Understandings of influenza and promoting influenza vaccination among high-risk urban dwelling Thai adults

Yupares Payaprom

Thesis submitted in fulfilment of the requirements for the degree of Doctor of Philosophy, 2011.

Cardiff University
School of Nursing and Midwifery Studies

ProQuest LLC
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106-1346

DECLARATION

This work has not previously been accepted in substance for any degree and is not concurrently submitted in candidature for any degree.

Signed..Yupa Paya.....(candidate) Date..1st..August..2011..

STATEMENT 1

This thesis is being submitted in partial fulfilment of the requirements for the degree of PhD.

Signed...Yupa Paya.....(candidate) Date..1st..August..2011..

STATEMENT 2

This thesis is the result of my own independent work/investigation, except where otherwise stated. Other sources are acknowledged by explicit references.

Signed....Yupa Paya.....(candidate) Date..1st..August..2011...

STATEMENT3

I hereby give consent for my thesis, if accepted, to be available for photocopying and for inter-library loan, and for the title and summary to be made available to outside organisations.

Signed.....Yupa Paya.....(candidate) Date...1st..August..2011..

STATEMENT 4: PREVIOUSLY APPROVED BAR ON ACCESS

I hereby give consent for my thesis, if accepted, to be available for inter-library loans after expiry of a bar on access previously approved by the Graduate Development Committee.

Signed....Yupa Paya.....(candidate) Date..1st August 2011

Yupa Paya 10 th August 2011

This thesis is dedicated to my parents, who instilled in me the value and importance of an education.

Acknowledgements

This thesis has been made possible through the support of many people. I would like to take this opportunity to convey my gratitude and appreciation to the following individuals and organisations for their invaluable contribution and support.

My deep gratitude to Prof. Paul Bennett, I truly appreciate his patience and tireless supervision through the years of my study. He has a unique way of guiding me through various stages in conducting research. His teaching style is relaxed, yet efficient and informative. He was the first person to introduce me to "health psychology". I have learnt a lot of interesting things under his supervision. Paul, I am so grateful for your unflinching encouragement and support that really help me get through the ups and downs of my PhD journey, and I hope this research will be the start of our future collaborations.

I am greatly indebted to Dr. Erica Alabaster for her guidance and advice during my years of study; spending time to read my thesis chapters thoroughly and providing me with excellent feedback and comments. Above of all, she provided great support and encouragement in many ways, especially during the final stage of my PhD study.

Dr. Katie Featherstone provided me invaluable advice and constructive comments on my qualitative study. And she helped make my fieldwork in Thailand possible. Thank you Dr. Katie, I am indebted to you. I also sincerely appreciate for all of the hard work you have done for us (PhD students).

I am grateful to Prof. Philip Burnard for his generous supervision during my first year study. He also spent his precious time for discussion with me about my first fieldwork during his stay in Bangkok; providing guidance for my qualitative data collection and analysis. My warmest appreciation goes to him.

For my fieldwork, I wish to thank the health authorities (Chiang Rai Provincial Health Office and Chiang Rai hospital) and the staff of health centres for their approval and coordination in implementing my research project. I extend my thanks to Dr. Sanga Intajak who gave me the generous support during my fieldwork, and my special thanks

to all the study participants for their kind participation and contribution to my research study.

Most importantly, this thesis would not have been completed without support, encouragement and patience of my family. My warmest gratitude goes to my mum, brother and sister. Also, my special thanks go in particular to Dr. Manus Potaporn, Dr. Hutsaya Tantipong, Ms. Kanokpan Pancharoen for their kind help and great support during my fieldwork as well as for their long-distance friends.

Finally, I would like to acknowledge the support from the Royal Thai Government for scholarship grant for my PhD study, and I wish to extend acknowledgement to the School of Nursing & Midwifery Studies, Cardiff University for partial financial support for my fieldwork in Chiang Rai province, Thailand.

Abstract

The 2004 outbreak of influenza A H5N1 and the WHO's recommendation for a national influenza pandemic plan has led the Thai Ministry of Public Health to develop an influenza vaccination programme for high-risk adults. One approach adopted by this programme has focus on implementing influenza vaccination in people with chronic medical conditions. However, influenza vaccination uptake rate among this high-risk group was relatively low, particularly in Chiang Rai province. Accordingly, the main objectives of this research were two-fold. This first objective was to explore beliefs about influenza and influenza vaccination, and the social influences on decisions whether or not to accept the influenza vaccination in a sample of urban-dwelling Thai adults. To reach this objective, a qualitative research approach was adopted. The second objective was to test the effect of a Health Action Process Approach (HAPA) based leaflet and action planning intervention on influenza vaccination behaviours among these high-risk individuals and to evaluate the impact of a HAPA-based leaflet on potential mediators of behavioural change. A controlled before and after trial was performed to evaluate the intervention effects. As the HAPA model was used as a conceptual framework for study two; the model's predictive utility was, thus, also examined. The results of the first study supported the development of the leaflet used in study 2.

A qualitative study using in-depth interviews was carried out with 20 high-risk individuals who were either (i) aged 65 and over, or (ii) under 65 years with chronic diseases that had clinical indications requiring influenza vaccination. Findings indicate that most participants had insufficient knowledge about influenza and influenza vaccination. Their decisions whether or not to get vaccinated against influenza were based on a number of factors, including salience of risk, influence of others, perception of the need for preventive health care, and the availability of influenza vaccine. These findings underscore the need to consider and understand factors underlying people's vaccination decisions to create an effective influenza vaccination programme.

Subsequently, a controlled before and after trial was conducted to compare the effects of a theory-based educational leaflet and action planning intervention with a standard government information leaflet on influenza vaccination behaviours among high-risk

urban dwelling Thai adults. Participants in the intervention group (n = 99) received a leaflet based on the HAPA and asking them to form an action planning as to where, when and how they would seek vaccination. Those in the comparison condition (n = 102) received a standard government information leaflet. The intervention had positive effects in changing risk perceptions, outcome expectancies, self-efficacy, and intention relative to the comparison condition. Stronger intentions to become vaccinated against influenza in the intervention group than the comparison group were explained by change in outcome expectancies and self-efficacy for arranging time and transportation. No significant difference in vaccination rates was observed between two groups. Influenza vaccination was predicted by self-efficacy and intention. A theory-based educational leaflet may be a useful tool to increase individual's vaccination intention, but larger trials are required to confirm these findings and to examine further the impact of similar interventions on influenza vaccination rates.

Publications

This thesis contains findings that have been presented in the following publications.

1. Payaprom, Y., Bennett, P., Burnard, P., Alabaster, E., & Tantipong, H. (2010). Understandings of influenza and influenza vaccination among high-risk urban dwelling Thai adults: a qualitative study. *Journal of Public Health*, 32 (1), pp. 26-31. doi: 10.1093/pubmed/fdp086 First published online: August 25, 2009

2. Payaprom, Y., Bennett, P., Alabaster, E., & Tantipong, H. (2011, May 2). Using the Health Action Process Approach and Implementation Intentions to Increase Flu Vaccine Uptake in High Risk Thai Individuals: A Controlled Before-After Trial. *Health Psychology*. Advance online publication. doi: 10.1037/a0023580

ABBREVIATIONS

ANCOVA-Analysis of Covariance

AE-COPD-Acute Exacerbation of Chronic Obstructive Pulmonary Disease

BSE-Breast Self-Examination

CDC-Centers for Disease Control and Prevention

CI-Confidence interval

COPD-Chronic Obstructive Pulmonary Disease

C&R-Circulatory and Respiratory

CSF-Cerebrospinal fluid

DFA-Direct Fluorescent Antibody test

ELISA-Enzyme-Linked Immunosorbent Assay

GBS-Guillain-Barré syndrome

GP-General Practitioner

HA- Haemagglutinin

HAI-Haemagglutination-inhibiting antibody

HAPA- Health Action Process Approach

HBM-Health Belief Model

HEF-Haemagglutinin-esterase-fusion

ICU-Intensive Care Unit

IFA-Immunofluorescent Antibody

IFN-α-Interferon-alpha

IL-6-Interleukin-6

IQR-Interquartile range

LAIV-Live, Attenuated Influenza Vaccine

M1-Matrix protein1

MAART-Medically Attended Acute Respiratory Illness

MANOVA-Multivariate Analysis of Variance

MAP-Model of Action Phase

NA- Neuraminidase

NI-Neuraminidase inhibiting

NS2- Non-structural protein

OR-Odds Raito

PB1-Polymerase protein

PBC-Perceived Behaviour Control

PCR-Polymerase Chain Reaction

P&I-Influenza and Pneumonia

PMT-Protection Motivation Theory

RNA-Ribonucleic acid

RNP-Ribonucleoprotein

RT-PCR-Reverse Transcriptase Polymerase Chain Reaction

RSV-Respiratory Syncicial Virus

SCT-Social Cognitive Theory

SLT-Social Learning Theory

T1-Time 1

T2-Time 2

TIV-Trivalent Inactivated Influenza vaccine

TPB-Theory of Planned Behaviour

TRA-Theory of Reasoned Action

WHO- World Health Organization

CONTENTS

LIST OF FIGURES

LIST OF TABLES

Chapter 1: Background and significance of the study

1.1 Introduction

The low influenza vaccination uptake among high-risk Thai adults, especially in Chiang Rai province, indicates a need for the development of an effective intervention programme to increase uptake in this population. To develop such an intervention programme, we first needed to understand how these high-risk people perceived influenza and the influenza vaccination and what influenced their decisions whether or not to be vaccinated. Factors underlying people's vaccination decisions need to be understood in order to guide the development of an intervention to promote influenza vaccination. In other words, knowing what high-risk people think about influenza and the influenza immunisation may help us to motivate them to take up immunisation. Thus, this thesis consists of two studies. The first study was designed to explore qualitatively high-risk Thai adults' beliefs regarding influenza and influenza vaccination, as well as other influences on their decisions. This was then used to inform the development of an intervention programme designed to increase vaccination rates among these high-risk individuals (study 2). Study 1 did not intend to test hypotheses; rather it investigated people's beliefs regarding influenza and influenza vaccination and identified factors underlying their vaccination decisions. A qualitative approach was therefore pursued in this study.

Subsequently, a controlled, before and after trial was conducted (study 2) to assess the effects of an intervention designed to promote influenza vaccination. This study was a pragmatic, randomised trial. The study design permits a precise assessment of the cause-and-effects relationships between an intervention programme and outcome, allowing the intervention to be modified and improved if necessary. As shown in previous studies, a number of factors have been associated with the people's decision of whether or not to get the influenza vaccine (e.g. Sengupta & Strauss, 2004; Burns, Ring, & Carroll, 2005; Jimenez-Garcia, Hernandez-Barrera, Carrasco-Garrido et al., 2006; Chen, Yi, Wu et al., 2007; Evans, Prout, Prior et al., 2007; Lau, Lau, & Lau, 2009). However, this study focused only cognitive factors influencing decision to vaccinate against influenza, as they are assumed to largely mediate the effects of other

factors and are more open to change than others. Thus, it is important to note that other factors, such as social and economic factors that were not assessed in this study, may also have a powerful effect on participants' decisions regarding influenza vaccination (Kroneman, Paget, & van Essen, 2003; Takahashi, Noguchi, Rahman et al, 2003; Gill, Taylor, & Watson, 20007). This chapter provides the background and the significance of the research project. The objectives that directed this research and hypotheses (study two) are presented. Finally, the overall structure of the thesis is outlined.

1.2 Background to the study

Influenza remains an important worldwide public health problem, although the effectiveness of influenza vaccine has been well established. The global burden of influenza epidemics in each year is estimated to be 3-5 million cases of severe illness, leading to 250,000-500,000 deaths (World Health Organization: WHO, 2003). Most cases of serious disease and death occur among high risk people: those over 65 years of age or who have chronic medical conditions such as cardiovascular diseases, chronic pulmonary diseases, diabetes and cancer (Centers for Disease Control and Prevention [CDC], 2007; Rothberg, Haessler, & Brown, 2008). The control and prevention of influenza have largely been accomplished through the use of vaccines (CDC, 2005, 2006; Kamps, Hoffmann, & Preiser, 2006). Although the effectiveness of influenza vaccine against influenza has been demonstrated since the 1940s, influenza vaccination coverage has often been suboptimal in most countries, even in North America and Europe and especially among older people with chronic disease. While influenza is recognised as an important health problem and public health efforts are made to increase immunisation rates in western countries (Humair, Buchs, Stalder, 2002; Zimmerman, Nowalk, Raymund et al., 2003; Bohmer, Jennings, Smith et al., 2004; CDC, 2006), but little is known about the burden of influenza in developing countries such as Thailand. Published data on human influenza in Thailand has been limited. This may have resulted from the lack of laboratory confirmation for influenza. Most cases have been diagnosed by using clinically diagnosed influenza (influenza-like illness).

However, influenza-associated morbidity and mortality has been a growing concern in Thailand since an outbreak of influenza A H5N1 in 2004, with a total of 17 confirmed human cases and 12 deaths. In addition, the WHO has strongly recommended that all countries develop or update their national influenza preparedness plans to prepare for and respond to threats and occurrences of pandemic influenza (Simmerman, Thawatsupha, Kingnate et al., 2004; Tiensin, Chaitaweesub, Songserm et al., 2005; WHO, 2005a). Together, these drive the need for the development of an influenza prevention and control programme in Thailand. One approach adopted by this programme has focused on implementing influenza vaccination among high-risk people aged over 65 years with chronic diseases and all healthcare workers involved in direct patient care (Ministry of Public Health: MOPH, 2008).

Influenza vaccine has been used in Thailand for many years but only in limited populations including healthcare workers, Thai pilgrims who attend the Hajj, and those who are able to afford for the cost of vaccination (Chunsuttiwat, 2002; Simmerman, Thawatsupha, Kingnate et al., 2004). Free influenza vaccine for high-risk older people was provided for the first time during the influenza vaccination period from 1 May to 30 June 2008. This programme was targeted at high-risk people aged over 65 years who had chronic diseases and with a history of inpatient hospital admission within the previous 12 months, and it will be expanded to cover more high risk Thai people in the coming years. In addition to providing free vaccine, an educational leaflet regarding influenza and influenza vaccine was designed and distributed to health professionals and high risk individuals. Despite these efforts, the overall immunisation rate in high-risk older people for the first year of the project in Chiang Rai province was relatively low (37.7 per cent); P. Sriwongpan, personal communication, March 6, 2009): insufficient to provide population protection against the influenza virus.

Data from a number of studies conducted in the United States and Europe indicate that the decisions whether or not to receive influenza vaccination are complex, and influenced by many medical and psychosocial factors. Cornford and Morgan (1999), for example, found that older people recognised that influenza could cause death, but few considered themselves to be at risk from it even though they had at least one chronic disease that did increase their risk of developing complications or death

attributable to influenza. As a consequence, many were reluctant to receive the influenza vaccination. Similarly, Gosney (2000) demonstrated that beliefs that the vaccine was both effective and free from side effects were associated with older adults' vaccination acceptance, while fear of side effects was negatively associated. Additionally, Telford and Rogers (2007) found that elderly peoples' decisions about whether to accept or refuse the influenza vaccination were influenced by trust or mistrust of modern medicine, prior experience of vaccination, and perceived risk from influenza. Other studies have found that the acceptance of influenza vaccination among older people was predicted by social influences, from sources such as health care providers, family members, and friends (e.g. Takahashi, Noguchi, Rahman, et al., 2003; Zimmerman, Nowalk, Raymund et al., 2003; Gallagher & Povey, 2006), and the costs and convenience of obtaining the vaccination (e.g. CDC, 1993; Nexøe, Kraqstrup, & Sogaard, 1999; Kroneman, Paget, & van Essen, 2003; Burns, Ring, & Carroll, 2005).

These factors provide a number of targets for any public health programme designed to increase uptake of influenza vaccine. Theoretical models also provide target variables to be addressed within any behaviour change intervention. They help determine the focus and content of any educational programme, and can be utilised to explain how interventions work to promote behavioural change (Fishbein & Yzer, 2003). The Health Action Process Approach (HAPA) (Schwarzer, 2001) provides one such explanatory model. This model has been widely applied to different behaviours and found to have good predictive utility in understanding health-related intentions and behaviours, including those related to nutrition (Schwarzer & Renner, 2000), breast self-examination (Luszczynska & Schwarzer, 2003), physical exercise (Sniehotta, Scholz, & Schwarzer, 2005; Scholz, Schuz, Ziegelmann et al., 2008), seat belt use (Schwarzer, Schuz, Ziegelmann et al., 2007), smoking (Scholz, Nagy, Gohner et al., 2009), and food hygiene (Chow & Mullan, 2010).

Crucially, evidence has shown that a theoretical approach to developing an intervention is more effective than interventions developed without theoretical basis (Abraham, Sheeran, & Johnston, 1998; Dishman & Buckworth, 1996). Using behaviour change theory to guide the development of interventions has many benefits. Firstly, theory identifies the variables that are hypothesised to cause change in

behaviour, thereby allowing researchers to target for the developing intervention. Secondly, using theory as a conceptual framework facilitates the accumulation of empirical evidence of effectiveness across different behaviours and population. Thirdly, theory-based intervention facilitates an understanding of the causal mechanisms of behaviour change and provides a basis for refining and revising a theory (Abraham & Michie, 2008; Michie, Johnston, Francis et al., 2008; Michie & Prestwich, 2010).

From the above, it can be concluded that developing effective interventions to maximise the uptake of influenza vaccination should be based on an understanding of the factors underlying people's vaccination decisions, and that behaviour change theory should be used to inform the design and development of any influenza vaccination programme. However, in Thailand where large-scale influenza vaccination programmes have yet to be undertaken, to date there is no available information on the theoretical basis of any intervention, and how to maximise the uptake of vaccine by the Thai population. Thus, this research is beginning to address this knowledge gap; it serves as a starting point for understanding Thai older people' beliefs about influenza and influenza vaccination (study 1), and for the development of an intervention to promote influenza vaccination among individuals with chronic disease, a group of people who are at risk of serious complication from influenza (study 2).

1.3 Significance of the study

This research is significant because it examines factors that influence high-risk Thai adults' decisions whether or not to receive influenza vaccine. It explores their beliefs about influenza and influenza vaccination, as well as other influences on their decision. The findings from this research can be used to guide the public health staff or other health professionals in developing tailored interventions to encourage influenza vaccination for such individuals. In addition, this research is also considered to be of value in providing a starting point for public health staff to develop a theory-based intervention to improve uptake of influenza vaccination. The findings of this research suggest that a relatively brief and simple intervention based on the HAPA model is effective in enhancing individual's vaccination intention, and has the

potential to change behaviour. The HAPA-based leaflet is inexpensive to reproduce; thus, it will be sustainable in routine practice. Accordingly, this research project provides one practical way to promote influenza vaccination in high-risk Thai adults living in the community, although other approaches are needed in primary care to raise influenza vaccination rate of this vulnerable group of people.

1.4 Aims of the research

As indicated above, this thesis reported on two research studies. The objective of the first study was to explore people's beliefs about influenza and influenza vaccination, and to investigate factors that affected the vaccination decision of a sample of urban-dwelling Thai adults. Study 2 was conducted with the objective of testing the effect of a HAPA-based educational leaflet and action planning intervention on influenza vaccination behaviours among these high-risk individuals, and evaluating the impact of this on potential mediators of behavioural change. In addition to assessing the intervention effects, this study also provided an opportunity to examine the predictive utility of the HAPA model in relation to both intention and subsequent vaccination behaviour in a certain high risk group in Thailand. The hypotheses for study two were as follows:

1. The implementation of a HAPA-based leaflet would lead to changes in key mediator variables (knowledge, risk perception, self-efficacy, outcome expectancies, and intention to seek vaccination), as well as higher rates of influenza immunisation than in a control group who received a standard information leaflet.

2. Risk perception, outcome expectancies, self-efficacy would predict the strength of intentions to obtain influenza vaccine.

3. Action planning, self-efficacy, and intention would significantly predict influenza vaccination in a sample of high-risk Thai adults.

1.5 Structure of the thesis

This thesis is organised into eight chapters.

Chapter two summarises issues relevant to influenza infection. The structure of the influenza virus is first presented. The chapter then describes how influenza virus changes every year (antigenic drift and shift). It also provides information about

pathology of influenza virus, clinical symptoms, complications of influenza, and mode of transmission. Finally, the chapter outlines the disease burden and cost.

Chapter three describes the influenza vaccine development process, type of vaccine, and the efficacy and safety of vaccination. A summary of immune responses to inactivated and live, attenuated influenza vaccines is also presented. Finally, recommendations for the use of seasonal influenza vaccine are outlined.

Chapter four reviews lay beliefs about influenza, influenza vaccine, and factors influencing the decision to be vaccinated against influenza among high-risk adults. The first part of this chapter presents the issues related to lay beliefs about influenza and influenza vaccine. It then focuses on the six categories of factors related to influenza vaccination: socio-demographic factors, health conditions, accessibility, knowledge and attitudes towards influenza vaccination, influence of others, and health beliefs and behaviour.

Chapter five presents a qualitative study of factors that influence high-risk urban-dwelling Thai adults'decisions whether or not to receive influenza vaccine. Study 1 findings are reported. Reported findings encompass participants' beliefs and their knowledge about influenza and influenza vaccination. It then presents four main themes that emerged from the data. This chapter finally draws out implications for clinical practice.

Chapter six details social cognition models, the Health Action Process Approach (HAPA) model which is used as a theoretical framework for this research (study 2), and the application of the HAPA model to health-related behaviours. This chapter further presents the formation of "if-then" plans (implementation intentions) and their effectiveness in changing health behaviour.

Chapter seven outlines the development and implementation of an intervention programme to increase influenza vaccine uptake in high-risk Thai individuals. It reports the results of a controlled before and after trial investigating the effects of a HAPA-based educational leaflet intervention on influenza vaccination. This chapter also presents findings on the applicability of the HAPA model in the context

of vaccination behaviour. It also considers the strengths and limitations of the study. Finally, the conclusion of the study is provided in the last section.

Chapter eight summarises the major findings from both studies. Theoretical and methodological implications are discussed. It then draws out implications for policy and practice. It also outlines the limitations of the research and discusses potential areas for future investigation. Finally, the chapter closes with the main conclusion.

Chapter 2: Influenza infection, epidemiology and burden of disease

2.1 Introduction

Few human infections have such a significant impact on hospitalisation, death, social disruption and economic cost as influenza. This chapter provides a review of the literature on the history and nature of influenza, including the influenza virus, antigenic drift, antigenic shift, pathology, clinical symptoms, diagnosis of influenza, influenza-related complications, antiviral treatment, mode of transmission, seasonality, and the burden of seasonal influenza.

2.2 A history of Influenza

The occurrence of influenza-like disease was described by Hippocrates as early as 412 BC. The name "influenza" has a Latin root and refers to the ancient belief that the disease was caused by supernatural influence; influenza epidemics were attributed to the "influence" of the stars. The first outbreak of influenza-like illness was reported in 1173-1174 (Hirsch, 1883 cited in Potter, 2001). Since then, there have been several reports of influenza-like epidemics throughout America and Europe. However, the outbreak of influenza which was firstly accepted as a global pandemic occurred in 1580 (Pyle, 1986, cited in Potter, 2001; Cunha, 2004). During the eighteenth century, at least three influenza pandemics (1729-1730, 1732-1733, and 1781-1782) were documented (Cunha, 2004). The data on influenza outbreaks has been more reliable since the first isolation of the influenza virus by Smith, Andrewes, and Laidlaw in 1933.

There are three main types of influenza viruses (influenza A, B and C viruses). Influenza A viruses can be further categorised into distinct subtypes (Cox & Subbarao, 2000). In the last century, there were three global influenza pandemics, which occurred in 1918-1919 (Spanish influenza), 1957-1958 (Asian influenza) and 1968-1969 (Hong Kong influenza) (Cox & Subbarao, 2000; Nguyen-Van-Tam & Hampson, 2003; Lerner & Lerner, 2008). The most destructive influenza pandemic in

human history was the Spanish influenza, with an estimated 40-50 million deaths worldwide (Potter, 2001; Lerner & Lerner, 2008; Gatherer, 2009). The virus that caused the pandemic was an influenza A H1N1 virus. The unique feature of this pandemic was that the vast majority of influenza-related deaths occurred mainly in healthy young adults (age range, 20-40 years) (Cox & Subbarao, 2000; Cunha, 2004). It was estimated that about ten times as many Americans died of influenza during this pandemic than died in the World War I (1914-1918) (Lerner & Lerner, 2008). The two subsequent pandemics had less of an impact than the Spanish influenza. The Asian influenza pandemic that was caused by influenza A virus subtype H2N2, killed approximately one to two million people worldwide (Nguyen-Van-Tam & Hampson, 2003; Lerner & Lerner, 2008). The Hong Kong influenza which was caused by a strain of influenza known as H3N3 was much milder than the previous two pandemics. There were an estimated 700,000 deaths worldwide during this pandemic (Lerner & Lerner, 2008).

As an influenza pandemic rapidly spreads and affects almost all people around the world, monitoring the global circulation of viruses, rapidly identifying new strains and timely reporting are essential to implement control measures, and the WHO is responsible for these activities. The WHO's Global Influenza Surveillance Network set up in 1952 comprises 131 National Influenza Centres in 102 countries working closely together with the four WHO collaborating centres: the National Institute for Medical Research, Mill Hill, London, United Kingdom, the Centers for Disease Control and Prevention, Atlanta, United States; the Commonwealth Serum Laboratories, Parkville, Melbourne, Australia, and the National Institute for Infectious Disease, Tokyo, Japan. According to the data collected by the network, WHO issues biannual recommendation for the vaccine components for the subsequent influenza season and related activities (WHO, 2010a). On June 11, 2009, the first influenza pandemic of the 21st century was officially declared by the WHO (Chan, 2009). A novel influenza A (H1N1) virus was determined the cause of this pandemic. As of 28 March 2010, the WHO has recorded over 17,483 people deaths in more than 213 countries as a consequence of the disease (WHO, 2010b).

2.3 Influenza virus

2.3.1 Structure of the virus

Influenza viruses are members of the Orthomyxoviridae family of RNA (ribonucleic acid) viruses, which comprise four genera: influenza virus A, influenza virus B, influenza virus C, and thogotovirus (Cox & Subbarao, 1999; Sutherland, 2002).
There are differences in host range and pathogenicity among the three types of influenza viruses (Taubenberger & Morens, 2008). All of them can cause disease in humans, but influenza A and B are mainly found infecting humans (Cox & Subbarao, 2000). Occasionally, influenza B causes local outbreaks of influenza. Both influenza A and B can cause annual epidemics in many parts of the world; however, only influenza A has caused human global pandemics (Zambon, 2001). Influenza A viruses are further classified into subtypes based on the antigenicity of two glycoproteins on the surface of the virus: haemagglutinin (HA) and neuraminidase (NA). There are 15 HA (H1-H15) and 9 NA (N1-N9) subtypes to date (Cox & Subbarao, 2000; Zambon, 2001; Nicholson, Wood, & Zambon, 2003; Lofgren, Fefferman, Naumov et al., 2007). All known subtypes of influenza A have been isolated in aquatic birds. However, only three haemagglutinin (H1, H2, H3) and two neuraminidase (N1 and N2) subtypes have been found circulating in human populations. Additionally, these subtypes have also been linked to epidemics and pandemics in humans since 1918 (Cox & Subbarao, 1999; Stephenson & Zambon, 2002; Nguyen-Van-Tam & Hampson, 2003; Nicholson, Wood, & Zambon, 2003; Bouvier & Palese, 2008).

Unlike influenza A, influenza B and C viruses are not categorised into subtypes. The structure of influenza B viruses is similar to influenza A. There are four envelope glycoproteins (HA, NA, NB, and BM2) for influenza B viruses. However, influenza C viruses have only one major envelope glycoprotein, namely hemagglutinin-esterase-fusion (HEF) protein (Whittaker, 2001; Bouvier & Palese, 2008; Taubenberger & Morens, 2008). Influenza virus particles are typically spherical, 80-120 nanometres in diameter, and they are enveloped RNA viruses. Influenza A and B viruses have two different glycoprotein spikes on the surface of a virus: haemagglutinin (HA) and neuraminidase (NA) (Sutherland, 2002; Treanor, 2005; Bouvier & Palese, 2008). Each virus particle contains approximately 500 molecules of HA and 100 molecules

of NA on its surface. The HA helps influenza virus penetration into host cells and initiates infection, whereas NA facilitates the release of newly produced virus particles from the host cell (Gubareva, Kaiser, & Hayden, 2000; Steinhauer & Skehel, 2002). These two viral proteins are also associated with the virulence of the influenza virus. For influenza A viruses (Figure 2.3.1), M2 protein is present at the surface of the influenza virion (a single infective viral particle). On the inner side of the envelope, the ribonucleoprotein (RNP) complex, which consists of helical segments of virion RNA coated with nucleoprotein (NP), M1 protein, and three polymerase proteins (PB1, PB2, PA), is responsible for transcription and replication of each virus gene. RNPs are surrounded by layer of matrix (M1) protein. M1 protein is the major component of virus particle. Additionally, the non-structural protein 2 (NS 2) is found within the virus particle, and it is believed to be involved in virus particle assembly and budding (Gubareva, Kaiser, & Hayden, 2000; Whittaker, 2001; Steinhauer & Skehel, 2002; Treanor, 2005; Bouvier & Palese, 2008; Taubenberger & Morens, 2008).

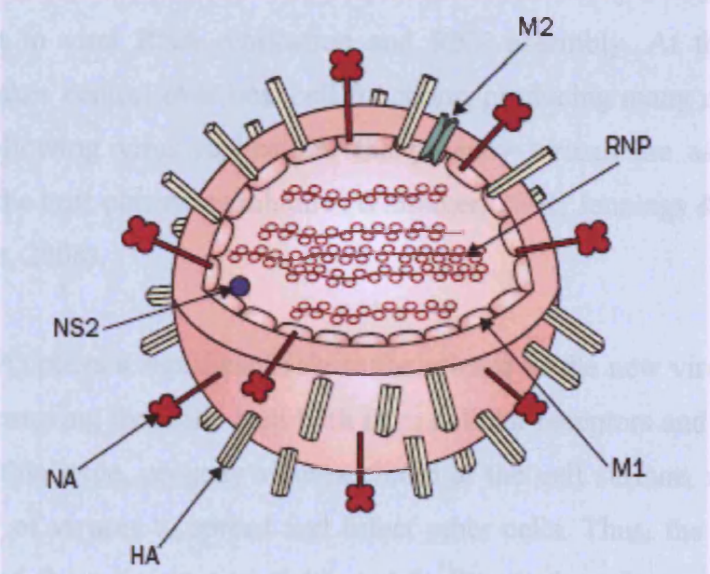


Figure 2.3.1. Schematic representation of influenza A virus
Source: Gubareva, Kaiser, & Hayden, 2000

2.3.2 The replication cycle of influenza virus

Figure 2.3.2 illustrates the replication cycle of influenza virus. The cycle consists of four distinct phases: virus attachment and entry; synthesis of viral RNA; synthesis of viral proteins and assembly of virion; and virus budding and release from host cell (Gubareva, Kaiser, & Hayden, 2000; Whittaker, 2001; Bouvier & Palese, 2008). The influenza virus initially attaches to specific receptors on the host cell (sialic-acid receptors) through the HA protein spikes and penetrates into the host cells. Once inside the host cell (cytoplasmic vesicles), influenza virion sheds its envelope, resulting in the release of the genetic material of the virus (RNP) into the host cell cytoplasm in order to be transcribed and translated. This process is called "uncoating" (Gubareva, Kaiser, & Hayden, 2000; Whittaker, 2001; Bouvier & Palese, 2008). The M2 protein is thought to function as an ion channel that allows the flow of hydrogen ions into the virion to facilitate ribonucleoprotien uncoating (Whittaker, 2001; Bouvier & Palese, 2008). The uncoated RNPs are transported to the host cell nucleus for replication. In the nucleus, all influenza virus RNAs are synthesized. In addition, the viral proteins (NP, M1, NS2 and the polymerases) are brought into the host cell nucleus to assist in viral RNA replication and RNP assembly. At this stage, the influenza virus takes control over host cell functions, producing many new influenza virus copies. Following virus replication, the progeny viruses are assembled and budded through the host plasma membrane (Whittaker, 2001; Jennings & Read, 2002; Bouvier & Palese, 2008).

Neuramidase (NA) plays a significant role in the release of the new viruses from the cell surface by removing the sialic acid both from cellular receptors and from the HA spikes. Without this stage, progeny viruses clump at the cell surface, resulting in a decreased ability of viruses to spread and infect other cells. Thus, the NA prevents the aggregation of the new virus particles and facilitates the release of new virion particles from infected cells, allowing them to infect a new host cell (Gubareva, Kaiser, & Hayden, 2000; Whittaker, 2001; Steinhauer & Skehel, 2002; Treanor, 2005; Bouvier & Palese, 2008).

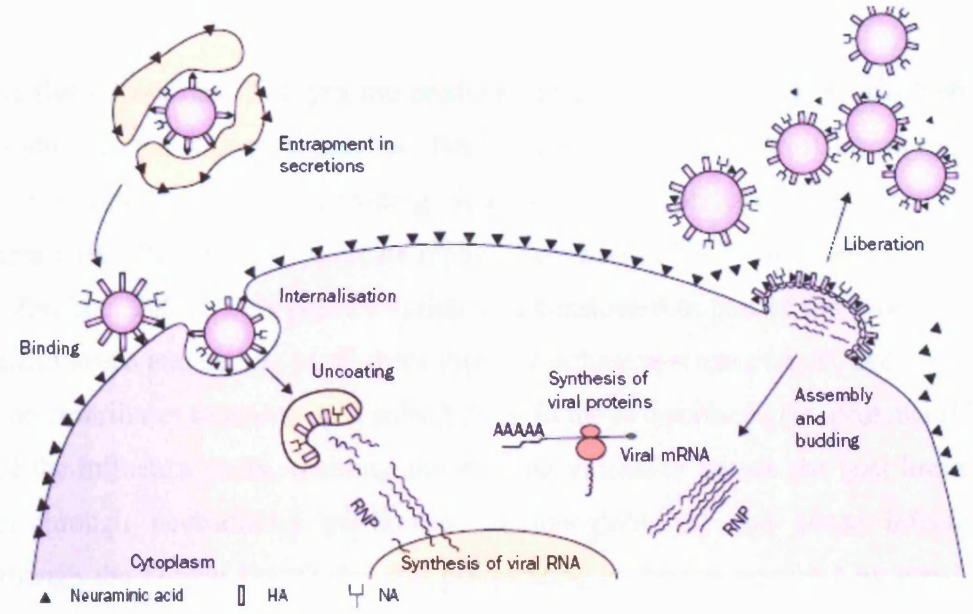


Figure 2.3.2 Influenza virus replication cycle

Source: Gubareva, Kaiser, & Hayden, 2000

2.3.3 Influenza virus nomenclature

Influenza viruses have a standard nomenclature. According to the WHO system (WHO, 1980), the full nomenclature for influenza virus isolates includes the host of origin, the geographical site, serial number, year of isolation, and then follows the year of isolation with the H and N variants in parentheses, for instance "A/swine/Iowa/3/70 (H1N1)". In the case of influenza virus isolated from humans, the host of origin is not given, e.g. A/Fujian/411/2002 (H3N2).

2.4 Antigenic drift and shift

There are two types of antigenic variation on envelope glycoproteins (HA and NA) of influenza A viruses: antigenic drift and antigenic shift. Such variations make people more susceptible to infection with a new virus strain that was not recognised by the human immune system. This results in influenza epidemics and pandemics (Cox & Subbarao, 2000; Nicholson, Wood, & Zambon, 2003).

"Antigenic drift" refers to the gradual accumulation of point mutations (minor changes) in the HA and NA genes of influenza virus that arises during the replication of the influenza genome (Cox & Subbarao, 2000; Stephenson & Zambon, 2002; Treanor, 2005). These changes in the genes occur because the viral RNA polymerase

enzyme that copies the viral genome produces an error. This enzyme is involved in transcription of the influenza genome, but lacks the ability to correct errors during RNA transcription (no proof-reading activity). It is estimated that the RNA polymerase of influenza viruses create replication errors in $1/10^4$ bases per replication cycle (Zambon, 2001). This genetic variation is considered as part of the evolution of influenza viruses and occurs in all three types of influenza viruses (A, B, and C). The mutation contributes to amino acid substitutions in the two surface glycoproteins (HA, NA) of the influenza virus, enabling the mutated viruses to invade the host immune system through neutralizing antibodies (immunoglobulins) and cause infection, even though the human population has pre-existing antibodies acquired by previous infection (Ferguson, Galvani, & Bush, 2003; Lofgren, Fefferman, Naumov et al., 2007).

The emergence of new variants is the reason for reassessing the components of influenza vaccine every year as part of public health programmes (Boni, 2008). In addition, there is evidence that the HA gene of influenza A viruses has a higher mutation rate than the HA gene of influenza B viruses ($3.60x10^{-3}$ nucleotide changes per nucleotide site per year and $1.60x10^{-3}$ nucleotide changes per nucleotide site per year, respectively). In other words, there is less antigenic drift in influenza B viruses than influenza A viruses. This may partially explain why influenza B outbreaks have occurred less frequently than influenza A viruses (Cox & Bender, 1995; Mc Cullers, 1999; Zambon, 2001).

A second type of variation is "antigenic shift", which has been observed only in influenza A viruses. Antigenic shift is a major change in the surface protein(s) of influenza viruses (the HA and/or NA) (Cox & Subbarao, 2000; Nguyen-Van-Tam & Hampson, 2003; Nicholson, Wood, & Zambon, 2003; Treanor, 2005). Influenza pandemic occurs with the emergence of a novel virus with completely new surface or internal proteins. The new subtypes of influenza viruses arise as a result of genetic reassortment (an exchange of a gene segment) between human and animal influenza viruses (Figure 2.4) (Zambon, 2001; Nicholson, Wood, & Zambon, 2003). Influenza A viruses infect both human and many animal species (bird, pig, duck, horse), and it is believed that wild aquatic birds are the primary natural reservoirs of influenza A viruses (Cox & Subbarao, 2000). These animals can be a source of HAs that are novel

to humans and increase the chance for the emergence of new pandemic viruses (Obenauer, Denson, Mehta et al., 2006). There is different receptor binding specificity of human and avian influenza viruses. The haemagglutinin of human influenza virus preferentially binds to sialic acid molecules with α-2,6-linkages, whereas avian influenza viruses favour attachment to sialic acid molecules with α-2,3-linkages. However, tracheal epithelium cells of pigs have both types of receptor binding. Thus, pigs may serve as "mixing vessels" for the genetic recombination of avian and humans influenza A viruses (Cox & Subbarao, 2000; Lofgren, Fefferman, Naumov et al., 2007).

Most of antigenic shifts are thought to have originated in China where agricultural practices allow people in close proximity to ducks, pigs, and domestic animals, as well as the high human population density, thereby facilitating the genetic reassortment of avian and human influenza A viruses (Zanbon, 2001; Nicholson, Wood, & Zambon, 2003). The segmented nature of the influenza A genome containing eight separate gene fragments allows the possibility of genetic recombination between influenza A viruses. It is estimated that up to 256 gene combinations during co-infection with human and animal viruses (Figure 2.4) (Nicholson, Wood, & Zambon, 2003).

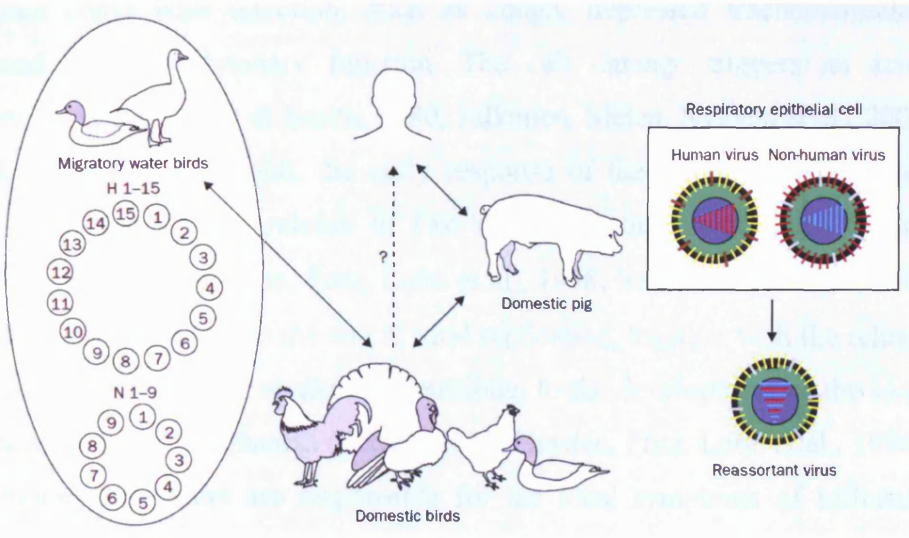


Figure 2.4 Origin of antigenic shift and pandemic influenza

Source: Nicholson, Wood, & Zambon, 2003

Although gene reassortment of two influenza A viruses may produce severe disease, stable adaptation to replicate in new host species is essential for new virus variants. Thus, influenza A viruses that have undergone antigenic shift have potential to cause major global pandemics if they have ability to adapt to human hosts and to spread from person to person. In addition, if most of population have little or no immunity against the new virus, the global influenza pandemic may occur (Cox & Subbarao, 2000; Nguyen-Van-Tam & Hampson, 2003; Taubenberger, Morens, & Fauci, 2007).

2.5 Pathology of influenza viruses

The pathogenesis caused by influenza viruses depends on the balance between the virulence of the infecting strain and the host's immune response. Typically, in non-fatal influenza infection, the viruses cause inflammation, congestion, and epithelial necrosis of the upper respiratory tract of humans (Jennings & Read, 2002; Suntherland, 2002; Treanor, 2005; Kuiken & Taubenberger, 2008; Guarner & Falcon-Escobedo, 2009). The inhaled virus attaches to ciliated epithelial cells of the trachea, bronchi, and bronchioles. After attachment, influenza viruses rapidly penetrate the cells, and intracellular replication is initiated. Viruses multiply in the epithelial cells of the respiratory tract and destroy the cilia. This causes many symptoms that come with infection, such as cough, depressed tracheobronchial clearance, and altered pulmonary function. The cell damage triggers an acute inflammatory response (Sweet & Smith, 1980; Julkunen, Melen, Nygvist et al., 2001; Suntherland, 2002). At this point, the early response of the host cell to pathogen invasion is the synthesis and release of two cytokines: interleukin-6 (IL-6) and interferon-alpha (IFN-α) (Hayden, Fritz, Lobo et al., 1998; Sutherland, 2002; Collier & Oxford, 2006). The damage at the site of viral replication, together with the release of cytokines and inflammatory mediators, contribute to the development of the local and systemic symptoms of influenza (Eccles, 2005; Hayden, Fritz, Lobo et al., 1998). The inflammatory mediators are responsible for the local symptoms of influenza (nasal obstruction, cough, sore throat), and cytokines (IL-6 and IFN-α) play a significant role in generating the systemic symptoms (headache, fever, chills, anorexia, myalgia) (Eccles, 2005; Sutherland, 2002; Collier & Oxford, 2006). Viral antigens also induce the B lymphocytes to produce specific antibodies. These

antibodies made against two glycoproteins (HA, NA) on the surface of a virus. Specific antibodies can block binding the host cell receptor, thus inhibit virus attachment and penetration. Antibodies can also cause aggregation of virions, thereby limiting them spread to new cells and making them more readily phagocytosed (Gubareva, Kaiser, & Hayden, 2000; Whittaker, 2001; Treanor, 2005; Bouvier & Palese, 2008).

However, in fatal cases of influenza, highly virulent strains (e.g. H5N1) cause alveolar damage and severe pneumonia. The main target organs for this high virulent of influenza A viruses are the lower respiratory tract and lungs. Co-incident bacterial pneumonia frequently occurs and increases the severity of disease (Guarner & Falcon-Escobedo, 2009). In addition to bacterial co-infection, other underlying medical conditions (e.g. asthma, chronic obstructive pulmonary disease, obesity, and diabetes) can contribute to the severe or fatal outcomes among these fatal cases (Taubenberger & Morens, 2008; Guarner & Falcon-Escobedo, 2009: Shieh, Blau, Denison et al., 2010).

2.6 Clinical symptoms

Uncomplicated influenza illness in healthy adults varies in severity from mild to severe. It is characterised by the abrupt onset of fever (38-40 °C) or feverishness, headache, muscle aches and pain, fatigue, sore throat, and a dry cough. Additional symptoms may include loss of appetite, runny or stuffy nose, a clear nasal discharge and sneezing (Cox & Subbarao, 1999; Jennings & Read, 2002; Cunha, 2004; Eccles, 2005; Treanor, 2005). The average duration of fever is three days, but it can last four to eight days (Jennings & Read, 2002; Treanor, 2005). Fever and cough have been identified as the best predictors of an influenza infection, with a positive predictive value of 79 per cent (Monto, Gravenstein, Elliott et al., 2000). Mild to moderate cases of uncomplicated influenza typically recover within 7 days. However, other symptoms, particularly cough, malaise, and fatigue can persist for weeks after recovery from the major clinical symptoms (Jennings & Read, 2002; Cunha, 2004).

Although most cases of influenza are mild and self-limited illness, more severe illness is observed in an elderly and people of any age with chronic medical conditions such as asthma, congestive heart failure, chronic obstructive pulmonary disease, diabetes, and chronic renal failure. In addition, the risks for complications, hospitalisation and death related to influenza are higher among these individuals (Jennings & Read, 2002; Hak, Wei, Nordin et al., 2004; Rothberg, Haessler, & Brown, 2008).

2.7 Diagnosis

Early diagnosis of influenza is crucial for antiviral treatment, chemoprophylaxis, and institutional outbreak management. Although the presence of high fever and cough was found to be the best clinical predictors for influenza infection in adults during influenza season, diagnosis of influenza based on clinical symptoms alone was imperfect. The study by Boivin, Hardy, Tellier et al. (2000) indicated that the positive predictive value (PPV: the percentage of test positive cases who have influenza), negative predictive value (NP: the percentage of test negative cases who do not have influenza) and the specificity of a clinical diagnosis (fever [temperature > 38 °C], and cough) were 86.8 per cent, 39.3 per cent and 55.0 per cent, respectively. By contrast, the PPV of clinical diagnosis using the same clinical symptoms was found only 44 per cent (95% CI, 30-58 %) in the study conducted in the southern region of the Netherlands (Govaert, Dinant, Aretz et al., 1998). However, the clinical diagnosis based on the acute onset of high fever and cough was more likely to predict influenza during influenza epidemics, with PPV ranging from 79 per cent to 87 per cent and NPV ranging from 39 per cent to 75 per cent). Moreover, the likelihood of confirmed influenza infection cases increases with higher temperature and acute presentation (within 36-48 hours of onset) (Gavin & Thomson, 2003; WHO, 2005b). The accuracy of clinical diagnosis of influenza is limited as the influenza symptoms can be confounded by symptoms from illness caused by other agents. Furthermore, clinical diagnosis of influenza may have been influenced by factors such as the circulating virus strain, duration of symptoms at presentation, preceding use of antipyretics, the patient's age, underlying medical conditions, and vaccination status (Gavin & Thomson, 2003).

Laboratory methods to detect influenza virus infection include: (1) virus isolation in cell culture; (2) direct antigen detection: direct fluorescent antibody test [DFA] or immunofluorescent antibody [IFA] test, and rapid enzyme and optical immunoassays for influenza antigen (rapid diagnostic tests); (3) detection of influenza-specific RNA by reverse transcriptase-polymerase chain reaction (RT- PCR); and (4) serologic diagnosis. These test methods vary in terms of the sensitivity and specificity of the assay, the turnaround time for reporting of assay results, and cost (Linde, 2001; Gavin & Thomson, 2003; Pachucki, 2005; WHO, 2005b; Petric, Comanor, & Petti, 2006).

2.7.1 Virus isolation in cell culture

Viral culture is considered to be the gold standard for laboratory diagnosis of influenza. There are two different techniques of viral culture: convention culture and shell vial culture. For conventional virus culture, the results are generally available in four to five days (range, 2-14 days), whereas shell vial culture (rapid culture technique) for detection of influenza virus takes one to three days after inoculation (Gavin & Thomson, 2003; Talbot & Falsey, 2010). Although shell vial culture provides results in less time compared with the conventional technique, it does not generate results quickly enough in guiding the clinical management of influenza patients (antiviral treatment, infection control, and management of close contacts). Nevertheless, this rapid culture technique provides confirmation of the influenza diagnosis. The specificity of shell vial culture for the detection of influenza virus is 100 per cent. Another advantage of virus culture methods is the detection of influenza A subtypes and strains. Thus, both conventional and shell vial culture methods can be used for monitoring the emergence of new influenza virus strains, and the information about the new virus strain circulating will be used to update the formulation of the influenza vaccine for the coming year (Steininger, Kundi, Aberle et al., 2002; Gavin & Thomson, 2003; WHO, 2005b; Petric, Comanor, & Petti, 2006; Talbot & Falsey, 2010).

2.7.2 Detection of virus antigen

There are two types of diagnostic tests for detection of influenza virus: 1) Direct fluorescent antibody tests (DFA) or immunofluorescent antibody (IFA) and 2) rapid enzyme/optical immunoassays or assay for NA enzymatic activity.

1) Direct fluorescent antibody tests (DFA) or immunofluorescent antibody (IFA)

Generally, the sensitivity of DFA is slightly lower than IFA, but the DFA test can provide the results in less time and is thereby more popular than IFA. Previous studies (Leonard, Leib, Birkhead et al., 1994; Doing, Jerkofsky, Dow et al., 1998; Chan, Maldeis, Pope et al., 2002; Gavin & Thomson, 2003) have shown that DFA is a fast and reliable technique for the detection of influenza, as well as relatively accurate results (sensitivity, range: 70-100 per cent; specificity, range: 80-100 per cent; PPV, range: 85-94 per cent; and NPV, range: 96-100 per cent).

2) Rapid enzyme/optical immunoassays or assay for NA enzymatic activity.

There are a number of commercial rapid influenza detection tests, and six of which are in general use for detecting influenza virus. Such tests include Directigen Influenza A, and Influenza A plus B tests (Becton Dickinson, Franklin Lakes, New Jersy), Binax Now Influenza A and B tests (Binax Inc., Portland, Maine), Biostar INFLUENZA OIA (Biostar, Inc., Boulder, Colorado), Quidel Quick vue (Quidel San Diego, Carifornia), and ZstatFlu test (Zyme Tx, Inc., Oklahoma City, Oklahoma). Most of these tests detect influenza viral antigen (viral neucleoprotein antigen). Only one diagnostic test (ZstatFlu test) detects influenza virus NA enzyme activity (Gavin & Thomson, 2003). Rapid diagnostic tests have been widely used for screening influenza A and B virus infections before confirmatory diagnostic testing using viral culture or PCR (polymerase chain reaction). These tests vary in terms of test complexity, the type of specimen tested, the ability of the test to detect types of influenza, and the time needed to produce results (WHO, 2005b). The rapid influenza tests can detect: (1) only influenza A virus; (2) both influenza A and B viruses, but does not differentiate between the two types; (3) both influenza A and B and

differentiate between the two types (CDC, 2009a). However, none of the rapid diagnostic tests distinguish influenza A virus subtypes. Most diagnostic tests can provide the results within 15-30 minutes, which facilitates timely diagnosis, antiviral treatment, prevention and outbreak management (CDC, 2009a). Various respiratory specimen types can be used for rapid diagnostic tests, including nasal aspirates, nasal washes, sputum, nasal pharyngeal swabs, nasal swabs, and throat swabs. Among these specimen types, nasal aspirates or washes yield the highest detection rates for influenza virus (WHO, 2005b; Hurt, Allexander, Hibbert et al., 2007; Smit, Beynon, Murdoch et al., 2007). Nasal aspirate specimens should be transported in sterile containers, while nasal or throat swabs should be collected and transported in virus transport media.

Most rapid diagnostic tests for the diagnosis of influenza have sensitivity of 70 to 75 per cent, compared to viral culture or reverse transcription polymerase chain reaction (RT-PCR), and their specificity is relatively high (median, 90-95 per cent) (Pachucki, 2005; WHO, 2005b). A further study (Hurt, Allexander, Hibbert et al., 2007) that tested six influenza diagnostic tests found that five of the rapid diagnostic tests (Binax Now influenza A & B, Directigen EZflu A+B, Denka Seiken Quick Ex-flu, Fujirebio Espline Influenza A&B-N, and Quidel Quick Vue Influenza A+B test) were 61-71 per cent sensitive for detecting influenza and 99-100 per cent specific compared with cell culture.

Although both the sensitivity and specificity of rapid diagnostic tests are relatively high, test results should be considered based on patients' clinical symptoms and epidemiologic information. The rapid influenza tests are most reliable when they are performed during periods of high influenza activity (at the height of the influenza season) and when samples were collected within four days of illness (high viral load). Therefore, when the prevalence of influenza in the community is low (at the beginning and end of influenza season), confirmation of rapid influenza test-positive by viral culture or RT-PCR may be necessary because a false-positive rapid test result is more likely to occur during low influenza activity. In particular, outside of the influenza season, positive rapid test results must be interpreted with caution, and confirmation of the results by other tests is warranted (Gavin & Thomson, 2003; WHO, 2005b; Petric, Comanor, & Petti, 2006; CDC, 2009a).

2.7.3 Detection of influenza-specific RNA by reverse transcriptase-polymerase chain reaction (RT- PCR)

Reverse transcriptase-polymerase chain reaction (RT-PCR) is the most sensitive and specific technique for detecting influenza virus. There are two types of RT-PCR methods: conventional RT-PCR and real-time RT-PCR. Reverse transcriptase-polymerase chain reaction methods can detect influenza virus, differentiate subtype and strains of influenza virus. Previous studies using RT-PCR have more accurately detected influenza virus than conventional viral culture (Taubenberger & Layne, 2001; Steininger, Kundi, Aberle et al., 2002). The study by Steininger, Kundi, Aberle et al. (2002) demonstrated that RT-PCR provided a higher detection rate of influenza (93 per cent) than virus culture (80 per cent) and antigen enzyme-linked immunosorbent assay (ELISA) (62 per cent). The sensitivity of RT-PCR was 10^3 times higher than viral culture and 10^6 to 10^7 greater than ELISA. However, RT-PCR methods for detection influenza virus are expensive and require high technical skills. Conventional RT-PCR can provide results in one to two days; however, its turnaround time is still limited in guiding clinical management decisions. The real time RT-PCT method has been developed as a quick, sensitive and reliable method. Real time RT-PCR can provide rapid results within four to five hours (Gavin & Thomson, 2003). Two studies by van Elden, Nijhuis, Schipper et al. (2001) and van Elden, van Kraaij, Nijhuis et al. (2002) showed that real time RT-PCR had greater sensitivity for detection of influenza virus than viral culture methods. Accordingly, real time RT-PCR may replace the current gold standard for confirming influenza which is viral culture in the future (van Elden, van Kraaij, Nijhuis et al., 2002).

2.7.4 Serologic diagnosis

Serologic diagnosis of influenza is based on the presence of a four-fold or higher rise in influenza-specific antibody titres between acute (within one week after initial infection) and convalescent serum samples (four to seven weeks after infection). Because this diagnostic method is time consuming; thus, its clinical value is limited. However, serological tests can be used for detecting influenza virus for epidemiological and research studies (Gavin & Thomson, 2003; Petric, Comanor, & Petti, 2006).

2.8 Complications of influenza

The complications of influenza may be divided into two categories: pulmonary complications and non-pulmonary complications.

2.8.1 Pulmonary complications

The most frequent complication of influenza is pulmonary complications, especially pneumonia. There are two clinical presentations of pneumonia associated with influenza: primary influenza pneumonia and secondary bacterial pneumonia (Treanor, 2005; Rothberg, Haessler, & Brown, 2008). Primary viral pneumonia is an uncommon complication associated with high mortality rate. However, the study by Hers et al. (1958, cited in Nguyen-Van-Tam & Hampson, 2003) found that there was a higher incidence rate of primary influenza pneumonia during the 1957-1958 influenza pandemic. In addition, it was evidenced that this pneumonia caused many deaths among young healthy adults in the 1918-1919 influenza pandemic (Treanor, 2005). The illness starts within 24 hours of the onset of fever with a dry cough, followed by a rapid progression of dyspnea, cyanosis, and respiratory failure. No significant bacteria were detected in the sputum Gram stain. Patients deteriorate and do not respond to antibiotic therapy, with a mortality rate of 80 per cent (Cox & Subbarao, 1999; Treanor, 2005; Louria et al., 1959, cited in Rothberg, Haessler, & Brown, 2008). At the present time, during the interpandemic periods, primary influenza pneumonia occurs predominantly in the people with underlying severe co-morbid conditions (cardiac disease, chronic obstructive pulmonary disease, diabetes, renal disease and immunosuppression), and the mortality rates are 6 per cent to 29.4 per cent (Oliverira & Marik, 2001; Murata, Walsh, & Falsey, 2007).

Secondary bacterial pneumonia occurs more frequently than primary viral pneumonia. Staphylococcus aureus, Streptococcus pneumoniae, Hemophilus influenza, and other Gram-negative bacilli are the most common causative agents of secondary bacterial pneumonia in older adults and those with chronic medical conditions. This pneumonia occurs in the early convalescent phase of a typical influenza. It is marked by the recrudescence of fever, cough, and sputum production. The areas of consolidation can be seen on a chest radiograph. A predominance of a bacterial pathogen was seen on

Gram's stain and culture. Most patients with secondary bacterial pneumonia respond to antibiotic therapy. During the outbreak of influenza, people may have primary viral pneumonia, secondary bacterial pneumonia or mixed viral and bacterial pneumonias. The response to antibiotic therapy varies among patient with mixed viral and bacterial infections (Cox & Subbarao, 1999; Treanor, 2005).

In addition, influenza virus is also the leading cause of acute exacerbation of chronic bronchitis and other chronic pulmonary diseases (e.g. asthma and chronic obstructive pulmonary disease: COPD) (Rothberg, Haessler, & Brown, 2008). Influenza viruses have been reported to be involved in COPD exacerbations in 25 per cent of cases (Rohde, Wiethege, Borg et al., 2003).

2.8.2 Non-pulmonary complications

Although pulmonary complications are common in influenza patients, the viruses can cause complication in other organs (influenza-associated extra-respiratory complications) such as myositis, myocarditis, and neurologic complications of influenza (Fujimoto, Kobayashi, Uemura et al., 1998; Cox & Subbarao, 1999; McCullers, Facchini, Chesney et al., 1999; Studahl, 2003; Rothberg, Haessler, & Brown, 2008).

Myositis (inflammation of muscle) may occur in both children and adults after being infected with influenza, but primarily in children. It has been reported to be associated with influenza B infection. The clinical symptoms include transient muscle pain in the lower extremities. In most cases, recovery is complete within one week (Cox & Subbarao, 1999; Treanor, 2005; Kuiken &Taubenberger, 2008).

Myocarditis—Although influenza infection can cause of exacerbations in patients with chronic heart diseases (such as congestive heart failure, ischemic heart disease), direct cardiac complications (pericarditis and myocarditis) are considered to be very rare (Onitsuka, Imamura, Miyamoto et al., 2001; Treanor, 2005; Rothberg, Haessler, & Brown, 2008). However, influenza viral antigen was detected within the myocardium of a person with marked myocardial necrosis (Ray, Icenogle, Minnich et al., 1989). A combination of the direct cytolytic effect of viral infection and the host

immune response may play an important role in the pathogenesis of the necrosis and inflammation in the myocardium (Kuiken & Taubenberger, 2008).

Neurologic complications of influenza include post influenza encephalitis, encephalopathy (Reye's syndrome), transverse myelitis, and Guillain–Barré syndrome (GBS). These complications may occur during influenza attack or after the influenza infection. Recently, encephalitis/encephalopathy associated with influenza has been increasingly reported in Japan, particularly in children aged younger than five years. The major clinical signs include altered or loss of consciousness, convulsion, cough and vomiting. Multiple-organ failure can occur in many cases, and the prognosis is generally poor (death or severe neurologic sequelae). The pathogenesis of encephalitis /encephalopathy associated with influenza has not been elucidated, but is thought to occur by direct viral invasion and host immune response. However, influenza virus RNA was detected in the cerebrospinal fluid (CSF) of the patients with acute encephalopathy associated with influenza-like illness (Fujimoto, Kobayashi, Uemura et al., 1998; McCullers, Facchini, Chesney et al., 1999; Morishima, Togashi, Yokota et al., 2002; Rothberg, Haessler, & Brown, 2008).

Reye's syndrome is one of the encephalopathies associated with influenza epidemics. It is an acute, non-inflammatory encephalopathy and occurs most often in children or adolescents, especially children aged less than 14 years who take or are given aspirin to reduce fever due to influenza and other viruses. This disease begins with severe vomiting and confusion, and these symptoms can progress to coma due to swelling of the brain. On this basis, aspirin use should be avoided in the children with febrile illness. In addition, the children and adolescents who require long-term aspirin therapy should be vaccinated against influenza every year in order to reduce the risk of Reye's syndrome (Treanor, 2005; Beigel, 2008; Rothberg, Haessler, & Brown, 2008).

Guillain–Barré syndrome is a post-infection autoimmune disorder and a rare disease. It has been previously suggested that there is a link between Guillain- Barré syndrome and influenza infection, but no definite causal connection has been established (Treanor, 2005). Recently, two studies by Tam, O' Brien, & Rodrigues (2006) and Sivadon-Tardy, Orlikowski, Porcher et al. (2009) have confirmed this causal

relationship; a positive association between the incidence of GBS and reported influenza illness was observed in both studies. The clinical symptoms of GBS may begin as early as 1-3 weeks after infection, and the symptoms include limb muscle weakness accompanied by absent or depressed deep tendon reflexes. Complete or partial functional recovery may occur over weeks or months (Koningsveld, Steyerberg, Moghes et al., 2007; Toovey, 2008).

2.9 Antiviral treatment

Currently, there are two classes of antiviral drugs against influenza: M2 inhibitors (amantadine and rimantadine), and neuraminidase inhibitors (zanamivir and oseltamivir).

2.9.1 M2 inhibitors or adamantanes (amantadine and rimantadine)

Adamantanes act to block the function of M2 ion channel, leading to prevent viral uncoating and the release of viral RNA in to the host cell, thereby inhibiting viral replication. Both amantadine and rimantadine are only effective against influenza virus A and are administered orally. Treatment of influenza is most effective when adamantanes are administered within 48 hours of symptom onset (Moscona, 2008; Nayak & Treanor, 2009; Schirmer & Holodniy, 2009). A recent Cochrane review of the amantadine and rimantadine regime for influenza A in adults indicated that these drugs have been shown to be similarly effective in alleviation of influenza symptoms in adults. In addition, neither amantadine nor rimantadine was effective in interrupting the spread of influenza. Adverse gastrointestinal effects were reported in both drugs, but amantadine can also cause serious side effects on the central nervous system (such as insomnia, dizziness, and difficulty in concentrating) (Jefferson, Demicheli, Pietrantonj et al., 2009). Similarly, a randomised, double-blind, placebo-controlled study comparing rimantadine to acetaminophen therapy in children by Hall, Dolin, Gala et al. (1987) found that children in the rimantadine group showed a more rapid decrease in fever and influenza symptoms during the first three days after they had taken the drug. The study also found that viral shedding was decreased during the first

two days, but the proportion of patients shedding virus increased in the subsequent days of therapy.

Additionally, the incidence of adamantanes resistance among influenza A viruses isolated worldwide has increased significantly from 1.8 per cent in 1995-2002 to 12.3 per cent in 2004 (Bright, Medina, Xu et al., 2005). In the United States, the incidence of adamantanes-resistance H3N2 was 92.3 per cent during the 2005-2006 influenza season (Bright, Shay, Shu et al., 2006). Consequently, the use of amantadine and rimantadine for the treatment or prophylaxis of influenza has been limited.

2.9.2 Neuraminidase inhibitors (zanamivir and oseltamivir)

Understanding the structure and function of viral neuramidase has yielded information that contributed to the development of anti-viral drugs. Recently, two neuramidase inhibitors (zanamivir: Relenza®, and oseltamivir: Tamiflu®) have been launched, and they are active against both influenza A and B viruses. These antiviral drugs inhibit the viral replication at the final stage by blocking the release of budded viruses from infected cells (Gubareva, Kaiser, & Hayden, 2000; Moscona, 2005) (Figure 2.9.2).

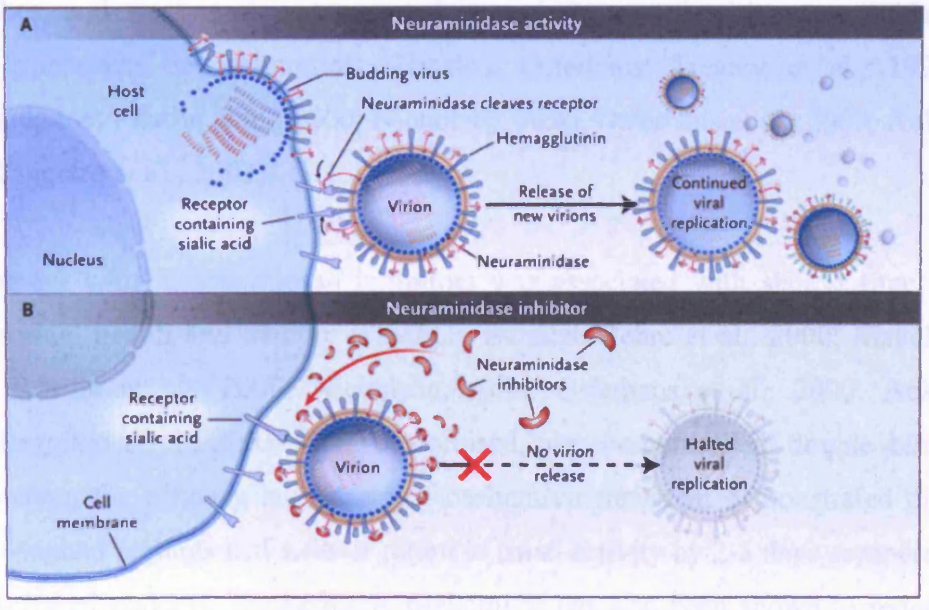


Figure2.9.2 Mechanism of Action of the Neuraminidase Inhibitors

Source: Moscona, 2008

Neuraminidase inhibitors, zanamivir and oseltamivir, are effective for both treatment and prophylaxis of influenza infection. Because viral replication in respiratory tract peaks between 24 and 72 hour after the onset of the illness, the early treatment with zanamivir or oseltamivir is more likely to provide benefits of neuraminidase inhibitor in prophylaxis and treatment of influenza (Makela, Pauksens, Rostila et al., 2000; Treanor, Hayden, Vrooman et al., 2000). The study by Aoki, Macleod, Paggiaro et al., (2003) indicated that total duration of illness is shortened by 41 per cent (3.1 days) when starting oseltamivir therapy within 12 hours after fever onset. Zanamivir is approved for treatment of influenza in persons five years and older, and it is inhaled through the mouth using a specific inhaler (Diskhaler). Unlike zanamivir, oseltamivir is administered orally and licensed for use in persons aged one year and over (Moscona, 2008; Nayak & Treanor, 2009). In randomised, double-blind placebo-controlled trials, both drugs have been shown to be effective in reducing the duration of illness by 1- 2.5 days compared with the placebo group (Hayden, Osterhaus, Treanor et al., 1997; Hedrick, Barzilai, Behre et al., 2000; Makela, Pauksens, Rostila et al., 2000; Nicholson, Aoki, Osterhaus et al., 2000; Treanor, Hayden, Vrooman et al., 2000; Aoki, Macleod, Paggiaro et al., 2003). Additionally, reduction in the severity of major influenza symptoms (such as headache, sore throat, feverishness, muscle aches, and weakness) was reported in patients treated with neuraminidase inhibitors (zanamivir or oseltamivir) (Hayden, Osterhaus, Treanor et al., 1997; Makela, Pauksens, Rostila et al., 2000; Nicholson, Aoki, Osterhaus et al., 2000; Aoki, Macleod, Paggiaro et al., 2003).

Early treatment with neuraminidase inhibitors was associated with shorter time to return to normal health and activity (Hedrick, Barzilai, Behre et al., 2000; Makela, Pauksens, Rostila et al., 2000; Nicholson, Aoki, Osterhaus et al., 2000; Aoki, Macleod, Paggiaro et al., 2003). One randomised, placebo-controlled, double–blind study evaluating the efficacy and safety of oseltamivir treatment demonstrated that oseltamivir-treated patients had a faster return to usual activity by 2-3 days compared to placebo-treated patients. Furthermore, oseltamivir has also been shown to reduce the secondary complications (bronchitis, sinusitis). Secondary complications were more likely to occur in the placebo recipients than the oseltamivir recipients (15 per cent vs. 7 per cent; p = .03) (Treanor, Hayden, Vrooman et al., 2000). The further study by Kaiser, Wat, Mills et al. (2003) also demonstrated that oseltamivir decreased

the incidence of influenza-related lower respiratory tract complications (e.g. bronchitis and pneumonia) and hospitalisations, resulting in a reduction in antibiotic use by 55 per cent. Similar treatment effects were also found in the high-risk group (Makela, Pauksens, Rostila et al., 2000; Lalezari, Campion, Keene et al., 2001). The study investigating the efficacy of zanamivir treatment in high-risk patients showed that zanamivir reduced the illness duration by 2.5 days, allowing a more rapid return to normal activity (3 days). Early treatment with zanamivir in high-risk adults also resulted in a 43 per cent reduction in the rates of influenza-associated complications compared to the placebo group (Lalezari, Campion, Keene et al., 2001). Additionally, a reduction in viral shedding during treatment was observed in patients treated with zanamivir or oseltamivir (Hayden, Osterhaus, Treanor et al., 1997; Hayden, Treanor, Fritz et al., 1999; Nicholson, Aoki, Osterhaus et al., 2000).

Overall, both zanamivir and oseltamivir were well-tolerated. The reported adverse events during treatment with both drugs were nausea, vomiting, diarrhoea and abdominal pain. These gastrointestinal events generally occur after starting the drugs and resolve spontaneously within 1-2 days (Hayden, Treanor, Fritz et al., 1999; Hedrick, Barzilai, Behre et al., 2000; Nicholson, Aoki, Osterhaus et al., 2000; Aoki, Macleod, Paggiaro et al., 2003; Treanor, 2005). Acute bronchospasm may rarely occur during using zanamivir, particularly in those with chronic obstructive pulmonary disease and asthma (Hedrick, Barzilai, Behre et al., 2000; Murphy, Eivindson, Pauksens et al., 2000; Treanor, 2005).

Several randomised, double-blind, placebo-controlled trials have shown that both oseltamivir and zanamivir are effective in preventing influenza illnesses in healthy adults and household contacts, with about 70-90 per cent protective efficacy (Hayden, Treanor, Fritz et al., 1999; Monto, Robinson, Herlocher et al., 1999; Monto, Pichichero, Blanckenberg et al., 2002). One study conducted in North America and Europe (76 centres) showed that the protective efficacy of oseltamivir against influenza in individuals and households exposed to influenza-infected index cases was 89 per cent and 84 per cent, respectively (Welliver, Monto, Carewicz et al, 2001). The study evaluating the efficacy of inhaled zanamivir for the prevention of influenza in families, also found that in the zanamivir group, the proportion of families in which at

least one household contact had symptomatic, laboratory-confirmed influenza was reduced by 79 per cent (Hayden, Larisa, Monto et al., 2000).

2.10 Mode of transmission

Human influenza is thought to be transmitted primarily via the large droplet (particles > 5 microns [μm] in diameter) and contact routes. Virus particles in the nasal secretions are expelled when infected person coughing or sneezing. These activities produce infectious aerosols of various sizes. The large droplets can travel through the air no more than 3 feet (one meter). Thus influenza virus transmission can occur within 3 feet of the source of infection (infected person). These large droplets deposit in the nose and upper airway of a new host. The viruses attach, invade and replicate in the epithelial cells of the upper respiratory tract, which will subsequently cause proinflammatory cytokines and necrosis of ciliated epithelial cells. In addition to generation of the large particle aerosol, coughing and sneezing can also produce small droplet nuclei or airborne particles (< 5 μm) which remain suspended in the air for long periods of time because they are small. Therefore, the droplet nuclei can spread to people far away from the source of infection and reach the lower respiratory tract of a new host. However, the airborne spread of influenza is relatively rare. By contrast, contact appears to be an important route of transmission for influenza. The influenza virus can be transmitted from person to person either through direct skin-to-skin contact with infected persons (e.g. hand shaking) or indirect contact by touching a surface or object contaminated with influenza viruses (e.g. door knobs, telephone receivers) (Bridges, Kuehnert, & Hall, 2003; Brankston, Gitterman, Hirji et al., 2007).

One study revealed that during influenza season, influenza viral RNA was detected on 23 per cent and 59 per cent of the fomites tested in day-care centres and home, respectively (Boone & Gerba, 2005). Influenza viruses enter mucous membranes when infected persons touch these contaminated surfaces or objects and then touch their eyes or nose. The typical incubation period for influenza virus averages two days (range, 1- 4 days). Influenza virus shedding occurs before clinical onset, and it usually continues for 5 -10 days. However, young children shed virus several days before

their illness onset, and the viral shedding is detectable for 10 days or more because of their relative lack of immunity to influenza (Cox & Subbarao, 1999; Whitley, Hayden, Reisinger et al., 2001; Jennings & Read, 2002; Treanor, 2005).

2.11 Seasonality

Influenza infection has a distinctive seasonality in temperate climates. In general, its incidence peaks during the winter months. In northern hemisphere, influenza mainly occurs from November to April, whereas in the southern hemisphere influenza infections are more prevalent between May and September (Simomsen, 1999). By contrast, the influenza viruses circulate throughout the year in the tropical and subtropical regions, and there is a remarkable increase in influenza cases in these regions during rainy seasons. Additionally, biannual pattern of influenza epidemics which occur both in spring and autumn have been observed in some subtropical and tropical countries (Chew, Doraisingham, Ling et al., 1998; Simonsen, 1999; Dosseh, Ndiaye, Spiegel et al., 2000; Shek & Lee., 2003; Simmerman, Thawatsupha, Kingnate et al., 2004; Nguyen, Saito, Ngiem et al., 2007; Moura, Perdigao, & Siqueira, 2009).

Many factors other than climate have been assumed to account for the seasonal variation of influenza. They include seasonal fluctuations in host immunity (e.g. melatonin in relation to the light/dark cycles and vitamin D), seasonal host-behaviour changes (e.g. school attendance, air travel, crowding indoors during cold or rainy weather), prevalence or virulence of the pathogen, and environment changes (temperature, relative humidity, rain, wind) (Dowell, 2001; Brownstein, Wolfe, & Mandl, 2006; Lofgren, Fefferman, Naumov et al., 2007; Lowen, Mubareka, Steel et al., 2007; Monto, 2008). However, only a few studies have directly examined the causal relationship between these factors and the seasonal variation of influenza.

The study by Curwen (1997) has shown the relationship between air temperature and the incidence of epidemic influenza and influenza-like illness in the UK; the peak incidence of influenza and influenza-like illness occurred at the period of lowest average temperature in February (Curwen, 1997, cited in Eccles, 2002). The most recent laboratory experiment using the guinea pig as a model host, revealed that

temperature and relative humidity were contributing factors to variation in influenza transmission; the increased viral shedding was more likely to occur at 5 °C, and low relative humidities of 20 per cent to 35 per cent were the most efficient transmission of influenza viruses among the guinea pigs. The influenza virus was not transmitted when the temperature reached 30 °C, and the relative humidity was 80 per cent (Lowen, Mubareka, Steel et al., 2007). It has been indicated that cold air exposure affects tracheal mucociliary clearance by reducing both ciliary beat frequency and the rate of secretion of mucus. In addition, cooling of the nasal mucosa also causes the depression of lymphocyte proliferation and other aspects of the immune response. This can lead to an increased incidence of upper respiratory tract viral infections in the winter, including influenza (Shephard & Shek, 1998; Eccles, 2002).

Relative humidity can have an influence on seasonal virus survival and transmission. At a low relative humidity, large droplets containing influenza virus can evaporate to become airborne particles (small droplet), promoting the spread of influenza viruses, as well as the survival of the virus in the air. In contrast, high relative humidity impedes the evaporation of water from exhaled virus droplets; thus these droplets fall to the ground more quickly (Lowen, Mubareka, Steel et al., 2007; Lipsitch & Viboud, 2009). Although the temperature and relative humidity have an effect on the incidence of influenza, there are still influenza epidemics in warm tropical climates. It has been proposed that the influenza virus transmission in tropical countries is predominantly by the contact route, and this transmission route may also reflect the sporadic outbreaks without a definite seasonal pattern in these regions (Lowen, Steel, Mubareka et al., 2008). In addition, influenza is likely to occur during rainy season in tropical countries (Shek & Lee, 2003; Simmerman, Thawatsupha, Kingnate et al., 2004). Influenza surveillance data covering January 2001-September 2003 from Thailand National Institute of Health also showed that peak periods of influenza cases were seen from June through October, which was the height of the rainy season (Simmerman, Thawatsupha, Kingnate et al., 2004).

2.12 The burden of seasonal influenza

Seasonal influenza causes a significant disease burden and costs in many parts of the world each year. However, it has been difficult to quantify the actual burden of

influenza on physician consultations, hospitalizations and mortality because influenza lacks pathognomonic features, and it causes a range of non-specific complication in individuals with chronic diseases (such as secondary bacterial infection, exacerbations of chronic lung diseases). Many influenza-related deaths occur from these complications, and a primary influenza infection may not be recognised. The confirmation of influenza infection by laboratory testing has been rarely performed. Additionally, influenza often concurrently occurs with other respiratory pathogens (e.g. respiratory syncitial virus). As a consequence, this may have underestimated the impact of influenza (Nicholson, Wood, & Zambon, 2003; Viboud, Alonso, & Simonsen, 2006).

Overall, influenza A outbreaks produced the greater burden of illness than influenza B virus. In particular, H3N2 subtype influenza A virus which is the most virulent strain of the currently circulating influenza viruses, causes more severe influenza and more hospital admissions, as well as influenza related deaths because antigenic drift has been found frequently in this strain (Frank, Taber, & Wells, 1985; Wright, Thompson, & Karzon, 1980; Simonsen, Fukuda, Schonberger et al., 2000; Thompson, Shay, Weintraub et al., 2003). Thus, most people have little or no pre-existing immunity to this variant virus, resulting in a more severe clinical course. The study by Fleming et al. (2000) using surveillance data covering 1987-1996 from sentinel general practice networks in England, Wales and The Netherlands found that the H3N2 influenza A epidemics were associated with higher consultation rates than influenza B virus, particularly in the age groups 0-4 years and 65 years and older.

2.12.1 Morbidity and mortality associated with influenza among adults in temperate countries

Although influenza morbidity varies substantially from year to year depending on the strain of virus and the immune status of the population, the average attack rates range from 10 to 20 per cent during influenza epidemics. However, these rates can reach as high as 40-50 per cent among susceptible individuals, such as elderly and people with chronic medical conditions. In addition, the highest attack rates were observed in school-age children. Accordingly, the higher occurrence of influenza was also reported in household contacts (Longini, Koopman, Monto et al., 1982; LaForce,

Nichol, & Cox, 1994; Cox & Subbarao, 2000; Treanor, 2005). In order to estimate the burden of influenza (influenza-attributable morbidity and mortality), indirect statistical modelling methods have been applied to analyse hospital discharge, cause of death, and virological surveillance data (Simmerman & Uyeki, 2008).

One retrospective study in USA (Mullooly, Bridges, Thompson et al., 2007) using data from four respiratory seasons (1996/1997-1999/2000) found that individuals with chronic medical conditions aged 50-64 years had significant excess pneumonia and influenza hospitalisations and circulatory and respiratory hospitalisations (123 and 232 per 100,000 person-periods, respectively). Moreover, persons older than 65 years with underlying chronic diseases had substantially higher influenza-associated rates of hospitalisations for pneumonia and influenza (556 per 100,000 person-periods) compared to healthy elderly persons (187 per 100,000 person-periods). Similarly, the study estimating influenza-related hospital admissions in older people from Swiss Sentinel Surveillance Network (SSSN) database over a 10-year period (1987-99 to 1996-97) revealed that the average rates of excess hospitalisations due to influenza epidemics each year was substantially higher in the elderly (110 per 100,000 population) than in those aged 51-65 years (6.56 per 10,000 population). The excess for both pneumonia and influenza and other respiratory conditions hospitalisations were highest among the oldest age-group (>65 years) (Scuffham, 2004). The increased risk for influenza-associated hospitalisations was also demonstrated in persons with chronic obstructive pulmonary disease (COPD). The study by Rohde, Wiethege, Borg al. (2003) showed that the respiratory viruses were found in 56 per cent of the patients with acute exacerbations of chronic obstructive pulmonary disease (AE-COPD) and in 19 per cent of the control patients. Influenza viruses accounted for 25 per cent of AE-COPD cases. Similarly, a longitudinal cohort study of older adults with COPD conducted in United States found that 45 per cent of COPD hospitalisations between December and March were attributed to respiratory viral infections, including influenza infections (Greenberg, Allen, Wilson et al., 2000). Another study conducted in Canada also showed a marked increase in physician visits, emergency room visits, and admission rates for influenza and pneumonia and chronic lung disease over four influenza seasons (1995-96 to 1998-99) among adults aged 65 and over (Menec, Black, MacWilliam et al., 2003).

Influenza infections also have a major impact on mortality, especially in the elderly and persons with underlying diseases. Excess mortality from influenza and pneumonia (P&I) deaths during influenza season have been considered as the primary index for assessing the severity of influenza seasons (Simonsen, Clarke, Williamson et al., 1997, Simonsen, 1999). However, excess pneumonia and influenza mortality may not reflect the overall picture of disease burden because influenza epidemics were also associated with an increase in hospitalisations and deaths in people with underlying disease such as COPD, congestive heart failure and secondary bacterial infection (Simonsen, 1999; Thompson, Shay, Weintraub et al., 2003). Therefore, the excess in mortality due to circulatory and respiratory (C&R) deaths and influenza-associated all-cause deaths have been used to estimate the total burden of deaths associated with influenza infections in several epidemiological studies (Simonsen, Clarke, Williamson et al., 1997; Simonsen, 1999; Thompson, Shay, Weintraub et al., 2003; Wong, Chan, Hedley et al., 2004; Chow, Ma, Ling et al., 2006).

The number of influenza-related deaths in France between 1980 and 1990 was estimated at 11-81 per 100,000 populations. However, this mortality rate was underestimated because many deaths attributable to influenza were registered as deaths from other causes (e.g. lung disease, heart disease). Final calculations of this statistic suggested total estimated death rates ranged from 28 per 100,000 populations (1988-89) to 482 per 100,000 populations (1985-86) (Carrat & Valleron, 1995). There were an estimated 30,000 excess deaths occurring during the 56 days of one influenza epidemic (17 November 1989 – 11 January 1990) in England and Wales (Ashley, Smith, & Dunnell, 1991). Additionally, the study conducted in the United States by Thompson, Shay, Weintraub et al. (2003) showed that annual estimates of influenza-associated deaths from pneumonia and influenza, respiratory and circulatory, and all causes increased markedly between 1976-77 and 1998-99. Influenza-associated deaths for pneumonia and influenza (P&I), circulatory and respiratory deaths (C&R), and all causes in persons aged 65 or older were 22.1, 98.3, and 132.5 per 100,000 person-years, respectively. Persons aged 65 years or older accounted for 90 per cent of deaths attributed to pneumonia and influenza during 1990-1999. Influenza caused more deaths than respiratory syncytial virus in all age groups, except for children younger than 1 year. Another study conducted in Canada by Menec, Black, MacWilliam et al. (2003) showed a similar result; significant excess mortality rates

due to influenza and pneumonia and chronic lung disease were evident among the elderly and nursing home residents. Influenza also posed a serious threat for diabetic persons. Excess mortality rates due to pneumonia and influenza were observed among these high-risk individuals in southern Wisconsin during 1980-1988 (Moss, Klein, & Klein, 1991).

Among pregnant women, there is concern that influenza during pregnancy is associated with an increase risk for maternal and foetal complications (Neuzil, Reed, Mitchel et al., 1998; Irving, James, Stephenson et al., 2000). Most previous studies have assessed the effect of influenza on pregnant women during influenza season. However, influenza-related hospitalisations in pregnant women have been measured in terms of excess hospitalisations for respiratory illness but not laboratory-confirmed influenza hospitalisation. During the influenza season, there was a higher rate of outpatient medical services for acute respiratory disease among pregnant women relative to non-pregnant women (Mullooly, Barker, & Nolan, 1986). In addition, hospitalised pregnant women with respiratory illness had a longer length of stay than those without respiratory illness. The average length of hospital stay among pregnant women with respiratory illness was 3.88 days for non-delivery and 6.36 days for delivery, whereas the average length of stay among those without respiratory illness was 2.69 days for non- delivery and 2.45 days for delivery (Cox, Posner, McPheeters et al., 2006).

Hospitalisations with respiratory illness among pregnant women were significantly higher in seasons when the prominent H3N2 influenza A circulating (Cox, Posner, McPheeters et al., 2006). A recent population-based cohort study of 33,775 pregnant women conducted over a study period of 13 years has found that the rate of third-trimester hospital admissions among pregnant women during influenza season was five times higher than the rate during the influenza season in the year before pregnancy (Dodds, McNeil, Fell et al., 2007). Moreover, the rate of hospital admissions during the third trimester of pregnancy was more than twice as high as the rate during the non-influenza season. An estimated 1,210 additional hospital admissions in the third trimester per 100,000 pregnant women with co-morbidities and 68 per 100,000 pregnant women without co-morbidities during the influenza season has been documented (Dodds, McNeil, Fell et al., 2007).

In a retrospective cohort study among 3975 pregnant women who were consecutively delivered at two Nottingham teaching hospitals, Irving, James, Stephenson et al. (2000) found significant differences in the pregnancy complications between the cases and controls. The pregnant women whose paired ante- and postnatal sera showed a rise in anti-influenza titres (cases) had more foetal, medical and obstetric complications (e.g. reduced fetal movements, preterm, pneumonia, pulmonary embolus, atrial fibrillation, bleeding, post dates induction) than the controls (106/181 vs. 73/180, p <0.001). By contrast, another study showed that there was no increased risk for adverse perinatal outcomes among pregnant women with respiratory hospitalisations during influenza season (Hartert, Neuzil, Shintani et al., 2003). The UK study also found a non-significant increased risk for low birth weight, low Apgar score and congenital anomalies among newborns of infected mothers with laboratory-confirmed influenza during the second and third trimesters of pregnancy (Irving, James, Stephenson et al., 2000).

2.12.2 Morbidity and mortality associated with influenza among children in temperate countries

Influenza illness is a leading cause of visits to medical practices and emergency departments among children younger than five years. A recent study conducted in the US. by Poehling, Edwards, & Weinberg (2006) revealed that the estimated rates of outpatient and emergency department visits associated with influenza were 50-95, and 6-27 per 1000 children younger than 5 years, respectively in the two consecutive influenza seasons (2002-03 and 2003-04).

A higher rate of outpatient visits or emergency department visits for infectious respiratory illness, including influenza among children younger than five years of age was also found in other studies (Neuzil, Mellen, Wright et al., 2000; Neuzil, Zhu, Griffin, et al., 2002; Bourgeois, Valim, Wei et al., 2006). The excess use of antibiotics in children younger than 15 years of age has also been observed during the influenza season (Neuzil, Mellen, Wright et al., 2000). In addition, Neuzil, Mellen, Wright et al. (2000) found that the rates of influenza-related hospitalisations were higher among infant and young children, and the hospital admission rates declined significantly with increasing age (104 per 10,000 children younger than 6 months, 50 per 10,000

children aged 6 months to less than 12 months, 19 per 10,000 children aged 1 year to less than 3 years, 9 per 10,000 children age 3 years to less than 5 years, and 4 per 10,000 children aged 5 years to less than 15 years).

Recently, a retrospective cohort study that measured hospitalisation rates for laboratory-confirmed influenza over three influenza seasons in children 18 years of age and younger provided similar results. The population-based rates of hospitalisation ranged from 6.3 to 252.7 per 100,000 children; hospitalisation attributable to influenza was highest in children younger than 6 months (252.7 per 100,000 children), and rates decreased in older children (Ampofo, Gesteland, Bender et al., 2006). In addition, a four-fold difference in the rate of hospitalisations from influenza was found between children aged up to 6 years old with asthma and healthy children of the same age (Miller, Griffin, Edwards et al., 2008). However, influenza-related deaths are rare among children. It is estimated that the excess number of deaths attributable to influenza is 8 per million in children younger than 15 years of age (Neuzil, Mellen, Wright et al., 2000).

2.12.3 Morbidity and mortality associated with influenza in tropical and subtropical countries

Unlike the temperate countries, the burden of influenza in tropical countries has not been well documented. This is partly because these countries are in the process of developing an influenza surveillance system, limiting the use of such surveillance data to reflect the true picture for influenza disease burden (Simonsen, 1999). Additionally, influenza occurs year-round, and seasonality is less defined in tropical country. These factors make it difficult to precisely quantify the burden of disease in this region because the year-round influenza activity probably prevents the detection of excess morbidity and mortality associated with influenza. However, recent studies have shown that influenza also causes an increase in hospitalisations and deaths in tropical and subtropical countries.

One study conducted in Hong Kong using the Poisson regression method to estimate influenza-related mortality found that influenza was responsible for approximately 29.3 additional pneumonia and influenza hospitalisations per 100,000 across all ages during 1996-2000 (Wong, Yang, Chan et al., 2006). This was comparable to those

reported in temperate countries such as the United States. The study by Thompson, Shay, Weintraub et al. (2004) using the same method to estimate excess influenza-associated hospitalisations during 1979-2001 found that the annual average rate of pneumonia and influenza hospitalisations was 36.8 per 100,000 population for all ages. Similarly, a retrospective study in a tertiary hospital in the tropics showed that influenza was associated with excess hospitalisations for pneumonia, acute exacerbations of COPD, and heart failure in persons aged 65 or older. Influenza activity accounted for 38.9, 7.5, and 45.6 of the variance in hospital admissions for pneumonia, COPD, and heart failure, respectively. The adjusted rates of excess influenza-related hospitalizations for these three diagnoses were 585, 200, 292 and 134 excess hospitalisations per 100,000 elderly persons in 1998, 1999, 2000, and 2001, respectively (Yap, Ho, Lam et al., 2004).

Ng, Pwee, Niti et al. (2002) assessed the burden of illness in the community in Singapore, and found that there were 630,000 cases of influenza-like illness, resulting in 520,000 medical visits each year. In Thailand, a prospective, population-based surveillance system and laboratory found that children younger than 5 years of age and the elderly have the greatest incidence of influenza pneumonia (236 per 100,000 and 375 per 100,000, respectively). It was estimated that there would be approximately 36,413 annual hospitalisations and 322 in-hospital deaths for influenza pneumonia in Thailand during 2005-2008 (Simmerman, Chittaganpitch, Levy et al., 2009).

Influenza-associated mortality rates, especially among elderly people in tropical and subtropical climates were higher in Singapore and Hong Kong than in the United States. Chow, Ma, Ling, et al. (2006) using a statistical model to estimate influenza-associated mortality in Singapore found that influenza-associated deaths for pneumonia and influenza (P&I), circulatory and respiratory deaths (C&R), and all causes in persons aged 65 or older were 46.9, 155.4, and 167.8 per 100,000 person-years, respectively. Moreover, these estimates of influenza-associated deaths were higher than those reported in Hong Kong (39.3 pneumonia and influenza deaths per 100,000 persons, 102.0 circulatory and respiratory deaths per 100,000 persons, and 136.1 all-cause deaths per 100,000 persons) and in the United States (22.1 per 100,000 persons from underlying P&I deaths, 98.3 per 100,000 persons from

underlying circulatory and respiratory deaths, and 132.5 per 100,000 persons from all-cause deaths) (Thompson, Shay, Weintraub et al., 2003; Wong, Chan, Hedley et al., 2004; Chow, Ma, Ling et al., 2006).

2.12.4 The costs associated with influenza

Seasonal influenza epidemics can have an economic impact on both society and the individual. A number of studies have attempted to assess the full economic impact of influenza, which includes direct medical costs and indirect costs, such as lost productivity from illness and lost earnings due to loss of life (Meltzer, Cox, & Fukuda 1999; Akazawa, Sindelar, & Palteil, 2003; Molinari, Ortega-Sanchez, Messonnier et al., 2007). A recent study estimating the annual impact of seasonal influenza in the US based on 2003 population demographics indicated that there were an estimated 41,008 deaths (610,660 life-years lost), 3.1 million hospitalised days and 31.4 million outpatient visits annually, resulting in direct medical costs of $US 10.4 billion (95% confidence interval [C.I.], $US 4.1 - $US 22.2) annually. The total annual economic burden of influenza in the United States has been estimated at $US 87.1 billion, including $US 10.4 billion in direct medical costs and $US 76.7 billion in indirect costs. The indirect costs of influenza were estimated to account for 88 per cent of the total economic burden of influenza; the majority of these indirect costs were produced as a result of lost productivity (Molinari, Ortega-Sanchez, Messonnier et al., 2007).

The economic burden of influenza was further illustrated in a cost analysis by Newall & Scuffham (2008) who found that annual epidemics of seasonal influenza resulted in an average of 310,000 general practitioner consultations, and 18,404 hospital admissions (95% CI: 15,918 - 20,889). The cost for the treatment of influenza-related illness alone in a typical season in Australia has been estimated at A$ 115 million per year (range A$ 72.3-A$ 170.1 million). In Thailand, a recent study that estimated the burden of influenza in hospitalised pneumonia and outpatient febrile respiratory illness with laboratory confirmed influenza has shown that the total economic costs of influenza has been estimated to be between US$ 23.4 and US$ 62.9 million during September 2003 and August 2004, and lost productivity accounted for 56 per cent of all costs (Simmerman, Lertiendumrong, Dowell et al., 2006).

Influenza illness also results in work loss. It was estimated that 10-12 per cent of all sickness absence from work is attributable to influenza (Keech, Scott, & Ryan, 1998). Moreover, after returning to work, approximately 80 per cent of adults had impaired work performance (Adams & Marano, 1994, cited in Keech & Beardworth, 2008). In the United States alone, it was estimated that influenza-like illness accounted for more than 79 million working days lost each year (Benson & Marano, 1998, cited in Keech & Beardworth, 2008). Similarly, a cost-of-illness study based on the data from German Sickness Funds indicated that the economic costs of influenza epidemic in 1997 was approximately two billion Deutschmarks (DM), and the costs were mainly associated with lost work productivity and medical treatment (Szucs, 1999). The indirect costs due to lost productivity from influenza illness were further demonstrated by Simmerman, Lertiendumrong, Dowell et al. (2006). This study conducted in Thailand and showed that hospitalised influenza pneumonia resulted in approximately 118,335 to 941,567 lost workdays. Additionally, a recent study quantifying the impact on working days lost due to influenza- like illness indicated that the mean number of missed work days after being diagnosed with influenza ranged from 3.7 to 5.9 days per episode (Keech & Beardsworth, 2008), and the average work loss due to influenza-like illness was estimated at US $137 per person (Akazawa, Sindelar, & Palteil, 2003).

With regard to the burden of influenza in children, a retrospective cohort study of children aged younger than 21 years who were hospitalised with laboratory-confirmed influenza by Keren, Zaoutis, Saddlemire et al. (2006) has shown that the burden of influenza-related hospitalisation in children is greater than previously appreciated. The mean total cost of hospitalisation attributable to influenza ranges from US$ 7,030 (interquartile range [IQR]: 3372 - 7309) for patients cared for exclusively on the wards to US$ 39,792 (IQR: 10634 - 44942) for those admitted to an ICU. Children with chronic disease (such as cardiac disease, neurological or neuromuscular disease) had higher mean total costs (US$ 15,269) than those in the low risk group (US$ 9,107). This retrospective cohort study over three influenza seasons at Primary Children's Medical Centre, Utah, USA also revealed that children aged two years and over had higher rates of pneumonia, intensive care stay, and mechanical ventilation than younger children, leading to longer hospital stays and higher hospital cost of care. The total direct cost attributable to the treatment of influenza over a 3-year

period (July 2001-June 2004) was US$ 2 million. Children aged two years and older were responsible for 55 per cent of the total direct costs. Moreover, forty five per cent of these children did not have chronic medical conditions that place them at risk of influenza complications (Ampofo, Gesteland, Bender et al., 2006).

The indirect burden of influenza in terms of secondary respiratory illness in families of children with influenza, work and school day loss was demonstrated by two studies. In Italy, a prospective study comparing clinical and socio-economic impact of influenza and respiratory syncytial virus (RSV) infection in children aged 15 years or younger who attended an emergency department found that children with influenza were absent significantly more than RSV-positive children (median, 12 vs. 5 days). Furthermore, secondary attack rates, medical visits, antipyretic use and the number of parent days lost from work were significantly higher in families of influenza-positive children compared with the families of RSV-positive children (Esposito, Gasparini, Bosis et al., 2005).

A recent study by Tsolia, Logotheti, Papadopoulos et al. (2006) also demonstrated an impact of influenza in healthy children and their families. Secondary respiratory illness was more prevalent in family members of influenza-positive children; the estimated secondary infection rate was 17 per cent. Parents lost an average of 1.34 workdays for taking care of sick children and 0.36 days for their own illness.

2.13 Conclusion

This chapter aimed to provide a greater understanding of influenza infection and its impact on health and society. It revealed that influenza is a highly contagious respiratory disease caused by the influenza virus and occurs globally, though is more prevalent in temperate countries during the winter months. Influenza epidemics pose a substantial burden on healthcare systems around the world. Influenza can affect people of all ages. However, older people and vulnerable populations can suffer more severe illness and a more rapid deterioration. Influenza infection is characterised by an abrupt onset of fever, muscles ache and pain, headache, fatigue, sore throat, and a dry cough. Influenza can be difficult to diagnose based on clinical features alone because its symptoms are similar to those of other upper respiratory conditions, such as a common cold. There are several laboratory methods for the detection of influenza

infection. These include virus isolation in cell culture, direct antigen detection, detection of influenza-specific RNA by reverse transcriptase-polymerase chain reaction (RT-PCR), and serologic diagnosis. The choice among these diagnostic tests depends on the turnaround time for reporting of the results and cost. Currently, there are four antiviral drugs (amantadine, rimantadine, oseltamivir, and zanamivir) available for the treatment and prophylaxis of influenza. The influenza vaccine is the best means of preventing influenza and its complications. More details about the vaccine development process, type of vaccine, and the efficacy and safety of influenza vaccination will be presented in the next chapter.

Chapter 3: Influenza vaccine

3.1 Introduction

Influenza viruses have long-been with humankind for centuries, causing seasonal epidemics every year and pandemics every few decades. It is generally accepted that "Influenza vaccine is the most effective preventive measure available" (WHO, 2005a). The vaccine has been proven to be safe and effective in preventing influenza and its serious complications across all age groups (Gross, Hermogenes, Sacks et al., 1995; Nichol, 2001, 2003; Hak, Buskens, van Essen et al., 2005; Looijmans-Van den akker, 2006; Poole, Chacko, Wood-Baker et al., 2006).

3.2 History of vaccine

The term "vaccination" is originally derived from Latin word "vacca" meaning cow, and it was first used in 1796 by Edward Jenner, who demonstrated the scientific principles of smallpox prevention by using cowpox virus to vaccinate people against the disease. Influenza vaccine successfully developed by the scientists in the 1940s, and was first used by the U.S military during the Second World War (Smith, Andrewes, & Laidlaw, 1933; Francis & Magill, 1937; Hilleman, 1998; Hilleman, 2000; Kamps, Hoffmann, & Preiser, 2006). Since then, significant progress has been made to develop a safe and effective influenza vaccine. At present, almost 300 million doses of trivalent influenza vaccines are distributed worldwide each year. Most of these vaccines are produced in nine countries: the United Kingdom, the United States, Germany, Canada, France, Italy, Netherlands, and Japan. Sixty two per cent of the influenza vaccines are also used in these countries. According to the current global vaccine-production capacity, it could be possible to produce around 900 million doses of pandemic vaccines (monovalent vaccine which contains only the pandemic influenza virus strain) when the next influenza pandemic occurs (Gerdill, 2003; van Essen, Palache, Forleo et al., 2003; WHO, 2004; Fedson, 2005; MIV study group, 2005).

3.3 The vaccine development process

The production of a new influenza vaccine is a complex process that involves several sequential steps and generally takes around six months. As two surface glycoproteins, HA and NA, of the influenza virus continually change by mutation, the WHO

coordinates the international surveillance network to monitor the global epidemiological situation. Biannually, the WHO announces the virus strains which are likely to be circulating in the forthcoming influenza season to aid the production of a matched vaccine. Influenza vaccine contains one influenza A (H3N2) virus, one influenza A (H1N1) virus, and one influenza B virus. The recommendation for influenza vaccine composition for use in the forthcoming influenza season will be made by the WHO in February for influenza vaccines for use in the northern hemisphere. Likewise, the recommended composition of influenza virus vaccines for use in the southern hemisphere will be issued in September.

As the circulation of influenza and seasonal pattern are less defined in equatorial regions, epidemiological considerations will influence which recommendations (February or September) are appropriate for vaccine used in these regions. Through this process, the influenza vaccine for use in the 2010-2011 Northern hemisphere winter will contain the following influenza viruses: A/California/7/2009(H1N1); A/Perth/ 16/2009 (H3N2); and B/Brisbane/60/2008. As the 2009 pandemic influenza A (H1N1) is expected to continue to occur during the 2010-11 influenza season, influenza A (H1N1) 2009 is included in the upcoming influenza vaccine, as well as the H3N2 influenza A component has been changed from A/Brisbane/10/2007 (H3N2) in the 2009-2010 to A/Perth/16/2009 (H3N2) in the 2010-2011 formulation. The influenza B virus strain used in this composition is the same strain used in the 2009 seasonal influenza vaccine. This recommendation was based on surveillance data related to epidemiology and antigenic characteristics of influenza virus strains circulating in the next year (WHO, 2010c; CDC, 2010a).

Once the recommendations for influenza vaccine composition for the forthcoming season have been issued, the preparation of vaccine virus needs to be done by the WHO in order to make the vaccine virus less dangerous and also safety. The seasonal influenza virus strain is mixed with an A/PR8/34 (a standard laboratory virus strain which is attenuated and unable to replicate in humans), and these viruses grow together, allowing the production of high-growth reassortants. These hybrid viruses contain both components of the laboratory strain and the seasonal influenza virus strain. The hybrid viruses are tested to make sure that they produce surface proteins (HA and NA) of the seasonal influenza virus and grow well in hen's eggs. After

verification of the vaccine strain, the hybrid vaccine viruses are then distributed to vaccine manufacturers for use in vaccine production. In parallel, the WHO collaborating centres produce official reference reagents (standardized substances) that are provided to all vaccine manufacturers. The reference reagents will be used to verify the antigenic content and the immunogenetic capacity of the commercial vaccines. The new vaccine viruses are injected into thousands of eggs which are incubated for two to three days to allow the virus to multiply. These viruses are then harvested, separated from the egg white, inactivated using formaldehyde or β-propiolactone and disrupted with detergent. The surface proteins of viruses (subunit hemagglutinin and neuraminidase) are subsequently purified, resulting in production of thousands of litres of purified virus protein for use as antigen which is the active ingredient in the influenza vaccine. In order to control quality, each lot of vaccine antigen is tested and verified with the WHO reference reagents. Finally the bulk vaccine is diluted to the desired concentration, packed, labelled and delivered. The summary of the influenza vaccine manufacturing process is shown in figure 3.3 (Gerdil, 2003; Treanor, 2004; Kamps, Hoffmann, & Preiser, 2006; WHO, 2009; CDC, 2010a).

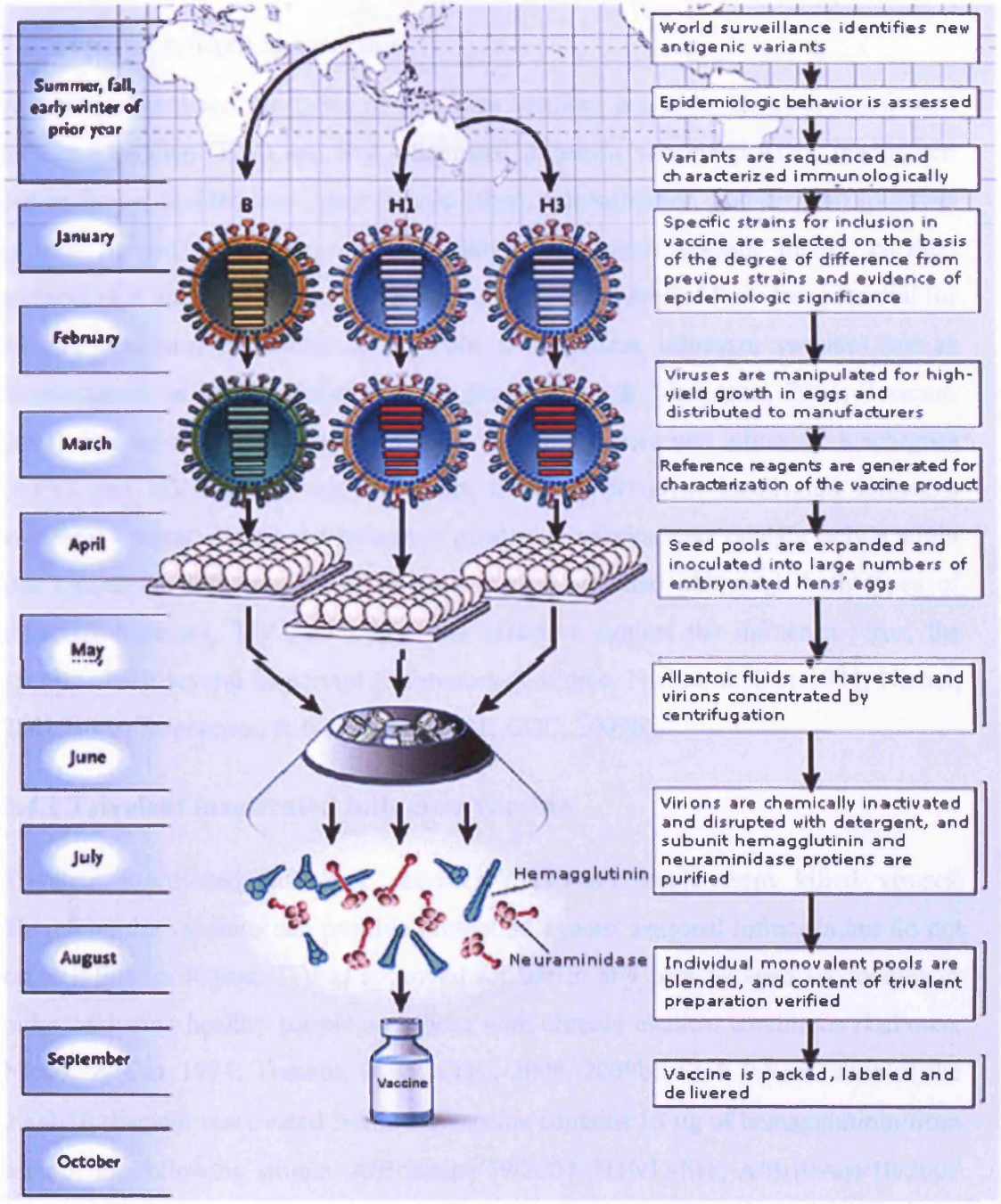


Figure 3.3 The process of development and manufacturing of influenza vaccines.

Source: Treanor, 2004

3.4 Type of influenza vaccine

At present, there are two types of influenza vaccines available: trivalent inactivated influenza vaccine (TIV) and live, attenuated influenza vaccine (LAIV). Inactivated can be further divided into intact (whole virus), split/subvirion, and sub-unit (purified surface antigen) influenza vaccines. Sub-unit vaccines contain highly purified antigens (HA and NA) instead of the whole virus, and therefore have less potential for adverse reactions, especially fever. Split and sub-unit influenza vaccines are as immunogenic as whole virion vaccine (Stephenson & Nicholson, 2001; Treanor, 2005). In inter-pandemic years, influenza vaccines contain two influenza A subtypes (H1N1 and H3N2), and one influenza B strain (trivalent inactivated influenza vaccine), whereas during the influenza pandemic, vaccine may contain only a strain that causes the influenza outbreak (monovalent vaccine). Although both types of influenza vaccines, TIV and LAIV, are effective against the influenza virus, the vaccines have several important differences (LaForce, Nichol, & Cox 1994; Nichol, 2001, 2003; Stephenson & Nicholson, 2001; CDC, 2009b).

3.4.1 Trivalent inactivated influenza vaccine

Trivalent inactivated influenza vaccines (TIV) are made from killed viruses. Therefore, the vaccines can provide protection against seasonal influenza but do not cause influenza illness. TIV is approved for use in any persons aged six months or older, including healthy people and those with chronic medical conditions (LaForce, Nichol, & Cox 1994; Treanor, 2005; CDC, 2008, 2009b). Each 0.5 mL dose of the 2009-10 trivalent inactivated influenza vaccine contains 15 μg of hemagglutinin from each of the following strains: A/Brisbane/59/2007 (H1N1)-like, A/Brisbane/10/2007 (H3N2)-like, and B/Brisbane 60/2008-likes. Preservatives (e.g. thimerosal) are added in multi-dose vials to prevent microbial growth. Inactivated, thimerosal preservative-free 0.5 mL, single dose vial or pre-filled syringes are also available (CDC, 2009b; WHO, 2009). TIV should be stored in a refrigerator between 2-8°C. Vaccine that is exposed to freezing temperatures must not be used (CDC, 2009b).

As the whole virus vaccine is associated with febrile reactions, only split-virus vaccine is recommended for children 12 years of age or younger (Campos-Outcalt,

2004). Accordingly, at present the whole virus vaccines are less frequently used than split or subunit vaccines and unlicensed in many countries (Stephenson & Nicholson, 2001). TIV is administered by intramuscular injection. The deltoid muscle is the recommended site of vaccination, and the needle should be one inch or more in length (> 25 mm) for adolescents and adults immunisations, as this length allows for penetration to reach in the muscle tissue. For infants and young children, the anterolateral aspect of the thigh is the preferred site for vaccination. A needle length of 7/8-1 inch should be used for children younger than 12 months of age. The dosage recommendations vary according to age groups (see Table 3.4.1). Children aged less than nine years need two doses of influenza vaccines for full immunity in the first year, and these should be separated by four weeks. If these children received only one dose of vaccine in their first year, they should receive two doses in the following year (Campos-Outcalt, 2004; CDC, 2009b).

Table 3.4.1 Influenza vaccine dosage, by age of patient

Age group	Product [a]	Dosage	Number of doses	Route
6-35 months	Split virus only	0.25 mL	1 or 2[b]	Intramuscular
3-8 years	Split virus only	0.50 mL	1 or 2[b]	Intramuscular
9-12 years	Split virus only	0.50 mL	1	Intramuscular
Over 12 years	Whole or split virus	0.50 mL	1	Intramuscular

Note: [a] Because of the lower potential for causing febrile reactions, only split-virus vaccines should be used in children. They may be labelled as "split", "subvirion", or "purified-surface- antigen" vaccine. Immunogenicity and side-effects of split-virus and whole-virus vaccines are similar in adults when vaccines are used at the recommended dosage.

[b] Two doses are recommended for children younger than 9 years of age who are receiving influenza vaccine for the first time.

Source: Campos-Outcalt, 2004; CDC, 2009b

3.4.1.1 Immune response

After influenza infection or immunisation with trivalent inactivated influenza vaccine, the protection against influenza virus is mainly connected with an increasing of haemagglutination-inhibiting (HAI) antibody in serum, which inhibits influenza virus

attachment to respiratory epithelial cells and neutralise virus infectivity (Kilbourne, Laver, Schulman et al., 1968; Clements, Betts, Tierney et al., 1986; Brydak & Machala, 2000; Brydak, Machala, Mysliwska et al., 2003). Haemagglutination-inhibiting antibody is first detectable between four and seven days after infection or immunisation, and peak titres were found at 14 - 21 days (Potter & Oxford, 1979; Gross, Russo, Dran et al., 1997). This HAI antibody in serum could persist for several months (or even years). Haemagglutination-inhibiting antibody titres of approximately 1:30 - 1:40 are considered positive for antibody against influenza infection and its complications (Potter & Oxford, 1979; Brydak & Machala, 2000; Stephenson & Nicholson, 2001; Hannoun, Megas, & Piercy, 2004). The presence of HAI antibody has also been found to reduce the severity of influenza illness (Morris et al., 1966 cited in Potter & Oxford, 1979; Brydak & Machala, 2000; Couch, 2000; Hannoun, Megas, & Piercy, 2004).

Additionally, antibody to the virus neuraminidase has been detected following immunisation with influenza vaccine and contributes to immunity against influenza virus infection (Kilbourne, Laver, Schulman et al., 1968; Kilbourne, Couch, Kasel et al., 1995; Brydak, Machala, Mysliwska et al., 2003). Unlike the HAI antibody, the neuraminidase inhibiting (NI) is non-neutralising antibody and plays a major role in limiting the spread of virus from infected cells; thus the NI antibody does not prevent infection, but helps to reduce the severity and duration of influenza infection (Kilbourne, Laver, Schulman et al., 1968; Kilbourne, Couch, Kasel et al., 1995; Brydak & Machala, 2000; Brydak, Machala, Mysliwska et al., 2003). This NI antibody has also been found to stimulate the immune response to subsequent influenza infection (Potter & Oxford, 1979). A lower incidence of influenza A infections which are caused by the influenza A/Hong Kong/68 (H3N2) containing a new haemagglutinin antigen (H3) but the same neuraminidase antigen (N2), was observed in individuals with NI antibody acquired by previous infection with influenza A H2N2 compared with those without NI antibody (Monto & Kendal, 1973).

In addition to producing the serum HAI and NI antibodies, local antibodies (e.g. IgA antibody to influenza haemagglutinin) can be produced following immunisation with inactivated influenza vaccine (Ruben, Potter, & Stuart-Harris, 1975; Potter & Oxford,

1979; Clements, Betts, Tierney et al., 1986). Local antibodies are detectable in nasal washing between four and seven days after infection or immunisation with influenza vaccine, reach their peak at two to three weeks and do not provide a long duration of immunity against influenza infection (Potter & Oxford, 1979; Couch & Kasel, 1983). Immunsation with inactivated influenza vaccine has also been reported to stimulate cytotoxic T-lymphocyte or cellular immune responses among individuals primed by previous influenza infection (Ennis, Yi-Hua, & Schild, 1982). T-cells might be important in recovery from influenza symptoms or reducing viral shedding, although they cannot prevent host cells from influenza infection (Yap & Ada, 1978; Ennis, Yi-Hua, & Schild, 1982; Bernstein, Kaye, Abrutyn et al., 1999). However, the importance of the local antibodies and cell-mediated immunity is probably less than that of specific humoral IgG antibody response to viral haemagglutinin (Ruben, Potter, & Stuart-Harris, 1975; Potter & Oxford, 1979; Clements, Betts, Tierney et al., 1986).

There is currently no estimate on a protective level of anti-neuraminidase antibody. Accordingly, most previous studies evaluating serological responses to influenza vaccination were more focused on the immunological response to haemagglutinin (Brydak & Machala, 2000; Brydak, Machala, Mysliwska et al., 2003). A number of studies have been shown a converse correlation between the level of HI antibody titres and the susceptibility to influenza infection (Dowdle, Coleman, Mostow et al., 1973; Masurel & Laufer, 1984; Brydak & Machala, 2000). The higher post-vaccination HI antibody titres (120-160) are associated with the lower risk of influenza infection (Masurel & Laufer, 1984; Hannoun, Megas, & Piercy, 2004). Dowdle, Coleman, Mostow et al. (1973) examined an association of post vaccine serum haemagglutination-inhibition and neuraminidase inhibition titres to protect against Hong Kong influenza infections during the influenza epidemic of 1968-1969. In this study, assessment of attack rate among influenza vaccinees using fever as an index of disease, the results showed that the influenza attack rate which caused by influenza A/Hong Kong/68 (H3N2) among volunteers without HAI and NI antibodies was 45 per cent, whereas in the volunteers with presence of NI antibody, the attack rate was reduced to 24 per cent. Those with both HAI and NI antibodies in serum (titres equal to or greater than 160) experienced an attack rate of 7 per cent.

The majority of healthy children and young adults develop high HAI antibody titres against influenza viruses after vaccination (Bridges, Thompson, Meltzer et al., 2000; Neuzil, Dupont, Wright et al., 2001; Demicheli, Pietrantonj, Jefferson et al., 2007). However, the influenza vaccine is less immunogenic in older people, individuals on immunosuppressive therapy and those with chronic diseases such as renal disease, diabetes mellitus, cancer and haemophilia (Ershler, 1988; Brydak & Machala, 2000; Treanor, 2005). Beyer (1989) reviewed thirty studies measuring the humoral immune response following vaccination, and the results showed a decreased humoral immune response with age in ten studies. In addition, there is evidence that the use of higher doses of influenza vaccine and administration of a booster dose one month after the first dose of vaccine have not been demonstrated to enhance immune response in the elderly (Gross, Weksler, Quinnan et al., 1987; Levine, Beattie, & Mclean 1987; Gravenstein, Miller, & Drinka, 1992).

3.4.1.2 The efficacy and effectiveness of trivalent inactivated influenza vaccine

The protective effect of inactivated influenza immunisation is influenced by a number of factors, including the degree of similarity between vaccine viruses and those in circulation, how the vaccine is administered, and the characteristics of the target population (e.g. age, co-morbidity, use of concurrent medications, prior influenza vaccination, and pre-vaccination HI antibody titres) (Demicheli, Jefferson, Rivetti et al., 2000; Hannoun, Megas, & Piercy (2004). The ability of a vaccine to elicit protective immunity can be assessed by considering the vaccine efficacy (the percent reduction in the incidence of influenza illness among vaccinated and unvaccinated persons in controlled trials) and vaccine effectiveness (the level of vaccine protection under ordinary field conditions). Thus, the effectiveness of a vaccine depends not only on its efficacy, but also on the conditions of its intended use and the characteristics of the target population (Comstock, 1994).

There are a number of multiple possible outcome measures that have been used to assess the efficacy and effectiveness of influenza vaccine in the previous studies such as the prevention of medically attended acute respiratory illness (MAART), prevention of lab-confirmed influenza infection and prevention of influenza-related to hospitalisations or deaths (CDC, 2008). Among these measures, lab-confirmed

influenza infection is considered "the gold standard" for many studies assessing vaccine efficacy, as it provides more specific outcome information than others (Nichol & Treanor, 2006; CDC, 2008).

A single dose of trivalent inactivated influenza vaccine injection has been found to elicit protective immune responses against influenza virus among healthy adults aged younger than 65 years of age. The trivalent inactivated influenza vaccine has been shown to be 70-90 per cent effective in preventing influenza infection among healthy adults in randomised controlled trials when the vaccine viruses are well matched to the circulating strains (Nichol, Lind, Margolis et al., 1995; Cambell & Rumley, 1997; Bridges, Thompson, Meltzer et al., 2000; Demicheli, Pietrantonj, Jefferson et al., 2007). In addition, vaccination has been shown to reduce absenteeism and the cost of influenza-like illness in healthy, working adults when there is well-match between vaccine and circulating viruses (Demicheli, Pietrantonj, Jefferson et al., 2007; Maciosek, Solberg, Coffield et al., 2006; Campbell & Rumley, 1997; Nichol, Lind, Margolis et al., 1995). A prospective study conducted in North Carolina workers showed that vaccinated employees were significantly less likely to report an influenza-like illness than unvaccinated employees (20 per cent vs. 49 per cent). This resulted in a substantial reduction in lost work days among vaccinated employees (43 and 93 lost work days in vaccinated and unvaccinated employees). The cost savings were estimated to be $22 per saved lost workday (Campbell & Rumley, 1997).

Similarly, a double-blind, placebo-controlled trial by Nichol, Lind, Margolis et al. (1995) found that vaccination against influenza in healthy adults in the workplace resulted in decreased absenteeism from work and physician visits by 43 per cent and 44 per cent, respectively. The potential cost-savings was also reported, and it was estimated to be $46.85 per person vaccinated (Nichol, Lind, Margolis et al., 1995). The ability of vaccine to reduce influenza-like illness and physician visits and work absenteeism was further demonstrated by Bridges, Thompson, Meltzer et al. (2000) who conducted a double-blind, randomised, placebo-controlled trial during two influenza seasons. Their results showed that significant lower rates of reported influenza-like illness, physician visits, and work absenteeism were reported among vaccine recipients. In addition, influenza vaccination of healthy working adults was shown to provide societal economic benefits in the year in which vaccine strains were

antigenically similar to the circulating viruses (Bridges, Thompson, Meltzer et al., 2000). In addition to conferring protection against influenza infection, the influenza vaccine was reported to decrease viral shedding by 38.8 per cent (Keitel, Cate, Couch 1997). This helps to reduce the risk of spreading the influenza virus to other people.

The vaccine's effectiveness appears substantially lower when vaccine viruses are not closely related antigenically to epidemic strains. A case-control study assessing the influenza vaccine effectiveness among people aged 50-64 years which was conducted in a season with suboptimal antigenic match, found that vaccine effectiveness was 60 per cent and 48 per cent (compared to 70-90 per cent immunity conferred by more closely matched vaccines) among individuals without and with high-risk medical chronic conditions, respectively (Herrera, Iwane, Cortese et al., 2007). A double-blind, randomised, placebo-controlled trial by Bridges, Thompson, Meltzer et al. (2000) also illustrated that vaccine efficacy was 50 per cent when there was a poor match between vaccine and the predominant circulating viruses.

A recent randomised, double-blind, placebo-controlled trial conducted in Michigan during the 2004-2005 influenza season, when vaccine viruses were antigenically dissimilar to the majority of circulating strains, indicated that the absolute efficacy of the inactivated influenza vaccine ranged from 67 per cent (95% CI, 16-87) to 77 per cent (95% CI, 37 to 92) in preventing laboratory-confirmed influenza in healthy adults, depending on the laboratory method for measurement of influenza antigen and antibody; the inactivated influenza vaccine had 77 per cent efficacy against laboratory-confirmed influenza for influenza cases diagnosed using isolating the virus in cell culture, 75 per cent efficacy for influenza cases diagnosed using either by isolating virus or real-time PCR and 67 per cent efficacy for influenza cases diagnosed using either by isolating virus or observing a rise in the serum antibody titre (Ohmit, Victor, Rotthoff et al, 2006).

Previous studies have reported conflicting results regarding the effectiveness of influenza vaccine in the high-risk populations. Several studies found that influenza vaccine offered less protection against influenza in older people and those with chronic medical conditions than healthy adults (e. g. pulmonary disease, renal disease, diabetes mellitus, heart disease, and cancer) (Keren, Segev, Morag et al., 1988;

Govaert, Thijs, Masurel et al., 1994; Beyer, Palache, Baljet et al, 1989; Brydak, Machala, Centkowski et al., 2006), while others have documented the effectiveness of inactivated influenza vaccine in these high-risk individuals, particularly its effectiveness in reducing hospitalisations and deaths among elderly people and those under age of 65 years with chronic medical conditions (Gross, Hermogenes, Sacks et al., 1995; Dorrell, Hassan, Marshall et al., 1997; Nichol, Wuorenma, & Sternberg, 1998; Plusa, Brydak, Jahnz-Rozyk, et al., 2004; Hak, Buskens, van Essen et al., 2005; Looijmans-Van den akker, Nichol, Verheij, et al., 2006; Poole, Chacko, Wood-Baker et al., 2006).

In Argentina, a randomised control study conducted by Gurfinkel, Leon de la Fuente, and Mendiz (2004) showed that in acute coronary patients, vaccination against influenza caused significantly lower incidence of cardiovascular deaths at one year in the vaccine recipients compared with unvaccinated groups (6 per cent vs. 17 per cent, hazard ratio 0.34; 95% CI, 0.17 to 0.71). Similarly, a more recent randomised, double-blind, placebo-controlled study conducted in Poland, during the 2004-2005 season in 658 coronary artery disease patients by Ciszewski, Bilinska, Brydak et al. (2008) found that vaccinated persons had a lower rate of coronary ischaemic events (major adverse cardiac events: MACE or hospitalisation for myocardial ischaemia) during the 12-month follow up compared to the placebo group (6.02 per cent vs. 9.97 per cent, hazard ratio 0.54; 95% CI, 0.29-0.99, $p = 0.047$).

However, at the moment, influenza vaccination has already been recommended for populations at high risk of influenza-related complications regardless of their age, it is unethical to conduct placebo-controlled trials. Accordingly, cohort or case control studies are used for the most recent research related to the assessment of efficacy, effectiveness of the influenza vaccine in the high-risk groups, including the elderly and persons with chronic diseases (CDC, 2008). Numerous observational studies of influenza vaccine have demonstrated substantial benefits of influenza vaccination among high-risk persons (Nichol, Wuorenma, & Sternberg, 1998; Hak, Buskens, van Essen et al., 2005; Looijmans-Van den akker, Nichol, Verheij, et al., 2006; Poole, Chacko, Wood-Baker et al., 2006). A case-control study of the clinical effectiveness of influenza vaccine conducted in the Netherlands during the 1999-2000 influenza season by Hak, Buskens, van Essen et al. (2005) found that influenza vaccination was

associated with a 87 per cent reduction in hospitalisation for acute respiratory disease or cardiopulmonary disease and a 78 per cent reduction in deaths attributable to any cause among adults aged 18-64 years with chronic medical conditions.

Similar results were observed by Looijmans-Van den akker, Nichol, Verheij, et al. (2006) who investigated the clinical effectiveness of influenza vaccination in adult and elderly diabetic patients in the Netherlands. A considerable reduction in the incidence of the combined outcome of a hospitalisation or death (reduction of 56 per cent), hospitalisation (reduction of 54 per cent), and death from any cause (reduction of 58 per cent) in patients with diabetes was reported. A case-control conducted in Leicestershire, England also demonstrated that influenza vaccination prevented 79 per cent (95% CI, 19-95%) of hospitalisations for people with diabetes (Colquhoun, Nichol, Botha et al., 1997). In the Unites States, Herrera, Iwane, Cortese, et al. (2007) indicated that the vaccine effectiveness was 36 per cent (95% CI, 0-63%) in preventing influenza-related hospitalisation among older adults aged 50-64 years with high-risk conditions, although the circulating viruses were drifted from the vaccine strains during the 2003-2004 influenza season.

In addition, two case-control studies by Hak, Buskens, Nichol et al., (2006) and Looijmans-Van den akker, Nichol, Verheij, et al. (2006) have shown that during the two influenza seasons (1998-1999 and 1999-2000), first-time influenza vaccination in adult persons with high-risk medical conditions was associated with a reduction in hospitalisation and mortality from any cause, and these benefits increased with repeat vaccination in subsequent the year. This was demonstrated by Looijmans-Van den akker, Nichol, Verheij, et al. (2006) in a case-control study assessing clinical effectiveness of first and repeat influenza vaccination in patients with diabetes. A 47 per cent reduction in hospitalisation and deaths was reported in adult diabetic patients vaccinated for the first time, and the reduction was 58 per cent in those who received vaccination in the subsequent year.

However, benefits associated with influenza vaccination among vaccinated recipients in these observational studies should be interpreted with caution because there are potentially differences (e.g. health status) between vaccinated and unvaccinated groups, thereby affecting the estimate of vaccine effectiveness (Jackson, Jackson,

Nelson et al., 2006; Simonsen, Taylor, Viboud et al., 2007). More recently, a systematic review of eleven randomised controlled trials by Poole et al. (2006) indicated that influenza vaccination has been shown to significantly reduce the number of exacerbations in patients with COPD. In contrast, a systematic review of influenza vaccination among people with asthma by Cates, Jefferson, & Rowe et al. (2008) was unable to demonstrate the beneficial effects of influenza vaccination on asthma exacerbations in these high-risk individuals.

It has been suggested that the ability of older people to produce protective antibody levels in response to influenza vaccine may be reduced due to the decreased number of B-lymphocytes (Ershler, 1988; Brydak & Machala, 2000; Hannoun, Megas, & Piercy, 2004). Although the influenza vaccine is less effective in preventing illness from influenza in elderly people, it is nevertheless effective in reducing hospitalisations and deaths attributable to influenza in these high-risk persons (Fleming, Watson, Nicholas et al., 1995; Ershler, 1988; Nichol, Wuorenma, & Sternberg, 1998; Nichol, Nordin, Nelson, 2007; Nordin, Machala, Poblete et al., 2001; Hak, Nordin, Wei et al., 2002; Looijmans-Van den akker, Nichol, Verheij, et al., 2006; Savulescu, Valenciano, de Mateo et al., 2010).

A randomised, placebo-controlled study conducted in the Netherlands during the 1991-1992 influenza season in 1,838 healthy adults aged 60 years or older, reported that influenza vaccine achieved an 58 per cent (95% CI = 26 % - 77%) efficacy in reduction of laboratory-confirmed influenza (Govaert, Thijs, Masurel et al., 1994). Several observational studies that used either cohort or case-control study were conducted to evaluate the clinical effectiveness of influenza vaccine in elderly people. Non-specific outcomes without laboratory confirmation of influenza virus infection, including influenza-like illness, pneumonia, influenza-related hospitalisation and death were assessed. A meta-analysis of twenty observational studies evaluating the efficacy of influenza vaccine in the elderly by Gross, Hermogenes, Sacks et al. (1995) found that influenza vaccination has been shown to prevent 35-45 per cent for pneumonia hospitalisations, 31 per cent to 65 per cent for hospital deaths from pneumonia and influenza, 43 per cent to 50 per cent for hospital deaths from all respiratory conditions, and 27 per cent to 30 per cent for deaths from all causes (Gross, Hermogenes, Sacks et al., 1995).

Likewise, a large cohort study by Nichol (2003) who assessed the effectiveness of influenza vaccine in community-dwelling elderly persons during the two influenza seasons (1998-1999 and 1999-2000) demonstrated a reduction in the risk of hospitalisation among these individuals. Vaccination against influenza reduced the risk of hospitalisation for cardiac disease by 19 per cent during both seasons. The risk reduction in hospitalisation for pneumonia or influenza was 32 per cent in the first season (1998-1999) and 29 per cent in the subsequent influenza season (1999-2000). In addition, a 48-50 per cent reduction in the risk of all-cause mortality during the two influenza seasons was also observed in this study.

Another study of Nichol, Baken, and Nelson (1999) also addressed the health benefits associated with influenza vaccination of elderly people with chronic lung disease over three influenza seasons in the urban area of Minneapolis-St. Paul, USA. Influenza vaccination resulted in a 52 per cent reduction in hospitalisation for pneumonia and influenza and a 70 per cent reduction in death from any cause. Other results included fewer outpatient visits for pneumonia and for all respiratory conditions during the 1993-1994, 1994-1995, and 1995-1996 influenza seasons.

Similar results were obtained in the other studies conducted in the United States; vaccination of elderly individuals resulted in the reduction of 19 per cent to 45 per cent in hospitalisation (Foster, Talsma, Furumoto-Dawson et al., 1992; Mullooly, Bennett, Hornbrook et al., 1994; Ohmit & Monto, 1995; Nichol, Wuorenma, & Sternberg, 1998; Nordin, Machala, Poblete et al., 2001), and was also associated with a 48 per cent to 61 per cent reduction in all causes of death (Nichol, Wuorenma, & Sternberg, 1998; Nordin, Machala, Poblete et al., 2001; Hak, Nordin, Wei et al., 2002). In observational studies from the UK, influenza vaccination was associated with a 63 per cent reduction in hospital admissions in 10 Leicestershire hospitals during the 1989-1990 influenza season (Ahmed, Nicholson, Nguyen-Van Tam et al., 1997), and a 75 per cent reduction in death in elderly people during the influenza epidemic of 1989-1990 (Fleming, Watson, Nicholas et al., 1995).

More recently, findings in a large cohort of 713,872 community-dwelling elderly people across 10 influenza seasons by Nichol, Nordin, Nelson et al. (2007) indicated that influenza vaccination had an overall protective effect of 27 per cent (adjusted

ratio, 0.73; 95% CI 0.68-0.77) against hospitalisation for pneumonia or influenza and 48 per cent (adjusted ratio, 0.52; 95% CI 0.50-0.55) against death in elderly persons. Even in two seasons where there was a sub-optimal match between the vaccine antigen and the circulating viruses, influenza vaccine was still associated with a 37 per cent reduction in mortality (adjusted odds ratio, 0.63; 95% CI, 0.57-0.69).

Among elderly persons in nursing homes, the influenza vaccine has been reported to be 23-43 per cent effective in preventing influenza-like illness and clinically diagnosed pneumonia (Patriarca, Weber, Parker et al., 1986; Monto, Hornbuckle, & Ohmit, 2001; Jefferson, Rivetti, Rivetti et al., 2005). A recent systematic review of the efficacy and effectiveness of influenza vaccines in elderly persons by Jefferson, Rivetti, Rivetti et al. (2005) has found the influenza vaccination was associated with a 23 per cent (95% CI, 6-36%) reduction in influenza illness cases, a 46 per cent (95% CI, 30-58%) reduction in pneumonia, and a 45 per cent (95% CI, 16-64%) reduction in hospitalisation in the nursing home populations. Additionally, influenza vaccine was 42 per cent (95% CI, 17 - 59 %) effective in reducing mortality from influenza or pneumonia and 60 per cent (95% CI, 23-79%) in reducing mortality from all causes.

3.4.1.3 Safety of trivalent inactivated influenza vaccines

Trivalent inactivated influenza vaccine has been found to be safe and well- tolerated with minor side-effects. The side-effects can include local reactions (e.g. soreness at the injection, redness swelling) and systemic reactions (muscle ache, headache, fever, and nausea). These side effects are usually mild and last for 1-2 days after vaccination and are more common in women than in men. The incidence of local side effects within 48 hours, especially arm soreness has been reported by 17.5 per cent to 70 per cent in adults (Al-Mazrou, Scheifele, Soong et al., 1991; Aoki, Yassi, Cheang et al., 1993; Govaert, Dinant, Aretz et al., 1993; Monto, Ohmit, Petrie et al., 2009). Two randomised, placebo-controlled trials showed systemic side-effects in 11 per cent to 14.2 per cent of vaccine recipients (Margolis, Nichol, Poland et al., 1990; Govaert, Dinant, Aretz et al., 1993). Generalised body aches, muscle soreness, fever, and headache have been commonly reported, and these reactions typically begin 6-12 hours after vaccination (Al-Mazrou, Scheifele, Soong et al., 1991; Govaert, Dinant, Aretz et al., 1993; Musana, Yale, Mazza et al., 2004).

Additionally, two randomised, placebo-controlled trials investigating adverse reactions to influenza vaccine in older people indicated that there was no significant difference in the rate of systemic reactions between vaccinated and placebo groups (Margolis, Nichol, Poland et al., 1990; Govaert, Dinant, Aretz et al., 1993). However, previous studies have shown that the systemic side-effects to influenza vaccine are more likely to occur among children and young adults, who have had no prior exposure to influenza vaccine antigens (Parkman, Galasso, Top et al., 1976; Scheifele, Bjornson, & Johnston, 1990). Systemic reactions occurred in 32 per cent of individuals aged 18-34 years compared with 7 per cent of those older than 35 years old (Wise, Dolin, Mazur et al., 1977). It has also been reported that split-viron influenza vaccines have fewer side-effects than the whole-virion influenza vaccines (Wise, Dolin, Mazur et al., 1977; Scheifele, Bjornson, & Johnston, 1990). This was demonstrated in the study by Al-Mazrou, Scheifele, Soong et al. (1991) who found that generalised aching was significantly less prevalent in the split-virion vaccine recipients than in the whole-virion vaccines group (13 per cent vs. 26 per cent). Fewer local adverse reactions were also observed in the split-virion vaccine recipients.

Serious adverse reactions to inactivated influenza vaccine have been rare. However, immediate hypersensitivity reactions (e.g. generalised urticaria, wheezing, swelling of the mouth and throat) have been reported among individuals with allergies to eggs (Davies & Pepys, 1976). Thus, inactivated influenza vaccines which are produced in fertilized chicken eggs are contraindicated for those who have severe anaphylactic reactions to egg or egg protein (Davies & Pepys, 1976; Treanor, 2005; CDC, 2009b).

In addition, vaccine-associated Guillan-Barré syndrome (GBS) has also been reported, particularly during the 1976-1977 season. In 1976, the national influenza immunisation programme against swine influenza has been launched in the United States. This programme was designed to provide the A/Swine/New Jersey/76 influenza vaccine for 45 million persons, including adults and children at high risk of serious complications from influenza. In the first 4 to 6 weeks following immunisation, the significantly increased incidence of GBS was observed among recipients of A/New Jersey influenza vaccine, which the estimated risk of vaccine-associated GBS was 1 in 100,000 vaccinations. Subsequent studies have been carried out to evaluate the relationship between GBS and influenza vaccines other than the

A/Swine/New Jersey/76 influenza vaccine, but no causal relationship has been found (Schonberger, Bregman, Sullivan-Bolyai et al., 1979; Treanor, 2005).

However, the study of GBS and influenza vaccines (the 1992-1993 and 1993-1994 seasons) by Lasky, Terracciano, Magder et al. (1998) found that the influenza vaccines were associated with 1-2 cases of GBS per million persons vaccinated (adjusted relative risk = 1.7; 95% CI, 1-2.8) during the 6 weeks after vaccination. The study investigating trends of GBS after receiving the influenza vaccine in adults from 1990 to 2003 conducted by Haber, DeStefano, Angulo et al. (2004), found that there was significantly decrease in the reporting rates of GBS from 0.17 per 100,000 vaccinees in 1993-1994 to 0.04 in 2002-2003. Recently, the study by Vellozzi, Burwen, Dobardzic et al. (2009) who assessed adverse events after receiving trivalent inactivated influenza vaccine in adults aged 18 years or older that reported to the US Vaccine Adverse Event Reporting System (VAERS), indicated that pain, fever, myalgia and headache were the most common local side-effects after vaccination among adults during 1990-2005. Guillan-Barré syndrome was the most common reported serious event, and the reporting rate of GBS was 0.70 per million vaccinations. The benefits of influenza vaccination clearly outweigh the potential risk of acquiring GBS after vaccination (CDC, 2009b).

3.4.2 Live, attenuated influenza vaccine (LAIV)

LAIV consists of live, attenuated influenza viruses. The vaccine is trivalent, with the three vaccine component strains used in trivalent inactivated vaccine (cold-adapted H1N1, H3N2, and B influenza viruses). The vaccine viruses are generated by reassortment between the cold-adapted master donor strains (A/Ann Arbor/6/60 (CA-A) and B/Ann Arbor/1/66 (CA-B) and the circulating wild-type viruses. The genetic reassortment methods involve a combination of six genes from the cold-adapted master donor strains, contributing six internal viral genes and two genes from the contemporary wild strain of influenza viruses, encoding the viral surface antigens (hemagglutinin and neuraminidase). Thus, the vaccine viruses in LAIV contain six genes (PB2, PB1, PA, NP, M, and NS) from a master donor strain that contributes to the attenuation and cold-adaptation of live influenza virus, and the HA and NA genes from the circulating virus strains recommended by the WHO which confer

antigenicity. LAIV is attenuated by cold adaptation, in which the vaccine viruses can replicate efficiently and survive at lower temperatures (25 °C) in the mucous membrane of the upper respiratory tract; thus LAIV does not produce systemic symptoms of influenza in vaccine recipients (Boyce, Gruber, Coleman-Dockery et al., 2000; Cha, Kao, Zhao et al., 2000; Treanor, Hayden, Vrooman et al., 2000; Nichol, 2001; Beyer, Palache, de Jong et al., 2002; Belshe, 2004; Belshe, Nichol, Black et al. 2004; Vesikari, Karvonen, Korhonen et al., 2006; CDC, 2009b).

The LAIV is thimerosal-free vaccine. Each 0.2 ml dose of the 2009-2010 vaccine includes three live, attenuated influenza virus strains: A/Brisbane/59/2007 (H1N1), A/Brisbane/ 10/2007 (H3N2), and B/Brisbane 60/2008 and is supplied in a prefilled, single-use sprayer (CDC, 2009). The vaccine is administered intranasally using 0.1 mL into each nostril while the recipient is in the upright position. LAIV has been used since 2003 and currently approved for immunisation of all healthy, non-pregnant persons between the ages of 2 and 49 years. The vaccine should be stored in a refrigerator between 2-8 °C (Block, Yogev, Hayden et al., 2008; CDC, 2009b; Wang, Tobler, Roayaei et al., 2009). Two 0.2 mL doses of the vaccine are recommended for children aged less than nine years in order to produce antibody levels that are sufficient for protection against influenza. Those who do not receive two doses in their first year of vaccination should have two doses in the following year (CDC, 2009b).

3.4.2.1 Immune response

As the LAIV is made from live, attenuated viruses and is administered via the intranasal route which is the natural route of infection, it is expected that the vaccine viruses can induce immune response in human equivalent to those induced by the natural influenza infection (Nichol, 2001; Belshe, 2004). A number of studies have shown LAIV to induce a broad range of immune response, including a mucosal IgA response (influenza-specific IgA nasal antibodies), systemic (serum antibodies) and cell mediated immune responses (T cell responses) (Clements, O' Donnell, Levine et al., 1983; Clements, Betts, Tierney, 1986; Gorse, Belshe, Munn 1986; Gorse, Belshe, & Munn, 1988; Murphy & Clements., 1989; Beyer, Palache, de Jong, et al., 2002). Data from a study by Clements and Murphy (1986) demonstrated that LAIV

stimulated both local and systemic immunity, although it induced lower titres of serum antibodies (IgA, IgG, and IgM HA antibody) compared with trivalent inactivated influenza A vaccine (TIV). In contrast, LAIV induced a nasal-wash IgA response more frequently than TIV (83 per cent vs. 38 per cent), and this antibody response reached a peak two weeks after vaccination.

Likewise, a randomised controlled trial investigating efficacy of LAIV and TIV against influenza by Edwards, Dupont, Westrich et al (1994) showed that nasal IgA antibody was significantly higher in response to LAIV than to TIV. Additionally, the study by Clements, Betts, Tierney et al. (1986) found that there was a difference between LAIV and TIV in the induction of different levels of antibody in serum or nasal wash after experimental challenge with wild-type influenza virus. HAI antibody in serum was associated with immune protection against influenza in TIV recipients, whereas local HA IgA antibody was responsible for resistance to influenza in LAIV recipients after experimental challenge with wild-type influenza virus.

Recently, a meta-analysis of 18 randomised clinical trials comparing LAIV and TIV with respect to systemic vaccine reactions, local and systemic antibody response, and vaccine efficacy confirmed that LAIV has demonstrated to be more effective than TIV in inducing a nasal wash IgA response (Beyer, Palache, de Jong et al., 2002). Accordingly, it has been suggested that local antibodies such as IgA HA antibody play a more important role in the immune response after immunisation with LAIV (Clements, O' Donnell, Levine et al., 1983; Clements, Betts, Tierney et al., 1986; Clements & Murphy, 1986; Gorse, Belshe, & Munn et al., 1988; Beyer, Palache, de Jong et al., 2002).

Additionally, a 2-year randomised, double-blind placebo-controlled trial assessing the safety and efficacy of LAIV in healthy children 15-71 months old by Belshe et al. (2000) revealed that serum HAI antibody and nasal wash IgA antibody were correlated with protection against H1N1 infection. Interestingly, the results of this study also showed that some vaccinated children (16 vaccinees) had neither serum HAI antibody nor nasal wash IgA antibody following experimental challenge with influenza A H1N1. Despite this, few influenza infections have been reported among these children. Thus, other protective mechanisms may be involved in immune

activation, including T cell responses and interferon (Tomoda, Morita, Kurashige et al., 1995; Murphy & Clements, 1989; Belshe, Gruber, Mendelman et al., 2000; Boyce, Gruber, Coleman-Dockery et al., 2000).

In another study, LIAV has been shown to stimulate influenza A virus-specific cytotoxic T-cell response in older, chronically ill adults. A higher level of influenza virus-specific cytotoxic T lymphocyte activity which has resulted in a cross-reactive immune response against different subtypes of influenza A viruses, was observed in older adults with chronic medical conditions who received LIAV (Gorse & Belshe, 1990). Cytotoxic T cells could have contributed to cross-protective immunity against influenza A subtypes because they can recognise internal virus antigens (internal virion proteins) expressed on the surfaces of infected cell, and these internal virus antigens are shared among influenza A viruses (Nichol, Mendelman, Mallon et al., 1999; Belshe, 2004). Although the mechanisms of LAIV protection have not been clearly defined, the vaccine appears to induce a broad immune response, including systemic, mucosal, and cell mediated immune responses (Clements, Betts, Tierney et al., 1986; Tomoda, Morita, Kurashige et al., 1995; Nichol, 2001; Belshe, 2004).

3.4.2.2 Virus shedding and transmission after immunisation with LAIV

There has been concern about the potential risk of transmission of the vaccine viruses after immunisation with LAIV from vaccine recipients to unvaccinated individuals; because LAIV virus strains infect and replicate in nasopharyngeal epithelial cells and are shed in the respiratory secretions (Talbot, Crocker, Peters et al., 2005; Vesikari, Karvonen, Korhonen et al., 2006; Block, Yogev, Hayden et al., 2008). A study conducted by Block, Yogev, Hayden et al. (2008) assessed virus shedding and immune response to LAIV in persons aged 5-49 years. The results revealed that the incidence of vaccine virus shedding decreased with increasing age; shedding incidence ranged from 44 per cent (aged 5-8 years) to 17 per cent (18-49 years). The duration of viral shedding was short. The vaccine virus was not recovered from any vaccinated person after 11 day post-vaccination. Serum strain-specific hemagglutinin inhibition titres had fallen below the limit of detection (<1 $\log_{10}$TCID $_{50}$/mL) after day 10 in children aged less than 9 years and after day 6 in individuals aged 9-49 years.

Additionally, Talbot, Crocker, Peters et al. (2005) found in their prospective surveillance study that viral shedding after LAIV vaccination in 20 adults (aged 18-49 years) had significantly decreased within one week after immunisation, and it was more likely to occur in younger age groups. The viral shedding among LAIV vaccinated persons was further demonstrated by Vesikari, Karvonen, Korhonen et al. (2006) who conducted a randomised controlled study assessing the transmissibility and genotypic stability of LAIV virus in 51 day care centres in Finland. This study showed that 80 per cent (78 of 98) of LAIV vaccinated children (aged 9-36 months) shed one or more vaccine virus strains after vaccination with LAIV. Although the shedding incidence was high, only one case of transmission has been reported among the placebo recipients (99 subjects), and the transmitted virus maintained its attenuated characteristics and did not cause clinical disease to a placebo recipient who had been infected inadvertently with vaccine virus. The probability of acquiring vaccine virus after close contact with a LAIV vaccinated child was estimated to be 0.58 per cent (95% CI, 0-1.7%). However, LAIV recipients have been advised to avoid contact with severely immunosuppressed individuals for 7 days after immunisation (CDC, 2009b).

3.4.2.3 The efficacy and effectiveness of live, attenuated influenza vaccine (LAIV)

LAIV has been shown to be efficacious in preventing laboratory-confirmed influenza and influenza illness in healthy adults. A double-blind, randomised controlled trial comparing efficacy of cold-adapted and inactivated influenza vaccines over the five influenza seasons (1985-1986 to 1989-1990) by Edwards, Dupont, Westrich et al. (1994) demonstrated that the efficacy of cold-adapted influenza vaccine was 85 per cent (95% CI, 70 - 92%) for prevention of culture-proven H1N1 influenza infection and 58 per cent (95% CI, 29 - 75%) for prevention of culture-proven H3N2 influenza infection.

The efficacy of LAIV against influenza was further illustrated in a randomised, double –blind, placebo-controlled trial conducted in the United States by Nichol, Mendelman, Mallon et al (1999) who evaluated the safety and effectiveness of LAIV in reducing influenza-like illness without laboratory confirmation, absenteeism, and medication use among working adults aged 18-64 years during the 1997-1998 season.

Despite a mismatch between the vaccine strains and circulating virus (H3N2), results showed that immunisation with LAIV has been found to significantly decrease the numbers of severe febrile illness by 18.8 per cent (95% CI, 7.4% - 28.8%) and febrile upper respiratory tract illness by 23.6 per cent (95% CI, 12.7%-33.2%). In addition, immunisation with LAIV also resulted in a reduction in the days of work lost (reduction by 28.4 per cent, 95% CI, 16.3% - 38.8%), the days of physician visits (reduction by 40.9 per cent, 95% CI, 30.1%-50.0%), and the days of antibiotic use for febrile upper respiratory tract illness (reduction by 45.2 per cent, 95% CI, 35.2%-53.6%). Treanor, Hayden, Vrooman et al. (2000) also found that there was no statistically significant difference in efficacy between LAIV and TIV; the efficacy of LAIV and TIV in preventing laboratory documented influenza illness was 85 per cent and 71 per cent, respectively.

Another study conducted in the US military basic training centres assessing vaccine effectiveness against laboratory-confirmed by Strickler, Hawksworth, Myers et al. (2007) also indicated that LAIV and TIV appeared to have equal efficacy; similar levels of protection against laboratory-confirmed among basic trainees were observed for LAIV relative to TIV. Additionally, LAIV and TIV have found to be equally or more effective in vaccine-naïve persons, including children and young adults who have no pre-existing antibodies for the influenza viruses or those who were seronegative at baseline. This may be due to the pre-existing immunity in some adults which may have resulted from their past infection with antigenically related strains of influenza A virus or vaccination; thus, LAIV efficacy has been shown to be similar to or better than TIV in vaccine-naïve persons (Belshe, Gruber, Mendelman et al., 2000; Nichol, 2001; Ohmit, Victor, Rotthoff et al., 2006; Wang, Tobler, Roayaei et al, 2009).

By contrast, two recent randomised, double-blind, placebo-controlled trials conducted in Michigan, comparing the efficacy of TIV and LAIV in healthy adults during the 2004-2005 (Ohmit, Victor, Rotthoff et al., 2006) and 2007-2008 influenza seasons (Monto, Ohmit, Petrie et al., 2009) reported that LAIV was found to be less efficacious than TIV for prevention of laboratory confirmed symptomatic influenza A in healthy adults. A randomised controlled trial by Ohmit, Victor, Rotthoff et al. (2006) showed that LAIV and TIV had an efficacy of 48 per cent and 77 per cent,

respectively, for preventing culture positive influenza among healthy adults. Monto, Ohmit, Petrie et al. (2009) also found an efficacy of 29 per cent (95% CI, -14 to 55 %) for LAIV and of 72 per cent (95% CI, 49 to 84 %) for TIV.

Similarly, a large cohort study of the US military personnel carried out to assess the effectiveness of LAIV and TIV over the three influenza seasons (2004-2005 to 2006-2007), revealed that LAIV efficacy was lower compared to TIV in reducing the incidence rate of pneumonia and influenza among the US military service members. A recent meta-analysis review of the effectiveness of influenza vaccines by Demicheli, Pietrantonj, Jefferson et al. (2007) has suggested that LAIV was less effective in preventing influenza than TIV among healthy adults.

3.4.2.4 Safety of live, attenuated influenza vaccine

LAIV has been demonstrated to be safe, and well-tolerated in adults. In a randomised controlled trial study of healthy, working adults, runny nose (44.3 per cent vs. 26.6 per cent) or sore throat (26.6 per cent vs. 16.3 per cent) during 7 days after vaccination has been reported more frequently in LAIV recipients compared with a placebo group. These adverse reactions were short lasting and did not result in additional medical treatment such as antibiotics, analgesics/antipyretics, or decongestants/ antihistamines. During 28 days after vaccination, there were no differences in the frequency of serious adverse events between vaccine and placebo recipients (0.18 per cent vs. 0.27 per cent), and none of the nine serious adverse events have been associated with this vaccine (Nichol, Mendelman, Mallon et al., 1999).

A randomised, double-blind, placebo-controlled trial of influenza vaccines assessing the efficacy of LAIV and TIV by Ohmit, Victor, Rotthoff et al. (2006) also found that runny nose/nasal congestion, cough, headache, and muscle aches were significantly more common in LAIV recipients compared with the placebo group. Four serious side-effects that occurred within 30 days after vaccination have been reported. Among these serious adverse events, one (acute pericarditis with moderate effusion) was judged to be probably related to the receipt of LAIV vaccination. The study of serum samples collected immediately before and after administration of the vaccine (four

weeks later) was performed; however, no evidence has been found to indicate that vaccine viruses caused acute pericarditis.

In a subset of healthy adults 18-49 years of age from a randomised controlled study evaluating the safety, efficacy and effectiveness of LAIV, side-effects following vaccination have been reported significantly more often in LAIV recipients than placebo group, including runny nose (44.5 per cent vs. 27.1 per cent), sore throat (27.8 per cent vs. 17.1 per cent), tiredness/weakness, (25.7 per cent vs. 21.6 per cent), cough (13.9 per cent vs.10.8 per cent), and chills (8.6 per cent vs. 6 per cent) (Belshe, Nichol, Black et al., 2004).

A further and more recent randomised, double-blind, placebo-controlled trial of influenza vaccines involving 1952 healthy adults during the 2007-2008 influenza season by Monto, Ohmit, Petrie, et al. (2009) showed that runny nose or congestion was significantly more common among LAIV recipients than placebo recipients (52.3 per cent vs. 37.7 per cent). LAIV has also been administered to elderly people with chronic medical conditions, although it has not yet been approved for use in persons aged 50 years or older. A randomised controlled study evaluating the safety of LAIV in simultaneous combination with TIV in the elderly with chronic diseases by Jackson, Holmes, Mendelman et al. (1999) indicated that TIV plus LAIV recipients were more likely than placebo plus TIV recipients to report sore throat during the seven days after vaccination (15 per cent vs. 2 per cent). Other reported symptoms, including fever, cough, runny nose, headache, muscle aches, tiredness, and chills did not differ between groups. Four serious adverse events were reported during the 28 days after vaccination. However, none of these adverse effects was considered related to the study vaccine.

In addition, a review of adverse events reported following LAIV administration to the US Vaccine Adverse Event Reporting System (VERS) during the two influenza seasons (2003-2004 to 2004-2005) indicated that a total of 460 adverse event had been reported to VERS after approximately 2.5 million doses of LAIV were distributed. Of these, forty reports were classified as serious: 15 respiratory events (e.g. influenza-like illness, pharyngitis, tracheitis, asthma, and pneumonia), seven allergic events (possible anaphylaxis, generalised urticaria, generalised itchy, rash on the back and chest), seven neurological events (e.g. Guillan-Barré syndrome, Bell

palsy, febrile seizures, encephalomyelitis), four constitutional symptoms (weakness/ tiredness, fever, headache, dizziness, and arthritis), three cardiovascular events (pericarditis, myocardial infarction), one abdominal symptom, one ocular symptom (retinal haemorrhage), and three other reports (serious chickenpox, rash/erythema, group A streptococcal infection) (Izurieta, Haber, Wise et al., 2005).

3.5 Recommendations for the use of seasonal influenza vaccine

The main objective for the use of influenza vaccine is to reduce the incidence of severe illness cases and death in the elderly and high-risk populations, which will, in turn, reduce the burden of care and pharmaceutical supplies. Recommendations for the use of influenza vaccine are different between countries. This difference is based on reliable data on the seasonal occurrence of influenza and its impact, as well as knowledge about the effectiveness of influenza control measures and the resources for the implementation of a seasonal influenza vaccination programme (WHO, 2000; van Essen, Palache, Forleo et al., 2003). However, the influenza vaccine is usually recommended in most countries for each of the following groups: (1) elderly residents of long-term care facilities or the disabled; (2) non-institutionalised elderly with one or more chronic disease requiring influenza vaccination; this includes elderly people with chronic cardiovascular, pulmonary, metabolic or renal disease, or who are immunocompromised; (3) individuals 60 or 65 years of age and older; (4) adults and children over 6 months of age who have chronic pulmonary, cardiovascular, metabolic or renal disease, or are immunocompromised; and (5) individuals who live with or care for people at high risk for severe complications from influenza such as health care personnel, household contacts and caregivers of high-risk persons. Nevertheless, for a country with limited resources to implement the influenza vaccine programme for all groups as listed above, it is recommended that the influenza vaccine should be given to residents of institutions for the elderly and disabled as a first priority. If more resources become available, the programme should be expanded to cover more high-risk individuals (WHO, 2000; van Essen, Palache, Forleo et al., 2003; Treanor, 2010).

In addition to the use of influenza vaccine in targeted the elderly and high-risk populations, universal mass vaccination of young children against the influenza has been implemented in some countries (e.g. Japan, Canada, and the United States) in order to disrupt the spread of influenza in the community (Treanor, 2010). In Japan, the influenza vaccination programme for schoolchildren was implemented between 1962 and 1987; most schoolchildren were vaccinated against influenza. Of particular note were findings that vaccination of Japanese children resulted in a significant reduction in influenza-related deaths among *older* persons during that period. Vaccination of school-aged children prevented about 37,000 to 49,000 deaths per year – or about one death for every 420 children vaccinated (Reichert, Sugaya, Fedson et al., 2001). By contrast, an increase in the influenza-related mortality rates among older adults has been reported since 1994 as the universal influenza vaccination program for school-aged children was discontinued.

Additionally, a single-blind, randomised controlled trial conducted by Hurwitz, Haber, Chang et al. (2000) showed that the vaccination of day care children has been shown to significantly reduce the incidence of febrile respiratory illness in household contacts, especially among school-aged household contacts (aged 5-17 years). As a consequence of reduction in febrile respiratory illness, more than 70 per cent reduction in physician visits, earaches, antibiotic prescribed, school-days lost and parental work-days lost were also reported in this study.

In the present, a major change has been made to guidance on the use of influenza vaccine for the 2010-2011 influenza season in the United States. The existing guidelines for seasonal influenza vaccination which focus on only certain groups (children between the age of 6 months and eighteen years; adults aged fifty years and older; those with chronic medical conditions; health care personnel, and household contacts and caregivers of high-risk persons) has been changed to include all persons aged 6 months or older who do not have contraindications to vaccination. The reasons for the expansion of seasonal influenza vaccination in the United States is the evidence that seasonal influenza vaccination is safe, and can also potentially provide benefits for all age groups. In addition, severe cases of influenza were observed in young adults (19-49 years) during the 2009 pandemic influenza A (H1N1) (Gianella,

Walter, Revollo et al., 2009; Jain, Kamimoto, Bramley, 2010; Kumar, Zarychannski, Pinto et al., 2009; CDC, 2010b), and the concerns that 2009 pandemic influenza A (H1N1) viruses will continue to circulate in the coming influenza season 2010-11; therefore, these young adults can remain at considerable risk of infection with this virus. The recommendations for influenza vaccination for the 2010-2011 influenza season are summarised in table 3.5 (CDC, 2010b).

Table 3.5 Groups recommended for influenza vaccination, 2010

- All individuals aged 6 months or older should be vaccinated annually
- If vaccine supply is limited, the following target groups are proposed as priority groups for influenza vaccination

Persons at high risk for influenza-related complications

- Children aged 6 months to 4 years (59 months);
- Children aged 6 months to 18 years receiving long-term aspirin therapy and therefore would be at increased risk for Reye's syndrome after influenza virus infection;
- Adults aged 50 years or older;
- Adults and children who are residents of nursing home and other chronic care facilities;
- Adults and children with chronic pulmonary (including asthma), cardiovascular (except hypertension), renal, hepatic, neurologic, hematologic, or metabolic disorders (including diabetes mellitus);
- Persons who have immunosuppression (including immunosuppression from medication or human immunodeficiency virus: HIV;
- Women who are or will be pregnant during the influenza season;
- Persons who are morbidly obese (body-mass index $\geq$ 40;

Persons who live with or care for people at high risk for influenza-related complications

- Health care personnel
- Household contacts and caregivers of children aged five years or less than and adults aged fifty years or older, with particular emphasis on vaccination of contacts of children aged lass than six months;
- Household contacts and caregivers of persons with medical conditions that put them at higher risk for severe complications from influenza

Source: Adapted from CDC, 2010b.

3.6 Conclusion

The literature related to the influenza vaccine, its effectiveness and side-effects was reviewed. Currently, there are two types of vaccine: trivalent inactivated influenza vaccine (TIV) and live, attenuated influenza vaccine (LAIV). As two surface glycoproteins (HA and NA) of the influenza virus continually change by mutation, the components of the vaccine need to be changed every year in order to match the circulating virus strains. The protective efficacy of influenza vaccine depends on several factors such as the characteristics of the target population, the degree of similarity between vaccine viruses and those in circulation, and how the vaccine is administered (Demicheli, Jefferson, Rivetti et al., 2000; Hannoun, Megas, & Piercy, 2004). Vaccine effectiveness is estimated to be between 70 and 90 per cent in young, healthy adults. Although the vaccine offers less protection against influenza illness for high risk populations such as the elderly and persons with chronic medical condition (approximately 58 per cent: CDC, 2009), it is effective in reducing hospitalisations for acute respiratory disease or cardiopulmonary disease and deaths by 87 and 78 per cent, respectively (Hak, Buskens, van Essen et al., 2005).

The inactivated influenza vaccine has been shown to be very safe and well-tolerated in older people and those with chronic disease. There have been rare reports of severe adverse reactions to the influenza vaccination. Common side-effects from the vaccine include soreness, redness, and/or swelling at the injection site, muscles ache, headache, and fever. These side effects occur soon after vaccination and are usually temporary. Influenza vaccination recommendations vary between countries. However, in most countries, annual influenza vaccination is recommended for high-risk populations (e.g. the elderly and persons with chronic medical condition) and those who live with or care for persons at high risk (e.g. health care workers, household contacts and caregivers of children less than six months of age). Despite strong recommendations and clear evidence for influenza vaccination efficacy in preventing influenza and its complications in high-risk older people, influenza vaccination rates remain relatively low in many countries. The following chapter will focus on lay beliefs about influenza, the influenza vaccine and the factors that affect the decision to be vaccinated against influenza among individuals aged 65 years or older and those aged less than 65 with chronic diseases.

Chapter 4: Understanding lay beliefs about influenza, the influenza vaccine and factors influencing influenza vaccination

4.1 Introduction

As described in the previous chapter, influenza vaccine has been shown to be safe and effective in reducing the risk of influenza and its disease-related complications such as bronchitis, pneumonia, acute exacerbations of chronic bronchitis, asthma, COPD, and heart failure (Ahmed, Nicholson, Nguyen-Van Tam et al, 1997; Nichol, Baken, & Nelson et al., 1999; CDC, 2010b; Treanor, 2010). Despite this, the rates of influenza vaccination in many countries are still below the WHO target for 2010 of vaccinating at least 75 per cent of the individuals aged 65 years or older (Kohlhammer, Schnoor, Schwartz et al., 2007; Ward & Draper, 2007; Blank, Freiburghaus, Schwenkglenks et al., 2008; Lau, Kim, Tsui et al., 2008; Lau, Lau, & Lau 2009; CDC, 2010b). A number of factors have been found to affect the decision to accept or decline vaccination (Telford & Rogers, 2003; Zimmerman, Nowalk, Raymund et al., 2003; Horby, Williams, Burgess et al., 2005; Evans, Prout, Prior et al., 2007; Lyn-cook, Halm, & Wisnivesky, 2007; Kohlhammer, Schnoor, Schwartz et al., 2007; Ward & Draper, 2007; Payaprom, Bennett, Burnard et al., 2010). This chapter addresses lay beliefs about influenza, the influenza vaccine and the factors affecting the decision to be immunised against influenza among high-risk adults: those aged 65 years or older and those aged less than 65 with chronic medical conditions. These can be grouped into six categories.

4.2 Lay beliefs about influenza

Previous studies have highlighted the importance of understanding lay beliefs about influenza, its causes, and its symptoms. These beliefs influence people's attitudes to influenza vaccination, and ultimately, their vaccination behaviours (Cornford & Morgan, 1999; Telford & Rogers, 2003; Adonis-Rizzo & Jett, 2006; Evans, Prout, Prior et al., 2007). Adonis-Rizzo and Jett (2006) investigated the health beliefs related to influenza prevention in the Haitian Americans. The findings showed that all participants thought that influenza was simply a "cold" or "a big cold". Based on this

belief, traditional preventive practices such as the use of herbal remedies, dressing warmly in cold weather, and eating healthy food were believed to be sufficient to prevent influenza. Perceptions regarding the seriousness of influenza were similar to those of previous studies which found that older people who refused influenza vaccination believed that influenza was not dangerous (e.g. Santibanez, Nowalk, Zimmerman et al., 2002; Tabbarah, Zimmerman, Nowalk et al., 2005). The interpretation of influenza as a mild infection can contribute to a low acceptance of vaccine recommendations. On the contary, perceiving influenza as serious can lead older people to comply with the influenza vaccination (Honkanen, Keistinen & Kivela, 1996; Rehmet, Ammon, Pfaff et al., 2002).

Few studies have examined what lay persons believe to be the cause of influenza, although more studies have explored folk beliefs and practices about the common cold. For example, a UK study found that lay people believed that the common cold occurred when certain body parts (such as the top of the head, the back of the neck, and the feet) were exposed to damp or draughts (Helman, 1978). The folk beliefs that exposure to cold weather or wearing wet cothes causes common cold and influenza have long been and continue to be influential among the lay persons (Baer, Weller, Pachter et al., 1999; CDC, 2003; Baer, Weller, de Alba Garcia, 2008; Prior, Evans, & Prout, 2010). These beliefs are, arguably, the descendents of the ancient Greek theory of bodily humors.

Hot-Cold imbalance is thought to lead to illness more widely (Harwood, 1971; Baer, Weller, de Alba Garcia, 2008). The hot-cold theory of illness influences explanations for causality of illness and the ways to treat it. For example, Young and Garro (1994) found that among Tarascan Indians, cold or flu was believed to be caused by eating "cold" foods, and the illnesses can both be treated by eating "hot" foods. Weller (1983) also reported that "flu" was classified by urban Guatemalans as needing "hot" remedies, whereas both the "cold" and "flu" were classified as needing "hot" remedies among the rural Guatemalans, showing that there is a different perspective, possibly culture (Weller, 1983 cited in Baer, Weller, Pachter et al., 1999). A study of community beliefs about medico-nutritional practices among Puerto Ricans conducted by Lieberman (1979) found that milk which was classified as "cold" should not be given to the child during illness. "Hot-cold" beliefs and practices are still prevalent; a

qualitative study conducted by the United States Centre for Disease Control and Prevention (2000, cited in CDC, 2003) revealed that many Hispanic Americans were unaware that influenza was a disease caused by a virus; they believed that changes in the weather caused influenza, and "not getting wet or chilled when outside in cold weather" was proposed as an important strategy for avoiding influenza.

A recent interview study on lay perceptions of symptoms and causes of cold and influenza among older British in South Wales, UK, conducted by Prior, Evans, and Prout (2010) pointed out that influenza has been associated with a wide range of etiological agents, including "viruses, bugs and germs; the environment in general and "stuffy" air in particular; being wet wearing damp cloths; the flu jab; and coughs and sneezes of other people" (p. 6). Additionally, lay persons believed that catching influenza depended not only on being exposed to these factors but, also, on the individual's health and immune system; exposure to viruses, bugs, the air and dampness was believed to have very little effect, if the individual's immune system was strong (Prior, Evans & Prout, 2010).

Some differences in the perception of influenza transmission between experts and lay people were documented in previous studies (Raude & Setbon, 2009; Prior, Evans & Prout, 2010). A national French survey on the public perception of the pandemic influenza threat showed that a large percentage of lay people believed that the spread of influenza from human to human via direct contacts with saliva or aerosol droplets from infected people was believed to be higher than via indirect contacts with contaminated fomites. The belief that influenza was not primarily transmitted through contact with infected surfaces was also common among older British people in South Wales (UK) (Prior, Evans & Prout, 2010). The results from these two recent studies suggest that campaigns seeking to promote hand hygiene probably do not work for preventing the spread of influenza in all settings (Raude & Setbon, 2009; Prior, Evans and Prout, 2010).

Previous studies have shown that lay people make a distinction between the common cold and influenza in terms of symptoms experienced (Baer, Weller, Pachter et al., 1999; Prior, Evans &Prout, 2010). Baer, Weller, Pachter et al. (1999) examined the conceptualisation of the common cold and the differences between the common cold

and influenza from a cross-cultural perspective. In this study, four groups of Latin Americans and a group of middle income Americans living in Tampa, Florida were studied. The authors found that influenza symptoms reported by the participants who lived in Tampa were nausea, stomach ache and diarrheoa, body aches and pains, fatigue, and fever, as well as upper respiratory symptoms. The gastrointestinal symptoms (nausea, stomach ache and diarrhoea) found in Baer et al. (1999)'s study appeared to be the same symptoms as "folk flu" that was identified in the study by McCombie (1987). McCombie (1987) noted that, in southern Arizona, lay people diagnosed influenza based on symptoms of nausea, vomiting, and diarrhoea. Gastrointestinal symptoms with influenza have also been noted among middle-income main stream Americans populations, African Americans, and English-speaking populations in the United States (Pachter, Niego, & Pelto, 1996; Baer, Weller, Pachter et al., 1999). Prior, Evans and Prout (2010) added that some older British people associated vomiting with influenza. However, an association between influenza and gastrointestinal symptoms did not appear in Latin American populations (Pachter, Niego, & Pelto, 1996; Baer, Weller, Pachter et al., 1999). In a study of lay diagnoses of common cold and influenza among older British people, Prior, Evans and Prout (2010) found that, although most of the influenza symptoms identified by participants were consistent with the biomedical understanding of major symptoms of influenza, lay people and health professionals used a different frame for the assessment of influenza symptoms. For lay people, pain and aching body involved more than just the muscles; "it was interpreted as a whole body illness" (p. 6). Influenza was also connected to behavioural correlates, for example, people with influenza can be bedridden and unable to function in their dialy lives.

In summary, there are agreements and differences between lay people's beliefs and professions' views regarding influenza, its causes, and symptoms. Most people have their own ideas and beliefs about influenza and its consequence, which may or may not be relevant to the biomedical theories. Furthermore, these beliefs vary across different cultures, and they need to be understood in order to facilitate patients' behaviour change. Previous studies have shown that lay beliefs played an important role in determining older people's acceptance or rejection of influenza vaccination (Cornford & Morgan, 1999; Telford & Rogers, 2003; Evans, Prout, Prior et al., 2007).

4.3 Lay beliefs about influenza vaccine and immunisation against influenza

Although multiple large-scale, randomised controlled studies have shown that the influenza vaccines are safe and efficacious, some lay people believe that the influenza vaccine might not be safe (e.g. Govaert, Dinant, Aretz et al., 1993; Armstrong, Berlin, Schwartz et al., 2001; Prislin, Dyer, Blakely et al., 1998; Wray, Jupka, Ross et al., 2007). In a survey of 659 African-Americans, carried out by Armstrong, Berlin, Schwartz et al., (2001), 20 per cent of the respondents were concerned that "there may be something they didn't know about in the flu shot", and this concern has been identified as a deterrent to acceptance of influenza vaccination among this low-income population (Armstrong, Berlin, Schwartz et al., 2001). Further, Wray, Jupka, Ross et al., (2007) conducted four focus groups (N= 35) and eight in-depth interviews with older African Americans. The findings revealed that participants were worried about the safety of vaccine components, and they were concerned that vaccination would give them the influenza or that the influenza vaccine would interact with prescription medications for chronic illness. Similar findings were observed among older Haitians; most participants were afraid of sickness that was believed to be caused by the vaccination itself and concerned that the influenza vaccine would exacerbate other health problems or cause another (Adonis-Rizzo & Jett, 2006).

Cornford and Morgan (1999) conducted 50 in-depth interviews with elderly people with chronic disease (aged over 75 years) regarding their beliefs about influenza vaccination. The authors noted that there were different ways of interpreting the vaccine side-effects between the elderly, relating to whether they viewed vaccination positively or negatively. Those with a negative view of vaccination highlighted the side-effects of painful arms, feeling unwell, getting influenza, and catching colds more frequently after having influenza vaccine. In contrast, those with positive views about vaccination felt that the vaccine side-effects might have been coincidental events, and they continued to have themselves vaccinated.

In a study of 54 British people aged 65 years and older, using interviews to explore lay beliefs about influenza vaccination, Evans, Prout, Prior et al. (2007) found the

reason given by refusers and defaulters for not wanting to have the vaccine was that the vaccine would make them ill or gave them influenza. Additionally, they also believed that the vaccine would not protect them, either because it contained the influenza strain that occurred last year or because many different strains were included in the vaccine. This suggests that some lay people have some knowledge about the influenza vaccine.

Previous studies suggest that the uptake of influenza vaccination among high-risk individuals remains low, partly because of mistrust of vaccines and fear of side-effects (Cornford & Morgan, 1999; Armstrong, Berlin, Schwartz et al., 2001; Telford & Rogers, 2003; Evans, Prout, Prior et al., 2007; Wray, Jupka, Ross et al., 2007). For example, Armstrong, Berlin, Schwartz et al.'s (2001) survey revealed that participants who were concerned about the undisclosed contents of the influenza vaccine were less likely to report having had an influenza immunisation. Santibanez, Mootrey, Euler et al. (2010) surveyed 8,710 American adults aged 50 years or older, and found that a higher chance of being vaccinated was observed among those who did not believe that they could get influenza from the vaccine, as compared to those who did believe this or who stated that they did not know.

In the United Kingdom, a qualitative study conducted by Cornford and Morgan (1999) found that among British older people aged over 75 years, the decision to receive influenza vaccination was based on lay beliefs about whether it could prevent or cause morbidity from colds and influenza and the importance of side-effects. A further study conducted by Evans, Prout, Prior et al. (2007) also revealed that persons who had been offered influenza vaccine but has always refused it and those who had been vaccinated but have relapsed, believed that the vaccine was not effective and it would give them various side-effects.

Other studies also found that fear of adverse reactions and the belief that the influenza vaccine may actually cause illness, were cited as the common reasons by the high-risk individuals for declining to vaccination (e.g. CDC, 1999; Pregliasco, Sodano, Mensi et al., 1999; Wray, Jupka, Ross et al., 2007).

In summary, some people's beliefs about the influenza vaccine and immunisation may be different from the medical knowledge. However, misconceptions about the vaccine safety must be corrected because vaccination misconceptions have been shown to affect markedly the influenza immunisation rates of high-risk older people (e.g. Abramson & Cohen-Naor, 2000; Armstrong, Berlin, Schwartz et al., 2001; Madhavan, Rosenbluth, Amonkar et al., 2003; Wray, Jupka, Ross et al., 2007). It has been suggested that people's lay beliefs can be changed in the light of new experiences and the availability of believable information (Donovan, 1991). Thus, health care workers should first acknowledge the patients'concerns and provide accurate information about the benefits and risks of the influenza vaccines, as well as correcting their misconceptions, to encourage them to take up the immunisation.

4.4 Factors influencing influenza vaccination

4.4.1 Socio-demographic factors

Socio-demographic factors (age, gender, marital status, education level, and socio-economic status) appeared to influence older adults' decisions in seeking vaccination, although the results of these many studies have been mixed (Russell & Maxwell, 2000; Bonito, Lenfestey, Eicheldinger et al., 2004; Chi & Neuzil, 2004; Mangtani, Breeze, Kovats et al., 2005; Tabbarah, Zimmerman, Nowalk et al., 2005; Bryant, Ompad, Sisco et al., 2006; Straits-Troster, Kahwati, Kinsinger et al., 2006; Damiani, Federico, Visca et al., 2007; Endrich, Blank, & Szucs et al., 2009; Zimmerman, Nowalk, Tabbarah et al., 2009; CDC, 2010; Chiatti, Rosa, Barbadoro et al., 2010; Jimenez-Garcia, Hernandez-Barrera, de Andres et al., 2010).

4.4.1.1 Age

Several studies have documented that older age was positively associated with influenza vaccine acceptance (Landi, Onder, Carpenter et al., 2005; Tabbarah, Zimmerman, Nowalk et al., 2005; de Andres, Carrasco-Garrido, Hernandez-Barrera et al., 2006; Lau, Yang, X., & Tsui, et al., 2006; Kohlhammer, Schnoor, Schwartz et al., 2007; Jimenez-Garcia, Jimenez, Carrasco-Garrido et al., 2008; Jimenez-Garcia, Hernandez-Barrera, Carrasco-Garrido, 2009). In the United States, Tabbarah,

Zimmerman, Nowalk et al. (2005) conducted a longitudinal survey to examine factors associated with influenza vaccination over the three influenza seasons (2000-2001, 2001-2002, and 2002-2003) in older Americans, and found that the proportion of people who reported having been vaccinated was nearly two times higher in the elderly people (62.6 per cent) than in individual aged 50 to 64 years (32.4 per cent) for all the three consecutive influenza seasons studied.

de Andres, Carrasco-Garrido, Hernandez-Barrera et al. (2006) analysed influenza coverage rates and their determinants among the Spanish elderly using data from five surveys of the non-institutionalised Spanish adult population (1993, 1995, 1997, 2001, and 2003). The results also showed a positive association between age and being vaccinated; elderly people (75 years or older) were 2.37 times more likely to report being immunised against the influenza than individuals aged 65 to 69 years. Although a total of 19,141 records of individuals aged 65 years or over were included in this study, the findings were perhaps limited by relying on the validity of self-reported data. In addition, this research study included only non-instutionalised people aged 65 years or over; therefore, its results cannot be generalized to the entire Spanish population.

Similar results were obtained from a survey study assessing influenza coverage in Spain by Jimenez-Garcia, Mayo-Montero, Hernandez-Barrera et al (2005). The study showed that older age was significantly associated with a greater likelihood of having been vaccinated (aged 50-64: OR = 2.28 [95% CI, 1.82-2.85]; aged 65-74: OR = 5.52 [95% CI, 4.36-6.99], and aged $\geq$ 75: OR = 7.18 [95% CI, 5.47-9.43]).

Additionally, an international observational study examining prevalence of influenza immunisation and factors associated with acceptance of the influenza vaccine among frail, elderly people living in the community in eleven European countries, found that older age has continued to be a positive predictor of influenza vaccination (OR=1.21, 95% CI, 1.01-1.46) in most of countries, except for four countries (Finland, Sweden, the Netherlands, and United Kingdom) (Landi, Onder, Carpenter et al., 2005). Similar results were obtained by Johansen, Sambel, & Zhao (2006) who analysed trends in influenza vaccination coverage rates in Canada in the year 2003. The results showed that two-third of people aged 65 to 79 years reported having been vaccinated, and a

higher percentage of people who received influenza vaccine was observed in people age 80 or older. More recently, a survey study that examined influenza vaccination uptake levels across two influenza seasons (2006-2007 and 2007-2008) in eleven European countries by Blank, Schwenkglenks, & Szucs (2009) demonstrated an upward trend in influenza vaccination coverage rates among the elderly (65 years or older) in all the countries studied.

The relationship between age and having been vaccinated against the influenza was likewise observed among older people with chronic medical conditions. The influenza vaccination rate has increased with age. Jimenez-Garcia, Carrasco-Garrido, Maya-Montero et al. (2005) explored the influenza vaccination status and its determinants in diabetic patients in Spain. The study revealed that the probability of getting vaccinated against the influenza in people with diabetes aged 65 year or older was 5.8 times higher than those under 50 years of age. Additionally, three recent studies evaluating influenza vaccination coverage rates and factors associated with influenza vaccination in patients with chronic diseases (COPD, chronic bronchitis, and cardiovascular disease) in Spain have also found that age was an important predictor of influenza vaccination, and the rate of immunisation with influenza vaccine among these high-risk individuals has risen with increasing age (Jimenez-Garcia, Mayo-Montero, Hernandez-Barrera et al., 2005; Jimenez-Garcia, Hernandez-Barrera, Carrasco-Garrido, 2006; Jimenez-Garcia, Hernandez-Barrera, Carrasco-Garrido, 2009). However, Honkanen, Keistinen, & Kivela (1996) investigating determinants of influenza vaccination among the elderly living in three districts in Finland, found no influence of age and sex on the acceptance of influenza vaccination in the elderly.

The finding that influenza vaccination coverage rates in older people increase significantly with age remains unclear. This may be influenced by government targets as routine influenza vaccination has been recommended for people in this age group in most countries (van Essen, Palache, Forleo et al., 2003). In addition, there is evidence that the prevalence of chronic disease requiring the need for influenza vaccination is high in individuals aged 65 or older. The study assessing influenza vaccination uptake in eleven European countries by Endrich, Blank, & Szucs (2009) indicated that people with chronic medical conditions across all countries studied consistently had a significant greater likelihood of being immunised than those who

reported that they did not have any underlying diseases. Jimenez-Garcia, Carrasco-Garrido, Maya-Montero et al. (2005) also found that the number of people who had underlying medical conditions rose significantly with increasing age in all the surveys. Thus, suffering from underlying diseases may be another explanation for an increased probability of being vaccinated in older people. However, it should be noted that these two studies have relied on retrospective, self-reported data of vaccination, and the information on chronic condition status could not be verified by medical records, which may lead to under-reporting or over-reporting by participants and thereby affect the validity of results. Nonetheless, several studies that compared self-reporting of influenza vaccination status with medical records have shown that the agreement between two methods was satisfactory (Mac Donald, Baken, Nelson et al., 1999; Zimmerman, Raymund, Janosky et al., 2003).

Also, high vaccination coverage levels may have been due to the fact that older people with chronic diseases are more frequent use of health care service, thus providing more chance to be offered or recommended influenza vaccine, especially in countries where general practitioners (GPs) play a key role in delivering influenza vaccination such as the UK. The study conducted by Booth, Coppin, Dunleavey et al. (2000) in central southern England during early 1998 showed that seventy-one per cent to eighty-two per cent of GPs reported that they routinely offered influenza immunisation to their at risk patients. Another British study revealed that one hundred and fifty-two older people reported having been offered vaccination and seventy-one percent of these individuals were subsequently vaccinated (Gosney, 2000).

4.4.1.2 Gender

Gender has been reported to be associated with the acceptance of influenza vaccination in some studies. However, the effect has varied between studies (Szucs & Muller, 2005; Jimenez-Garcia, Hernandez-Barrera, Carrasco-Garrido et al., 2006; Jimenez-Garcia, Jimenez, Carrasco-Garrido et al., 2008; Jimenez-Garcia, Hernandez-Barrera, Carrasco-Garrido, et al., 2009, Jimenez-Garcia, Hernandez-Barrera, de Andres et al., 2010; Kee, Lee, Cheong et al., 2007; Bean-Mayberry, 2009; Endrich, Blank, & Szucs, 2009). A population-based study to assess influenza vaccination coverage rates in five European countries over two influenza seasons (2001-2002 and

2002-2003) conducted by Szucs & Muller (2005), indicated that a significant higher vaccination rate was found for women in comparison to men.

Similarly, Russell and Maxwell (2000) examined the prevalence and factors relating to influenza vaccination in a home care population. The results of this study showed that the percentage of people who reported having been vaccinated against influenza was higher among women than men (63.1 per cent vs. 54.9 per cent). Recently, in South Korea, Kee, Lee, Cheong et al. (2007) also found that women relative to men were significantly more likely to be immunised against influenza (OR = 1.41, 95% CI, 0.97 – 2.06).

In contrast, other studies have shown that the percentage of people who reported having been vaccinated was higher in men than in women (Bonito, Lenfestey, Eicheldinger et al., 2004; Jimenez-Garcia, Hernandez-Barrera, Carrasco-Garrido, 2006, Jimenez-Garcia, Hernandez-Barrera, Carrasco-Garrido et al., 2009, Jimenez-Garcia, Hernandez-Barrera, de Andres et al., 2010; Endrich, Blank, & Szucs, 2009). The study that explored influenza vaccination uptake among non-institutionalised Medicare Beneficiaries during 2000-2002, indicated that there was a significant difference in vaccination rates between the genders over the study period; a higher proportion of vaccinated people was found in men (Bonito, Lenfestey, Eicheldinger et al., 2004). A survey study of predictors of influenza vaccination in eleven European countries showed that the likelihood of receiving the influenza vaccine was higher among men than women in Italy (OR = 1.43), Portugal (OR = 1.41), Spain (OR = 1.37), Czech Republic (OR = 1.34), Poland (OR = 1.29), France (OR = 1.26), and the UK (OR = 1.21), but not in Germany, Austria, Finland, and Ireland (Endrich, Blank, & Szucs, 2009).

Likewise, a study of gender influence on the acceptance of influenza vaccination among Spanish by Jimenez-Garcia, Hernandez-Barrera, de Andres et al. (2010) has also shown that men had better influenza coverage rates than women; the likelihood of being vaccinated against influenza was 12 per cent higher in men than in women (OR = 1.12, 95% CI, 1.06 - 1.18). Moreover, three recent studies exploring influenza coverage rates and the determinants of influenza vaccine uptake in high-risk people with chronic diseases (COPD, cardiovascular, and chronic bronchitis) in Spain,

indicated that the use of influenza vaccine has been higher in men than in women among high-risk individuals with chronic disease (Jimenez-Garcia, Hernandez-Barrera, Carrasco-Garrido et al., 2006; Jimenez-Garcia, Hernandez-Barrera, Carrasco-Garrido et al., 2009). In addition, Jimenez-Garcia, Jimenez, Carrasco-Garrido et al. (2008) examined predictors of influenza immunisation among diabetic adults in Spain. The study also showed that the likelihood of being vaccinated was higher among men than women (OR = 1.37, 95% CI, 1.01-1.87). The reasons for the low uptake of influenza vaccine among women were unclear. However, the authors speculated that less social support, differences in the health status and provider bias might be responsible for gender differences in influenza vaccine uptake in Spain (Jimenez-Garcia, Hernandez-Barrera, de Andres et al., 2010). The relationship between influenza vaccination and gender has also been recently reported in the United States; a prospective study of 9,164 older people (65 years or older) using data drawn from the Health and Retirement Study (HRS) also revealed that women were less likely than men to receive an influenza vaccine and to get a cholesterol screening (Cameron, Song, Manheim et al., 2010).

4.4.1.3 Marital status

Being married was found to be a positive predictor of influenza vaccination (Russell & Maxwell, 2000; Andrew, McNeil, Merry et al., 2004; Nowalk, Zimmerman, Shen et al., 2004). Nowalk, Zimmerman, Shen et al. (2004) conducted a survey study to examine barriers to pneumococcal and influenza vaccination among elderly people living in the community. The result of this study revealed that married people were more likely to report having the influenza vaccination during 2000-2001 influenza season than those who were widowed, single, or divorced/ separated (83 per cent vs.73 per cent widowed, 66 per cent single, 62 per cent divorced/separated). In Canada, the study by Russell and Maxwell (2000) also revealed that influenza vaccination was higher among married (56.8 per cent) and widowed (68.9 per cent) persons than those who were never married (46 per cent) or divorced (37.5 per cent). Similarly, a significant higher rate of influenza immunisation was observed among married British aged over 74 years relative to non-married individuals (Mangtani, Breeze, Kovats et al., 2005). A positive association between marital status and influenza immunisation was further illustrated in a population-based cohort study by

Andrew, McNeil, Merry et al. (2004) that investigated the factors involved influenza vaccine uptake in older people aged 65 or older living in the community. The study showed that being married was a strong predictor of influenza vaccination among these individuals (OR= 1.29, 95% CI, 1.14 -1.47). The study determining the influenza of gender on influenza vaccination also found that among other factors, being married was the predictor of influenza vaccination in Spanish women (Jimenez-Garcia, Hernandez-Barrera, de Andres et al., 2010). It was suggested that there was more social support from within the family among married persons than those in other marital categories; therefore, married people were more likely to receive preventive services, including influenza vaccination (Russell & Maxwell, 2000).

4.4.1.4 Living with others

In line with the explanation afforded by Russell and Maxwell (2000), living with others has also been associated with an increased probability of being immunised (Nexøe, Kraqstrup, & Sogaard, 1999; Lau, Kim, Choi et al. 2007). One study exploring factors related to influenza vaccine uptake among the elderly in Denmark conducted by Nexøe, Kraqstrup, & Sogaard (1999), for example, showed that living together with another person was significantly associated with higher likelihood of immunisation (OR = 1.59, 95% CI, 1.03 – 2.48). Likewise, Lau, Kim, Choi et al. (2007) assessed the prevalence and determinants of influenza vaccine uptake in people aged 65 years and over. The study has shown that the odds of being immunised were significantly greater among the elderly living with family members than those living alone (OR = 2.05, 95% CI, 1.27 – 3.33).

By contrast, living alone appeared to be negatively associated with influenza vaccination (Burns, Ring, & Carroll, 2005; Landi, Onder, Carpenter et al., 2005; Jimenez-Garcia, Hernandez-Barrera, de Andres et al., 2010). The percentage of people who reported having been vaccinated against influenza vaccine, was significantly lower in older people who lived alone compared to those who lived with others (74 per cent vs. 87 per cent, OR = 2.25, 95% CI, 1.35 – 3.73) (Burns, Ring, & Carroll, 2005). A recent study assessing influenza coverage rates in eleven European countries conducted by Landi, Onder, Carpenter et al. (2005) confirmed the negative relationship between living alone and influenza vaccination; living alone was

significantly associated with a lower likelihood of being immunised in eight European countries (the Netherlands, Denmark, Norway, Sweden, United Kingdom, Germany, Iceland, and Italy) (OR = 0.78, 95% CI, 0.67 – 0.90).

4.4.1.5 Socio-economic status

Socio-economic status is typically indicated by education attainment, occupational status and income. Socio-economic factors have been shown to have significant influence on influenza vaccine uptake. However, the findings are inconsistent (Sarria-Santamera & Timoner, 2003; Bonito, Lenfestey, Eicheldinger et al., 2004; Nowalk, Zimmerman, Shen et al., 2004; Burns, Ring, & Carroll, 2005; Mangtani, Breeze, Kovats et al., 2005; Damiani, Federico, Visca et al., 2007; Mayo-Montero, Hernandez-Barrera, Carrasco-Garrido et al., 2007; Blank, Schwenkglenks, & Szucs, 2009; Endrich, Blank, & Szucs, 2009; Chiatti, Rosa, Barbadoro et al., 2010).

The study among people aged 65 or older conducted by Burns, Ring, and Carroll, (2005) indicated that the likelihood of being immunised against influenza was significantly higher for individuals with a higher occupational status (OR = 1.47, 95% CI = 1.09 - 1.98) than the economically less advantaged. Household income was also found to be significantly associated with influenza vaccination among the elderly living in community during the 2000-2001 influenza season in the study conducted by Nowalk, Zimmerman, Shen et al. (2004); persons with higher incomes were more likely to receive influenza vaccine than those with lower incomes. In the UK, the study conducted by Mangtani, Breeze, Kovats et al. (2005) yielded similar results; a lower vaccination rate of 10 per cent was observed in lower socioeconomic status people aged over 74 years (those without central heating or in rented accommodation) as compared to those of higher socio-economic status.

Likewise, the study by Landi, Onder, Carpenter et al. (2005) found that economic problems were associated with a lower probability of receiving influenza vaccine among the elderly (OR = 0.58, 95% CI, 0.45-0.74). In Italy, the study assessing the influence of socioeconomic level on influenza vaccine uptake conducted by Damiani, Federico, Visca et al. (2007) showed that significant lower percentages of people who reported receiving the vaccine were among lower educated persons and those in lower occupational classes than individuals in higher categories, especially among

individuals under 65 years of age. Recently, a survey study examining factors related to influenza vaccination among the elderly by Lau, Kim, Choi et al. (2007), also found that perceived financial barriers were associated with influenza vaccination among the elderly in Hong Kong; people who did not perceive financial barriers were more likely to get vaccinated than those who perceived such barriers (OR = 2.14, 95% CI, 1.48 – 3.10).

In addition to the influence of income and social class, higher rates of influenza immunisation have been found to be associated with higher levels of education. Bonito, Lenfestey, Eicheldinger et al. (2004) analysed vaccination coverage rates and factors related to disparities in influenza vaccination among elderly Medicare Beneficiaries over three years (2000 – 2002). The results of this study also found that influenza vaccination rates rose significantly with levels of education. This relationship was confirmed in a Canadian study; Andrew, McNeil, Merry et al. (2004) have observed that high-level education was significantly associated with influenza vaccination among Canadian seniors (OR = 1.05, 95% CI, 1.03-1.07).

Additionally, a prospective study comparing two cohorts of older adults (vaccinated and unvaccinated against influenza and pneumococcal infections) in Stockholm County, Sweden by Christenson and Lundbergh (2002) also revealed that vaccination rates for both influenza and pneumococcal infections were significantly higher among older people (aged 65 or older) with higher education than those with little education. Similar results were obtained from the US Behavioural Risk Factor Surveillance System (BRFSS); the elderly with higher levels of education were more likely to be immunised against influenza than those with less than a high school education (CDC, 2001).

Nevertheless, a negative influence of socioeconomic level on influenza vaccine uptake has been reported (Jimenez, Larrauri, Carrasco-Garrido et al., 2003; Nowalk, Zimmerman, Shen et al., 2004; Szucs & Muller, 2005; Blank, Schwenkglenks, & Szucs, 2009; Endrich, Blank, & Szucs, 2009; Chiatti, Rosa, Barbadoro et al., 2010). The results of a study conducted by Nowalk, Zimmerman, Shen et al. (2004), for example, revealed that a significantly higher proportion of people who completed vocational or technical school received influenza vaccine during the 2000-2001

influenza season than that among those with college degrees. Two recent studies conducted by Blank, Schwenkglenks, and Szucs (2009) and Endrich, Blank, and Szucs (2009) have also found that a higher education level was negatively associated with influenza vaccination. Also, Damiani, Federico, Visca et al. (2007) observed a greater likelihood of being vaccinated against influenza in persons without any qualification relative to those with a university degree among individuals aged 25-44 years (OR = 2.07, 95% CI, 1.41 – 3.04).

A survey study analysing trends in influenza vaccination coverage rates in five European countries by Blank, Schwenkglenks, and Szucs (2009) also showed that, while vaccination rates were lower among individuals with higher education levels compared to lower educated person in Italy (OR = 0.6), the reverse effect was found for Spain; a greater proportion of persons who reported having been vaccinated was found among graduates (OR = 1.4). Likewise, the study among people with chronic obstructive pulmonary disease has also shown that individuals who had no formal education had the highest likelihood of obtaining the influenza vaccination (OR = 3.19, 95% CI, 2.47 – 4.13) (Jimenez-Garcia, Mayo-Montero, Hernandez-Barrera et al., 2005).

With regard to a negative effect of household incomes on influenza vaccine uptake, Jimenez, Larrauri, Carrasco-Garrido et al. (2003) explored influenza vaccination coverage rates and their determinants in individuals aged 50-64 years. The result of this study found that low-income people (less than €600 per month) had a higher prevalence of influenza vaccination, as compared to those with higher incomes (more than €1,200 per month) (OR = 1.71, 95% CI, 1.14 - 2.56). Szucs and Muller (2005) have observed a greater vaccination rate in persons with a monthly income of less than €1,000 relative to those with monthly income over € 2,000 per month (29.9 per cent vs. 21.0 per cent).

Similar results were obtained in a study examining influenza vaccination coverage levels in five European countries (The United Kingdom, Germany, Italy, France, and Spain) by Blank, Schwenkglenks, and Szucs (2009). The study also showed that in Germany and Spain, people with a lower income (less than € 2,499 per month) were significantly more likely to receive influenza vaccine than those with a higher income

(≥ € 2,500 per month). Chiatti, Rosa, Barbadoro et al. (2010) recently reported findings that a higher likelihood of being immunised against influenza has been observed among individuals in lower social classes as compared to those from upper social classes (OR = 1.21, 95% CI, 1.11-1.33). However, no association was seen between educational levels, household incomes and influenza vaccination in the study conducted in Spain by Sarria-Santamera and Timoner (2003).

One may predict that higher socioeconomic status would positively influence influenza vaccine uptake. Individuals with higher education level and monthly income can access more information on influenza and its consequences; therefore they can better understand and potentially make the decision to receive influenza vaccine (Blank, Schwenkglenks, & Szucs, 2009). However, the impact of socioeconomic status on influenza vaccination is controversial. One possible explanation may be that other factors such as mistrust of modern medicine and the perception of good health may exert influence on the decision to receive influenza vaccine (Conford & Morgan, 1999; Telford & Rogers, 2003). Additionally, the provision of free vaccination for older people in many countries may partially explain why higher socioeconomic status did not have a positive influence on influenza vaccine uptake (Mangtani, Breeze, Kovats et al., 2005; Blank, Schwenkglenks, & Szucs, 2009; Endrich, Blank, & Szucs, 2009).

4.4.2 Health status/conditions

4.4.2.1 Healthy lifestyles

A higher influenza vaccination rate among people with healthy lifestyles (such as non-smokers and those who exercise regularly) has been found previously (Nicholson, Kent, & Hammersley, 1999; Sarria–Santamera & Timoner, 2003; Mangtani, Breeze, Kovats et al., 2005; de Andres, Carrasco-Garrido, Hernandez-Barrera et al., 2006; Jimenez-Garcia, Hernandez-Barrera, Carrasco-Garrido et al., 2006; Nowalk, Zimmerman, Tabbarah et al., 2006; Kee, Lee, Cheong et al., 2007; Mayo-Montero, Hernandez-Barrera, Carrasco-Garrido et al., 2007). A survey study conducted in South Korea by Kee, Lee, Cheong et al. (2007) revealed that people who took regular exercise were more likely to get vaccinated than those who did not exercise (OR = 1.49, 95% CI, 1.09 - 2.03).

Likewise, the study assessing trends in influenza vaccination coverage rates and factors associated with influenza vaccination over five influenza seasons among the elderly in Spain by de Andres, Carrasco-Garrido, Hernandez-Barrera et al. (2006) found a greater likelihood of being immunised among ex-smokers (OR = 1.81 95% CI, 1.35 - 2.41) and those who had never smoked (OR = 1.64, 95% CI, 1.22 – 2.20), as compared to active smokers. Additionally, Nicholson, Kent, and Hammersley (1999) indicated a 13 per cent decrease in the odds of being immunised against influenza in individuals current smoking status relative to the ex-smokers and non-smokers (OR = 0.87, 95% CI, 0.76 – 0.99). The study among individuals with chronic respiratory diseases conducted by Mayo-Montero, Hernandez-Barrera, Carrasco-Garrido et al. (2007) found that ex-smokers (OR = 2.62, 95% CI, 2.04 - 3.37) and those who had never smoked (OR = 1.97, 95% CI, 1.57 – 2.47) were more likely to receive influenza vaccine than smokers.

In addition, Sarria-Santamera and Timoner (2003) found that smoking was a negative determinant of influenza immunisation (OR = 1.92, 95% CI, 1.24 – 2.96). More recently, the study conducted by Jimenez-Garcia, Hernandez-Barrera, Carrasco-Garrido et al. (2009) also found that the higher probability of getting vaccinated against influenza was seen in people with healthy lifestyles such as non-smokers (OR = 1.80, 95% CI, 1.23 – 2.62), ex-smokers (OR = 1.73, 95% CI, 1.20 – 2.50), and those who took physical exercise (OR = 1.46, 95% CI, 1.13-1.88) compared to people with less healthy lifestyles (smokers and those who did not exercise). As people with healthy lifestyles may be more concerned about their health, and may have more interest in the use of preventive services, including influenza vaccination; therefore, this may be credited with the higher rate among these individuals (Andrew, McNeil, Merry et al., 2004; Kee, Lee, Cheong et al., 2007).

4.4.2.2 Cognitive impairment

Cognitive impairment has been shown to be associated with lower rates of influenza vaccination in older adults (Landi, Onder, Carpenter et al., 2005; Mangtani, Breeze, Kovats et al., 2005). The study conducted by Landi, Onder, Carpenter et al. (2005) in eleven European countries (Czech Republic, Denmark, Finland, France, Germany, Iceland, Italy, The Netherlands, Norway, Sweden, and the UK), indicated that the

odds of being immunised were significantly lower for individuals with cognitive impairment in all the countries studied (OR = 0.69, 95% CI, 0.59 – 0.80). Similarly, Mangtani, Breeze, Kovats et al. (2005) also found disparities in influenza vaccination uptake between people aged over 74 years who had cognitive impairment and those with no cognitive problems.

4.4.2.3 Presence of underlying chronic medical conditions

A number of studies have shown that the existence of co-morbidities was associated with influenza vaccination, both for older people (aged 65 years or older) and those under 65 years with chronic medical conditions aged (Jimenez, Larrauri, Carrasco-Garrido et al., 2003; Jimenez-Garcia, Mayo-Montero, Hernandez-Barrera et al., 2005; Jimenez-Garcia, Hernandez-Barrera, Carrasco-Garrido et al., 2006; Horby, Williams, Burgess et al., 2005; Landi, Onder, Carpenter et al., 2005; de Andres, Carrasco-Garrido, Hernandez-Barrera et al., 2006; Chen, Yi, Wu et al., 2007; Chiatti, Rosa, Barbadoro et al., 2010). Although there were consistent findings across theses studies, the findings were limited by their cross-sectional designs. In addition, data on influenza vaccination uptake and chronic medical conditions were based on self-report.

A cross-sectional study that analysed trends in influenza immunisation coverage levels (1993-2003) among elderly people in Spain by de Andres, Carrasco-Garrido, Hernandez-Barrera et al. (2006) found that there was a 1.58-fold increase in the odds of being vaccinated in elderly people who presented with co-morbidity compared to those without co-morbidity (OR = 1.58, 95% CI, 1.34 – 1.86). A population-based study that assessed the influenza vaccination coverage levels in eleven countries by Landi, Onder, Carpenter et al. (2005) has shown that the presence of co-morbidity increased the odds of having influenza vaccination among the elderly in eleven European countries (OR = 1.26, 95% CI, 1.08 – 1.47). In addition, Blank, Schwenkglenks, and Szucs (2009) indicated that the presence of chronic diseases and being older augmented the adjusted odds ratio of being vaccinated (odds ratios = 20.1, 95% CI, 16.6 – 24.4) in all five European countries (the United Kingdom, Germany, Italy, France, and Spain) in the 2007-2008 influenza season.

The association between presence of chronic disease and having influenza vaccination in older people was further illustrated in the study conducted in Italy by Chiatti, Rosa, Barbadoro et al. (2010). The study demonstrated that the chance of being vaccinated in older Italians increased with disease severity (mild disease: OR = 1.43, 95% CI, 1.33-1.55; severe disease: OR = 1.97, 95% CI, 1.82-2.14). In Spain, Jimenez-Garcia, Jimenez, Carrasco-Garrido et al. (2008) also found that among the elderly, the likelihood of vaccination increased with age and the presence of underlying chronic disease.

Several authors have found that having chronic disease was significantly associated with a greater probability of getting vaccinated among adults aged less than 65 years (Jimenez, Larrauri, Carrasco-Garrido et al., 2003; Jimenez-Garcia, Mayo-Montero, Hernandez-Barrera et al., 2005; Jimenez-Garcia, Hernandez-Barrera, Carrasco-Garrido et al., 2006; Horby, Williams, Burgess et al., 2005; Chen, Yi, Wu et al., 2007). In Spain, Jimenez, Larrauri, Carrasco-Garrido et al. (2003) conducted a survey study among adults aged 50 to 64 years. The results showed that the probability of being vaccinated was three times higher if the person had a chronic disease (OR = 3.07, 95% CI, 2.18 – 4.33). A further study describing the evolution of influenza vaccination coverage rates in adults from 1993-2001 indicated that the presence of chronic medical conditions had an important influence on influenza vaccination; a significantly higher number of persons who reported having been vaccinated was seen in individuals with chronic diseases (asthma, diabetes, chronic bronchitis, and cardiovascular disease) throughout the studied period, regardless of age group, as compared to those without such diseases (age < 65 years: 31.24 per cent vs. 9.17 per cent; age ≥ 65 years: 61.86 per cent vs. 47.95 per cent) (Jimenez-Garcia, Mayo-Montero, Hernandez-Barrera et al., 2005).

Other studies conducted in Australia and Canada, have also found the influence of high-risk medical conditions on influenza vaccine uptake. A national survey assessing the influenza vaccination coverage rates and factors related to influenza immunisation among Australian adults by Horby, Williams, Burgess et al. (2005), found that medical risk factor has been shown to be a significant predictor of influenza vaccination among individuals aged 40 to 64 years (OR = 4.8, 95% CI, 3.1- 3.4).

Despite a large sample size (63,317) in this national survey, the results should be interpreted with caution due to the relatively low response rate (30%), indicating that this could have resulted in selection bias and limited generalisability of the results.

Additionally, analysis of data drawn from the Canadian Community Health Survey by Chen, Yi, Wu et al. (2007) indicated that the higher number of chronic diseases, the greater the likelihood of being immunised; there were two to three times greater proportion of influenza vaccination among individuals with four chronic conditions compared to those with only one chronic condition. Jimenez-Garcia, Hernandez-Barrera, Carrasco-Garrido et al. (2006) examined trends in influenza vaccination coverage in Spain from 1993 to 2003 among cardiovascular disease (CVD) sufferers. The odds of being immunised against influenza among CVD patients who also suffered from respiratory chronic diseases was significantly higher, as compared to those without a concomitant respiratory disease (OR = 1.97, 95% CI, 1.46 – 2.67). Also, Mayo-Montero, Hernandez-Barrera, Carrasco-Garrido et al. (2007) observed that people with chronic respiratory disease who had a concomitant disease were significantly more likely than those without concomitant diseases to have received influenza vaccination (OR = 1.21, 95% CI, 1.03 – 1.50). The same results were obtained for people with chronic bronchitis; more patients with chronic bronchitis who had concomitant asthma or diabetes tended to be immunised than those without these concomitant diseases (asthma: OR = 1.45, 95% CI, 1.11 – 1.90; diabetes: OR = 1.54, 95% CI, 1.08 – 2.19).

An explanation related to the higher rate of influenza vaccination in people with chronic medical conditions may be because these high-risk individuals considered themselves as being in poor health and more frequently visited physicians; thus providing more opportunity to be immunised against influenza (Kohlhammer, Schnoor, Schwartz et al., 2007).

4.4.3 Beliefs, knowledge and attitude about influenza and the influenza vaccine

Individual-level factors such as knowledge, attitude towards and beliefs about influenza and influenza vaccine have been found to have a significant influence on the decision to receive influenza vaccine (Honkanen, Keistinen, & Kivela, 1996; Gosney,

2000; Santibanez, Nowalk, Zimmerman et al., 2002; Takahashi, Noguchi, Rahman,et al., 2003; Zimmerman, Nowalk, Raymund et al., 2003; Chi & Neuzil, 2004; Nowalk, Zimmerman, Shen et al., 2004; Brunton, Weir, & Jennings, 2005; Adonis-Rizzo & Jett, 2007; Keenan, Campbell, & Evans, 2007; Lyn-cook, Halm, & Wisnivesky, 2007; Kwong, Lam, & Chan, 2009). In the United States, Santibanez, Nowalk, Zimmerman et al. (2002) examined knowledge and beliefs influencing the decision to get vaccinated against influenza and pneumococcal diseases. The study showed that the unvaccinated were significantly more likely than vaccinated persons to report that they did not know the symptoms of influenza. In addition, a significantly higher proportion of those vaccinated mentioned the severity of the influenza as a motivating factor for influenza immunisation (i.e. "feel so miserable, never want to get it again").

A case-control study investigating the determinants of influenza vaccine uptake among Japanese people by Takahashi, Noguchi, Rahman et al. (2003) showed that knowledge about the influenza vaccine was significantly associated with acceptance of influenza immunisation (OR = 3.06, 95% CI, 1.02 – 9.20). Additionally, a cross-sectional study that examined influenza coverage rates in former West Germany in the 1999-2000 influenza season demonstrated that the decision to be vaccinated against influenza was influenced by positive attitude towards vaccination and the belief that influenza was a severe disease (OR = 7.8, 95% CI, 1.9 – 68.9; OR = 3.1, 95% CI, 0.7 – 28.3, respectively) (Rehmet, Ammon, Pfaff et al., 2002).

Likewise, Brunton, Weir, and Jennings (2005) explored knowledge, attitude and beliefs toward influenza immunisation among the elderly (aged 65 and older) in New Zealand during the 2001-2002 influenza seasons. The study has found some significant differences in knowledge, attitude, and beliefs between the vaccinated and unvaccinated persons. These differences included: "an influenza injection will reduce your risk of becoming seriously ill from influenza and from the complications of influenza" (91 per cent vs. 45 per cent), "healthy older people are at just as much risk of getting influenza as older people with chronic illness" (54 per cent vs. 43 per cent), "people can get influenza from the flu shot" (21 per cent vs. 54 per cent), "people can get sick from the flu shot" (22 per cent vs. 52 per cent), and "I don't need an influenza injection as I rarely get sick" (5 per cent vs. 64 per cent).

Other studies have also shown that positive beliefs about influenza and influenza vaccine significantly increased the likelihood of vaccination among the elderly aged 65 or older and people with chronic medical conditions aged less than 65 years, including "persons who does not get flu shot will probably get the flu" (OR = 5.4, 95% CI, 2.4 – 12.0), "flu shots are a good idea (OR = 3.4), "getting the flu shot is wise" (OR = 13, 95% CI, 6.2 – 26) "Influenza vaccination gives a good protection against the flu" (OR = 2.05, 95% CI, 1.45 – 2.89), "I would rather have a flu shot than get the flu" (OR = 2.7), "If I don't get vaccinated will probably get the flu" (OR = 3.7, 95% CI, 2.2 – 6.3) (Santibanez, Nowalk, Zimmerman et al., 2002; Zimmerman, Nowalk, Raymund et al., 2003; Chi & Neuzil, 2004; Nowalk, Zimmerman, Shen et al., 2004; Keenan, Campbell, & Evans, 2007).

In addition, a positive association between the perceived seriousness of influenza and influenza vaccine acceptance has been previously documented. For example, a study conducted in Finland by Honkanen, Keistinen, and Kivela (1996) found that when 383 elderly people were asked to express their opinion about the seriousness of influenza, 15 per cent of the 383 persons considered that influenza was a mild disease, and 33 per cent of these individuals had been immunised. Sixty-six per cent of the 383 persons felt that it was quite serious, and 52 per cent of these people had been vaccinated. Only nineteen per cent of the 383 persons thought that influenza was serious; of these, seventy per cent of these individuals reported having been immunised against influenza.

People are also more likely to vaccinate if they perceived influenza vaccine to be effective in preventing influenza and its complications. A national survey study assessing influenza vaccination coverage levels and their determinants conducted by Horby, Williams, Burgess et al. (2005) indicated that the belief that influenza vaccine was effective strongly predicted influenza immunisation in elderly Australians (aged 65 years and older) (OR = 13.5, 95% CI, 10.6 – 17.2). Gosney (2000) revealed that ninety-five per cent of vaccinated people thought that the influenza vaccine was effective in preventing influenza and its complications, compared with only 30 per cent of unvaccinated persons. Similar perceptions have been reported in other studies. These include: "vaccination prevents me from catching influenza" (OR = 12.18, 95% CI = 3.61-41.07, "If I get vaccinated, I will decrease the frequency of medical

consultation" (OR = 8.12, 95% CI, 2.70 – 24.38), "The flu vaccine can prevent influenza" (OR = 10.55, 95% CI, 3.42-32.49), and "Influenza vaccine was effective for the prevention of an asthma attack" (OR = 7.21, 95% CI, 2.25 – 23.10) (Takahashi, Noguchi, Rahman, et al., 2003; Lyn-cook, Halm, & Wisnivesky, 2007; Kwong, Lam, & Chan, 2009).

Conversely, a number of studies have shown that a perceived lack of efficacy of influenza vaccine, and that "getting a flu shot is more trouble than it is worth" (OR = 0.12, 95% CI, 0.03 – 0.45), that "the side-effects of influenza vaccination interfere with my usual activities" (OR = 0.04, 95% CI, 0.01 – 0.13), that " immunisation is inconvenient" (OR = 0.14, 95% CI, 0.05-0.36), and that "influenza vaccination is painful" (OR = 2.73, CI, 1.55 – 4.81) were significantly associated with the likelihood of not being vaccinated (Frank, Henderson, & McMurray, 1985; Armstrong, Berlin, Schwartz et al., 2001; Takahashi, Noguchi, Rahman et al., 2003; Zimmerman, Nowalk, Raymund et al., 2003; Nowalk, Zimmerman, Shen et al., 2004; Kwong, Lam, & Chan, 2009).

Additionally, the study evaluating prevalence and determinants of influenza vaccination uptake among the elderly living in the community conducted by Lau, Kim, Choi, et al. (2007) showed that the likelihood of immunisation was significantly lower among those who did not know about the duration of immunity after influenza vaccination (OR = 0.54, 95% CI, 0.30 – 1.00), and those who did not know about the place to get vaccination (OR = 0.21, 95% CI, 0.11 – 0.39). Evans and Watson (2003) also found an association between a negative view on the effectiveness and safety of the influenza vaccine and non-uptake of influenza vaccination in community-dwelling elderly people.

The research reviewed here suggests that beliefs, knowledge, and attitudes about influenza and the influenza vaccine undoubted play a significant role in the decision-making process on influenza vaccination, although other factors such as influence of others (i.e. health care providers, family and friends), cost of influenza vaccine, convenient access to vaccination services, self-perceived health status, previous experience of influenza vaccination, and the use of healthcare services also affect such decisions. These factors are discussed in subsequent sections in more detail.

4.4.4 Influence of others

Health care provider's recommendation or prompt from family/ friends has been identified as a strong predictor of influenza vaccination (CDC, 1988; Honkanen, Keistinen, & Kivela 1996; Evans & Watson, 2003; Zimmerman, Nowalk, Raymund et al., 2003; Nowalk, Zimmerman, Shen et al., 2004; Sengupta, & Strauss 2004; Tabbarah, Zimmerman, Nowalk et al., 2005; Kohlhammer, Schnoor, Schwartz et al., 2007; Lyn-cook, Halm, & Wisnivesky, 2007; Blank, Freiburghaus, Schwenkglenks et al., 2008; Lau, Lau, & Lau, 2009). According to a survey of knowledge, attitudes, and practices about influenza and pneumococcal vaccinations among the elderly aged 65 or older in DeKalb and Fulton counties, Georgia by the CDC, the strongest factor associated with influenza immunisation was a provider recommendation for vaccination. Advice from health care providers is markedly important, even among people who had a negative attitude to vaccination. The result showed that among those with negative attitudes towards influenza vaccination (such as influenza vaccine was not effective against influenza, and the vaccine was unnecessary), a significantly higher vaccination rate was found among those whose health care providers strongly recommended the vaccine as compared to those whose health care providers did not so recommend (prevalence ratio = 10.8, 95% CI, 7.3 – 16.0) (CDC, 1988).

Honkanen, Keistinen, and Kivela (1996) has also documented this phenomenon among Finnish people; the information received from health visitors contributed to increasing influenza vaccine acceptance, even among those with an unfavourable attitude to vaccination. A further study exploring the determinants of non-vaccination among the elderly aged 65 and older conducted by Nowalk, Zimmerman, Shen et al (2004) showed that a belief that "my doctor thinks I should get the flu shot" was significantly associated with a greater likelihood of being immunised (OR = 11.4, 95% CI, 3.9 – 33.3). Additionally, Zimmerman, Nowalk, Raymund et al. (2003) found that a large percentage of the people who reported having been vaccinated were influenced by advice or information provided by a health professional (98 per cent vs. 63 per cent). The results of this study confirmed that a strong association existed between the likelihood of vaccination and provider recommendation on influenza immunisation (OR = 6.4, 95% CI, 2.5 – 17).

Sengupta, and Strauss, (2004) interviewed 28 non-institutionalised elderly aged 65 and older in North Carolina, and found that a reminder from physician to get vaccinated against influenza and the perceived effectiveness of the influenza vaccine were identified as important facilitators of influenza vaccination.

Similar results were seen in the study by Tabbarah, Zimmerman, Nowalk et al. (2005) that investigated the predictors of influenza vaccination across three influenza seasons (2000-2001 to 2002-2003). The study found that the decision about influenza immunisation was strongly affected by advice from health care providers, family members or friends, together with perceived risk for influenza (OR = 15.03, 95% CI, 5.53 – 40.85).

Other studies have also shown that provider recommendation was found to be strongly predictive of influenza vaccination (Evans & Watson, 2003; Kohlhammer, Schnoor, Schwartz et al., 2007; Lyn-cook, Halm, & Wisnivesky et al., 2007; Lau, Lau, & Lau, 2009). Perenboom and Davidse (1996) demonstrated the value of personal invitation by the general practitioner in promoting influenza vaccination uptake in the Netherlands, showing that influenza vaccination coverage rates increased from 42 per cent to 75.5 per cent. This study confirms that recommendation or reminder from the health care provider strongly influences older people's decisions to be vaccinated.

On the other hand, a lack (or perceived lack) of recommendations from health care providers has been found to correlate with lower acceptance of vaccination against influenza (Fiebach &Viscoli, 1991; Nichol & Zimmerman, 2001). Fiebach and Viscoli (1991) investigated the factors related to non-acceptance influenza vaccine among elderly people aged 65 years or older. The results of this study revealed that the likelihood of non-vaccination was 5.8 times higher for people who reported that their providers had not recommended influenza vaccine compared with those whose health care providers recommended it (OR = 5.8, 95% CI, 2.5 – 13.2). The study that examined factors associated with non-vaccination by Evans and Watson (2003) also found that lack of advice from a doctor or nurse predicted the non-uptake of influenza vaccination in community-dwelling elderly people.

Additionally, Evans, Prout, Prior et al. (2007) conducted 54 in-depth interviews with people aged 65 and older regarding their lay beliefs about influenza vaccination in South Wales, United Kingdom. The authors found that six vaccine defaulters and four vaccine refusers would be vaccinated against influenza if the General Practitioners (GPs) recommended that they should get influenza vaccine. More recently, a study examining influenza vaccination coverage trends 2001-2002 to 2006-2007 in the UK also showed that no recommendation from health care providers was cited as the most important reason for non-compliance with influenza vaccination (Blank, Freiburghaus, Schwenkglenks et al., 2008).

In reviewing the research on determinants of influenza vaccination, several large-and medium-scale studies emphasised a health care worker's recommendation, especially the recommendation of a doctor, as a key factor influencing uptake. Thus, doctors and other healthcare workers have a substantial opportunity to improve influenza vaccination coverage by providing clear information about influenza and the benefit of vaccination to their patients and actively promoting influenza vaccination programmes.

In addition to the influence of health care professionals, family or friends appeared to influence the decision to be vaccinated among older people. The study by Takahashi, Noguchi, Rahman et al. (2003) found that the recommendation by a family member and /or a close friend was significantly associated with the acceptance of influenza vaccination among Japanese patients (OR=17.74, 95% CI, 1.95-161.7). Similarly, the study assessing prevalence and determinants of influenza vaccination among non-institutionalised elderly people conducted by Lau, Lau, and Lau (2009) indicated that the elderly were more likely to receive influenza vaccine if they receive a prompt about influenza vaccination from family members or friends (OR = 3.02, 95% CI, 1.61 – 5.68).

Other studies have also shown that encouragement from family and friends had a significant impact on influenza immunisation uptake (Zimmerman, Nowalk, Raymund et al., 2003; Tabbarah, Zimmerman, Nowalk et al., 2005; Nowalk, Zimmerman, Tabbarah et al., 2006). In contrast, a British study that examined the influenza vaccination rates and determinants of non-compliance with influenza

vaccination among the elderly living in the community by Evans and Watson (2003) found that the advice from friends was associated with a lower likelihood of being vaccinated; the elderly who had received advice from friends were less likely to receive the influenza vaccine than those who reported that they did not receive advice from friends (OR = 0.4, 95% CI, 0.2 – 0.7). Some studies conducted in the US and other western countries also found that advice from family and friends was not significant predictor of influenza vaccination (Nicholas, Fiebach, Catherine et al., 1991; Nichol, Mac Donald, & Hauge, 1996; van Essen, Kuyvenhoven, & de melker, 1997).

The influence of family and friends has been shown to have a positive effect on older people's decisions about whether or not to receive the influenza vaccine in some countries, and this effect appears to be strong in Chinese and Japanese culture (Takahashi, Noguchi, Rahman et al., 2003; Lau, Lau, & Lau, 2009). Therefore, it is reasonable to take this factor into account when developing strategies for promoting influenza vaccination.

4.4.5 Accessibility factors

The accessibility factors include the cost of influenza vaccine and convenient access to vaccination services. Previous studies have shown the importance of accessibility factors in predicting influenza immunisation (Nexøe, Kraqstrup, & Sogaard, 1999; Burns, Ring, & Carroll, 2005; Lau, Kim, Choi et al., 2007). In Denmark, the likelihood of getting vaccinated against influenza was higher among the elderly who lived in Copenhagen where influenza vaccines were offered free-of-charge (OR = 6.17, 95% CI, 3.20 – 11.90) (Nexøe, Kraqstrup, & Sogaard, 1999).

The study conducted by Kroneman, Paget, and van Essen (2003) indicated that countries that provided free influenza vaccines for the elderly achieved higher rates of influenza vaccination than other countries where co-payment systems have been implemented. In addition, one study conducted in the United States has shown that health insurance was a significant predictor of influenza immunisation, especially among adults aged less than 65 years (Figaro & Belue, 2005). A further study that explored prevalence and factors associated with influenza vaccination among non-

institutionalised elderly people in Hong Kong by Lau, Lau, and Lau (2009) also showed that "consideration of vaccination if all people aged 65 or above were eligible to receive free vaccination" significantly predicted influenza vaccination (OR = 3.02, 95% CI, 1.5 – 6.08).

Convenient access to vaccination service was also found to be associated with influenza vaccination (Nichol, Lofgren, & Gapinski, 1992; Burns, Ring, & Carroll, 2005). Burns, Ring, and Carroll (2005) examined factors related to influenza vaccination uptake among elderly people living in the community. The results of this study showed that having a car or being able to walk to the vaccination clinic increased the likelihood of receiving an influenza vaccine (OR = 1.67, 95% CI, 1.00-2.78). On the other hand, a survey study of influenza vaccination among high-risk outpatients by Nichol, Lofgren, and Gapinski (1992) revealed a lower probability of being vaccinated among people who reported difficult access to services (OR = 0.42, 95% CI, 0.31 – 0.57).

Other studies have found the correlation between size of living residence and influenza vaccination rates (Jimenez, Larrauri, Carrasco-Garrido et al., 2003; de Andres, Carrasco-Garrido, Hernandez-Barrera et al., 2006). The study investigating factors associated with influenza vaccination coverage among individuals aged 50-64 years conducted by Jimenez, Larrauri, Carrasco-Garrido et al. (2003) has shown that persons who lived in small towns with less than 10000 inhabitants were more likely to receive influenza vaccination as compared to those living in a town or city with more than 100,000 inhabitants (OR = 1.45, 95% CI, 1.01-2.10).

Two further studies conducted in Spain yielded similar results; a survey study among people with chronic obstructive pulmonary disease has shown that living in a small town (< 10,000 inhabitants) was significantly associated with the highest likelihood of vaccination (OR= 1.65, 95% CI, 1.42 – 1.92) (Jimenez-Garcia, Mayo-Montero, Hernandez-Barrera et al., 2005). The study of trends in influenza vaccination coverage rates in Spain from 1993 to 2003 conducted by de Andres, Carrasco-Garrido, Hernandez-Barrera et al. (2006) also found that residence in towns with less than 10000 increased the odds of receiving influenza vaccination (OR = 1.36, 95% CI, 1.16 – 1.59).

In the United States, one study examined the use of preventive health care services between rural and urban elderly residents. The study showed that for influenza vaccination, a higher vaccination rate was found for rural residents as compared to those living in the urban areas, although the difference did not reach statistical significance (58 per cent vs. 55 per cent) (Zhang, Tao, & Irwin, 2000). It was suggested that the close proximity and convenient access to an immunisation clinic might contribute to differences in influenza vaccination rates between sizes of living residence (Jimenez, Larrauri, Carrasco-Garrido et al., 2003; de Andres, Carrasco-Garrido, Hernandez-Barrera et al., 2006).

4.4.6 Health beliefs and behaviours

4.4.6.1 Self-perceived health status

A number of research studies suggested that the decision to vaccinate has been depended on individuals' perceptions of their own health. Self-perceived health status can have a positive or negative influence on the decision about influenza vaccination (van Essen, Kuyvenhoven, & de Melker, 1997; Cornford & Morgan, 1999; Evans & Watson, 2003; de Andres, Carrasco-Garrido, Hernandez-Barrera et al., 2006; Chen, Yi, Wu et al., 2007; Evans, Prout, Prior et al., 2007; Chiatti, Rosa, Barbadoro et al., 2010).

In the Netherlands, the study examining the factors related to non-compliance with influenza immunisation among elderly people conducted by van Essen, Kuyvenhoven, and de Melker, (1997) showed that those who considered themselves to be healthy were less likely to have influenza vaccine compared to those who perceived themselves to be in poor health (OR = 57.9, 95% CI, 4.4 – 770). Evans, Prout, Prior et al. (2007) carried out a qualitative study of 54 elderly people aged 65 years or older. The authors found that both vaccinated and unvaccinated did not perceive themselves to be at risk of getting influenza and developing its serious complications. They believed that although they got influenza, they were unlikely to suffer from any serious consequences. Thus, they did not feel that they needed influenza vaccine. In this study, the authors have pointed out that other factors such as individual prompts by GPs appeared to be an important motivator to obtain influenza vaccination.

Other studies have also documented this phenomenon. For example, a qualitative study using semi-structured interviews with 25 immunised and 25 unimmunised individuals aged over 75 years conducted by Cornford and Morgan (1999), revealed that most older people viewed themselves as healthy and remained active and independent despite having a chronic disease. They did not feel at severe risk of influenza, and therefore the perceived need for influenza vaccination was low among these high-risk individuals. Colley (2008) interviewed 12 older people with a long-term condition, and found that four unvaccinated people did not consider themselves as being in one of the high-risk groups for which influenza vaccination was strongly recommended.

A small study to examine health beliefs about influenza immunisation among Chinese older people aged 65 years or older conducted by Kwong and Lam (2008), also found that most older people (74.3 per cent) felt that they were in good or very good health, and eighty-three per cent of the total sample (n = 70) thought that their chances of catching influenza were relatively low. In addition, other strategies such as using traditional Chinese medicine (herbal tea and soup), staying warm, and avoiding cold drinks and food were perceived to be effective in preventing influenza. The study concluded that perceived good health and the perceived effectiveness of the traditional medicine and other measures adopted for the prevention and cure of influenza were the most important reasons for non-compliance with influenza vaccination among unvaccinated persons.

Moreover, a survey study to assess trends in influenza vaccination coverage rates in Canada by Johansen, Sambel, and Zhao (2006) found that 66 per cent of elderly people who had not been vaccinated in the previous year stated that they thought influenza vaccine was unnecessary, either because of their own judgment about their health or health care provider's attitudes regarding influenza vaccination for elderly.
Conversely, in the study of Chen, Yi, Wu et al. (2007), adults who reported poor general health were 2.5 times more likely to be immunised against influenza, as compared with those who reported very good or excellent health (OR = 2.49, 95% CI, 2.23 – 2.79). This is supported by the study of de Andres, Carrasco-Garrido, Hernandez-Barrera et al. (2006) in which the likelihood of being vaccinated was

higher in people who had a negative perception of their general health, as compared to those with a positive perception of their health (OR = 1.24,95% CI, 1.07 – 1.46).

Recently, a national survey examining the influenza vaccination coverage levels over four influenza seasons and factors associated with influenza vaccination uptake in Spain carried out by Mayo-Montero, Hernandez-Barrera, Carrasco-Garrido et al. (2007) also found that in persons with chronic respiratory diseases, poor perception of health increased the odds of vaccination among these high-risk individuals (OR = 1.40, 95% CI, 1.14 – 1.72).

Similar results were observed by Chiatti, Rosa, Barbadoro et al. (2010) who investigated the socio- economic effects on influenza vaccination uptake among older Italians aged 65 years and older. The study revealed that lower influenza vaccination rates were associated with self-perceived good health; older people who reported being in good health were significantly less likely to be immunised than those who reported being in fair health (OR = 0.73, 95% CI, 0.68 – 0.76).

Results from previous research have indicated that perceived "good health" was associated with vaccine non-compliance in high-risk older people. Therefore, healthcare workers should pay more attention to those people who consider themselves to be healthy and provide them with more information about the risk of influenza and serious influenza-related complications, emphasising that influenza vaccination is recommended for all high-risk individuals, regardless of their general health status. This may help to improve influenza vaccination for this particular group.

4.4.6.2 Previous experience of influenza-like illness or the influenza vaccination

Apart from self-perceived health status, several studies have shown that previous experience of influenza-like illness or influenza vaccination appeared to be a powerful predictor of influenza immunisation (Kee, Lee, Cheong et al., 2007: Davis, Fujimoto, Chan et al., 2009; Li & Liu, 2009). A survey study exploring barriers and facilitators of influenza vaccination conducted by Kee, Lee, Cheong et al. (2007), showed the relationship between having been vaccinated in the previous year and the higher odds

of obtaining the influenza vaccination; older people who had been vaccinated in the previous year were significantly more likely to be immunised against influenza in the following year than those unvaccinated (OR = 17.94, 95% CI, 13.21 – 24.37).

This is supported by the study of Li and Liu (2009), which showed that the likelihood of getting vaccinated increased if people had been vaccinated in the previous season. The elderly who had previously been vaccinated were ten times more likely to be immunised than those who were unvaccinated (OR = 10.22, 95% CI, 9.82-10.64).

Other studies conducted in the United States and Australia, have also found that prior immunisation with influenza vaccine led to an increase in the probability of getting vaccinated for the next influenza season (odds ratio range 5.9 to 10) (Lewis-Parmar & McCann, 2002; Davis, Fujimoto, Chan et al., 2009). One possible explanation for a higher rate of influenza vaccination among those who had been repeatedly vaccinated may be that having received an influenza vaccination has become part of their healthy lifestyle behaviours. These individuals were therefore more willing to get vaccinated annually (Gallagher & Povey, 2006).

Telford & Rogers (2003) interviewed 20 people aged 75 or older, and found that either personal experience with influenza vaccination or others' experience with influenza or the influenza vaccination could have both positive and negative influence on the decision of whether to vaccinate, depending on what experience people have had. The authors noted that lay experience and personal perceived risk from influenza appeared to have great influence on the likelihood of vaccination.

In addition, a survey study among community dwelling adults in South Korea conducted by Kee, Lee, Cheong et al. (2007) has also shown that those who had an experience with influenza-like illness were two times more likely to be vaccinated against influenza (OR = 2.30, 95% CI, 1.33 – 3.99). In contrast, a lack of experience with influenza vaccination or influenza-like illness, or knowing someone who had had a negative experience with influenza immunisation, or listening to people who claimed that influenza vaccine gave them an influenza has been found to be associated with non-acceptance of influenza vaccine (Telford & Rogers, 2003; Sengupta & Strauss, 2004).

4.4.6.3 Use of healthcare service

Previous studies have shown that the use of healthcare service was positively associated with higher rates of influenza vaccination among older people. A population-based survey study conducted in Switzerland demonstrated that the higher the number of physician visits, the greater the likelihood of being vaccinated; the odds ratio for people with at least one physician visit, and those who had seen a physician twice or
more were 2.52 (95% CI, 2.05 – 3.10), and 4.51 (95% CI, 3.65 – 5.57), respectively (Luthi, Mean, Ammon et al., 2002). In former West Germany, a cross-sectional survey assessing influenza vaccination coverage levels during the year 1999-2000 conducted by Rehmet, Ammon, Pfaff et al. (2002) also found that individuals who had visited a physician during the autumn were more likely to be immunised than those who had not seen a physician (OR = 4.4, 95% CI, 2.2 – 9.6). Furthermore, in this study, physician's advice regarding immunisations during consultation increased the probability, 13.5-fold, of people reporting have been immunised (OR = 13.5, 95% CI, 6.7 – 27.9). Other studies have also shown that a visit or a consultation with health care professionals increased the likelihood that an older adult would receive the influenza immunisation (Stehr-Green et al., 1990; Davis, Fujimoto, Chan et al., 2009; Li & Liu, 2009; Jimenez-Garcia, Hernandez-Barrera, de Andres et al., 2010).

Similar results were observed for individuals with chronic medical conditions. The study of influenza immunisation among people with chronic obstructive pulmonary disease in Spain has also shown that the probability of getting vaccinated increased with a greater number of general practitioner (GP) visits in the preceding 12 months; those who had visited a physician more than ten times had the highest likelihood of receiving the influenza vaccination (OR = 2.78, 95% CI, 2.26 – 3.43), and the adjusted odds ratio of having been vaccinated were 2.15 (95% CI, 1.83 – 2.52), and 1.79 (95% CI, 1.54 – 2.08) for those who had visited their GP six to ten times, and three to five times, respectively (Jimenez-Garcia, Mayo-Montero, Hernandez-Barrera et al., 2005). A further study of influenza immunisation among diabetic patients has also shown that those who reported seeing a physician during the influenza season were more likely to have been immunised (OR = 1.46, 95% CI, 1.12 – 1.96) (Jimenez-Garcia, Jimenez, Carrasco-Garrido et al., 2008)

On the other hand, older people who had less contact with health care providers were less likely to obtain an influenza vaccination. In Spain, a survey study conducted by Sarria-Santamera and Timoner (2003) has shown that older adults who had not visited their health care providers more than six months since the last clinic visit were more likely to be associated with non-acceptance of influenza vaccination (OR = 2.13, 95% CI, 1.52 – 2.98). Recently, Bryant, Ompad, Sisco et al. (2006) also found that the likelihood of obtaining influenza vaccination was significantly lower among those who did not have access to routine medical care (OR = 0.51, 95% CI, 0.34 – 0.76).

4.5 Conclusion

In summary, researchers have found a number of mismatches between many professionals and lay perceptions of influenza, its symptoms and causes, as well as its consequences (McCombie, 1987; Baer, Weller, Pachter et al., 1999; Telford & Rogers, 2003; Adonis-Rizzo & Jett, 2006; Prior, Evans, & Prout, 2011). Mistrust of the vaccine contents, anecdotal stories of previous bad experiences with vaccination, fear of adverse reactions, and the belief that influenza vaccination causes other serious health problems have also been found to be associated with the low acceptance of influenza vaccine (Findlay, Gibbons, Primrose et al., 2000; Armstrong, Berlin, Schwartz et al., 2001; Adonis-Rizzo & Jett, 2006; Evans, Prout, Prior et al., 2007; Wray, Jupka, Ross, 2007). In addition to lay beliefs about influenza and influenza vaccine, the existing literature on determinants of influenza vaccination has indentified a variety of individual and social factors that may affect the influenza vaccine uptake. Although these studies vary in terms of design quality, data collection and analysis methods, the extant body of research literature on this topic provides enough information to indicate that decisions whether or not to receive influenza vaccination are complex, and influenced by several medical, psychological and social factors, including the knowledge, attitude and beliefs about influenza and influenza vaccination, perceived risk of contracting influenza, health status, health beliefs, concerns about the efficacy and side effects of vaccine, previous experience of influenza vaccination, the influence of others (healthcare workers, family members and friends), and the costs and convenience of obtaining the vaccination (e.g. Telford

& Rogers, 2003; Sengupta & Strauss, 2004; Burns, Ring, & Carroll, 2005; Jimenez-Garcia, Hernandez-Barrera, Carrasco-Garrido et al., 2006; Evans, Prout, Prior et al., 2007; Chen, Yi, Wu et al., 2007; Lau, Lau, & Lau, 2009; Payaprom, Bennett, Burnard et al., 2010).

These factors provide a number of targets for any public health programme designed to increase uptake of influenza vaccine. However, the degree of influence of these factors may vary widely between individuals and populations. Identifying factors underlying people's vaccination decisions is an essential first step in the development of a tailored intervention to raise influenza vaccination rates among high-risk groups. Accordingly, the present study sought to explore Thai older people's beliefs about influenza and influenza vaccination, and other factors that influence their decisions whether or not to accept the influenza vaccination (study 1). The study's findings were then used to inform the development of the HAPA-based educational leaflet and questionnaire for study two. In the following chapter, the methodology and the results of the research will be presented.

Chapter 5: Understandings of influenza and influenza vaccination among high-risk urban dwelling Thai adults

5.1 Introduction

This study employed qualitative methods, drawing on a grounded theory approach to explore people's beliefs about influenza and influenza vaccination, and to examine factors influencing urban-dwelling Thai adults' decisions whether or not to have the vaccine. In this chapter, the methodology and procedures used in this study are described. This includes an overview of qualitative approach and the rationale. The chapter also provides information about the setting, participants, and details on data collection and analysis. The findings of the study are reported. Following this, the discussion of findings and implications for clinical practice are provided. Finally, a conclusion is outlined.

5.2 Qualitative approach

Qualitative research uses an interpretive approach to social reality (Denzin & Lincoln, 2005; Holloway, 2005; Yin, 2010). A qualitative research method provides an in-depth description of a phenomenon being studied. One of the major purposes of qualitative research is to understand the phenomenon of interest from the participants' perspectives.

Accordingly, the events or ideas emerging from research findings explore the meanings given to real-life events by the participants, not meanings held by the researchers (Creswell, 1998; Yin, 2010). The purpose of this study was to explore people's beliefs about influenza and influenza vaccination and to identify factors influencing urban-dwelling Thai adults' decisions whether or not to receive influenza vaccine. A qualitative research methodology was chosen for this study because it attempts to make sense of, or interpret phenomena from the participant's perspective (Denzin & Lincoln, 2005). Thus, it allows for the exploration of participants' beliefs about influenza and influenza vaccine, as well as the influences on their decisions of

whether to accept or refuse the influenza vaccination. Additionally, Strauss and Corbin (1998, p. 11) also pointed out that "qualitative methods can be used to obtain the intricate details about phenomenon such as feelings, thought processes, and emotions that are difficult to exact or learn about through more conventional research methods". In other words, a qualitative approach may produce greater depth and breadth of information on complex issues, rather than conventional research methods. Data from a number of studies (e.g. Cornford & Morgan, 1999; Telford & Roger, 2003; Zimmerman, Nowalk, Raymund et al., 2003) conducted in western countries indicates that the decisions whether or not to receive influenza vaccine are complex, and influenced by many factors. Accordingly, a qualitative approach was used for the present study to get an in-depth understanding of the factors underlying people's vaccination decisions to create an effective influenza vaccination programme.

5.3 The rationale for choosing grounded theory method

Within the qualitative paradigm, there are many approaches that could have been used to inform the data collection and analysis (Creswell, 1998; Denzin & Lincoln, 2005). In this study, in-depth interviews were considered as appropriate methods. In-depth interviews permit the researcher to gain access to the participant's perspective (Patton, 2002; Charmaz, 2006). Therefore, the interviewer's questions ask the participants to describe their beliefs or express their views in their own words. This involves using a flexible technique that allows the important ideas and issues to emerge naturally during the interview (Patton, 1987; Kvale, 1996; Charmaz, 2006). In-depth interviews can also be useful tool for exploration of complex topics and sensitive experiences, which may not be possible through other data collection methods such as survey (Taylor, 2005; Charmaz, 2006). According to Jones (1985, p. 46), "To understand other persons' constructions of reality we would do well to ask them (rather than assume we know merely by observing their overt behaviour) and ask them in such a way that they can tell us in their terms (rather than those imposed rigidly and *a priori* by ourselves)". Therefore, an in-depth interview was the method used to collect data.

In addition, a grounded theory approach was particularly suitable for exploring and gaining insights into a previously unknown area (Glaser & Strauss, 1967). In

Thailand, to our knowledge, no studies to date have examined people's beliefs about influenza and influenza vaccination. Therefore, the focus of this study fitted this criterion. Although the main purpose of grounded theory is the generation of theory from the data, it can also be used to explore and understand how complex phenomenon occurs (Willig, 2001; Corbin & Straus, 2008). According to Glaser (1987), grounded theory, unlike other qualitative research methods, not only provides meaning, understanding and description of the phenomenon under study, but is also theory-generating. Central to this study is the understanding of people's beliefs about influenza and influenza vaccination and identification factors influencing the decision whether or not to get the influenza vaccine among high-risk Thai individuals. Thus, a grounded theory approach was drawn on the exploration of the complexity of personal decision-making in influenza vaccination. The study findings could then inform the development of effective interventions to encourage uptake of influenza vaccination by such high-risk individuals.

5.4 Methodology

5.4.1 Setting and participants

The study was conducted in the Muang district, an urban community of Chiang Rai province with a population of 223, 936. Chiang Rai is the northernmost province of Thailand and has an adult literacy rate of 93 per cent (National Statistical Office, 2006). This study was approved by the research ethics committee, Chiang Rai Province, Thailand.

The study population was adults who were either (i) aged 65 and over, or (ii) under 65 years with chronic diseases with clinical indications requiring influenza vaccination such as coronary heart disease, chronic pulmonary disease, asthma and diabetes mellitus. Potential participants were selected from one health centre's database. The selected participants were determined by the emerging concepts, and evolving data analysis informed each subsequent interview. Their medical records were scrutinized to confirm the suitability of participants for interview. Those with severe chronic conditions (i.e. bed bound or acutely ill), severe mental health problems, or communication difficulties were excluded. Letters of introduction were sent to 30 potential participants: fifteen letters in each group. Twenty potential individuals

agreed to participate; a response rate of 66.7 per cent. These individuals were contacted by the researcher and gave informed consent to participate in the study.

5.4.2 Interviews

In-depth interviews were conducted between February and March 2008, either in participants' homes or at a health centre depending on their preference. On each occasion, written consent was obtained before the interview. A semi-structured schedule was used to guide the interviews (see Appendix 6). It explored participants' understandings of influenza and influenza vaccination, and factors that may influence their decision whether to accept or decline the influenza vaccination in the forthcoming vaccination period. Interviews lasted between 30 and 60 minutes, and were tape-recorded with the permission of interviewees.

5.4.3 Data analysis

The interviews were fully transcribed in Thai language and analysed following the grounded theory approach (Strauss & Corbin, 1998). The data analysis was based on the constant comparative method. After data (one interview) were collected and transcribed, the first transcript was read thoroughly a number of times and analysed line-by-line, closely examined and compared for similarities and differences, then code concepts were developed. The coded concepts described the main idea of what the participants stated. During coding of data and constant comparative analysis, emerging concepts from the data determined what kinds of data would be sought next. As more data were examined, the coded concepts were revised and cross-referenced with the data as a whole, and similar code concepts were grouped together. The analysis process continued, similarities and differences were identified and the cluster codes that seem to fit together (similar or related properties) were further grouped into categories. At this stage, categories were developed and linked with subcategories (Strauss & Corbin, 1998).

In this study, all the transcripts were coded in Thai by two researchers (Y. P. and H. T. who is an internist and has social sciences training) to increase reliability, and the discrepancies in coding were resolved through discussion; both researchers

performed open coding separately. Additionally, two participants who could correctly verify the texts transcribed from their interviews were asked to validate their contribution and provided feedback. The sampling method achieved data saturation with respect to our research objectives; the evolving analysis informed the subsequent data collection. This process continued until new data did not add to the insights already gained (or no new categories emerged) (Corbin, 1986; Strauss & Corbin, 1998; Charmaz, 2006). After extensive data analysis, the transcripts were translated into English and back-translated into Thai language by an independent translator. The back-translated transcripts were then compared with the original, and the points of divergence were noted and corrected to more closely reflect the meaning of the original Thai language. The English translation of transcripts is reported here.

5.5 Findings

In total, 20 community dwelling Thai adults were interviewed: 11 aged ≥ 65 years and nine aged < 65 years with chronic diseases. The mean age was 64.9 years, with the oldest participant being 75 years old. The study population presented a range of socio-demographic characteristics, including age, gender, and socio-economic status. There were eleven female participants and nine male participants. All men were married, whereas the majority of women were widowed. Twelve of participants had completed primary school (6 years of schooling), four had completed secondary school, two had attainted vocational/technical programmes, and two had no formal education. While the majority of older people aged ≥ 65 were unemployed, most individuals aged < 65 with chronic disease had occupations (such as merchant, farmer, and labourer). All participants lived with others. The study also included both takers and non-takers of influenza vaccination as well as those who had experienced influenza illness and those who had not. As such, the study population may be considered to reflect a variety of different views, beliefs and experiences regarding influenza and influenza vaccination (see Table 5.5.1).

Table 5.5.1 Demographic characteristic of participants

Age	Sex	Marital status	Educational Level	Occupation	Living arrangements	Health problems	Had flu in the past	Immunisation status
72	F	Married	Primary school	None	Children and spouse	None	No	never
60	F	Widowed	Primary school	None	Children	Diabetes	No	never
58	F	Widowed	Primary school	Merchant	Children	Asthma	Yes	never
60	M	Married	Primary school	Farmer	Children and spouse	COPD	No	immunised
75	M	Married	Primary school	None	Children and spouse	None	No	never
69	F	Married	Secondary school	Merchant	Spouse	None	No	immunised
66	M	Married	Primary school	Labourer	Children and spouse	None	No	never
56	M	Married	Primary school	Merchant	Spouse	Diabetes	No	never
54	M	Married	Secondary school	Labourer	Children and spouse	Diabetes	Yes	never
61	M	Married	Primary school	Labourer	Children and spouse	COPD	Yes	immunised
65	M	Married	Vocational/Technical	Labourer	Children and spouse	None	No	never
70	F	Widowed	None	None	Children	None	Yes	never
52	F	Married	Primary school	Merchant	Children and spouse	Diabetes	No	never
72	F	Married	Vocational/Technical	Pensioner	Children and spouse	None	No	immunised
73	M	Married	Secondary school	Pensioner	Children and spouse	None	Yes	immunised
61	F	Married	Secondary school	Pensioner	Spouse	Asthma	No	immunised
62	F	Widowed	Primary school	None	Children	Diabetes	No	never
74	F	Widowed	None	None	Children	None	No	never
70	M	Married	Primary school	None	Children and spouse	None	No	never
69	F	Widowed	Primary school	None	Children	None	No	never

Two major themes emerged from the data (see Table 5.5.2), and under these all of the data collected were supported.

Table 5.5.2 Emerged themes and their subcategories

Categories	**Subcategories**
Understanding of influenza and influenza vaccination	- Knowledge of influenza and influenza vaccination - Source of information
Factors affecting decision-making in influenza vaccination	- Salience of risk - Influence of others - Perception of the need for preventive health care - Availability

5.5.1 Understanding of influenza and influenza vaccination

5.5.5.1 Knowledge of influenza and influenza vaccination

Participants were asked to explain what they understood influenza to be. Most of them reported that they knew little about influenza, and they did not know how to describe it. In terms of its cause, a number of participants thought influenza was associated with the changes of weather, particularly from rainy to winter season, while only one person stated that influenza was caused by 'germs'. A few participants aged less than 65 years with chronic diseases thought that their underlying diseases placed them at increased risk for influenza.

> *"It's easy for me to catch the flu because my resistance is down. I have lung disease also the changing the weather is a contributing factor"* Mr. K. (ID 10), p.2

In addition, some participants reported they did not consider that influenza was a communicable disease.

> Interviewer: - *"If one of this house members catches flu, do you think you may catch it from him?*
> Mr. N.:- *"No, I have not heard that influenza is a contagious disease...you can get ill from other people only in case of common cold."*
> Mr. N. (ID 7), p.1

With regard to the symptoms of influenza and its seriousness, most participants confused the symptoms of the common cold and other respiratory illnesses with influenza.

> *"When you have flu, you have a fever, sneezing, runny nose with watery secretions during the first few days, then these become thick and dark mucus, and you also feel headache...flu is more serious than a cold"*
> Mrs. J.T. (ID 20), p. 2

Although they considered influenza to be a serious health problem, only few participants felt that it could cause death.

> *"Haemorrhagic fever can kill you, but not influenza"* Mr. N. (ID 7), p 1

and:

> *"It's possible that flu can make elderly people very ill and even cause death because they have weak immune system.* Mr. Y. (ID 4), p.2

and:

> *"If you are not cured in time, you may die of influenza. However, I haven't heard of people dying of it."* Mr. C. (ID 8), p. 2

Participants were asked how they protected themselves from getting influenza. Almost all participants proposed general protective measures to avoid influenza. Few participants mentioned getting influenza vaccine. Others had different strategies:

> *"...I walk around the house for 5 rounds in the evening every day. When the weather is cold, I shower with lukewarm water. I also drink lukewarm water."* Mrs. V (ID 13) p.1

and:

> *"I work a little at home which to me is an exercise, I keep myself warm in cold weather. On the day I feel hot and cold; I go to bed early, so I get enough rest, and my daughter, she is a nurse, suggested me to get the flu shot."* Mr. M, (ID 15), p. 2

In summary, most participants were not appropriately knowledgeable about influenza; influenza was frequently associated with the changes of weather rather than a virus. Many participants commonly confused influenza with the common cold or other upper respiratory diseases. They generally stated that influenza was more debilitating than the common cold. Significantly, the majority of participants did not consider influenza to be a potentially deadly disease.

When participants were asked whether they knew about the influenza vaccination, most participants reported that they knew little or nothing about it. In other words,

lack of knowledge about influenza vaccine was clearly evident among our participants. A typical comment was:

> "*I had heard about the vaccine for children. Is there the influenza vaccine for elderly people? Well, I have not heard of it"* Mrs. V, (ID 13), p.3

and:

> "*Nobody probably knows about the vaccine. Only the village health volunteers probably know about it."* Mr. D, (ID 9), p. 3

Participants were also asked "How effective do you think that a flu shot will protect you from getting the flu?" The majority of participants reported that they did not know how effective the vaccine would be against influenza. However, a few of them expressed a positive view toward influenza vaccination. One participant stated that:

> *"When I caught influenza, I felt so sick, and I got extremely fatigued. I could not even get up as my muscle was aching. Any pain killer could not help my conditions. I think that getting the flu shot is necessary for me, and it should be 100 percent or nearly 100 percent in preventing the flu."* Mr. M. (ID 15), p. 3

Additionally, some participants had misconceptions about influenza vaccination; they believed that it could also prevent them from catching a cold. One participant mentioned that influenza vaccine would seriously weaken her immune system.

> *"After received it* [influenza vaccination], *I have not been ill. Previously, if a person who got cold sneezed or coughed toward me, I would certainly catch a cold."* Mr. K. (ID 10). p.4

and:

> *"In the elderly, immune systems are not as strong as in younger. If I get a flu shot, it may weaken my immune system."* Mrs. R. (ID 1), p 3.

Interestingly, vaccine side-effects were not a substantial barrier to vaccination for our participants. Most felt that these were not a major concern for them. They thought

that any side-effects would be the same as other vaccines. However, a few participants stated that they needed to be reassured that the vaccine was safe.

> *"I probably will have a fever for a few days* [after vaccination], *like when I was young"*, Mrs. P. (ID 12), p. 3

and:

> *"It's the same as other vaccine injection. If the public health staffs give the elderly people more information, there should not be any problem"*
> Mr. Y, (ID 4), p. 5.

and:

> *"Few people may have* [concerns about side effects of vaccine]. *However, if the vaccine comes from the public health staff, and the information is provided on vaccine safety, these should help lessen the people's concerns"*
> Mr. S.T. (ID 11), p. 4

5.5.5.2 Source of information

Participants were asked whether they had ever had influenza and how they had learned about the condition. A number of participants reported that they had had influenza at some time in the past. Other participants had heard about influenza from others.

> "[I've heard] *from elderly people. Now, less people catch It* [influenza]. *I have rarely heard of someone catching it."* Mr. N. (ID 7), p.1

and:

> *"It has been a long time since I heard people talking about it* [influenza].
> Mrs. V. (ID 13), p.1

and:

> *"They've probably heard of influenza for a long time, but they do not understand it. And I think no one in this community remembers what the disease is."* Mr. D, (ID 9), p. 2

Additionally, four participants reported that they had received information about influenza from public media such as television and radio, but they did not get enough information about it. As for the influenza vaccination, most participants stated that

they had never heard about influenza vaccination from their healthcare providers or from public media.

> Interviewer: - *"Have you ever heard about Influenza vaccine from T.V.?"*
> Mr. Y: - *"No, just influenza"*
> Interviewer:-: *"Do you think you have received enough influenza information from TV?"*
> Mr. Y: - *"I did not receive any details from it, just got rough information."*, Mr. Y. (ID 4), p. 3.

and:

> *Most television programme talks about Haemorrhagic fever, but not much about Influenza.*" Mr. N. (ID 7), p. 2

and:

> *"The public health staff...give(s) us a health check-up, but they never mention the influenza vaccine."* Mrs. V. (ID 13), p.3

5.5.2 Factors affecting decision-making in influenza vaccination

5.5.2.1 Salience of risk

Though most participants held generally positive views on influenza vaccination, decisions whether to accept or refuse influenza vaccination were also based on their perceived risk of contracting influenza. Some participants reported that they would only seek influenza vaccine if there was an outbreak of influenza within their community or in nearby communities.

> *"Even it is free. If we do not have this kind of epidemic* [influenza epidemic] *in our community, there is no need to receive the injection"*, Mr. N. (ID 7), p. 5

and:

> *"I would receive the vaccine injection for my protection if an outbreak happens in the community or in the nearby community such as Banpong which is 6 Km. from here."*, Mr. ST (ID11),p. 3

and:

> *"Yes, I can wait till there actually is* [influenza epidemic]. *I can have the injection immediately after the outbreak. That should be in time. The village health volunteers will tell us when there is an epidemic of influenza".*
> Mr. D (ID 9), p. 6

A few participants thought that they had a low risk of contracting of influenza because it was not a major health problem in their community. Accordingly, influenza vaccination was not necessary for them. One participant commented that:

> *Why do that?* [getting influenza vaccination] *I'm still healthy and this illness is not one of our community's problems"* Mr. D (ID 9), p. 5

By contrast, those who had previously been vaccinated considered themselves to be at risk of developing influenza and that it would affect them seriously:

> *I have the underlying disease which is lung disease...I should get a flu shot because I could get the flu easily."* Mr. Y. (ID 4), p. 4.

and:

> *I'm afraid of catching the flu at old age. People my age, once get sick, will get worse and need medical treatment at the hospital. I have to protect myself."*
> Mrs. S. (ID 14), p. 4.

As mentioned above, some participants perceived themselves as having a low risk of contracrting influenza due to a low prevalence of disease in the community, whereas others cited their age or their underlying chronic illness as increasing their risk.

5.5.2.2 Influence of others

When asked "Could you make your own decision to get the flu shot?", a number of participants expressed that they could not make decision by themselves and many cited reasons why they needed to ask their children or other people in the community.

"I have to ask my children before that. If they say I should, I'll receive this injection. If they say no, I will not receive it... I've to ask them whether or not to have a flu shot, it is necessary" Mrs. V. (ID 13), p. 4

and:

I will talk with my friends...people of the same age and with the same health condition could help us decide whether to get the flu shot or not. If they decide against it, I do not want to do it either." Mr. N. (ID 7), p. 5

and:

In this community, we follow each other. Because if you do not get the flu shot when most people in the community do, you can get blamed if anything happens.... That's why you get sick." Mrs. JT. (ID 20), p. 6

There was a strong sense that individuals were influenced by their peers and felt a need or responsibility to conform. This conveys a sense of responsiblity to the community.

In addition, some participants, particularly those who had chronic medical conditions reported that their decision about whether to receive the influenza vaccine relied heavily on their healthcare providers, regardless of their own views. These participants also noted that health care staff were knowledgeable about influenza and vaccination, and they were also the people who took care of them when they became sick. Therefore, they trusted in the recommendations given by their healthcare providers.

" I've been healthy for about the last 2-3 years, and I've never caught a cold once. So I think it is not necessary to get the flu shot. But if the doctor advised me to have the vaccine, I'll do it" Mrs. CH. (ID 2), p. 5

and:

"We believe the doctor. If the doctor suggests us to get the flu shot, we must follow." Mr. C (ID 8), p. 4

and:

"The public health staffs also studied, so we believe them as well. If they had not studied about it, they would not have told you.", Mr. Y (ID 4), p. 3

Clearly, the participants' decisions about whether to accept the influenza vaccination were affected by social influences, from sources such as doctors, other health care professionals, family members and friends. Where family members are also health workers, such as in the case of Mr. M (p. 118) their views might be perceived as having added credibility.

5.5.2.3 Availability

Two different issues contributed to the availability of the vaccine: the cost of vaccine and having a convenient place for people to get vaccinated. The cost of vaccine was considered an important factor that influenced the participants' decisions concerning vaccination. Most participants stated that they would consider having the vaccination if it was provided free of charge.

> *"No, I do not have any money for a vaccine. I will only do it, if it is free."*
> Mrs. T. (ID 17), p 6.

and:

> *Vaccine is basically for protection disease. But if it costs you money, not many people will receive it. If it is free, many people will be happy to get the flu shot."* Mrs. JT. (ID 20), p 5.

and:

> *They should...* [get vaccination]. *But what would they do? Elderly people without any income and support can only live day by day.*
> Mr. S.T (ID 11), p. 4

By contrast, some participants could afford for influenza vaccination, but they nevertheless expected the government to provide them with it free of charge as they were now senior citizens.

> *"I think that the government will support us. Like when we get free medical treatment from the hospital because we are senior citizens. So I will not get the flu shot until the free vaccine service is launched."* Mrs. A. (ID 18), p 6

and:

"Yes, of course senior citizens should be supported by government, so not many people will pay for the vaccine if it cost money. I think that free vaccine will be provided to help us." Mrs. P. (ID 12), p. 4

The cost of vaccine played an influential part in participants' decisions about whether to get vaccinated. The chance of being immunised seems able to increase if the vaccine was made available to high-risk people free of charge. In contrast, when the vaccine was not available free of charge, a number of participants commented that although they knew about the benefits of vaccine, they would decline the vaccination because they were dependent on their children for support. The following comments are representative of many participants' opinions about this issue.

"Most of elderly people have to rely on their children's support. If you have money, the vaccine does not seem so expensive. If you don't, the cost of vaccine [400 baht; £6] *is pretty much money....So you will not get the flu shot. Everyone dies at the end anyway."* Mrs. T. (ID 17), p. 4

and:

"The ones without their children's support must find it difficult to pay for the vaccine. It should be free, same as the medicines." Mrs. CH. (ID 2), p. 3

Besides providing free vaccine, most participants proposed that the vaccination service should take place at a health or community centre because elderly people could easily access such places. Two participants commented that:

"The health centre is fine. It's near our houses, and it's not crowded. If it's the hospital, you have to spend one day because the hospital service is very slow, and my children have to take me there." Mrs. A. (ID 18), p. 4

and:

Some elderly people they must pay for the bus fare to travel to the hospital. It's tough for us [old people] *to travel."* Mr. ST. (ID 11), p. 5

5.5.2.4 Perception of the need for preventive health care

A perceived need for preventive health care appeared to be another factor influencing participants' immunisation decisions. Some participants believed that getting immunised helped to prevent severe illness, including exacerbation of underlying conditions. They reported that they would consider getting vaccinated because they were concerned that influenza might exacerbate any illness and would make them feel a burden on other people.

> *"I'm afraid of getting sick. I have asthma. I think that my breathing may become difficult. So I have to protect myself."* Mrs. W, (ID16), p.3

and:

> *"I have lung disease* [asthma]. *I feel tired when I breathe, my children bring me to the hospital and they lose their income for one day. I think I will get it* [influenza vaccine]*"* Mrs. SJ. (ID 3), p. 4

By contrast, several participants in the study, especially those who perceived themselves as healthy, considered the influenza vaccination to be unnecessary for them, even though they could afford to pay for the vaccine. These participants were prepared to take the risk of not having the vaccination and developing influenza. Consequently, paying for influenza vaccination was ranked behind other expenses.

> *"I've never caught it so I am not afraid of it. I'm healthy because I exercise every day. I've a strong immune system.* Mr. PS (ID 5), p. 3

and:

> Interviewer: - *"you are not afraid of catching influenza if you do not get a flu shot?"*
>
> Mrs. V.:- *"I don't know. If I catch it, I will receive the treatment at the hospital.*
>
> Interviewer: - *"You mean you want to take the chance?"*
>
> Mrs. V.:- *"Yes."* Mrs. V. (ID 13), p. 4

and:

"Many people do not want to pay for the vaccine because they say they have more important expense. They do not get sick when they are getting the vaccine so they think it is not necessary." Mr. K. (ID 10), p. 4

5.6 Discussion

Although previous research carried out in developed countries of temperate climate has explored high-risk individuals' understandings influenza and factors associated with uptake of the influenza vaccine (e.g. CDC, 2003; Burns, Ring, & Carroll 2005; Evans, Prout, Prior et al., 2007; Kroneman, Paget, & van Essen, 2003; Telford & Rogers, 2003; Zimmerman, Nowalk, Raymund et al., 2003), to our knowledge, this study is the first known to describe these issues in Thailand which has a tropical climate.

The results of the study revealed that high-risk community dwelling Thai adults had low levels of knowledge regarding influenza and influenza vaccination. Many were unsure about its cause and symptoms of influenza, mode of transmission, the seriousness of influenza and its complications. Most participants were not aware that influenza is caused by a virus. Rather, they associated developing influenza with the changes of weather, particularly from rainy to winter season. Exposure to cold weather or a change in the weather is a commonly held-belief on the cause of common cold and influenza in many other cultures such as British, American, Chinese and Malay (CDC, 2003; Chan, 2006; Tan, Lim, Teoh et al., 2007; Prior, Evans, Prout, 2010; Sigelman, 2011). This lay belief is inconsistent with published scientific data about the cause of influenza (Couch, 2000; Cox & Subbarao, 2000; CDC, 2009), and can affect the ways people seek to prevent influenza illness. When influenza is considered to be caused by a change in the weather, general protective measures such as dressing warmly in cold weather, not getting wet, eating healthy food, doing the exercise are perceived to be sufficient in preventing influenza (Adonis-Rizzo & Jett, 2006). This can lead many high-risk individuals to be reluctant to get vaccinated against influenza.

With regard to the influenza symptoms, few participants correctly described the symptoms of influenza, while others confused the symptoms of the common cold or other respiratory illnesses with influenza. Symptoms of influenza commonly recognised by most participants included fever, sneezing, runny nose, and headache; other symptoms such as muscle aches and pains, or fatigue were named by few participants. However, influenza was considered to be more severe than the common cold. These findings may not be specific to this population: one study in the United States found that only 44 per cent of their sample was able to describe typical influenza symptoms (Santibanez, Nowalk, Zimmerman et al., 2002). Lack of knowledge about the symptoms of influenza has also been noted among older people in Singapore; Tan, Lim, Teoh et al.'s (2007) study exploring knowledge, attitudes and practices about influenza and influenza immunisation among people aged over 50 years in Singapore found that runny nose (rhinorrhoea) was viewed as a major symptom of influenza among most participants. Our results, together with the results from previous studies (Santibanez, Nowalk, Zimmerman et al., 2002; Tan, Lim, Teoh et al., 2007; Santibanez, Mootrey, Euler et al., 2010), point to the need for public information about influenza, its transmission and spread, clinical symptoms, and its consequences.

Consistent with previous findings (CDC, 2003; Findlay, Gibbons, Primrose et al., 2000), most participants regarded influenza as a serious disease. However, many did not fully understand how serious influenza can be, considering it to be no worse than a "bad cold". Very few participants thought that it could cause death. These beliefs appear to have contributed to a reluctance to seek the vaccine among some individuals (see also Sengupta & Strauss, 2004), and may have resulted, at least in part, from the lack of information regarding the burden of influenza illness available to our participants. An association between lay belief that influenza is not dangerous and a low uptake of influenza vaccine has also been found in previous studies (van Essen, Kuyvenhoven & de Melker, 1997; Santibanez, Nowalk, Zimmerman et al., 2002; Tabbarah, Zimmerman, Nowalk et al., 2005).

Understanding community perceptions of influenza and its severity is essential to develop educational materials and design an effective intervention to increase uptake of influenza vaccine among individuals at high-risk. In the present study, most

paricipants believed that influenza was no worse than a "bad cold". The interpretation of influenza as a "bad cold" reduces its perceived potential for being lethal and may lead high-risk people to ignore vaccination recommendations. This result suggests that, in addition to providing information on the cause of influenza and its symptoms, educational materials designed to promote influenza vaccination among high-risk Thai adults should emphasise the severity of influenza, the risk of developing influenza-related complications and the need for influenza vaccination.

Unlike some previous studies (CDC, 2003; Adonis-Rizzo & Jett, 2006; Kwong & Lam, 2008), no respondents reported the use of herbs or other traditional medicines for prevention and treatment of influenza. Possible explanations may be related to the universal coverage of health insurance in Thailand that has been implemented since 2001. Additionally, this study was conducted in an urban community among people who usually sought care at a health centre or community hospital. Such individuals are now most likely to seek care from medical/health professionals, with a minimal reliance on traditional healers (Clague, Chamany, Burapat et al., 2006).

Most participants reported that they knew little or nothing about the influenza vaccination. This finding is understandable, as the use of influenza vaccine in Thailand has, until recently, been limited to a small group of people such as healthcare workers and other concerned workers, Thai pilgrims who attend the Hajj, and those who are able to afford for the cost of vaccination (Chunsuttiwat, 2002; Simmerman, Thawatsupha, Kingnate et al., 2004). It is also interesting to note that side-effects following vaccination were not a major concern among our participants, in contrast to some studies which have reported that fear of side-effects has been a significant factor in decisions not to receive the vaccination (e.g. Cornford & Morgan, 1999; Evans & Watson, 2003; Burns, Ring, & Carroll 2005; Evans, Prout, Prior et al., 2007; Wray, Jupka, Ross et al., 2007). By contrast, salience of risk did appear to play an important role in decision-making in influenza vaccination. A number of participants reported that their decisions whether or not to seek vaccination depended on there being an outbreak of influenza within their community or in nearby communities. Other participants considered their risk of contracting influenza to be very low, making the influenza vaccination unnecessary for them. Such beliefs will clearly reduce the probability of seeking or accepting the vaccination (van Essen,

Kuyvenhoven, & de Melker, 1997; Cornforn & Morgan, 1999; Gosney, 2000; Telford & Rogers, 2003; Brewer, Chapman, Gibbons et al., 2007; Weinstein, Kwitel, McCaul et al., 2007).

Participants' vaccination decisions were also influenced by family members and peers. In Thai Buddhist culture, taking care and supporting of aged parents have long been recognized as virtues and a prime responsibility of adult children. Most older Thais live with their children; living in residential care is uncommon in Thailand (Choowatanapakorn, 1999). Accordingly, it is possible that their decisions concerning influenza vaccination will be more influenced by their children than in cultures where the generations are more separated. Data here are lacking, although one study by Adonis-Rizzo & Jett (2006) found that the children of older Haitian adults, with similar patterns of inter-generational care, were also highly involved in such decisions. Besides peers and family members, a number of participants reported that their vaccination decisions relied heavily on their healthcare providers, regardless of their own views. These data add support to similar findings in previous studies (CDC, 1988; Evans, Prout, Prior et al., 2007; Zimmerman, Nowalk, Raymund et al., 2003). Advice from health care professionals was found to be a powerful motivator for high-risk people to comply with influenza vaccination, even among those who had a negative attitude to vaccination (CDC, 1988; Honkanen, Keistinen & Kivela, 1996). The US Center for Disease Control and Prevention (1988) found that among people with unfavourable attitudes to influenza vaccine, those whose health care providers strongly recommened the vaccine had a significantly higer rate of immunisation than those who did not get that advice. This suggests that, if influenza vaccination rates are to be improved, healthcare workers should take an active role in educating and recommending the influenza vaccination to their patients.

Financial barriers also appear to be another important factor that affected participants' immunisation decisions, particularly those who were unable to support themselves. These findings are similar to those of other studies (CDC, 1993; Kroneman, Paget, & van Essen, 2003; Nexøe, Kraqstrup, & Sogaard, 1999; Zwar, Hasan, Harris et al., 2007). Clearly, free vaccination is likely to result in higher levels of vaccination than paid for vaccination. Although starting from a higher baselines level (55 per cent), Gill, Taylor, and Watson (2007) provided some evidence of the likely benefits of such

an approach, reporting an increase in vaccination rate of 27 per cent following the provision of free influenza vaccination in South Australia.

Apart from these factors, decision-making was affected by the individual's perception of the need for preventive health care. A number of participants with chronic diseases stated that they would seek the influenza vaccination, even if it was not provided free of charge. These data are consistent with findings reported by the Centers for Disease Control and Prevention (2001) and Chen, Yi, Wu et al. (2007), who found that the presence of chronic diseases, poor self-reported health and hospital admission strongly predicted influenza vaccination in elderly people among other cultures. A Similar result was observed in a Spanish study; the likelihood of being immunised was higher in people who had a negative perception of their general health, as compared to those with a positive perception of their health (de Andres, Carrasco-Garrido, Hernandez-Barrera et al., 2006). By contrast, some participants who perceived themselves as healthy considered that being vaccinated against influenza was unnecessary for them, and were prepared to take the risk of not having the vaccination. This is supported by Cornford and Morgan's (1999) study which found that most of the participants aged over 75 years perceived themselves as healthy and remained active and independent even though they had at least one chronic disease that placed them at an increased risk for severe complications or death attributable to influenza. Their perception of being in "good health" renders the influenza vaccination unnecessary.

5.7 Implications for clinical practice and the proposed intervention

Our findings suggest that in Thailand, as well as in other countries with tropical climates where large-scale influenza vaccination programmes have yet to be undertaken, the publicising of knowledge on influenza and influenza vaccination to the public will be necessary before launching the programme. This educational programme should both emphasise the symptoms and severity of influenza as well as explaining why the influenza vaccine should be applied to all high-risk groups. The educational messages should also clearly explain that the influenza vaccine prevents influenza, but not colds or other respiratory illnesses, and should be had before, rather

than following, the onset of an influenza epidemic. This information should be provided in a manner appropriate to the culture and to the level of understanding of older people. It may also be targeted at younger people who will not have the vaccination themselves, but who may influence the vaccination decisions of their parents and others. Maximising uptake also appears to be predicated on the vaccine being free and available in local health care centres or community organisations, as well as more centralised hospitals. Doctors and other health care workers (including out-reach workers) should also be prepared and encouraged to discuss vaccination with their patients.

5.8 Strengths and limitations of the study

The strengths were the use of several styles of questions and probing techniques. As influenza symptoms can be confounded by symptoms from illness caused by common cold as well as other respiratory diseases, and the decision whether or not to vaccinate is a complex issue; thus, several styles of questions (essential questions, extra questions, and probing questions) that were appropriate for the informants' backgrounds, and probing techniques (silent and echo probes) were used during the interview to ensure mutual understanding of the issues. Nevertheless, there were limitations to this study. The main limitation is its wider generalisablilty. It was conducted in one selected urban community; potentially restricting its implications to only high-risk Thai adults living in Muang district, Chiang Rai, Thailand. Another limitation is that there were ten potential participants who refused to participate in this study: four felt generally unwell, four did not have enough time for interview, and two were not interested. Accordingly, while a good response rate for qualitative research was obtained, it is possible these individuals might have different views on influenza and influenza vaccination from those who participated in the study. Despite these cautionary notes, however, our findings provide information relevant to the development of public health interventions to promote the use of influenza vaccine among high-risk groups in tropical countries such as Thailand where large-scale implementation of influenza vaccination programme have yet to be established. Nonetheless, further research needs to be done in various settings to provide a complete understanding of the knowledge, beliefs regarding influenza and

vaccination, as well as the facilitators and barriers to get vaccinated among high-risk urban dwelling Thai adults.

5.9 Conclusion

Our study clearly demonstrated that the decision whether or not to vaccinate is a complex issue that is influenced by several medical, psychological and social factors. This study has important implications for the promotion of influenza vaccination, as its findings offer potential insights into how health promotion professionals could develop an effective programme to raise influenza vaccination rate of vulnerable groups in populations. In the light of study findings, efforts to develop the effective influenza vaccination programme should aim to address as far as possible all the direct and indirect influences, as well as the knowledge and beliefs about influenza and influenza vaccination held by high-risk people. It has been suggested that the design of behaviour change interventions should be based on behavioural models, as these provide change targets and provide an explanation for an outcome (Dishman & Buckworth, 1996; Abraham, Sheeran, & Johnston, 1998; Michie & Abraham, 2004; Michie, Johnston, Francis et al., 2008; Michie & Prestwich, 2010). According to the behaviour model, it is assumed that when the factors identified as possible causes of target behaviour were modified appropriately, this will engender the targeted health behaviour change (Michie, Johnston, Francis et al., 2008; Michie & Prestwich, 2010; Thomas, Russell, & Lorenzetti, 2010). In study 2, the Health Action Process Approach (HAPA) was used as a conceptual framework to guide intervention and implementation. Thus, the HAPA model will be the focus of the following chapter.

Chapter 6: Changing health behaviour: theory and application

6.1 Introduction

An individual's decisions about changing health behaviours is a complex process influenced by numerous factors, including personal, social, environmental, and economic factors (Abraham, Sheeran, & Johnston, 1998; Conner & Norman, 1998, 2005). Interventions are therefore needed to address these in order to change a given behaviour. In promoting influenza vaccination, for example, some people have worked on changing a system of vaccination (e.g. setting up an express vaccination clinic, and providing the vaccine free of charge, standing orders and physicians consistently offering influenza vaccination to all high-risk patients during the influenza season) (Nichol, Korn, Margolis, 1990; Humair, Buchs, & Stalder, 2002; Kroneman, Paget, & van Essen, 2003), others have tried to change perceptions and motivate high-risk people to get annual influenza vaccination (LaVela, Cameron, Priebe et al., 2008; Wray, Buskirk, Jupka et al., 2009). In addition, some people have focused on the development of influenza vaccination policies such as lowering the age for universal vaccination (WHO, 2000; CDC, 2010). These are all useful approaches, but they are based on different conceptual frameworks for promoting change. In this study, the intervention to promote influenza vaccination was based on the HAPA model which is a psychological model; thus, it focuses on the individual (Schwarzer, 2001).

Evidence has shown that a theoretical approach to developing an intervention is more effective than interventions developed without theoretical guidance (Dishman & Buckworth, 1996; Abraham, Sheeran, & Johnston, 1998). In addition, Godin and Shephard (1990) pointed out that although an intervention programme without a theoretical basis can demonstrate a positive change in health behaviour, the reasons which underpin its successful change remain unclear due to the lack of theory to support the intervention. This makes it difficult to implement such interventions on a large scale or nation-wide. This chapter provides an overview of social cognitive models and three commonly used models (Health Belief Model [HBM], Protection

Motivation Theory [PMT], and Social Cognitive Theory [SCT]), the Health Action Process Approach model (HAPA), implementation intentions, and the application of the HAPA model to health-related behaviours (Becker, 1974; Rosenstock, 1974; Rogers, 1975, 1983; Bandura, 1977, 1986, 1997; Schwarzer, 1992, 1999, 2001; Gollwitzer & Brandstatter, 1997; Gollwitzer& Schaal, 1998; Gollwitzer, 1999; Conner & Norman, 1998, 2005; Armitage & Conner, 2000; Rutter & Quine, 2002). Three social cognitive models (HBM, PMT, and SCT) are reviewed as they are historical antecedents to the HAPA.

6.2 Social cognition models

A number of factors have been found to be involved in the decisions to perform health-related behaviour, including demographic factors, social factors, emotional factors, personality factors, factors associated with access to medical care, and cognitive factors (such as knowledge, attitudes, and beliefs) (Conner & Norman, 2005; Morrison & Bennett, 2006). Among these factors, cognitive factors appear to mediate the effects of other factors upon the performance of health behaviours. They are also amenable to change, and thus provide targets for interventions designed to change health behaviours (Conner & Norman, 1998, 2005; Rutter & Quine, 2002). The social-cognitive approach emphasises human cognitions or thoughts. The models are derived from expectancy-value theory and subjective expected utility theory, which describe individual behaviour as being based intentionally rational judgment and aimed at utility maximisation (Edwards, 1954; Conner & Norman, 2005). When making a decision to perform a particular behaviour, people are assumed to evaluate options by assessing probabilities, weighing up of the potential costs and benefits of them, and ranking all of the options in order to make a decision. These assessment processes are assumed to be a rational (Edwards, 1954; Conner & Norman, 2005). For more than 40 years, various social cognitive models have been developed and used to explain and predict health behaviours. Finding the weakness in these models has led to the development of new models or refinement of existing ones (Rutter & Quine, 2002). In this chapter, three social cognitive models are reviewed: Health Belief Model (HBM), Protection Motivation Theory (PMT), and Social Cognitive Theory (SCT) (Becker, 1974; Rosenstock, 1974; Rogers, 1975, 1983; Bandura, 1977, 1986, 1989, 1997, 2004).

6.2.1 Health Belief Model

The Health Belief Model (HBM) was originally developed in the 1950s and 1960s by a group of the U.S. public health service researchers, including Hochbaum, Kegeles, Leventhal, and Rosenstock (Rosenstock, 1974; Becker, 1974), to help explain why people did or did not participate in the preventive programme and screening tests such as x-ray screening for tuberculosis or accepting immunisation (Becker, 1974; Rosenstock, 1974). Subsequently, it has been applied to other health-related behaviours, including patients' responses to symptoms of illness, adherence to penicillin prescriptions and compliance with a diet regimen for diabetes mellitus (Janz & Becker, 1984). The model has its root in the Lewinian theory of goal setting which assumes that individual behaviour is determined by the value placed by individual on a particular goal (positive or negative) and the consequences of behaviour related to achieving that goal (Maiman & Becker, 1974).

The HBM proposes that the motivation to perform behaviour arises from the individual's perception of a threat to personal health. Threat perception is determined by two key beliefs: perceived susceptibility to a disease or health problems and the perception of the seriousness of that disease. At the same time, behaviour is evaluated from an estimate of the perceived benefits of the recommended treatment or preventive behaviours in terms of reduce susceptibility or severity of the health problems. The benefits are then weighed against the costs or barriers of performing that behaviour; people who perceive more benefits than barriers are more likely to take action than those perceiving more barriers than benefits. In addition, the model stipulates that a cue to trigger appropriate behaviour is important. The cues may be internal (e. g. perceptions of symptoms) or external (e.g. information from health education leaflets, receiving a reminder postcard from health care providers). Additionally, demographic factors and physiological characteristics are thought to influence individual's perception. Therefore, they indirectly have an effect on health-related behaviour (Rosenstock, 1974; Becker, 1974; Janz & Becker, 1984; Mullen, Hersey, & Iverson, 1987). The model has been refined over the years. The construct "health motivation" to reflect one's motivation to engage in health behaviour was added to the original model (Rosenstock, 1974; Becker, 1974; Rutter & Quine, 2002). In addition, the concept of self-efficacy was added to the model by Rosenstock,

Strecher, & Becker (1988). Generally, these six components are to be treated as independent predictors of health behaviour, thus up to six independent variables may account for variance in behaviour (Abraham & Sheeran, 2005). A schematic description of the Health Belief Model is shown in figure 6.2.1.

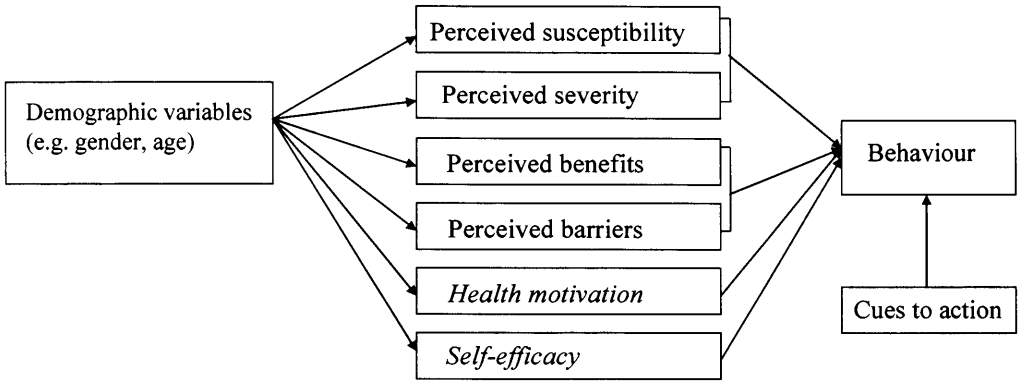


Figure 6.2.1 The Health Belief Model (original, plus additions in italics)

The model has been applied to the prediction of a wide variety of health-related behaviours, including smoking (Knight & Hay, 1989), exercise (Godin & Shephard, 1990), attendance at health checks (Norman & Conner, 1993), mammography and cervical screening (Fischera & Frank, 1994; Orbell, 1996; Champion & Miller, 1996), adherence to safe-sex behaviours (Abraham, Sheeran, Spears et al., 1992; Bakker, Buunk, & Siero, 1997), adherence to antipsychotic medication (Hughes, Hill, & Budd, 1997; Budd, Hughes, & Smith 1996), breast self-examination (Friedman, Hoffman, Nelson et al., 1994; Millar, 1997), and compliance with influenza vaccination (Nexøe, Kraqstrup, & Sogaard, 1999; Mok, Yeung, & Chan 2006; Lyn-cook, Halm, & Wisnivesky, 2007).

In relation to vaccination behaviour, the HBM predicts that an individual will seek the influenza vaccination if they perceive that they are susceptible to the influenza, that influenza infection can cause serious complications, that the benefits of obtaining influenza vaccine are high, and that the costs/barriers of getting vaccinated are comparatively low. In addition, cues to action such as a reminder postcard from health care providers or information from the media may prompt them to seek or receive the vaccine. Similarly, if one is motivated to stay healthy during the influenza season. Finally, the revised model suggests that if he/she has the confidence to either seek or cope with the side-effects of vaccination uptake is more likely.

According to Janz and Becker's (1984) review of the studies applying the HBM published between 1974 and 1984, there were four studies that used the HBM as a conceptual framework for explaining swine influenza and influenza vaccination uptake. The results of these researches supported the predictions of the HBM; perceived susceptibility, perceived efficacy and safety of the vaccine were significantly associated with vaccination behaviour. Subsequently, a cross-sectional study of factors influencing the decision on influenza immunisation conducted by Nexøe, Kraqstrup, & Sogaard (1999) revealed that three major HBM variables: perceived barriers, perceived benefits, and perceived severity were significantly related to influenza vaccination status among the older people. More recently, Mok, Yeung, & Chan (2006) included factors specified in the HBM in the study examining correlates of intention to be immunised in Hong Kong Chinese adults aged 65 years and older. The results of this study showed that the perception of susceptibility to influenza ("I am likely to get the flu if I do not get a yearly flu shot") appeared as a significant predictor of vaccination intention among these individuals. Similar results were obtained by Raftopoulos (2007) who explored the knowledge, the beliefs about and the attitudes towards influenza and pneumococcal vaccination among community-dwelling older people in Greece. This qualitative study found that perceived benefits of influenza vaccination emerged as key facilitators of receipt of influenza vaccine.

Despite these generally positive findings, a meta analysis of studies of the HBM conducted by Harrison, Mullen, and Green (1992) indicated that although the HBM has been consistently found to be predictive of health behaviours, the relationship between the model's components and health behaviours across the studies was weak (effect sizes ranging from 0.01 to 0.30). Aside from the weak predictive power, the model has also been criticised for emphasising individuals and their cognitive processing. Other variables that could influence behaviours, including social support systems and emotional factors, have not been included. In addition, the operational definitions of the variables and the rules for combining variables (such as perceived susceptibility and perceived severity) are not clear. Accordingly, different methods have been used to measure HBM constructs. For example, susceptibility has been used to assess either personal vulnerability to specific disease/threat or general vulnerability to disease/ threat compared to others (Simon, Morse, Balson et al., 1993;

Rutter & Quine, 2002). Also, different combinations of variables have been used in the studies applying the HBM model, including adding or multiplying susceptibility and severity, or subtracting barriers from benefits (Hill, Gardner, & Rassaby, 1985; Rutledge, 1987; Wyper, 1990). Furthermore, the model has not been clearly specified any particular relationship among the core set of beliefs, how these beliefs should be measured and how they can combine to influence behaviour (Hill, Gardner, & Rassaby, 1985; Montano, 1986; Wyper, 1990; Strecher & Rosenstock, 1997; Armitage & Cornner, 2000; Rutter & Quine, 2002; Abraham & Sheeran, 2005; Morrison & Bennett, 2006). Finally, it has been pointed out that the HBM conceptualises behaviour change as a static process rather than a dynamic process. Various beliefs seem to occur simultaneously, and there is no room in these beliefs for change or development (Schwarzer, 1992).

Despite these conceptual flaws, the model has been used extensively to predict a range of health-related behaviours. In addition, some of the model's components (susceptibility and severity) have been incorporated into the new models such as Health Action Process Approach model and Protection Motivation Theory (Rogers, 1975, 1983; Schwarzer, 1999; Rutter & Quine, 2002).

6.2.2 Protection Motivation Theory (PMT)

Protection Motivation Theory shares some features with the HBM (Rosenstock, 1974). It was developed by Rogers (1975), who aimed to provide a framework for research on fear appeals and attitude change. According to PMT, an individual's decision whether or not to adopt a particular health behaviour is guided by two cognitive processes: threat appraisal and coping appraisal. Threat appraisal refers to an individual's evaluation of risks posed by the threat. This appraisal is based on perceived susceptibility, perceived severity, and fear. Fear is labelled as an intervening variable between perceived severity and susceptibility and threat appraisal; the greater the perceived threat, the more fear will be elicited. Theoretically, as perceptions of susceptibility and severity increase, the likelihood of adopting unhealthy behaviour decreases. However, there may be a number of intrinsic rewards (e.g. pleasure) and extrinsic rewards (e. g. peer approval) that increase the likelihood

of performing the unhealthy behaviour. As the PMT has been revised in 1983, rewards of not adopting the recommended behaviour and self-efficacy have been specified and added to the model (Rogers, 1975, 1983; Maddux & Rogers, 1983; Maddux, 1993; Armitage & Conner, 2000; Milne, Sheeran, & Orbell 2000; Norman, Boer, & Seydel, 2005).

The second appraisal process is coping appraisal which is influenced by response efficacy (an individual's estimation of the effectiveness of the recommended coping strategy in reducing appraised threat) and self-efficacy (an individual's perception of his or her ability to perform the behaviour). It is expected that response efficacy and self-efficacy increase, the probability of engaging in preventive behaviour increases. However, the likelihood of an adaptive response is decreased by the perceived response costs or barriers such as the lack of availability of resources. In addition, the PMT identifies two types of sources of information: environmental (e.g. verbal persuasion, observational learning) and intrapersonal (e.g. prior experience), and this information influences susceptibility, severity, fear, response efficacy, and self-efficacy, which induce either an adaptive response or a maladaptive response (Rogers, 1975, 1983; Maddux & Rogers, 1983; Maddux, 1993; Armitage & Conner, 2000; Milne, Sheeran, & Orbell 2000; Norman, Boer, & Seydel, 2005).

The PMT describes protection motivation to perform health behaviour as a result of the two appraisal processes (threat appraisal and coping appraisal). Protection motivation is seen as a proximal predictor of protective behaviour, and it is assumed that intention is the most appropriate measure of protection motivation (Prentice-Dunn & Rogers, 1986). Protection motivation is an intervening variable that "arouses, sustains, and directs activity" (Rogers, 1975, p. 98). According to Rogers (1983), four beliefs are assumed to increase protection motivation (a positive linear function) : the threat is severe, the individual regards his or herself as susceptible to the threat, the recommended behaviour will be beneficial in reducing the threat, and the individual has the ability to perform the coping response. Two further beliefs operate in a negative linear function: rewards from the maladaptive responses and the perceived costs or barriers of the adaptive behaviour (see Figure 6.2.2). Thus, the highest amount protective motivation will be elicited if all positive beliefs are high and the two negative beliefs are low (Rogers, 1975, 1983; Maddux & Rogers, 1983; Prentice-

Dunn & Rogers, 1986; Armitage & Conner, 2000; Milne, Sheeran, & Orbell 2000; Norman, Boer, & Seydel, 2005).

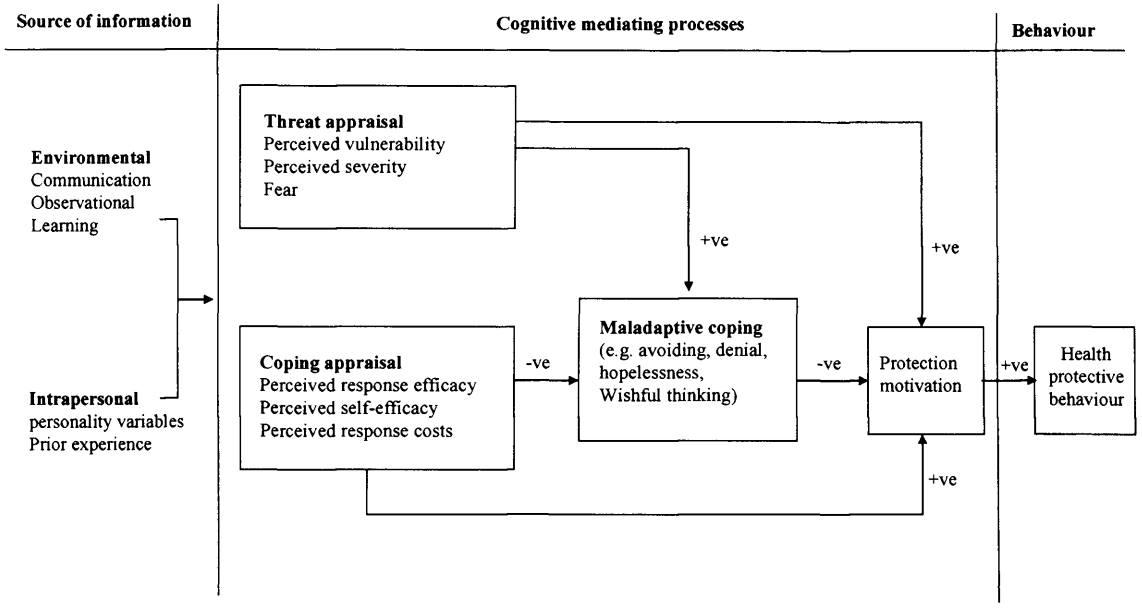


Figure 6.2.2 Schematic representation of protective motivation theory (adapted from Rogers, 1983): +ve = positive association; -ve = negative association Source: Milne, Sheeran, & Orbell, 2000

Floyd, Prentice-Dunn, & Rogers (2000) conducted a meta-analysis of PMT studies. The findings of this study provide support for the use of the PMT framework in predicting intentions and behaviour; all PMT components were significantly associated with intentions, and self-efficacy was the strongest predictor of both protection motivation (intention) and behaviour.

In another meta-analysis of PMT studies, carried out by Milne, Sheeran, and Orbell, (2000), their analyses also showed that all variables specified by PMT were significantly predictive of intentions and concurrent behaviour. With regard to the prediction of intention, the effect sizes (r_+: sample weighted average correlations) were larger for the coping appraisal variables (perceived response efficacy [$r_+ = 0.29$], self-efficacy [$r_+ = 0.33$] and response costs [$r_+ = -0.34$]) than the threat appraisal variables (perceived severity [$r_+ = 0.10$] and susceptibility [$r_+ = 0.16$]). In other words, coping appraisal variables were stronger in predicting protection motivation or

intention than threat appraisal variables. This pattern of results was also found in measures of association with concurrent behaviour. However, when considering the prediction of future behaviour, only four PMT variables proposed in PMT (perceived vulnerability, self-efficacy, response costs and protection motivation (intention) have been found to be significant predictors of future behaviour. Furthermore, the effect sizes for these four variables (susceptibility [$r_+ = 0.12$], self-efficacy [$r_+ = 0.22$], response costs [$r_+ = -0.25$], and protection motivation [$r_+ = 0.40$]) were in the small to medium range according to Cohen's (1988) guideline, and protection motivation (intention) was found to have the largest effect size ($r_+ = 0.40$), followed by self-efficacy ($r_+ = 0.22$). However, Milne, Sheeran and Orbell's (2000) review of PMT studies was based on a relatively small number of studies that examined the relationship between PMT variables and future behaviour.

In addition, the PMT has been used to predict cancer-preventive intentions and behaviours (Seydel, Taal, & Wiegman, 1990). The study showed that the PMT was superior to the HBM in the prediction of preventive behaviour related to cancer; self-efficacy expectancy and outcome expectancy were found to be predictors of actual behaviour – ordering leaflets ("The seven warning signs" and "Breast self-examination) from the national information centre of the Dutch Cancer Society. Wurtele and Maddux (1987) also found that perceived vulnerability to heart disease and perceived exercise self-efficacy increased intention to adopt an exercise program among undergraduate women, but persuasive communications did not have significant effects on exercise behaviour.

Unlike the HBM and other social cognitive models (e.g. Theory of Reasoned Action [TRA], Theory of Planned Behaviour [TPB] (Ajzen & Fishbein, 1980; Ajzen, 1991; Ajzen, 2005), the PMT has been evaluated through the use of a number of experimental manipulations (Beck & Lund, 1981; Milne, Sheeran, & Orbell, 2000; Milne, Orbell, & Sheeran, 2002; Norman, Boer, & Seydel, 2005). Beck and Lund (1981) applied the PMT to oral hygiene behaviour, and found that feelings of fear, perceived susceptibility, perceived severity, intention and oral hygiene behaviour (flossing) were significantly higher among dental patients exposed to a "high seriousness" version of a threat communication designed to change their beliefs about periodontal disease than those patients exposed to their "low seriousness" version.

The study conducted by Wurtele (1988) revealed that perceived vulnerability to osteoporosis had a significant influence on adoption intention and recommended behaviour for preventing osteoporosis (dietary intake of calcium and picking up a free calcium supplement) among female undergraduates. Other studies also found that PMT manipulations had positive effect on intentions to adopt the adaptive response (Stanley & Maddux, 1986; Rippetoe & Rogers, 1987; Yzer, Fisher, Bakker et al., 1998).

The PMT differs from the original HBM, in which it includes self-efficacy and protection motivation which is generally measured by intention (Prentice-Dunn & Rogers, 1986). These two variables (self-efficacy and intention) have been found to be positively associated with behaviours in multiple studies (e.g. Beck & Lund, 1981; Wurtele, 1988; van der Velde & van der Pligt, 1991; Weinstein, 1993). Also, consistent with other models such as the Theory of Planned Behaviour (TPB) (Ajzen, 1991; Ajzen, 2005), the PMT suggests that protection motivation functions as an intervening variable that stimulates, sustains, and directs coping response (Rogers, 1975, 1983; Prentice-Dunn & Rogers, 1986). Thus, according to the PMT, protection motivation is an important predictor of behaviour, and forming protection motivation leads to the adoption of precautions or behaviour change (Prentice-Dunn & Rogers, 1986). This may explain why the PMT has been found useful for explaining and predicting health-related behaviours (Prentice-Dunn & Rogers, 1986; Weinstein, 1993; Floyd, Prentice-Dunn, & Rogers, 2000; Milne, Sheeran, & Orbell, 2000; Norman, Boer, & Seydel, 2005).

In contrast to the previous discussion, some studies have found that PMT interventions had no effect on actual behaviour (Milne et al., 2002; Wurtele and Maddux, 1987). For example, a study that investigated the impact of PMT-based intervention on subsequent changes in exercise cognitions, intention and behaviour carried out by Milne, Orbell, and Sheeran (2002) found that a motivational intervention based on PMT made a significant contribution to changing exercise cognitions (threat and coping appraisals) and intention, but had no significant impact on subsequent exercise behaviour. The finding that motivational interventions grounded in PMT was found to have a strong influence on health-related behavioural intentions but not subsequent behaviour may not be specific for the PMT. One

explanation for these findings is that there is frequently a disjunction between intention and behaviour, known as the "intention-behaviour gap" (Armitage & Conner, 2000; Sheeran, 2002; Sheeran, Milne, Webb et al., 2005). The intention-behaviour relationship may be disrupted by unforeseen barriers or the face of temptations; thus, people do not perform a particular behaviour according to their intentions (Sheeran, 2002; Sniehotta, Scholz, & Schwarzer, 2005; Schwarzer, Luszczynska, Ziegelmann et al., 2008).

Findings from meta-analyses showed that intentions accounted for 20 per cent to 30 per cent of the variance in health behaviour on average (Sheppard, Hartwick, & Warshaw, 1988; Randall & Wolff, 1994; Godin & Kok, 1996; Sheeran & Orbell, 1998, Sheeran, 2002). This suggests that other predictors of health behaviours (e.g. planning and volitional self-efficacy) may be responsible for the intention-behaviour gap (Abraham et al., 1998; Armitage & Conner, 2000; Sheeran, 2002; Sheeran, Milne, Webb et al., 2005).

Although manipulation of PMT variables tends to have a small impact on subsequent behaviour, the model provides useful insights for the design of interventions to enhance intention and, perhaps, behaviour. Additionally, it has been suggested that changing behaviours may require other volitional strategies such as implementation intentions to bridge the gap between intentions and behaviour (Milne, Orbell, & Sheeran, 2002; Sheeran, Milne, Webb et al., 2005; Norman, Boer, & Seydel, 2005). In the following session, the implementation intentions will be discussed in more detail.

6.2.3 Social Cognitive Theory (SCT)

Social Cognitive Theory (STC) is seen as a comprehensive theory of behaviour change. Central to the SCT is the concept of self-efficacy which is now included in most of health behaviour models (Bandura, 1977, 1986, 1997; Armitage & Conner, 2000). The SCT is derived from the Social Learning Theory (SLT) (Bandura, 1986). Like other Social Cognition Models, the SCT aims to predict and explain health behaviour using a core set of determinants: self-efficacy, outcome expectations, goals, facilitators and impediments. In addition, the model also specifies the mechanisms involved in the behaviour change. According to the SCT, human behaviour can be

described in terms of triadic reciprocal causation in which behaviour, personal factors (cognitive, affective, and biological factors), and environmental factors all interact and influence each other (see figure 6.2.3.1), and health behaviour change lies in these interactions (Bandura, 1986; 1989).

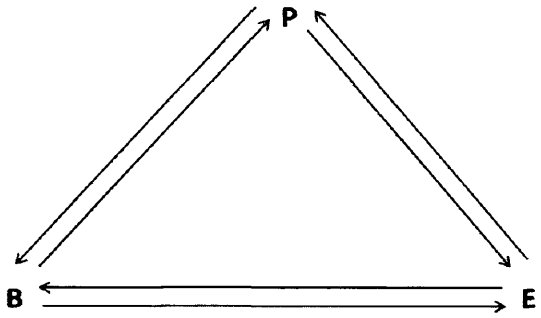


Figure 6.2.3.1 Schematic representation of triadic reciprocal causation.
Note: B represents behaviour; P the internal personal factors in the form of cognitive, affective, and biological events; and E the external environment
Source: Bandura, 1986

The core constructs of the SCT include goals, self efficacy, outcome expectations, facilitators and impediments (Bandura, 2004; Luszczynska & Schwarzer, 2005). Social Cognitive Theory suggests that in initiating and maintaining health behaviour, individuals first establish a goal, and then they consider the likely consequences of performing a given behaviour in relation to that goal (outcome expectations) before they decide whether to engage in a given behaviour. Such outcome expectancies can be classified into three categories: physical outcome expectations, social outcome expectations and self-evaluative outcome expectations. Outcome expectations are considered to be important in the initial formulation of the goals. Physical outcome expectations are related to the anticipation of physical effects, such as the expectations of discomfort or disease symptoms, which might be experienced after behaviour change. Social expectancy refers to the consequences of performing a particular behaviour that may be determined by others or society. Self-evaluative outcome expectations are related to the internal reactions that might expected after behaviour change such as being proud of oneself and being ashamed. However, these outcome expectancies lose their influence in the phases of action control, and self-efficacy appears to have more powerful effect on behaviour. Perceived self-efficacy is

related to the beliefs about one's own ability to perform a particular behaviour (Bandura, 1977, 1986, 1989, 1997, 2004; Luszczynska & Schwarzer, 2005).

Self-efficacy beliefs are crucial to successful change of health behaviours. They have direct impact on personal behaviour, and they can also influence goals, outcome expectancies, and perceived facilitators and barriers (Bandura, 2004). Individuals with stronger self-efficacy tend to set higher goals for themselves and commit to their goals more strongly, which in turn influence actual behaviour (Bandura, 1989; Locke & Latham, 1990). Perceived self-efficacy also shapes the outcome expectations of an individual. Individuals with high generalised self-efficacy will expect their efforts to attain favourable outcomes, whereas those who perceive low self-efficacy tend to view poor outcomes (Bandura, 1989, 2004). Behaviours that guarantee valued outcomes may not be pursued if the person doubts his or her ability to engage in them (Beck & Lund, 1981; Bandura, 1994). A typical study of this phenomenon, conducted by Williams and Bond (2002), confirmed the role of self-efficacy in influencing health behaviour change; people with diabetes who had less confidence in their self-care abilities were unlikely to comply with a diabetic regimen (diet, exercise, and blood glucose testing), although they believe that following the regimen would be beneficial to their general health.

Additionally, SCT suggests that goal setting is affected by sociostructural factors (facilitators and impediments). Social Cognitive Theory proposes that the perceived facilitators and barriers could potentially influence behaviour (Bandura, 2004; Luszczynska & Schwarzer, 2005). Self-efficacious persons believe that they have the capacity to exercise control, even in the face of difficulties or barriers. On the contrary, those with low self-efficacy are less likely to persevere in the face of obstacles, and are eventually likely to abandon their goal when they encounter difficulties and setbacks (Bandura, 1977, 1989, 2004). Bandura (1977) suggested that an individual's persistence and efforts in behaviours as well as the quality of the performance are related to his or her level of self-efficacy.

All social cognitive constructs of social cognitive theory are illustrated in figure 6.2.3.2. However, within social cognitive theory, outcome expectations and self-efficacy beliefs are considered as central determinants of behaviour, and are the main

focus of research attention. According to this perspective, persons are more likely to engage in certain health behaviours if they believe that performing them will lead to desirable outcomes, and they are confident in their abilities to perform the recommended behaviour, even in the face of difficulties or barriers.

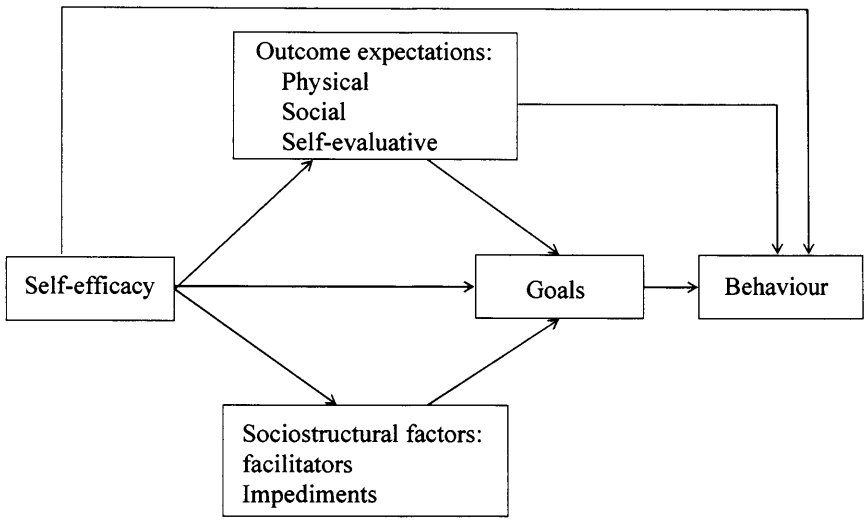


Figure 6.2.3.2 An illustration of social cognitive theory
Source: Bandura, 2004

One's self-efficacy can develop through four major sources. These sources include performance attainment, vicarious experience, verbal persuasion, and physiological state (Bandura, 1977, 1986, 1997). Performance accomplishments are believed to be the most potent sources of efficacy information as they provide information about past success. Successful experiences boost self-efficacy, whereas failure undermines it (Bandura, 1977).

The second source of self-efficacy is vicarious experience, which refers to learning through modelled attainment or observing others' achievements. A trial of vicarious experience can be particularly useful for people who are doubtful about their ability to perform a particular behaviour. Seeing others perform an activity can help these individuals believe that they can possess the ability to perform the recommended behaviour (Bandura, 1977, 1986; Parent & Fortin, 2000). However, the effectiveness of enhancing self-efficacy through vicarious experience depends on the similarity between the model and the observer (Bandura, 1977, 1986; Strecher, DeVellis, Becker et al., 1986).

A third source is verbal persuasion. Persuasive techniques are widely used by health educators because of their relative simplicity and ease of use. By using verbal persuasion to enhance self-efficacy, individuals are led through suggestion to believe that they have the capability to do and to accomplish a particular outcome (Bandura, 1977, 1997).

Finally, physiological and emotional states can also have an effect on the individual's efficacy beliefs. For example, anxiety, and depression can diminish self-efficacy and discourage continued efforts to engage in a specific behaviour. People are less likely to initiate and continue behavioural efforts if they are tense and viscerally agitated (Bandura, 1977, 1989, 1997). Accordingly, reducing emotional arousal is viewed as one way of improving an individual self confidence. In addition, for some people who are prone to misinterpret their physical state or emotional arousal as symptoms of physical illness (e.g. incorrectly interpreting muscle aches and pains after beginning an exercise programme as signs of weak physical efficacy), diminishing negative bias in interpretation of bodily states may maintain feelings of self-efficacy (Bandura, 1977, 1986, 1997; Strecher, DeVellis, Becker, 1986; Luszczynska & Schwarzer, 2005).

The SCT has been extensively used to study a variety of health-related behaviours such as adherence to antiretroviral therapy, compliance with a diabetic regimen, unprotected sexual behaviour, physical exercise, nutrition and weight control, breast self-examination, smoking, and substance use (Seydel, Taal, & Wiegman, 1990; Ellickson & Hays, 1992; Wulfert & Wan, 1993; Anderson, Winett, & Wojcik, 2000; Catz, Kelly, Bogart et al., 2000; Dijkstra & DeVries, 2000; Kremers et al., 2000; Schnoll & Zimmerman, 2001; Christiansen et al., 2002; Rodgers, Hall, Blanchard et al., 2002; Williams & Bond, 2002). Such studies have shown that outcome expectancies and perceived self-efficacy play an influential role in explaining and predicting a wide variety of health behaviours, although self-efficacy was found to be the most important factor in affecting motivation and subsequent behaviour (Seydel, Taal, & Wiegman, 1990; Wulfert & Wan, 1993; Kremers, Mesters, Pladdet et al., 2000; Christiansen, Vik, & Jarchow 2002; Rodgers, Hall, Blanchard et al., 2002; Williams & Bond, 2002). As a consequence of the strong relationship between self-efficacy and behaviour in multiple studies, it has been incorporated into several

conceptual models of health behaviours, including Health Belief Model, Protection Motivation Theory, and Health Action Process Approach (Rosenstock, 1974; Rogers, 1983; Schwarzer, 1992)

Social Cognitive Theory has also been used as a framework in developing behaviour change interventions in several studies (e.g. O'Leary, Shoor, Lorig, & Holman 1988; Stanton, Li, Ricardo et al.,1996; Parent & Fortin, 2000; Dijkstra & De Vries, 2001; Carson, Gillham, Kirk et al., 2002; Baranowski, Baranowski, Cullen et al., 2003; Dishman, Motl, Saunders et al., 2004). For example, an SCT-based intervention involving vicarious experience through peer support enhanced self-efficacy following coronary artery bypass graft surgery (CABG) more than a standard treatment control (Parent & Fortin, 2000). Walking, stair climbing, and 'general activity' were also more prevalent among patients in the intervention group five days after surgery (Parent & Forbin, 2000).

Similar results were obtained by Dishman, Motl, Saunders et al (2004) who demonstrated the effects of a comprehensive school-based intervention aimed at enhancing physical activity self-efficacy in adolescent girls. The study showed that increased self-efficacy led to increased physical activity. In addition, self-efficacy was found to partially mediate intervention program effects on physical activity among these individuals. Baranowski, Baranowski, Cullen et al. (2003) also showed that a psychoeducational, multimedia game based on SCT had positive effects on fruit, juice and vegetable consumption among pre-adolescents participating in an intervention programme; children in the intervention condition increased intake by 1.0 serving more than the children who did not receive the intervention at the end of the 5-week, ten-session programme (Baranowski, Baranowski, Cullen et al., 2003).

However, some studies have revealed that interventions designed in line with SCT have had limited success in promoting long-term behaviour changes, such as physical activity, and condom use (Stanton, Li, Ricardo et al. , 1996; Pinto, Friedman, Marcus et al., 2002). In a study conducted by Pinto, Friedman, Marcus et al. (2002), the telephone linked communication-physical activity (TLC-PA) was developed to promote physical activity in sedentary adults. While the intervention participants were asked to call TCL-PA, those in the control group were informed to call TLC-Eat

(telephone linked communication-healthy eating). The contents regarding physical activity for weight loss were not provided to the comparison group (TLC-Eat). The intervention was available for six months. The results showed that at three months, the higher proportion of participants who met recommendation for moderate-intensity or vigorous-intensity physical activity was found in the intervention group, as compared with the control group. Also, those in the intervention group reported higher daily kilocalorie energy expenditure than the control group. However, after six months of intervention, the intervention effects were not maintained. The weak effects of the TLC-PA intervention might have been due to a significant decrease in the number of users over six months; thirty three per cent of the participants did not continue to use the system.

Stanton, Li, Ricardo et al. (1996) found that the HIV-risk-reduction treatment based on SCT had positive effects on condom used at six months among African-American youths 9-15 years of age, but there was no significant difference in condom use rates between the intervention and control groups at 12-month follow-up. In this study, the finding that the SCT-based intervention had no long-term effects on condom use among early adolescent was unclear. However, similar results have been noted in drug prevention study that targeted pre-adolescents (Ellickson, Bell, & McGuigan, 1993).

In summary, all three models have been widely used to predict a wide variety of behaviours with a fair degree of success. Intentions or personal goals (as defined in social cognitive theory) are regarded as proximal determinants of behaviour (Bandura, 2004; Luszczynska & Schwarzer, 2005). However, recent developments in social cognition models suggest that intentions alone are not sufficient to drive behaviour change (Weinstein, 1993; Abraham, Sheeran, & Johnston, 1998; Armitage & Conner, 2000; Sheeran, 2002; Schwarzer & Luszczynska, 2008).

A meta-analysis of 47 experimental studies conducted by Webb and Sheeran (2006), for example, found that a medium-to-large change in intention produced a small-to-medium change in behaviour. This study confirms that behaviour change is not exclusively determined by an individual's intentions. Therefore, in order to better understand why and how people change their health behaviour, attention has shifted from motivational processes (intention formation) to the post-intentional volition

processes that are involved in health behaviour change and maintenance behaviour change over time (Abraham, Sheeran, & Johnston, 1998; Armitage & Conner, 2000; Sniehotta, Scholz, & Schwarzer, 2005; Schwarzer, 1996, 2008). Stages of change models such as Transtheoretical Model [TTM] (Prochaska & DiClemente, 1983) and Health Action Process Approach [HAPA] (Schwarzer, 1992, 2001) describe the processes of health behaviour change, and may be able to overcome some of limitations of motivational models.

6.3 The Health Action Process Approach (HAPA) model

The HAPA model was developed by Schwarzer at the Free University of Berlin, Germany. It aims to predict health behaviour and provide a better understanding of the mechanisms of health behaviour change than motivational models of health behaviour (Schwarzer, 1992, 2008). The HAPA integrates the motivational components of Social Cognition Models (such as Health Belief Model, and Social Cognitive Theory) and Volitional Theories (Heckhausen & Gollwitzer, 1987; Schwarzer, 1992, 2001, 2008). The HAPA suggests a distinction between the pre-intentional motivation processes that involve the formation of intentions and post-intentional volition processes which address the processes in the translation of goal intentions into action.

The HAPA can serve as an alternative to other health behaviour change models that do not include the post-intentional factors, including the HBM, PMT, TRA, and TPB (Luszczynska & Schwarzer, 2005; Sniehotta, Scholz, & Schwarzer 2006; Schwarzer & Luszczynska, 2008). These models (also called "continuum models") assume that an individual's behaviour occurs as the result of a conscious intention, and the intention formation is governed by beliefs and attitude (Amitage & Conner, 2000; Schwarzer, 2008). Accordingly, many health behaviour change models attempt to explain and predict a given health-related behaviour by identifying a set of social cognitive factors that influence behaviour (such as personal susceptibility, disease severity, perceived costs, perceived self-efficacy, and social norm), and then combining these variables into a linear prediction equation. This equation provides us information about the likelihood of behaviour which lies somewhere along the

continuum of action (Weinstein, Rothman, & Sutton., 1998; Schwarzer, 2008). The action initiation is supposed to be the same for everyone because the prediction of behaviour is based on a single equation (Weinstein, Rothman, & Sutton., 1998). This implies that interventions designed to change behaviour based on continuum models try to modify all changeable variables in all individuals.

In contrast, stage models posit that health behaviour change passes through a series of stages (Weinstein, Rothman, & Sutton., 1998). It is assumed that individuals at the same stage experience similar barriers and those in different stages face different barriers of translating intentions into action. Additionally, the factors that influence the transition from one stage to another are different (Weinstein, Rothman, & Sutton., 1998). According to this perspective, the optimal intervention can be designed to match a person's stage. The HAPA can be regarded as a stage model because it implies the existence between pre-intentional motivation processes and post-intentional volition processes (Schwarzer, 2008). The distinction between motivational and volitional stages is based on the idea that there is a shift in the mindset of a person from the first stage to the second one (Schwarzer, 2008). Within the two processes or stages of behaviour change, the role of cognitive variables may be different. The motivation phase in which individuals form an intention to act is influenced by risk perceptions, outcome expectancy, and self-efficacy (Schwarzer, 1992, 2001).

Risk perceptions or threat include perceived vulnerability (a person's perception of the risk of contracting a disease) and perceived severity (an individual's perception of the seriousness of a disease). Although risk perceptions have found to be a poor predictor of health behaviour change, they are a necessary prerequisite for the motivation processes; a minimum level of concern about a health threat has to exist in order to help a person to deliberate and make a decision about health behaviour change (Schwarzer, 1992, 2001, 2008; Schwarzer & Luszcynska, 2008). A person also needs to understand the possible consequences of the action before making a decision about whether to engage in particular behaviour. *Outcome expectancies* are a person's beliefs about the positive and negative consequences of performing a specific behaviour. It is assumed that the greater perceived positive outcome and the lower perceived negative outcome of a behaviour change, the more likely people are to

develop an intention to change their behaviour. The HAPA suggests that outcome expectancies and self-efficacy are considered to be the major predictors of intention. Nevertheless, in a situation in which people have no experience with the behaviour they are contemplating (and thus no specific efficacy beliefs), outcome expectancy may be more powerful in influencing motivation to change (Schwarzer, 1992, Bandura, 1997).

In addition to being aware of a health threat and considering the consequences of performing a particular behaviour, the HAPA proposes that people also need to believe in their ability to perform a desired behaviour (*perceived self-efficacy*). Self-efficacy beliefs influence the individuals' goals, and reflect how much effort they will expend in reaching a goal and how long they will persist in the face of difficulties and setbacks (Bandura, 1997, 2004; Schwarzer, 2001). The model also specifies phase-specific self-efficacy beliefs: pre-action self-efficacy (or action/task self-efficacy), maintenance self-efficacy (or coping self-efficacy), and recovery self-efficacy. *Pre-action self-efficacy* is necessary in the motivation phase in which people develop their intentions (Schwarzer & Renner, 2000; Schwarzer, 2008; Schwarzer & Luszczynska, 2008; Schwarzer et al., 2008). There is now convincing evidence that risk perceptions, outcome expectancies and self-efficacy significantly contribute to intentions to perform specific behaviours (Garcia & Mann, 2003; Sniehotta, Scholz, & Schwarzer, 2005; Chow & Mullan, 2010; Schwarzer & Luszczynska, 2008). Thereafter, once goals have been established, risk perceptions and outcome expectancies exert less influence. Only self-efficacy plays a crucial role at all stages in the health behaviour change process (Bandura, 1997; Schwarzer, 2001).

After an intention to perform specific behaviour has been formed, people pursue their goals in the subsequent volition phase. In order to translate intention into action, the intended behaviour is needed to be planned, initiated, maintained, and restarted when problem or failure occurs. This involves self-regulatory strategies (Schwarzer, 1992, 2001; Scholz, Schuz, Ziegelmann et al., 2008).

According to the HAPA, *action planning* plays an influential role in bridging the gap between intentions and behaviour. Action planning is defined as a prospective self-regulatory strategy that links behavioural responses to situational cues by specifying

when, where, and how to perform a behaviour (Gollitwer, 1999; Schwarzer, 2003; Sniehotta, Scholz, & Schwarzer, 2005; Scholz, Schuz, Ziegelmann et al., 2008). Intentions are most likely to be acted on if the individual develops an action plan (Gollwitzer, 1999; Schwarzer, 1992, 2001; Luszczynska & Schwarzer, 2003; Schwarzer & Luszczynska, 2008). The action planning specifies about when, where, and how to carry out the intended behaviour. By forming a specific plan detailing where, when and how to perform the intended behaviour, individuals are more likely to recognise their intentions and carry out the desired behaviours when the specified situation is entered (Gollwitzer, 1999; Schwarzer, 1992, 2001).

Once a new behaviour has been initiated, it has to be maintained through the development of self-regulatory skills and strategies (Schwarzer, 2001; Schwarzer, Luszczynska, Ziegelmann et al., 2008). Self-regulation is broadly defined as any effort that individuals have undertaken in order to alter their own motivation and behaviours, such as setting attainable sub-goals, creating incentives, and mobilising support from other people (Carver & Scheier, 1996; Schwarzer, 2001). In the HAPA, "*action control*" refers to the self-regulatory processes that people can use to control their actions, including focusing attention on the task at hand, resisting temptations, and maintaining emotional balance (Schwarzer, 2001, 2008). The action control is strongly influenced by self-efficacy.

Maintenance self-efficacy describes one's perceived capability to act and sustain healthy behaviour and to deal with unexpected barriers that arise during the maintenance period (Luszczynska & Schwarzer, 2003; Sniehotta et al., 2005; Schwarzer, 2008; Schwarzer & Luszczynska, 2008). Once a new behaviour is established, people with high maintenance self-efficacy exert more effort and persist longer in the face of difficulties and obstacles than those with lower self-efficacy.
However, it should be noted that a new health behaviour might be difficult to maintain over the years without a lapse. *Recovery self-efficacy* represents one's capability to regain some control over behaviour after a setback or failure (Luszczynska & Schwarzer, 2003; Schwarzer, 2008; Schwarzer & Luszczynska, 2008; Schwarzer, Luszczynska, Ziegelmann et al., 2008). Recover self-efficacy has been shown to be important predictor in promoting to long-term maintenance of behaviour change (Luszczynska, Mazurkiewicz, Ziegelmann et al., 2007; Schwarzer,

Luszczynska, Ziegelmann et al., 2008). After the desired behaviour has been performed, the individual evaluates it as successful or failing. Many people sometimes disengage from their goals (Schwarzer, 1992, 2001). *Disengagement* from the goal implies failure of self-regulation. In the case of health-compromising behaviours, effective self-regulation skills are required to improve the maintenance of behaviour (Schwarzer, 2001). However, if the goals were set too high or if situations have changed and become more difficult than before, disengagement or scaling back the goal might be seen as an adaptive strategy because it can have a positive effect such as decreased psychological distress (Carver & Scheirer, 1990; Schwarzer, 2001; Wrosch, Miller, Scheier et al., 2007; Schwarzer, 2008).

Finally, the HAPA suggests that the perceived and actual environment also affect health behaviour change. For example, people may be willing and able to perform the recommended behaviour, but situation barriers as well as opportunities may prevent them from engaging in such behaviour (Schwarzer, 1992, 2001). A schematic representation of Health Action Process Approach model has been shown in figure 6.3.

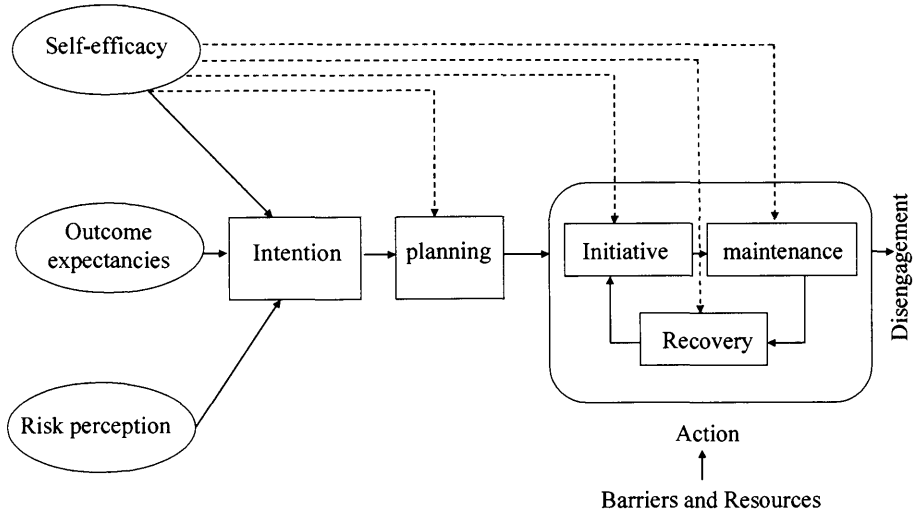


Figure 6.3 Schematic representation of Health Action Process Approach model
Source: Schwarzer (1992); http//usepage.fu-berlin.de/~health/hapa.htm

With regard to the design of health behaviour change interventions, the HAPA suggests that there are three distinct stages involved in designing and implementing specific-stage interventions: pre-intention, intention, and action stages (Lippke, Ziegelmann, & Schwarzer., 2005; Schwarzer, 2008; Wiedemann, Lippke, Reuter et

al., 2009). Individuals with different mindsets can be identified in order to receive a specific intervention/treatment. In a *pre-intention stage*, individuals are classified as non-intenders. At this motivation stage, they are developing their intentions to perform a behaviour. After the intentions have been set, people enter the volition phase. This volition stage is further subdivided into two sub-stages: intention and action stages. While in the *intention stage* individuals hold an intention to act, but they have not yet acted (intenders), people in the *action stage* already act according to their intentions (actors).

A number of studies (e.g. Lippke, Ziegelmann, & Schwarzer., 2005; Schüz, Sniehotta, Mallach et al., 2009) have shown that the specific cognitive factors that move people from one stage to the next are different; risk perception is crucial in forming an intention for people in the pre-intention stage who have no pre-existing intention, whereas self-efficacy has been found to influence the transition through three stages of change for all groups: non-intenders, intenders and actors (Lippke, Ziegelmann, & Schwarzer., 2005; Schüz, Sniehotta, Mallach et al., 2009). This implies that effective intervention aimed at changing health behaviours should be tailored to their stages of change (Lippke, Ziegelmann, & Schwarzer, 2004, 2005; Lippke & Ziegelmann, 2008; Schwarzer, 2008). For example, individuals in the pre-intention stage should benefit from motivational intervention, whereas people in the intention stage should benefit from an action planning intervention to help them translate their intentions into actual behaviour. For individuals in the action stage, an intervention designed to promote self-efficacy beliefs (coping self-efficacy and recovery self-efficacy) may be useful to help them maintain their healthy behaviours (Lippke, Ziegelmann, & Schwarzer, 2004; Lippke & Ziegelmann, 2008; Schwarzer, 2008).

6.4 The application of the HAPA model: research on health-related behaviours using the HAPA model

The HAPA model has shown to predict health behaviours, including dental flossing, seat belt use, dietary behaviour, physical activity, breast self-examination, low-risk, single-occasion drinking, and smoking (Schwarzer & Renner 2000; Murgraff,

McDermott, & Walsh, 2003; Schwarzer & Luszczynska, 2003; Schwarzer, Schuz, Ziegelmann et al., 2007; Schwarzer & Luszczynska, 2008; Schwarzer, Luszczynska, Ziegelmann et al., 2008; Chow & Mullan, 2010). Moreover, Garcia and Mannn (2003) compared the ability of five social-cognitive models, including the HBM, revised HBM (including self-efficacy), TRA, TPB, and HAPA in predicting intentions to engage in two different health behaviours (resisting dieting and performing breast self-examination). The HAPA yielded the greatest predictive explanatory power for both behaviours. According to prior studies, the model explained between 30 percent and 69 percent of the variance in intentions, and between 29 per cent and 73 per cent of the variance in behaviours (Schwarzer & Renner 2000; Garcia & Mann, 2003; Luszczynska & Schwarzer, 2003; Murgraff, McDermott, & Walsh, 2003; Luszczynska, 2004; Schwarzer, Schuz, Ziegelmann et al., 2007; Schwarzer, Luszczynska, Ziegelmann et al., 2008; Schwarzer & Luszczynska, 2008; Chow & Mullan, 2010).

6.4.1 The HAPA model: predicting intention and health behaviours

The HAPA model has been used to predict a wide range of health-related behaviours. For example, Garcia and Mann (2003) assessed the ability of the HAPA to predict intentions to resist dieting. All motivational variables specified by the HAPA (risk perception, outcome expectancies, and self-efficacy) were measured. The results of this study revealed that risk perception, outcome expectancies, and self-efficacy were significantly related to intention to resist dieting.

Likewise, Schwarzer and Renner (2000) applied the HAPA model to predict nutrition behaviours (low fat and high-fibre dietary intake) in 524 residents of Berlin. Participants completed questionnaires at baseline (time 1) and six months later (time 2). Risk perception, outcome expectancies, action self-efficacy, and intentions were measured at time 1. Coping self-efficacy, low-fat dietary intake, and high-fibre dietary intake were measured at time 2. The results of this study revealed that risk perception, outcome expectancies, and action self-efficacy significantly predicted intention. Nutrition behaviours (low fat and high-fibre dietary intake) were predicted by intentions and coping self-efficacy.

In addition, Murgraff, McDermott, and Walsh (2003) assessed the usefulness of HAPA model in predicting drinking behaviour in a sample of 160 female undergraduates. Self-efficacy, action planning, action control, intention, social barriers, and past drinking frequency were measured at two time points. The first questionnaire was completed at recruitment into the research study, and the second one was completed two weeks later. Drinking behaviour at follow-up was predicted by self-efficacy for action planning and action control (equivalent to coping self-efficacy), and past drinking frequency. Intentions did not predict drinking behaviour either directly or indirectly.

The HAPA has also been shown to predict detection behaviour such as breast self-examination. Luszczynska and Schwarzer (2003) reported an application of the HAPA model to breast self-examination (BSE) in 418 young women. Participants completed assessments at baseline and twelve to fifteen weeks later. At time 1, all HAPA motivational variables (risk perception, outcome expectancies, and action self-efficacy) were measured. Action planning, maintenance self-efficacy, recovery self-efficacy, and BSE were measured at time 2. Intention to perform BSE was predicted by outcome expectancies and action self-efficacy, but not risk perception. Breast self-examination was predicted by planning, maintenance self-efficacy and recovery self-efficacy.

The model has also proven useful in predicting preventive behaviours. Schwarzer, Schuz, Ziegelmann et al. (2007) conducted four studies to investigate the applicability of the model across four preventive behaviours (dental flossing, seat belt use, dietary behaviour, and physical activity. Three predictors of intention (risk perception, outcome expectancies, and self-efficacy) and three proximal predictors of behaviours (intention, action planning, and recovery self-efficacy) were included in these studies. The findings showed that action planning and recovery self-efficacy emerged as significant predictors of all four of the investigated preventive health behaviours.

Sniehotta, Scholz, & Schwarzer (2005) applied the HAPA model to physical exercise behaviour in a sample of 307 cardiac rehabilitation patients. Participants were asked to complete questionnaires at the rehabilitation centre (time 1), two months after discharge (time 2), and four months after discharge (time 3). At time 1, risk

awareness, outcome expectancies, action self-efficacy, and intentions were measured. All of these variables and maintenance self-efficacy, action planning, and action control were measured at time 2. Physical exercise was measured at time 3. The study showed that intention to exercise in the patients with coronary heart disease was predicted by risk perception, outcome expectancy and self-efficacy. Physical exercise four months after discharge was predicted by intention, planning, maintenance self-efficacy, and action control. The effects of intention on exercise behaviour were lower than the direct effects of the three volition constructs. Recently, three longitudinal studies examining long-term exercise adherence in rehabilitation patients (cardiac and orthopaedic patients) conducted by Schwarzer, Luszczynska, Ziegelmann et al. (2008) also showed that planning and recovery self-efficacy were significant predictors of exercise adherence across three studies. The authors reported that between 14 per cent and 39 per cent of the variance in exercise behaviour was explained by these two predictors. In addition, in all three longitudinal studies, risk perception was not significantly associated with other variables under study. This may indicate that in the context of cardiac and orthopaedic rehabilitation patients, a different strategy (e.g. intervention focusing on planning and recovery self-efficacy) may have a significant impact on changing physical activity than risk communication (Schwarzer, Luszczynska, Ziegelmann et al., 2008).

Scholz, Schuz, Ziegelmann et al. (2008) conducted a 5-week longitudinal study to examine whether adding action planning and coping planning would improve the overall prediction of exercise behaviour. The study showed that all motivational HAPA variables (risk perception, outcome expectancies, and self-efficacy) accounted for 17 per cent of variance in exercise activity five weeks later, and only self-efficacy was a significant predictor of intention to exercise. However, when adding action planning and coping planning into the model, the amounts of variance in Time 2 exercise behaviour were increased to 23 per cent. In other words, the inclusion of action plan and coping plan contributes to the better prediction of exercise behaviour, as compared with intentions alone. Additionally, this study showed that only active individuals (maintainers) benefited from coping planning (Scholz, Schuz, Ziegelmann et al., 2008). Other studies also revealed that coping planning is effective in maintaining long-term behavioural change (Sniehotta, Scholz, & Schwarzer, 2005; Sniehotta, Schwarzer, Scholz et al., 2005; Ziegelmann, Lippke, & Schwarzer, 2006).

Finally, Scholz, Nagy, Gohner et al (2009) examined the usefulness of the HAPA in predicting two different behaviours (smoking and low-fat diet). It was hypothesized that change in HAPA motivational variables would predict change in intentions and that change in volitional variables (intentions, self-efficacy, action planning, and action control) would predict change in behaviour. In the first study, participants viewed a commercial web-based nutrition programme that included an online diet-diary, feedback on weight change over time, recipe suggestions and weekly "coaching letters", whereas the participants in study two viewed smoking-related web pages. Participants in both studies were asked to fill out the online questionnaires. Data were collected at two time points. The results showed that neither change in risk perception nor change in outcome expectancies predicted change in intentions. Only change in self-efficacy was found to be associated with change in intentions in both behaviours (smoking and low-fat diet). For predicting change in behaviours, it was found that change in number of daily cigarettes smoked was significantly related to change in action control and change in self-efficacy. Change in eating a low-fat diet was predicted by change in intentions (marginally significant direct effect), change in action planning, and change in action control. The findings from this study suggest that action control may be a promising target for designing effective interventions for changing repeated behaviours such as smoking and eating low-fat foods because change in action control had the strongest effect on change in both investigated behaviours (Scholz, Nagy, Gohner et al, 2009).

In summary, a number of studies applying the HAPA have provided support for the important role of volitional variables in predicting health-related behaviours. Therefore, the volitional factors should be included in the motivational models of health behaviour. Schwarzer (1992, 1999, 2001) argued that in the volition phase, where individuals plan the details, perform the desired behaviour, persist, possibly fail to maintain their health behaviour, and then recover, volitional constructs such as action planning, maintenance self-efficacy, recovery self-efficacy, and action control help to bridge the gap between intention and behaviour.

6.4.2 The HAPA model: intervention studies

The HAPA model is increasingly being used to inform the development of behaviour change interventions. Recently, three intervention studies have evaluated the effect of planning interventions in samples of cardiac and orthopaedic disease patients. Lippke, Ziegelmann, & Schwarzer (2004) conducted an experimental randomised prospective design to evaluate the effectiveness of planning intervention in 560 orthopaedic patients. Participants were randomised to either (1) intervention group (a planning intervention) or (2) control group (no-planning). Intervention participants were encouraged to form up to three action plans about where, when, and how they would exercise after discharge from rehabilitation. In addition, participants were also encouraged to think about any difficulties that might hinder the implementation of their exercise plans and then formed a coping plan to overcome those difficulties or obstacles. The participants were asked to complete three assessments at baseline (prior to exercise therapy), two weeks, and four weeks after discharge. The authors reported that the planning intervention had no effect on intention in any patient group, but resulted in a significant increase in action plans and higher rates of exercise behaviour. When the sample was divided into three groups (divided according to their intentions to exercise) : non-intenders, intenders, and actors, a significantly higher exercise adherence rate was found only in intenders.

Similarly, Sniehotta, Scholz, Schwarzer et al. (2005) investigated the effects of two interventions (planning intervention and personalised weekly diary intervention) on changes in physical exercise in 240 coronary heart patients. Participants were randomly assigned to one of three groups: standard care control group, planning group, and planning plus diary group. All participants were asked to complete questionnaires. The first questionnaire was collected at the rehabilitation centre. Follow-up questionnaires were completed two months (time 2), and four months after discharge (time 3). Intentions, self-efficacy, and planning were assessed at all three times. Action control was measures at time 2 and time 3. Participants in the two intervention groups were encouraged to develop a specific plan for their physical activity. In addition to forming an action planning, participants in the planning plus diary group were encouraged to keep a weekly diary to self-monitor their physical activity for six weeks after discharge from the rehabilitation centre. Participants in the

two intervention groups showed greater adherence to exercise at follow-up than those in the standard care group. Those in the planning plus diary group had higher levels of action control and more stable intentions. There was also a trend towards higher levels of exercise in the planning plus diary group.

Sniehotta, Scholz, and Schwarzer (2006) found similar results in their study that assessed the effect of planning interventions designed to promote regular physical exercise after discharge from cardiac rehabilitation in 211 cardiac patients. Participants were randomly assigned to a standard care control group, action planning group, or combined planning group (both action planning and coping planning were formed). While patients in the action planning were encouraged to form a specific plan about when, where and how they would exercise after discharge, patients in the combined planning group were additionally asked to develop up to three coping plans regarding strategies for dealing with anticipated difficulties in complying with the exercise programme. Data were collected at two time points: the second week of the rehabilitation programme (time 1) and two months after discharge (time 2). The results of this study showed that participants in the combined planning group had significantly higher adherence to exercise after discharge than those in the action planning and control groups. Also, a trend towards higher rates of exercise was observed in the action planning group.

A more recent intervention study based on the HAPA model (Schüz, Sniehotta, & Schwarzer, 2007) examined stage-specific effects of an action control intervention on dental flossing. A total of 151 university students completed questionnaires at baseline (time1), two weeks after time1 (time 2) and four weeks after time 2 (time 3). A dental flossing calendar was designed and used as self-monitoring tools. Participants were classified into the motivational and volitional stages. An action control intervention resulted in increased action control levels at follow-up in all participants. Nevertheless, significantly higher levels of action control were found in volitional participants. Additionally, change in dental flossing in volitional participants was predicted by change in action control. Intention was not significantly related to change in dental flossing among participants in this group. This is consistent with the theoretical assumptions, which propose that individuals who are in the volition stage profit from self-regulatory efforts (Schwarzer, 2008).

These studies have provided evidence for the effectiveness of HAPA-based interventions in improving or changing health behaviours. Although the HAPA is an appealing model in health behaviour research for designing effective health behaviour change intervention, a number of criticisms have been brought against it. This includes the validity of stage assessment and the lack of specification of the factors that influence stage transitions (Sutton, 2005, 2008; Conner, 2008). As the stage models will be most useful to design the matching intervention when certain groups of individuals in each stage have been correctly identified. Therefore, the stage algorithm must identify homogenous group of individuals to stages according to their change process (Weinstein, Rothman, & Sutton, 1998; Schwarzer, 2008). While in the Transtheoretical Model of behaviour change (TTM), the passage of time is used as the main criterion for grouping people in each stage (Prochaska, DiClemente, & Norcross, 1992; Weinstein, Rothman, & Sutton, 1998), the HAPA uses psychological variables (intention and behaviour) to group people into three categories: non-intenders, intenders, and actors (Lippke, Ziegelmann, & Schwarzer 2004; Schwarzer, 2008).

In the HAPA, the term stage is used as synonymous with phase or process. During the behaviour-change process, individuals can cycle and recycle in the motivation and volition phases (Schwarzer, 2008). Outcome expectancies, self-efficacy, and risk perceptions are expected to be the factors that move individuals from pre-intenders to intenders (Schwarzer, 2008), whereas action planning, coping planning, and self-efficacy are supposed to facilitate in the second transition, from intenders to actors (Schwarzer, 2008; Schüz, Sniehotta, Mallach et al., 2009). Although the validity of stage assessment poses an interesting debate, recent studies have shown that matching treatment to individual in a particular stage is a promising intervention and a pragmatic approach (e.g. Lippke, Ziegelmann, & Schwarzer, 2004; Schüz, Sniehotta, & Schwarzer, 2007). However, more research on the stage assessment validity and on the potential impact of misclassification of individual at each stage is required.

6.5 The translation of intention into action: implementation intentions

It has long been argued that individual's intention to perform a behaviour is the most proximal predictor of subsequent behaviour (Locke & Latham, 1990; Ajzen, 1991, Bandura, 1977, 2004). However, according to a recent meta-analysis of 47 experimental studies conducted by Webb and Sheeran (2006), a medium-to-large change in intention (effect size; d =.66) results in a small-to-medium change in behaviour (d = 0.36). This finding suggests that the intention has positive effect on behaviour, but the effect size is small to medium only (R^2 = .03). In an attempt to examine the intention-behaviour gap, Orbell and Sheeran (1998) differentiated between people with positive intentions who do not perform behaviour according to their intentions (inclined abstainers) and individuals with negative intentions who perform behaviour (disinclined actors). The authors found that discrepancies between intentions and behaviour were caused by inclined abstainers rather than by disinclined actors. In addition, a review of health behaviours (e.g. exercise, condom use, and cancer screening) by Sheeran (2002) indicated that individuals with positive intentions translated their intentions into action only 53 per cent of the time. This indicates that there is a substantial "gap" between individuals' intentions and their subsequent behaviour (Sheeran, 2002; Sheeran, Milne, Webb, et al., 2005; Gollwitzer & Sheeran, 2006).

Implementation intentions have been proposed as a powerful tool to bridge the intention-behaviour gap. Forming implementation intentions is part of the Model of Action Phases (MAP) (Heckhausen & Gollwitzer, 1987; Gollwitzer & Sheeran, 2006). According to the MAP, forming of a goal intention is the first step to goal attainment. Intention formation is influenced by individuals' beliefs about the desirability (i.e., expectancy and value) and feasibility of the goal. Following the goal setting processes, in order to attain the goal, the person must deal effectively with self-regulatory problems (such as failing to get started and getting derailed) in goal striving (Heckhausen & Gollwitzer, 1987; Gollwitzer & Sheeran, 2006).

An implementation intention is a specific plan, which specifies exactly when, where, and how one will act in order to achieve his or her goal (Gollwitzer, 1999; Gollwitzer

& Sheeran, 2006). Although both implementation intentions and action planning represent a mental "if-then" association that links specified behavioural response to specific situational cues, plans in the form of implementation intentions are usually provided by the researcher in a pre-worded if-then sentence (Sniehotta, 2009; Chapman, Armitage, & Norman, 2009). Implementation intentions are distinct from intentions as they specify both the situational context and behaviour that helps to realise the desired behaviour. While, a goal intention has a form "I intend to do X" or "I will do X", implementation intentions take on the specific form of "I intend to do X in time and place Y" (Gollwitzer, 1999; Sheeran, 2002; Gollwitzer & Sheeran, 2006). Implementation intentions are hierarchically subordinate to goal intentions, and they are formed in the service of the goal. Forming plans in the form of implementation intentions requires an individual to identify a response that will enhance goal attainment and anticipate a suitable occasion to initiate that response (Gollwitzer & Oettingen, 1998; Gollwitzer & Sheeran, 2006; Sheeran, Milne, Webb, et al., 2005).

Theoretically, implementation intentions facilitate goal attainment through two component processes: increasing the activation of the anticipated situational cue (specified in the if-component of the plan) and automating the goal-directed response to that cue (specified in the then-component of the plan) (Gollwitzer, 1999; Gollwitzer & Sheeran, 2006; Parks-Stamm, Gollwitzer, & Oettingen, 2007). An individual who forms an implementation intention selects a specific situational cue for the if-part of the plan, this means that they decide in advance which of the possible opportunities will be used to achieve the intended goal. Therefore, the person is "perceptually ready" to encounter that situation, leading to heightened activation of the mental representation of the specified situational cues. As a consequence, individuals who form implementation intentions are better able to detect, attend to, and recall specified cue when that cue is encountered (Gollwitzer, 1999; Gollwitzer & Sheeran, 2006).

Forming implementation intentions also involves the selection of an effective goal-directed response (specified in the then-component of the plan) upon encountering the specified situation. This means that a mental link is created between the chosen situational cue and the intended goal-directed response in the form of if-then plans. The consequence of this strong link leads to the automatic action initiation once the

critical situation is encountered. Accordingly, the predetermined responses are initiated immediately, efficiently and with less need for conscious intent (Gollwitzer & Brandstatter, 1997; Brandstatter, Lengfelder, & Gollwitzer et al., 2001; Gollwitzer & Sheeran, 2006; Sheeran, Milne, Webb, et al., 2005; Parks-Stamm, Gollwitzer, & Oettingen, 2007; Webb & Sheeran, 2007). Implementation intentions do not affect individuals' motivation or intention (Sheeran & Orbell, 1999; Gollwitz & Sheeran, 2006; Sniehotta, Soares, & Dombrowski, 2007; Webb & Sheeran, 2007). Rather, by forming if-then plans, people pass the control of the behaviour over to anticipated critical situational cues (Gollwitzer & Brandstatter, 1997; Gollwitzer, 1999).

There is now significant evidence that encouraging individuals to make implementation intentions significantly increases the likelihood of them achieving behavioural change (e.g. Sheeran & Orbell, 2000; Milne, Orbell, & Sheeran, 2002; Armitage, 2007; Luszczynska, Sobczyk, & Abraham, 2007; Sniehotta, Soares, & Dombrowski, 2007; Webb & Sheeran, 2007; Prestwich, Ayres, & Lawton, 2008; van Osch, Reubsaet, Lechner et al., 2008). Sheeran and Orbell (1999), for example, conducted two experiments to test the effects of implementation intentions in relation to vitamin supplement use. Participants were given bottles of vitamin pills and asked to fill out the time 1 questionnaire. Follow-up questionnaires were collected ten days later (time 2) and three weeks later (time 3). The implementation intention intervention was a questionnaire manipulation. Intervention participants were asked to write down when and where they would take a vitamin C tablet every day for the next three weeks, whereas those in the control group were asked to complete the questionnaire without implementation intention manipulation. Behaviour (taking vitamin C tablets) was measured by self-report and pill count at time 2 and time 3. The results showed that no significant difference was found between the two groups in the number of missed pills (both the pill count and self-report) at time 2 (ten days into the intervention). However, after three weeks, participants in the intervention group missed significantly fewer pills than those in the control group. In the second experiment, the results confirmed that there was significant difference in the number of missed pills between the two groups at three weeks.

Implementation intentions have been shown to increase attendance for cervical screening (Sheeran & Orbell, 2000). Participants were 114 women who registered at a

medical practice in England. These women received a standard postal reminder from their medical practitioner encouraging them to attend for a smear test within the next three months. Then, questionnaires based on the Theory of Planned behaviour (TPB) with implementation intention manipulation were sent to the participants in the intervention group. The following written instructions were included to the postal questionnaire for the intervention participants "You are more likely to go for a cervical smear if you decide when and where you will go. Please write in below when, where, and how you will make an appointment". Space was included to allow participants to write down their implementation intentions. For the control group, the questionnaires were identical in all respects apart from this item. The results of this study showed that cervical screening attendance rate was significantly higher (92 per cent) in participants who formed implementation intentions than those who did not form if-then plans (69 per cent).

Armitage (2004) assessed the effectiveness of an implementation intention-based intervention for reducing dietary fat intake. Participants were asked to complete questionnaire based on the TPB at baseline and one month later. Participants in the intervention group (n = 138) received the implementation intention-based intervention (questionnaire with implementation manipulation). The same questions were administered to the control group (n = 126) but without the implementation intention manipulation. Multivariate analysis of variance (MANOVA) indicated that there were significant differences between the intervention and control in the total fat intake, saturated fat intake, and proportion of energy derived from fat; all the three indexes of dietary intake significantly decreased over time in the intervention group but not in the control group.

Implementation intentions have also been found to be an effective intervention in changing oral self-care behaviour (Sniehotta, Soares, & Dombrowski, 2007). Participants were 140 undergraduate students recruited after a lecture. All participants completed a questionnaire based on the TPB at baseline and received a coded sample of dental floss together with a flossing guide. In addition to TPB variables, intentions and perceived behaviour control (PBC) were measured at time 2 in order to assess whether the manipulation has effects on participants' motivation. Participants were randomly assigned to either the intervention group or the control group. Intervention

participants were asked to form an implementation intention specifying when and where they would use dental floss. Behaviour was determined from self-report flossing and the measurement of residual floss at two weeks and two months after the intervention. The results showed that compared with a no-intervention control condition, implementation intention-based intervention had no effect on TPB motivation variables, but led to a significant increase in flossing by intervention participants two weeks and two months after intervention (Sniehotta, Soares, & Dombrowski, 2007).

Milne, Orbell, and Sheeran (2002) tested the efficacy of motivational interventions augmented by implementation intentions in promoting physical activity. They compared the motivational intervention based on the Protection Motivation Theory (PMT) with a combined motivational and volitional (implementation intentions) intervention. The study was conducted in 248 undergraduate students in the UK. Participants were randomly assigned to either the control group or one of two intervention groups: PMT-based motivational intervention (experimental group 1) and PMT-based motivational intervention plus implementation intentions (experimental group 2). Participants were also informed that an exercise session must be at least 20 minutes long. Data were collected at three points in time. At time 1, the motivational intervention was implemented; participants in the two intervention groups were asked to read a health educational leaflet regarding coronary heart disease and the benefits of exercise, whereas the control group were asked to read the opening three paragraphs of a novel.

Following the implementation of the PMT-motivational intervention, PMT variables (perceived severity, perceived vulnerability, response efficacy, and self-efficacy) and intention were measured. At time 2, one week later, exercise behaviour was measured. Then all participants were asked to complete the PMT questionnaire; PMT variables and intentions were assessed a second time. In addition to completing the PMT questionnaire, participants in the experimental group 2 (PMT-based motivational intervention plus implementation intentions) were asked to form implementation intentions specifying when and where they would carry out exercise in the following week. One week later, at time 3, all the three groups were asked to complete the PMT questionnaire again, and exercise behaviour was also measured. The study showed

that PMT-based motivational intervention had been effective in changing PMT cognitions and intention to engage in exercises, but it had no significant effect on exercise behaviour. By contrast, the PMT-based motivational intervention plus implementation intentions led to significantly increase exercise participation (91 per cent) among the experimental group 2. Additionally, this study found that there were no significant differences in intention (assessed at time 3) between experimental group 1 and experimental group 2 after the implementation of an 'if-then' plan intervention. Thus, a significant increase in subsequent exercise behaviour could not be explained by PMT-based motivational intervention (Milne, Orbell, & Sheeran, 2002).

Recently, a meta-analysis of 94 studies with participants of different age and gender conducted by Gollwitzer and Sheeran (2006) indicated that implementation intentions were effective in enhancing people's achievement of their goals and had overall effect size of .65 on goal attainment. Nevertheless, although implementation intentions are generally highly effective in translating intention into behaviour, some recent studies have failed to show if-then plans intervention effects on behaviour (Michie, Dormandy, & Marteau, 2004; Jackson, Lawton, Knapp et al., 2005; Jackson, Lawton, Raynor et al., 2006; Rutter, Steadman, & Quine, 2006; De Vet, Oenema, Sheeran et al., 2009). It has been argued that the lack of effects of implementation intentions may be based on several reasons, including types of health behaviours (single one-off/repeated behaviour, simple/complex behaviour), types of goals (difficult/easy goals), the study populations (student, clinical population/non-clinical population), the setting of the study (clinic/ non-clinic settings), the follow-up time periods, and the validity and reliability of the outcome measures used (Dewitte, Verguts, & Lens, 2003; Michie, Dormandy, & Marteau, 2004; Jackson, Lawton, Knapp et al., 2005; Jackson, Lawton, Raynor et al., 2006; Rutter, Steadman, & Quine, 2006; De Vet, Oenema, Sheeran et al., 2009).

Michie, Dormandy, and Marteau (2004), for example, tested the efficacy of implementation intention intervention in increasing the rates of antenatal screening uptake. Women were asked to form a specific plan during their visit for an ultra-sound dating scan (12 weeks gestation). Participants were also asked to complete the questionnaire that measured attitude towards undergoing screening and screening

intention. Screening behaviour was assessed from laboratory records. The results of this study showed that no statistically significant differences in uptake between the intervention and control groups. However, only 63 per cent of women (25/40) in the intervention group completed a specific plan in the questionnaire. Within the intervention group, the higher screening uptake was observed in woman who formed implementation intentions, as compared with those who did not (84 per cent vs. 47 per cent, $p = 0.017$). Also, there were trends towards positive attitude and stronger intentions in the woman who formed if-then plans. The findings suggest that implementation intention interventions may be less effective in a clinic setting than in the settings used in studies of students (a lecture theatre setting) because in a busy place such as an antenatal clinic, women also underwent a medical procedure, were referred for counselling, and possibly looked after their children. These activities may have contributed to the low rate of compliance for developing implementation intentions in these individuals.

Jackson, Lawton, Knapp et al. (2005) found that the formation of implementation intentions had no significant effect on promoting adherence to antibiotics. A possible explanation may be that participants in this study were sufficiently motivated to take the short-term course of antibiotics (7 days). A study examining the effects of implementation intentions in relation to vitamin supplement reported by Sheeran and Orbell (1999) also found similar results; no significant difference between intervention and control groups in the number of missed pills after ten days following an implementation intention intervention. For short-term, simple behaviour, strong intentions are possibly sufficient to change behaviour without requiring an implementation intention. Rather, the formation of implementation intentions may be needed in the cases of repeated behaviours (dental flossing, Sniehotta et al., 2007) or long-term, complex behaviours such as physical activity, smoking, and a healthy diet (e.g. Milne, Orbell, & Sheeran, 2002; Armitage, 2004; Armitage, 2007; Prestwich, Ayres, & Lawton, 2008).

6.6 Conclusion

In summary, this chapter has reviewed the social-cognitive models of behaviour change and the application of the theoretical models to health-related behaviours. Much consideration has been given to the Health Action Process Approach (HAPA) model and the use of implementation intentions to facilitate the translation of intentions into behaviour, as they provide a framework for study 2. The HAPA identifies both pre-intentional and post-intentional factors relating to behaviour change. The existing research literature demonstrates that the HAPA model has been successfully applied to the prediction of a wide range of health-related behaviours (e.g. Schwarzer & Luszczynska, 2003; Schwarzer, Schuz, Ziegelmann et al., 2007; Schwarzer & Luszczynska, 2008; Schwarzer, Luszczynska, Ziegelmann et al., 2008; Chow & Mullan, 2010). In the following chapter, the HAPA model, in combination with the qualitative data gathered in study 1, will be used to guide an intervention to promote influenza vaccination in high-risk Thai adults. The chapter will also present the research methodology and the results of a randomised trial investigating the effects of a HAPA-based educational leaflet intervention and action planning on influenza vaccination, as well as the findings on the applicability of the HAPA model in the context of vaccination behaviour.

Chapter 7: Using the HAPA and implementation intentions to increase influenza vaccine uptake

7.1 Introduction

This chapter outlines the research design, description of study population, research setting, and the development and implementation of intervention programme to increase influenza vaccination rates. It also describes data collection tool, procedures, and data analysis. The chapter then presents the results of the study along with the discussion. It further considers the strengths and limitations of the study. Finally, a conclusion is provided.

7.2 Methodology

7.2.1 Study setting

The study was conducted in the Muang district, an urban community of Chiang Rai province with a population of 223,936. Chiang Rai is the northernmost province of Thailand and has an adult literacy rate of 93 per cent (National Statistical Office, 2006). Two geographically separated communities were chosen to limit contamination between trial arms. These two areas were similar in overall population size, the number of people with chronic diseases requiring influenza vaccination within them, and the baseline influenza vaccination rate among high-risk people. The two geographically separated communities were assigned randomly to an intervention or comparison areas.

7.2.2 Design and participants

A controlled before and after trial was carried out. This study compared the effect of a HAPA-based educational leaflet with a standard government information leaflet on influenza vaccination behaviours among high-risk urban dwelling Thai adults.

The study was powered to detect between group differences in influenza vaccination rates of 22% (between the previous year's vaccination rate of 38% and a predicted rate of 60%). This required a sample size of 177 participants with a power of 0.80 at a significance level of 0.05 (Fleiss, Levin, & Paik, 2003).

The study was confined to people aged 45-65 years with chronic diseases with clinical indications requiring influenza vaccination. These included heart disease, chronic obstructive pulmonary disease, asthma, chronic renal disease and diabetes mellitus. Potential participants were identified from the National Health Security Office list. They were excluded from the study if they reported to a research assistant (a local health volunteer) any of the following: (1) known or suspected allergy to egg protein; (2) hypersensitivity to any component of the vaccine; (3) severe chronic conditions (i.e., bed bound or acutely ill); (4) dementia or suspected dementia, or (5) being unable to read and write. The research ethics committee, Chiang Rai province, Thailand approved the study, and all participants signed informed consent.

Potential participants were identified from the list patients who were offered free vaccination from the National Health Security office (NHSO). Of the 594 potential participants (two communities), 401 met all the eligibility criteria: (1) people aged 45-65 years with chronic diseases with clinical indications requiring influenza vaccination, and (2) being able to read and write. Of these, 105 were randomly selected from one community (comparison area) to participate in the study using a lottery method without replacement. The random selection process was repeated. One hundred potential participants were randomly selected from another community (intervention area). Four participants withdrew before starting the study (before completing the baseline questionnaire). Accordingly, a total of 201 high-risk Thai adults were included in the study (99 in the intervention group and 102 in the comparison group) (see Figure 7.2.2).

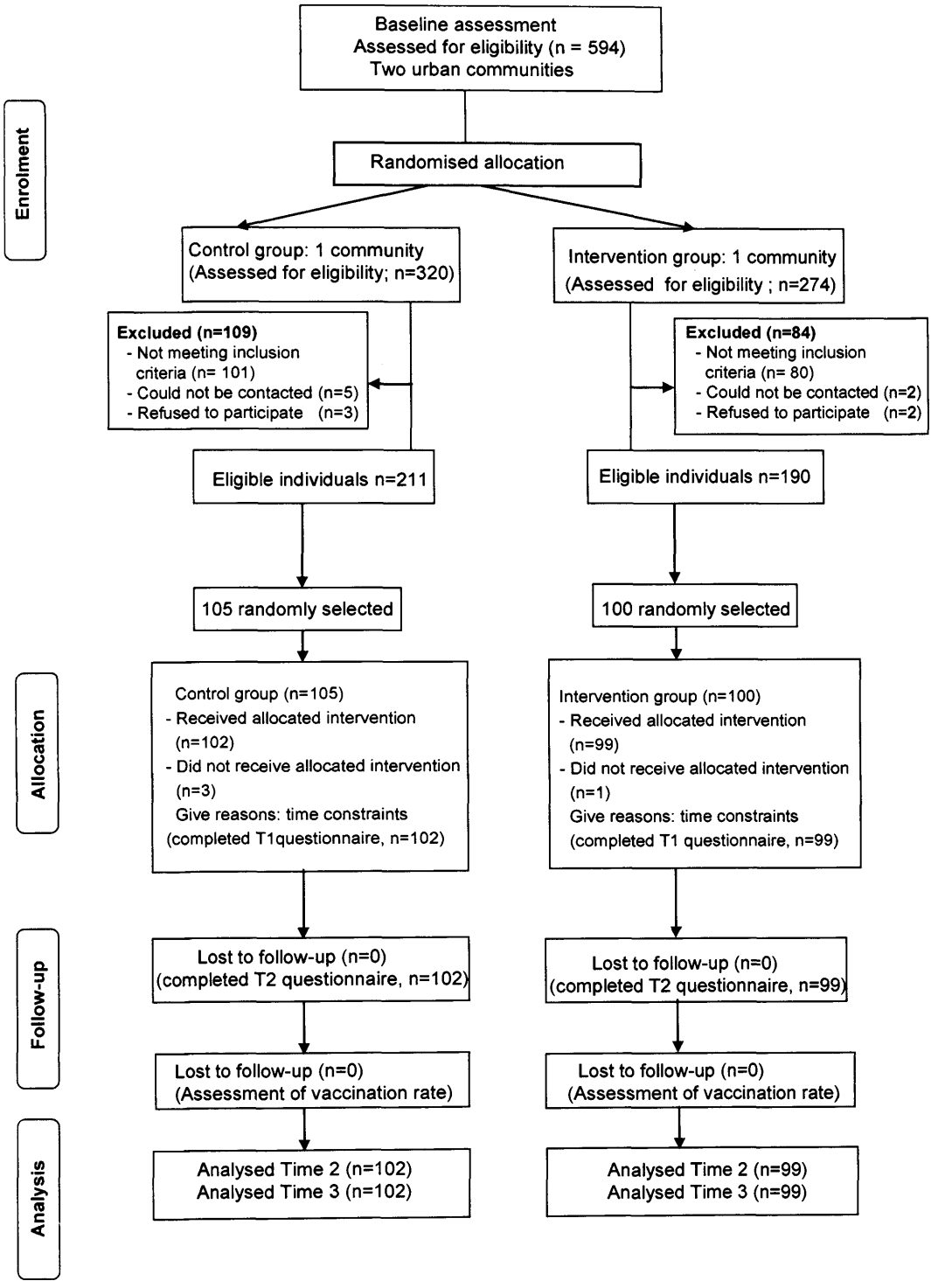


Figure 7.2.2 Flow diagram of participants' progress through the randomised trial

7.2.3 Intervention

The interventions were conducted during a 6-week period before the influenza vaccines were available for all high-risk people. As data from study 1 showed a wide range of perceptions about influenza and influenza vaccination; for example, few people believed that influenza was a serious disease and could cause death, whereas others considered it to be no worse than a "bad cold". Some participants with chronic diseases viewed influenza vaccination as a mean to prevent exacerbation of their underlying conditions. By contrast, several participants in the study, especially those who perceived themselves as healthy, considered the influenza vaccination to be unnecessary for them. Additionally, the findings showed that salience of risk, influence of others, perception of the need for preventive health care, and the availability of influenza vaccine emerged as important influences on the decision whether to accept or refuse the influenza vaccination.

Based on the responses of our participants, suggestions for focal points to consider in the message development for influenza vaccination education materials are the emphasis on the seriousness of influenza, risk of developing influenza-related complications, the benefits of getting immunised, and the need for influenza vaccination. Using a combination of the qualitative data gathered in study 1 and a theoretical model of behaviour change (HAPA model), an educational leaflet was created to target high-risk Thai adults. As described previously in Chapter 6, the HAPA posits two processes involved in changing individual behaviour: motivation (the formation of intention) and volition (the translation of intentions into behaviour) processes. In the motivational phase, the HAPA suggests that an indiviual's intention to perform a behaviour is influenced by risk perception, outcome expectancy, and self-efficacy. After a goal intention has been developed, intended behaviour must be planned, initiated, maintained, and restarted when problem occurs (Schwarzer, 1992, 1999, 2001). Accordingly, the behaviour change techniques used in the leaflet, included providing information about the behaviour-health link (Abraham & Michie, 2008). This involved highlighting the susceptibility to influenza and its complications in high-risk people with chronic disease (e.g. "You are at high risk for severe complications such as pneumonia, and blood infections. This may put you in the hospital, so why risk it?"). These health risk messages focused on increasing

perceptions of personal risk rather than arousing fear of disease (see Ruiter, Abraham, & Kok, 2001).

A second behaviour change technique involved providing information on the benefits of vaccination. This involved phrases such as "Taking the flu shot will help you a lot through the flu season: Don't get the flu! Don't spread the flu! Don't have serious complications, Reduce the risk of going into hospital, and Stay healthy during the influenza season". The leaflet also sought to increase participants' efficacy in relation to their ability to both benefit from and cope with the vaccination by including the personal accounts of people who had received the influenza vaccination (e.g. "I have asthma, I need to protect myself. At first, I had not agreed to get the flu shot because I was afraid of allergies and breathing difficulty, but I was fine after the injection"). These accounts also sought to increase normative beliefs favouring vaccination.

Finally, the leaflet encouraged participants to develop a specific plan (Gollwitzer, 1999, Schwarzer, 2003) detailing where, when and how they would obtain the influenza vaccination (prompt specific goal setting). Additionally, participants were asked to consider how they would go to the clinic to receive influenza vaccine (prompt barrier identification). As action planning (Schwarzer 2001) is analogous with implementation intentions ("if-then" plans) (Gollwitzer, 1999). Thus, "if- then" statement was used in this study. In order to facilitate the forming of the plans and to ensure consistency, examples were also provided by the researcher. The following instructions were included in the HAPA-based leaflet for the intervention group.

> "Getting a flu vaccination: Plan ahead! You are more likely to go for having the flu shot, if you decide now about where, when and how you will go. Please write in below when, where and how you plan to get a flu vaccine.
>
> "If I get an appointment letter to have the flu vaccine, then I will .....(please write down **what you plan to do**, e.g. go for taking the flu shot) at.....(please write down **Where**, e.g. Chiang Rai hospital, private clinic), and I'm going to get there by.....(please write down **How** you go to that

place, e.g. walking, taking a bus or asking son/daughter/relatives to take you to get the flu vaccine)"

A HAPA-based educational leaflet was pretested with five patients with chronic renal diseases to assess its content and its format. The patients' feedback was positive. They reported that the leaflet would be useful to high-risk people, and the written content in leaflet was clear and easy to understand. They felt that the educational message was very persuasive and informative. However, two patients suggested using larger font size to improve readability. The leaflet was adapted before being used in the study.

Participants in the comparison group received the standard government information leaflet. This was initially used for the people with chronic disease aged 45-65 years in the previous year's (2009) vaccination programme. The leaflet provided general information about the symptoms of influenza, brief details about influenza vaccine, possible side-effects following vaccination, and the general benefits of influenza vaccination, including 'flu shots help prevent the flu and its serious complications'. No details about the complications of influenza and other benefits of influenza vaccination were addressed. Accordingly, the key techniques in this leaflet were to provide information about the behaviour-health link and the consequences of vaccination (Abraham & Michie, 2008). In addition to leaflet distribution, an appointment letter detailing the date and time of vaccination was sent to all high-risk individuals by the public health staff.

7.2.4 Outcome measures

The outcome measures for this study included the psychosocial determinants of influenza vaccination behaviour and immunisation rates among high-risk urban dwelling Thai adults. These were measured by questionnaires at baseline (Time1: T1) and two week follow-up (after implementation of the educational leaflet and action planning intervention: time 2 [T2]). At T1, risk perception, outcome expectancies, self efficacy, and intention to receive influenza vaccine were measured. Additionally, all of these variables and action planning were measured at T2, to assess the changes in any of HAPA variables and to test for intervention effects. The vaccination rates were assessed during the subsequent two months in the intervention and control areas.

7.2.4.1 Questionnaire

The questionnaire was designed based on the HAPA model. It consisted of items assessing risk perceptions, outcome expectancies, self efficacy, action planning, and intention to obtain influenza vaccine in the forthcoming vaccination period. Questions related to influenza symptoms and side effects following the vaccination were also included. In addition, participants were asked to provide the demographic information about their age, gender, marital status, level of education and occupation, as well as a history of prior influenza immunisation. A draft of questionnaire was pilot tested by 20 Thai adults and subsequently revised based on analysis of their responses. The final version contained 37 questions in three sections: (a) demographic variables and history of prior influenza immunisation, (b) knowledge of influenza symptoms vaccine side-effects, and (c) the questions on HAPA variables: risk perception, outcome expectancies, self-efficacy, action planning, and intention to obtain influenza vaccine (the questionnaire is available in Appendix 7 of this thesis). The items were assessed as follows:

7.2.4.2 Knowledge

Knowledge of influenza symptoms and vaccine side effects was assessed by presenting the participants with a list of 13 symptoms (e.g. fever, muscles ache, watery eyes) and eight potential side-effects following vaccination (e.g. pain at the vaccination spot, vomiting, feeling generally unwell) (see Appendix 7). There were eight correct answers out of 13 for influenza symptoms and four correct answers out of eight for vaccine side effects. Participants were asked to tick yes, no, or not sure to the symptom and vaccine side effects checklist. The percentage of correct responses on knowledge about influenza symptoms and vaccine side effects was calculated.

7.2.4.3 Risk perception

For the measure of risk perception, participants were asked to indicate their level of agreement or disagreement with 15 statements referring to (i) the risk of developing influenza and (ii) the consequences of influenza to their lives, for instance "If someone in my family develops flu, everyone else will", "I do not think that I am personally at risk of contracting the flu", "Flu can make my existing illness worse", and "If I catch the flu, I may have to go to hospital". Risk perceptions were measured

on a five-point Likert scale from one (strongly disagree) to five (strongly agree). Total risk perception scores were calculated by summing the scores on all items, ranging from 15 to 75. A high score represents higher levels of perceived risk. Cronbach's alpha for the risk perception subscales had sufficient internal consistencies at pre- and post-intervention (risk of developing influenza α=0.79 and 0.68; severity of influenza α = 0.75 and 0.70, respectively).

7.2.4.4 Outcome expectancies

Outcome expectations after receiving influenza vaccine were assessed with 10 items. These items included both positive and negative consequences of influenza vaccination such as "If I get the flu shot my chance of getting the flu will be decreased, "If I get the flu shot, it can prevent me from getting a more severe case of the flu", and "If I get the flu shot, it will weaken my immune system". All 10 items were rated on a four-point Likert scale from one (not at all true) to four (exactly true). These items were summed to provide a total outcome expectancy score. Total scores range from 10 to 40. A high score on this ten-item scale reflects more positive expectations with receiving influenza vaccine. Cronbach's alphas were 0.72 and 0.71 at pre-and post-intervention, indicating sufficient reliability.

7.2.4.5 Self-efficacy

In the present study, the self-efficacy measurement was designed to assess participants' confidence in their ability to obtain vaccination against influenza. Self-efficacy was measured by asking participants to rate their level of confidence in receiving influenza vaccine in the forthcoming vaccination period with seven items, for instance "I am confident that I can cope with side effects after receiving the flu vaccine", "I am confident that I can find the time to get vaccinated against the flu" and "I am confident that I can arrange the transportation for myself to get vaccinated". Responses for these items were reported on a four-point Likert scale from one (not at all true) to four (exactly true). A total self–efficacy score was computed by summing the scores on all items, ranging from seven to 28. A high score indicates higher levels of self-efficacy in their confidence in their ability to obtain influenza vaccination. Conbach's alphas for self-efficacy subscales were high at pre- and post-intervention

(self-efficacy in coping with vaccine side-effects α = 0.72 and 0.81; self-efficacy in arranging time and transportation α = 0.84 and 0.91, respectively).

7.2.4.6 Intention

To measure behavioural intention, participants were required to indicate their level of intention to obtain influenza vaccination with two statements: "I intend to receive a flu shot in the forthcoming vaccination period" and "I want to get vaccinated against the flu in the next vaccination period". Answers were given on a 5-point scale from one (definitely do not) to five (definitely do). These items were added to form a sum score of intention. Total scores range from two to 10, with higher scores representing greater intention to obtain influenza vaccine. The Pearson correlation between two items was 0.61 at pre-intervention and 0.67 at post-intervention.

7.2.4.7 Action planning

Action planning was measured by responses to three questions: "I have made a plan **when** I'm going to vaccinate during the next vaccination period", "I have made a plan **where** I'm going to have the flu shot in the next vaccination period", and "I have made a plan **how** I'm going to get vaccinated against the flu". The response alternatives were "Yes" and "No". The participants were also required to bring the leaflet to the researcher at the time 2 data collection in order to check whether they had made an action plan.

7.3 Procedure

The study was conducted between April and August 2009. A briefing meeting was held in each community in April in order to provide information about the activities of the research project. It was attended by the public health staff, village health volunteers and key persons in the community. Additionally, five research assistants were trained on data collection and documentation by the principal researcher. The training programme included lecture and practice sessions. They were instructed to explain the aims of the study to potential participants, to obtain written infored consent if these individuals agreed to participate, to answer any questions that participants may have, and to administer the questionnaire. In addition, the research

assistants were accompanied by the principal researcher in the first three cases of data gathering in order to enhance their confidence in collecting data.

Potential participants in both the intervention and control areas were approached by village health volunteers who gave them an invitation letter together with a reply slip. This stated that the study would examine whether an information leaflet would help people in two selected communities understand more about the influenza and the influenza vaccination, and whether it would influence their decisions related to vaccination. Those approached were asked to complete a reply slip, indicating whether they were willing to consider participating in the study. For those who agreed to consider participation, the volunteers arranged a date, time and venue for them to see a research assistant, either in their home or at a health centre. On the meeting day, the research assistants provided the participants with an information sheet providing details of the study, and answered any questions the participants had. If they were willing to participate, a written informed consent was obtained from each participant prior to data collection.

Following the informed consent, participants were asked to complete the baseline questionnaire. A trained research assistant explained about the questionnaire and how to complete it to the participant. For some participants, especially those with limited literacy, a trained researcher read the statements or questions out loud and asked participants to score their own responses. All participants were unaware of their group assignment. After completing the baseline questionnaire, participants were thanked and offered a gift (a ceramic coffee mug) for their participation in the study.

After T1 data collection was completed, leaflets were enclosed in a plain brown envelope, and were distributed by the village health volunteer of each community to participants. The volunteers were blinded to the randomised allocations. Leaflets were distributed by the village health volunteer to participants in both groups. The HAPA intervention group received a HAPA-based educational leaflet, whereas the comparison group received a standard government information leaflet developed by the Ministry of Public Health.

T2 data were collected two weeks after implementing the intervention, using a personal identity code to match T1 data with the follow up to maintain anonymity. The previous data collection procedure was repeated. Participants in both intervention and control groups were asked to complete the questionnaires assessing HAPA variables. Although implementation intentions (action planning) have been shown to promote health behaviour change, insufficient evidence exists to suggest how long the implementation intention effects last (Jackson, Lawton, Knapp et al., 2005). Previous studies revealed that the effects of this intervention varied over periods of time between one week and one month, depending on the type of behaviour change (Sheeran & Orbell, 1999; Armitage, 2004; Prestwich, Ayres, & Lawton, 2008). Accordingly, T2 questionnaires were collected within 10 days.

The assessors were blinded to the treatment allocation because the leaflets were distributed by the village health volunteer independently. However, the outcome assessors were able to identify the trial group when they asked specific questions regarding participants' action plans at time 2 because the action plans were verified at this stage. Three of the questions regarding action plan were located in the final part of the questionnaire. In some cases, participants could not be free to meet with the researcher on the appointment date. The village health volunteers arranged a new appointment for them; each volunteer was responsible for contacting seven to ten participants. In the few cases that volunteers failed to reach the participants, these participants were contacted by the public health staff or the principal researcher.

Finally, influenza vaccination rates were assessed up to two months after the intervention by using vaccination clinic records. The process of data collection in both intervention and control groups is shown in the flow chart below (Figure 7.3).

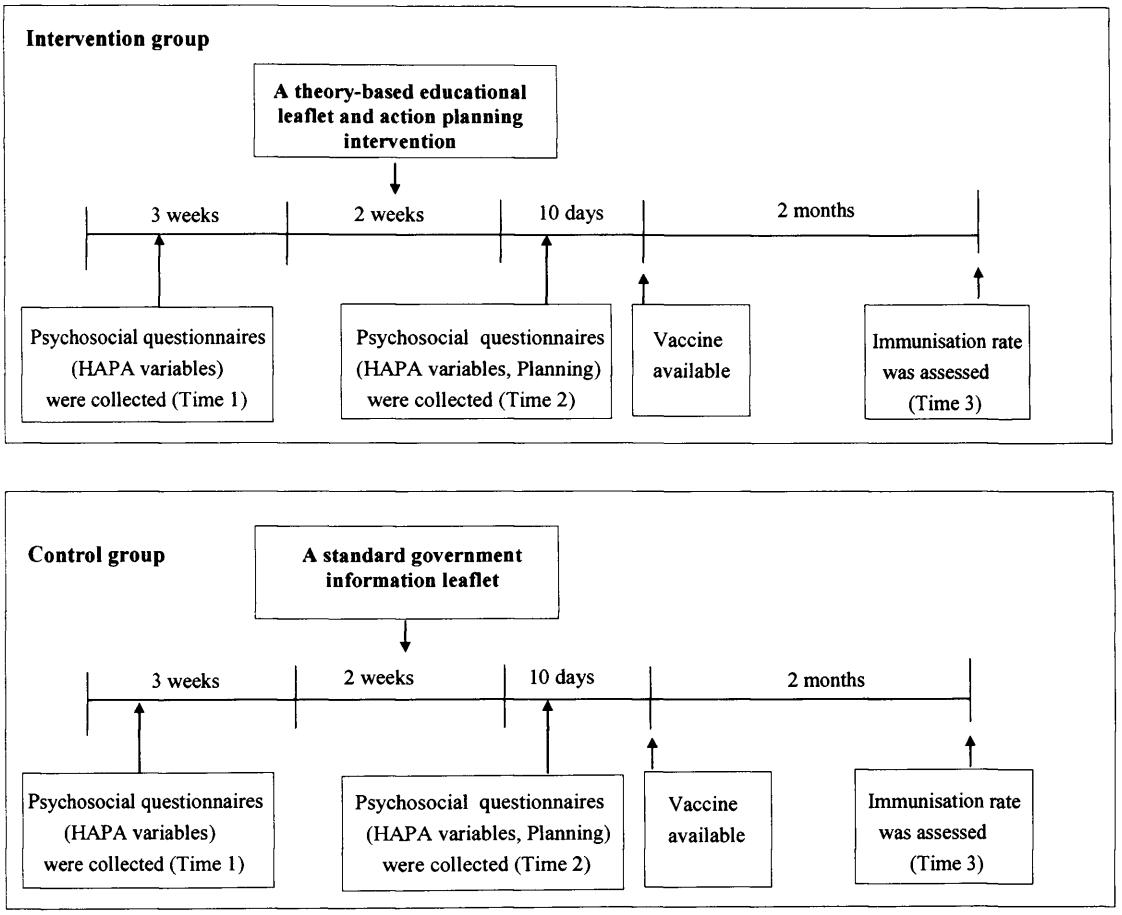


Figure 7.3 The data collection process in two communities.

7.4 Data access/storage

Research data were stored securely in either a locked filing cabinet or on password protected files. The completed questionnaires were kept in a locked filing cabinet, separately from the identifying data to preserve anonymity. All computerised data were stored in a password-protected computer. Additionally, access to these data was limited solely to the principal researcher and the head of health centre.

7.5 Data Analysis

Analyses were performed on an intention-to-treat basis. Baseline characteristics of participants in the intervention and control groups were compared using Chi-square test for categorical variables and Student's t-test for continuous variables. McNemar's test was used to compare the proportions of correct responses on knowledge about influenza symptoms and vaccine side effects at baseline and after intervention within groups, Chi-square or Fisher's exact test where appropriate was used to test for differences between groups on categorical data. Means and standard deviations were calculated for all HAPA variables at baseline and at T2. In order to assess the changes in any of HAPA variables over time and to identify differences between intervention and control groups on the outcome measures, a series of one-way ANCOVA was used on T2 data. In this analysis the T2 score was the dependent variable and the corresponding T1 score was a covariate (Pallant, 2005). The assumptions of ANCOVA were tested before performing the analysis.

When multiple testing is performed at set p-values, it increases the chance of a false-positive findings (type I errors) due to random variability. Therefore, a number of procedures (e.g., Bonferronni correction, Holm correction, and Benjamini and Hochberg False Discovery Rate) have been recommended for use in controlling the false-positives; the p-value or the significance level needs to be adjusted. However, this will also raise the probability of type II errors (false negatives) (Rothman, 1990; Feise, 2002). In the present study, statistical advice on multiple comparisons was sought. The statistician advised to report actual p-value instead of the adjusted p-value in this case because we had an a priori expectation of the direction of change in any HAPA variables after the intervention.

Relationships between the hypothesised predictor variables and the outcome measures were first tested by Pearson's product moment correlations. Multivariate analyses were then performed to examine the effects of the predictor variables on the outcome measures: a linear regression was used to predict the participants' intentions to obtain the influenza vaccine at Time 1, and a logistic regression was conducted to examine predictors of vaccination behaviour at T2. Finally, Chi-square test was used to

compare the differences in influenza vaccine uptake between the intervention and comparison groups.

7.6 Results

7.6.1 Data management

The data were checked and cleaned for out-of-range values or non-permitted values by running the frequencies of all the variables. Checks were also carried out to ensure consistency within questionnaires and to ensure that negative items were inversely coded. For the parametric statistical tests, data were checked for assumptions of normality and homogeneity of variance. Where appropriate, variables were logarithmically transformed to meet a normality assumption. All statistical analyses were conducted using SPSS® version 16.0 for Windows.

7.6.2 Sample Characteristics

A total of 201 high-risk Thai adults were included in the study (99 participants in the intervention group and 102 participants in the control group). The study population had a mean age of 56.24 [SD = 5.86] years, with a range of 45-65 years. The demographic characteristics of the sample are presented in Table 7.6.2. Independent–sample t-test and Chi-square analyses revealed that participants in the intervention and control groups did not differ with regard to age (t=1.7, df =199; p = 0.09), gender (χ^2= 1.76; p = 0.18), marital status (χ^2= 7.05; p = 0.07), educational level (χ^2= 4.96; p = 0.17), occupation (χ^2= 2.24; p = 0.53) and prior immunisation with influenza vaccine (χ^2 = 3.14; p = 0.08). These findings indicate that randomisation procedure was successful.

Table 7.6.2 The demographic characteristics of the study sample.

Characteristics	Control group (N=102)	Intervention group (N=99)	*p*-value
Age, Mean (SD)	55.55 [5.98]	56.95 [5.67]	0.09
Gender (%)			
Male	33.33	42.42	0.18
Female	66.67	57.58	
Marital status (%)			
Single	5.88	2.02	0.07
Married	88.24	86.87	
Divorced or Separated	5.88	6.06	
Widowed	0	5.05	
Educational Level (%)			
Primary school	94.12	90.91	0.17
Secondary school	3.92	7.07	
Vocational/Technical	0	2.02	
Bachelor's Degree	1.96	0	
Occupation (%)			
Unemployed	26.47	33.33	0.53
Farmer	24.51	19.19	
Labourer	18.63	22.22	
Merchant	30.39	25.26	
Prior immunization with influenza vaccine (%)			
Yes	0	3.03	0.08
No	100	96.97	

7.6.3 Measuring the impact of the intervention

7.6.3.1 Knowledge of influenza symptoms and vaccine side-effects

The percentage of correct responses to symptoms and vaccine side-effects in the questionnaire for both groups of participants was computed. "Not sure" responses were considered to be incorrect. Additionally, responses of "not sure" or "no" were combined into a single percentage score for comparison analysis. The results are presented in Table 7.6.3.1-7.6.3.2

Table 7.6.3.1 shows the proportions of participants' responses to the question regarding influenza symptoms. Participants in both groups mistakenly associated seizure, common cold symptoms (watery eyes and itching in nose, throat or eyes) and gastrointestinal symptoms with influenza at time 1. However, McNemar's test for comparison of paired proportions indicated that there were significant changes in the knowledge regarding influenza symptoms at time 2 in the intervention group; a large proportion of participants accurately described the main symptoms of influenza, including fever (from 79.8 per cent to 100.0 per cent, $p < .001$), muscle aches (from 77.8 per cent to 97.0 per cent, $p < .001$), extreme tiredness (from 71.7 per cent to 82.8 per cent, $p = 0.05$), dry cough (from 45.5 per cent to 76.8 per cent, $p < .001$), headache (from 76.8 per cent to 90.9 per cent, $p = 0.01$), and sore throat (from 65.7 per cent to 82.8 per cent, $p = .004$).

For the control group, McNemar's test revealed a significant increase in accurately describing two typical influenza symptoms: fever (from 72.5 per cent to 98 per cent, $p < .001$), and muscle aches (from 80.4 per cent to 94.1 per cent, $p = .007$) at time 2. When comparing knowledge of influenza symptoms between two groups, no statistically significant differences were observed at time 1. However, participants in the control group were less likely to describe seizure as an influenza symptoms than the intervention group at time 2 (47.1 per cent vs. 67.7 per cent, $\chi 2 = 6.45$; $p = .01$), whereas intervention participants were more likely to describe two typical symptoms of influenza: sneezing (78.8 per cent vs. 65.7 per cent, $\chi 2 = 4.29$; $p = .03$) and dry cough (76.8 per cent vs. 60.8 per cent, $\chi 2 = 5.96$; $p = .01$) than those in the control group.

Table 7.6.3.1 Knowledge of participants regarding influenza symptoms at two time points.

Symptoms	Correct answer	group	Time 1			Time 2			$\chi 2$ test *p*-value
			%Yes	%No	%Not sure	%Yes	%No	%Not sure	
Fever (38 C or higher)	Yes	Control Intervention	72.5 79.8	4.9 2.0	22.6 18.2	98.0 100.0	1.0 0	1.0 0	.16
Muscle aches and pains	Yes	Control Intervention	80.4 77.8	5.9 6.1	13.7 16.1	94.1 97.0	1.0 0	4.9 3.0	.33
Seizure	No	Control Intervention	24.5 24.2	40.2 44.4	35.3 31.4	23.5 10.1	47.1 67.7	29.4 22.2	.01
Extreme tiredness	Yes	Control Intervention	69.9 71.7	11.8 9.1	18.6 19.2	81.4 82.8	10.8 7.1	7.8 10.1	.79
Diarrhoea	No	Control Intervention	20.6 19.2	43.1 45.5	36.3 35.3	13.7 10.1	59.8 70.7	26.5 19.2	.43
Watery eyes	No	Control Intervention	38.3 41.4	33.3 30.3	28.4 28.3	44.1 49.5	39.2 41.3	16.7 10.2	.45
Runny or stuffy nose	Yes	Control Intervention	72.5 64.6	14.7 17.2	12.8 18.2	74.5 77.8	19.6 17.2	5.9 5.0	.59
Itching in nose, throat or eyes	No	Control Intervention	44.1 46.5	24.5 19.2	31.4 34.3	50.0 62.6	33.3 27.9	16.7 9.5	.07
Sneezing	Yes	Control Intervention	63.7 72.7	16.7 8.1	19.6 19.2	65.7 78.8	23.1 17.2	11.2 4.0	.03
Nausea	No	Control Intervention	25.5 27.3	36.3 43.4	38.2 29.3	30.4 35.4	48.0 48.5	21.6 16.1	.45
Dry cough	Yes	Control Intervention	49.0 45.5	27.5 24.2	23.5 30.3	60.8 76.8	29.4 17.2	9.8 6.0	.01
Headache	Yes	Control Intervention	75.5 76.8	13.7 11.1	10.8 12.1	84.3 90.9	10.8 6.1	4.9 3.0	.16
Sore throat	Yes	Control Intervention	70.6 65.7	11.8 12.1	17.6 22.2	73.5 82.8	20.6 14.1	5.9 3.1	.11

Note * A comparison between groups, using the T2 data

Participants were asked to identify what they thought were the side-effects of influenza vaccine, and table 7.6.3.2 presents the proportions of participant's responses to this question. McNemar's tests were conducted to assess changes in the proportion of participants describing the vaccine side-effects at baseline and follow-up. There was a significant increase in accurate description of vaccine side-effects in both groups at time 2; the vaccine side-effects, including a low grade fever (intervention group: from 66.7 per cent to 94.9 per cent, p <.001; control group: from 64.7 per cent to 88.2 per cent, p <.001), generally feeling unwell and mild or moderate muscle aches for 1-2 days (intervention group: from 75.8 per cent to 92.9 per cent, p =.001; control group: from 78.4 per cent to 94.1 per cent, p = .002).

There was also a significant increase in identifying pain/soreness at the vaccination site by the control group (from 83.3 per cent to 97.1 per cent, p = .001). There were no statistically significant differences in the description of vaccine side-effects between the two groups at time 1. However, more participants in the comparison group incorrectly identified breathing difficulties or swelling of the face as side-effects of vaccination than those in the intervention group at T2 (17.6 per cent vs. 4.0 per cent, $\chi 2 = 9.54$; p = .002).

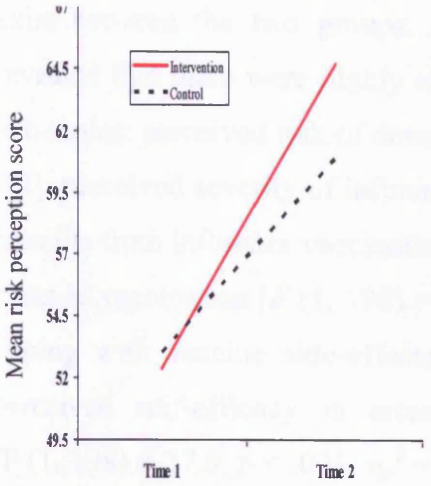
Table 7.6.3.2 Knowledge of participants regarding side-effects of influenza vaccination at two time points.

Side-effects	Correct answer	Group	Time 1			Time 2			χ^2 test p-value
			%Yes	%No	%Not sure	%Yes	%No	%Not sure	
There are no side-effects.	No	Control Intervention	0 2.0	93.1 92.9	6.9 5.1	0 0	96.1 100.0	3.9 0	N/A
A slight fever for 8-24 hrs after vaccination.	Yes	Control Intervention	64.7 66.7	8.8 3.0	26.5 30.3	88.2 94.9	1.0 1.1	10.8 4.0	.08
Soreness, pain at the vaccination spot.	Yes	Control Intervention	83.3 87.9	9.8 4.0	6.9 8.1	97.1 92.9	1.0 4.1	1.9 3.0	.18
Swelling around the vaccination spot.	Yes	Control Intervention	62.7 62.6	18.7 17.2	18.6 20.2	69.6 72.7	11.8 18.2	18.6 9.1	.63
Vomiting, diarrhoea, and being nauseous.	No	Control Intervention	13.7 13.1	56.9 51.5	29.4 35.4	12.7 6.1	62.7 69.7	24.6 24.2	.10
A fever, runny nose with dark and thick secretions.	No	Control Intervention	39.2 39.4	29.4 34.3	31.4 26.3	31.4 29.3	53.9 54.5	14.7 16.2	.75
Feeling generally unwell and mild or moderate muscle aches for 1-2 days.	Yes	Control Intervention	78.4 75.8	9.8 8.0	11.8 16.2	94.1 92.9	1.0 5.1	4.9 2.0	.73
Difficult breathing or swelling of the face	No	Control Intervention	16.7 11.1	50.0 63.6	33.3 25.3	17.6 4.0	65.7 77.8	16.7 18.2	.002

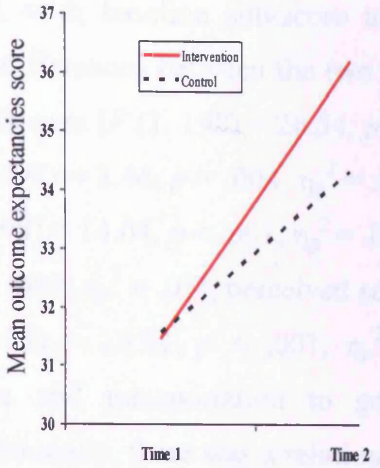
Note * A comparison between groups, using the T2 data

7.6.3.2 Changes in HAPA variables following the intervention

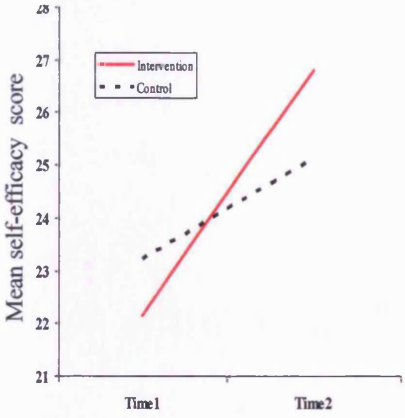
To understand how the intervention impacted on potential mediators of behavioural change, changes in risk perceptions, outcome expectancies, self-efficacy, and behavioural intention over time between intervention and control groups were analysed. The results are reported in Figure 7.6.3.2. Participants in the intervention group showed a greater increase in the mean scores of all variables compared with the control group between T1 and T2. This was evidenced by series of analyses of covariance (ANCOVA) with baseline score on each variable as a covariate. The results indicated significant differences between the groups at T2 in risk perception [F (1, 198) = 20.07, p< .001, partial eta squared (η_p^2) = .09], outcome expectancy [F (1,198) =18.65, p< .001, η_p^2 = .08], self-efficacy [F (1, 198) = 58.8, p < .001, η_p^2 = .23], and intention scores [F (1, 198) = 33.56, p <.001, η_p^2 = .15]. In addition, there was a relationship between the baseline (T1) and follow-up (T2) scores on all variables, with effect sizes (partial eta squared) ranged from .10 to .25



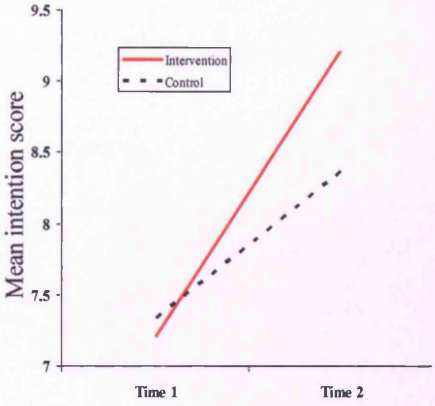
Mean risk perception score in the intervention and control groups at two time points



Mean outcome expectancies score in the intervention and control groups at two time points



Mean self-efficacy score in the intervention and control groups at two time points



Mean intention score in the intervention and control groups at two time points

Figure 7.6.3.2 Changes in risk perception, outcome expectancies, self-efficacy, and behavioural intention following the intervention

In Table 7.6.3.2.1 the scores for risk perception, outcome expectancies, and self-efficacy are broken down into sub-scores in order to examine whether differences exist between the two groups. ANCOVA with baseline sub-score as a covariate revealed that there were highly significant differences between the two groups on all sub-scales: perceived risk of developing influenza [F (1, 198) = 26.54, p < .001, η_p^2 = .12], perceived severity of influenza [F (1, 198) = 8.44, p = .004, η_p^2 = .04] perceived benefits from influenza vaccination [F (1, 198) = 14.04, p < .001, η_p^2 = .07], perceived costs of vaccination [F (1, 198) = 6.95, p = .009, η_p^2 = .03], perceived self-efficacy in coping with vaccine side-effects [F (1, 198) = 16.93, p < .001, η_p^2 = .08], and perceived self-efficacy in arranging time and transportation to get vaccinated [F (1, 198) = 27.0, p < .001, η_p^2 = .12]. Additionally, there was a relationship between the baseline (T1) and follow-up (T2) scores on all subscales, with effect sizes ranging from .07- .14 except for the perceived costs of vaccination [F (1,198) = 2.68, p = .10, η_p^2 = .01]

Table 7.6.3.2.1 Mean [and Standard Deviation] for subscales of risk perception, outcome expectancies, self- efficacy, and intention to obtain influenza vaccine at two time points (n = 201).

Variables	Total possible score	Group	Time1 Mean [SD]	Time 2 Mean [SD]	*p*-value
Threat perception:					
- Risk of developing influenza	35	Control	24.51 [3.01]	27.93 [3.63]	< .001
		Intervention	24.09 [3.06]	30.12 [3.33]	
- Severity of influenza	40	Control	28.51 [3.68]	32.98 [4.56]	.004
		Intervention	28.27 [3.41]	34.59 [4.14]	
Outcome expectancies:					
- Perceived costs of vaccination	12	Control	10.32 [1.86]	11.17 [1.36]	.009
		Intervention	10.35 [1.59]	11.59 [0.82]	
- Perceived benefits from influenza vaccination	28	Control	21.25 [3.71]	23.17 [2.93]	< .001
		Intervention	21.13 [3.81]	24.61 [2.97]	
Self-efficacy:					
- Coping with vaccine side effects	12	Control	6.35 [1.63]	7.15 [1.12]	< .001
		Intervention	6.17 [1.38]	7.66 [0.88]	
- Arranging time and transportation	16	Control	13.43 [2.75]	14.42 [1.96]	< .001
		Intervention	12.74 [2.58]	15.48 [1.25]	
Intention	10	Control	7.34 [1.51]	8.38 [1.36]	< .001
		Intervention	7.21 [1.52]	9.24 [1.20]	

A mean score for each question on the HAPA variables of before and two weeks after the intervention in both groups was analysed. ANCOVA with baseline scores as a covariate was conducted to determine whether there were differences in mean scores for each question between groups at Time 2.

Table 7.6.3.2.2 shows mean scores for each question on risk perception in both groups. The results of ANCOVA with baseline score as a covariate illustrated that there were significant differences between the two groups in the mean scores on the following statements: "influenza spreads between people very easily" [F (1,198) = 6.3, p = .01, η_p^2 = .03], "I am likely to catch the flu if other people in my district develop it" [F (1,198) = 4.8, p = .03, η_p^2 = .02], "If someone in my family develops flu, everyone else will" [F (1,198) = 4.5, p = .03, η_p^2 = .02], "I have a good health, so I don't need to get a flu vaccine" [F (1,198) = 17.5, p < .0005, η_p^2 = .08], "I do not think that I am personally at risk of contracting the flu" [F (1,198) = 7.1, p = .008, η_p^2 = .04], and "my body could fight off the flu because I have a strong immune system" [F (1,198) =10.2, p = .002, η_p^2 = .05].

This indicates a higher perceived risk of developing influenza among intervention participants. Additionally, the results of ANCOVA demonstrated a significant difference in perceived severity of influenza between the two groups. The participants in the intervention group were more likely to believe that "Flu can kill people in poor health" [F (1,198) = 5.9, p = .02, η_p^2 = .03], and they were more inclined to disagree with the statements, "Flu is not serious enough to interfere with my daily activities" [F (1,198) =7.0, p = .009, η_p^2 = .03] and "Flu is a very minor health problem" [F (1,198) =8.7, p = .003, η_p^2 = .04].

Table 7.6.3.2.2 Mean [and Standard Deviation] for risk perception in the intervention and control groups at two time points (the total possible score for each item = 5)

Item	Group	Time 1 Mean [SD]	Time 2 Mean [SD]	*p*-value
Risk of developing influenza				
1. Flu spreads between people very easily.	Control	3.97 [.75]	4.46 [.61]	.01
	Intervention	3.83 [.61]	4.65 [.50]	
2. I am likely to catch the flu if other people in my District develop it.	Control	3.36 [.94]	4.22 [.86]	.03
	Intervention	3.34 [.72]	4.44 [.66]	
3. If someone in my family develops influenza, everyone else will.	Control	4.06 [.54]	4.41 [.76]	.03
	Intervention	4.03 [.59]	4.61 [.57]	
4. Compared to other people, the likelihood that I will get the flu is very large.	Control	3.46 [.94]	4.26 [.82]	.16
	Intervention	3.41 [.77]	4.40 [.73]	
5. I do not think that I am personally at risk of contracting the flu. [a]	Control	3.09 [.93]	3.59 [1.21]	.008
	Intervention	3.04 [.81]	3.98 [.95]	
6. My body could fight off the flu because I have a strong immune system. [a]	Control	2.99 [.87]	3.05 [1.16]	.002
	Intervention	2.80 [.83]	3.54 [1.13]	
7. I have a good health, so I don't need to get a flu vaccine. [a]	Control	3.58 [.91]	3.94 [1.17]	<.001
	Intervention	3.64 [.75]	4.51 [.68]	
Severity of influenza	Control	3.84 [.82]	4.43 [.76]	.84
1. Influenza is a serious disease.	Intervention	3.69 [.66]	4.42 [.81]	
2. If I get the flu I will become very sick	Control	3.74 [.79]	4.29 [.79]	.39
	Intervention	3.56 [.63]	4.37 [.68]	
3. Flu is a very minor health problem. [a]	Control	3.25 [.94]	3.87 [1.11]	.003
	Intervention	3.28 [.83]	4.27 [.77]	
4. Flu is not serious enough to interfere with my daily activities. [a]	Control	2.88 [1.02]	3.20 [1. 23]	.009
	Intervention	2.93 [.86]	3.65 [1.16]	
5. Flu can make my existing illness worse.	Control	3.80 [.84]	4.25 [.91]	.15
	Intervention	3.62 [.71]	4.35 [.79]	
6. If I catch the flu, I may have to go to hospital.	Control	3.64 [.78]	4.32 [.82]	.15
	Intervention	3.67 [.73]	4.48 [.72]	
7. Flu can be very serious for people with poor health.	Control	3.92 [.77]	4.48 [.71]	.24
	Intervention	3.84 [.65]	4.58 [.66]	
8. Flu can kill people in poor health.	Control	3.43 [.83]	4.14 [.91]	.02
	Intervention	3.70 [.71]	4.45 [.63]	

Note: [a] Negative items

Table 7.6.3.2.3 presents the mean scores of participants in the intervention and control groups on vaccine outcome expectancy scales. The results of ANCOVA indicated that participants in the intervention group held more positive beliefs about the influenza vaccine and its effectiveness in preventing influenza and influenza-related complications than those in the control group at T2 after controlling for baseline scores.

Significant between group differences were found for measures of "If I get the flu shot, it can prevent me from getting a more severe case of the flu [F (1,198) =11.74, p = .001, η_p^2 = .06], "If I get the flu shot, I will feel more confident about not having the flu" [F (1,198) =11.44, p = .001, η_p^2 = .06], "If I get the flu shot, I could protect my family and friends from flu" [F (1,198) =5.68, p = .02, η_p^2 = .03], and "If I get the flu shot, I will be less of a burden to my family" [F (1,198) = 9.42, p = .002, η_p^2 = .05]. It also revealed that the participants in the intervention group were more inclined to disagree with the statements; "If I get the flu shot, I will be more likely to get other illnesses" [F (1,198) = 4.8, p = .03, η_p^2 = .02], and "If I get the flu shot, It will weaken my immune system" [F (1,198) = 4.5, p = .04, η_p^2 = .02].

Table 7.6.3.2.3 Mean [and Standard Deviation] for outcome expectation after getting influenza vaccine in the intervention and control groups at two time points (the total possible score for each item = 4)

Item	Group	Time 1 Mean [SD]	Time 2 Mean[SD]	*p*-value
If I get the flu shot.....				
1. My chance of getting the flu will be decreased.	Control Intervention	3.06 [.75] 2.95 [.67]	3.36 [.66] 3.46 [.61]	.20
2. It can prevent me from getting a more severe case of the flu.	Control Intervention	3.18 [.76] 3.05 [.67]	3.34 [.62] 3.62 [.55]	.001
3. I will feel more confident about not having the flu.	Control Intervention	3.16 [.67] 3.21 [.73]	3.41 [.62] 3.69 [.51]	.001
4. I will be more likely to get other illnesses. [a]	Control Intervention	3.28 [.92] 3.37 [.85]	3.66 [.69] 3.85 [.46]	.03
5. I could protect my family and friends from flu.	Control Intervention	2.67 [1.06] 2.58 [1.04]	2.92 [1.09] 3.23 [.96]	.02
6. It will weaken my immune system. [a]	Control Intervention	3.49 [.83] 3.40 [.86]	3.69 [.66] 3.85 [.41]	.04
7. I will be less of a burden to my family.	Control Intervention	3.04 [.79] 3.10 [.73]	3.29 [.71] 3.58 [.55]	.002
8. My family won't worry about my chances of getting a serious case of the flu.	Control Intervention	3.08 [.84] 3.09 [.79]	3.33 [.69] 3.48 [.61]	.10
9. I will get sick with the flu. [a]	Control Intervention	3.55 [.77] 3.58 [.72]	3.82 [.57] 3.89 [.35]	.34
10. It will help me stay healthy during the flu season.	Control Intervention	3.07 [.76] 3.15 [.75]	3.50 [.59] 3.55 [.61]	.74

Note. [a] Negative items

The mean scores of perceived self-efficacy in obtaining influenza vaccination are reported in Table 7.6.3.2.4. At T2, participants in the intervention group were more confident in their ability to receive influenza vaccine in the next vaccination period than those in the control group. In support this, the ANCOVA with baseline score as a covariate indicated that there was a significant effect for group in the perceived self-efficacy in relation to getting vaccinated against influenza, with intervention participants reporting greater confidence in their ability to receive the influenza vaccine in the forthcoming vaccination period compared to the control group [F (1,198) = 10.59, p = .001, η_p^2 = .05]. In addition, there was a significant main effect for group with respect to self-efficacy related to coping with vaccine side effects; participant in the intervention group reported significantly high levels of confidence in coping with side-effects after receiving influenza vaccine relative to the control group [F (1,198) = 26.31, p < .001, η_p^2 = .12].

Similarly, there were statistically significant main effects for group on the self-efficacy for arranging time and transportation subscales; intervention participants reported greater levels of confidence in their ability to find the time to get vaccinated against influenza [F (1,198) =13.37, p < .001, η_p^2 = .06], obtain the influenza vaccine even though they were quite busy [F (1,198) = 20.63, p < .001, η_p^2 = .09], and receiving an influenza vaccine would not interfere with they daily routine [F (1,198) = 17.23, p < .001, η_p^2 = .08]. Moreover, the participants in the intervention group reported greater levels of confidence in their ability to arrange the transportation to go for the influenza vaccination [F (1,198) = 9.88, p = .002, η_p^2 = .05]. No significant between-group differences were observed for dealing with a fear of needles or shot [F (1,198) =1.24, p = .27, η_p^2 = .006].

Table 7.6.3.2.4 Mean [and Standard Deviation] for self-efficacy to receive vaccination against influenza in the intervention and control groups at two time points (the total possible score for each item = 4)

Item	Group	Time 1 Mean[SD]	Time 2 Mean[SD]	*p*-value
I am confident that.....				
1. I will get the flu shot in the forthcoming vaccination period.	Control Intervention	3.43 [.76] 3.24 [.73]	3.76 [.53] 3.92 [.34]	.001
2. I can cope with side effects after receiving the flu vaccine.	Control Intervention	2.97 [.97] 2.89 [.79]	3.44 [.76] 3.87 [.39]	<.001
3. I can deal with a fear of needles or shot.	Control Intervention	3.38 [.84] 3.28 [.81]	3.72 [.57] 3.79 [.59]	.27
4. I can find the time to get vaccinated against the flu.	Control Intervention	3.46 [.74] 3.31 [.66]	3.75 [.53] 3.94 [.28]	<.001
5. Receiving a flu shot will not interfere with my daily routine.	Control Intervention	3.35 [.79] 3.12 [.72]	3.62 [.59] 3.90 [.42]	<.001
6. I will get a flu shot even though I am quite busy during the vaccination period.	Control Intervention	3.10 [.89] 2.91 [.83]	3.35 [.77] 3.74 [.55]	<.001
7. I can arrange the transportation for myself to get vaccinated.	Control Intervention	3.52 [.64] 3.39 [.71]	3.70 [.63] 3.91 [.32]	.05

Table 7.6.3.2.5 shows mean scores on the behavioural intention scale at two time points. The results of the ANCOVA found statistically significant differences between groups for intention scores on the following statements: "I intend to receive a flu shot in the forthcoming vaccination period" [F (1,198) =23.10, p<.001, η_p^2 = .10], and "I want to get vaccinated against influenza in the next vaccination period" [F (1,198) = 27.55, p< .001, η_p^2 = .12]. Additionally, there was a strong relationship between the baseline (T1) and follow-up (T2) scores on the behavioural intention for both items, with an effect size of .17 and .16, respectively.

Table 7.6.3.2.5 Mean [and Standard Deviation] for intention to obtain influenza vaccine in the intervention and control groups at two time points (the total possible score for each item = 5)

Item	Group	Time 1 Mean [SD]	Time 2 Mean [SD]	p-value
1. I intend to receive a flu shot in the forthcoming vaccination period.	Control Intervention	3.79 [.88] 3.81 [.83]	4.31 [.76] 4.74 [.58]	<.001
2. I want to get vaccinated against the flu in the next vaccination period.	Control Intervention	3.55 [.83] 3.40 [.83]	4.13 [.73] 4.57 [.70]	<.001

7.6.3.3 Vaccination behaviour

In addition to the measurement of changes in any of HAPA variables over time, the present study examined the difference in the rate of influenza vaccine uptake between the intervention and control groups. Eighty nine participants (89.90 per cent) in the intervention group were vaccinated compared with 86 (84.31 per cent) in the control group; this difference was not significant (χ^2 =1.39, df = 1, p = .23) (Table 7.6.3.3).

Table 7.6.3.3 Effects of the intervention on influenza vaccination rate

Group	Vaccinated		Non-Vaccinated		χ^2	*p* value
	n	%	n	%		
Intervention (N=99)	89	89.90	10	10.10	1.39	0.23
Control (N=102)	86	84.31	16	15.69		

7.7 Testing the predictive utility of the HAPA model

As well as investigating the intervention effect, the current study also provides an opportunity to determine the predictive utility of the HAPA model in relation to both intention and subsequent vaccination behaviour among high-risk urban dwelling Thai adults. In a test of HAPA model, it was hypothesised that risk perception, self-efficacy, outcome expectancies, would predict strength of intention to receive the influenza vaccine, and that action planning, self-efficacy, and intention would significantly associated with influenza vaccination behaviour of high-risk Thai adults.

In order to examine the relationship between hypothesised predictor variables and intention to obtain influenza vaccine, Pearson correlations were computed between all variables measured at T1 and T2. The results of these analyses are reported in Table (Table 7.7.1-7.7.2). Results indicated that risk perceptions (susceptibility and severity), outcome expectancies (perceived benefit and perceived cost of vaccination), and self-efficacy (self-efficacy for coping with vaccine side-effects and self-efficacy in arranging time and transportation) were all significantly correlated with intention to obtain influenza vaccine at both T1 and T 2 (r =.29 to .66, p = .01).

Table 7.7.1 Pearson's correlation matrix of HAPA variables at Time 1

Variables	1	2	3	4	5	6	7	8
1. Age	1.00	.03	.41	.09	.10	-.06	-.03	-.02
2. Perceived risk of developing influenza	.03	1.00	.59**	.58**	.33**	.43**	.39**	.47**
3. Perceived severity of influenza	.04	.59**	1.00	.62**	.26**	.45**	.44**	.49**
4. Perceived benefits from influenza vaccination	.09	.58**	.62**	1.00	.08	.53**	.49**	.58**
5. Perceived costs of vaccination	.10	.33**	.26**	.08	1.00	.12	.15*	.29**
6. Self-efficacy for coping with vaccine side effects	-.05	.43**	.45**	.53**	.12	1.00	.84**	.62**
7. Self-efficacy in arranging time and transportation	-.02	.39**	.44**	.49**	.15*	.84**	1.00	.66**
8 Intention	-.01	.47**	.49**	.58**	.29**	.62**	.66**	1.00

Note $^{*}p = 0.05$, $^{**}p = .01$

Table 7.7.2 Pearson's correlation matrix of HAPA variables at Time 2

Variables	1	2	3	4	5	6	7	8
1. Age	1.00	.07	.12	.06	-.01	.05	.13	.12
2. Perceived risk of developing influenza	.07	1.00	.64**	.39**	.08	.36**	.32**	.29**
3. Perceived severity of influenza	.11	.64**	1.00	.44**	.11	.35**	.32**	.33**
4. Perceived benefits from influenza vaccination	.06	.39**	.44**	1.00	.12	.54**	.33**	.56**
5. Perceived costs of vaccination	-.01	.08	.11	.12	1.00	.02	.12	.33**
6. Self-efficacy for coping with vaccine side effects	.05	.36**	.35**	.54**	.02	1.00	.62**	.61**
7. Self-efficacy in arranging time and transportation	.13	.32**	.32**	.33**	.12	.62**	1.00	.62**
8. Intention	.12	.29**	.33**	.56**	.33**	.61**	.62**	1.00

Note ** $p = 0.01$

In addition, a linear regression was used to assess for independent association between the various independent variables measured at time 1 and intention. The results of this analysis revealed that overall the model had an adequate fit to the data (Adj. $R^2 = .55$, $F = 42.83$, $p < .001$). The HAPA variables were able to explain 55 per cent of the variance of intentions to vaccinate against influenza among our participants. Perceived benefits from influenza vaccination (Beta =. 29, $p < .001$), perceived costs of vaccination (Beta =.18, $p = .001$) and self-efficacy (Beta =. 39, $p < .001$) were significantly associated with intentions at T1 (Table 7.7.3).

Table 7.7.3 Prediction of intention to obtain influenza vaccine from risk perception, outcome expectancies, and self–efficacy at time 1.

Predictor variable	**Beta**	***t***	***p* value**
Perceived risk of developing influenza	.015	.35	.73
Perceived severity of influenza	.061	.61	.54
Perceived benefits from influenza vaccination	.29	4.26	< .001
Perceived costs of vaccination	.18	3.5	.001
Self-efficacy for coping with vaccine side effects	.94	1.05	.29
Self-efficacy in arranging time and transportation	.39	4.41	< .001
Adj. $R^2 = .55$, $F = 42.83$, $p < .001$			

The change score in T1 and T2 variables was also assessed by subtracting the baseline scores (T1) from follow-up scores (T2) on each variable. Pearson correlations were then used to identify the association between the change in each of the independent variables and intentions. Results indicated that changes in risk perceptions (susceptibility and severity), outcome expectancies (perceived benefit and cost of vaccination), and self-efficacy (self-efficacy for coping with vaccine side-effects and self-efficacy in arranging time and transportation) were significantly associated with changes in intentions (Table 7.7.4).

Table 7.7.4 Pearson product moment correlations between change scores in risk perception, outcome expectancies, self-efficacy subscales, and intention

Variable	1	2	3	4	5	6	7	8
1. Age	1.00	-.03	.14	-.04	-.10	.08	.09	.13
2. Change in perceived risk of developing influenza	-.03	1.00	.48**	.31**	.13	.18*	.16*	.17*
3. Change in perceived severity of influenza	.14	.48**	1.00	.27**	.15*	.26**	.27**	.20**
4. Change in perceived benefits from influenza vaccination	-.04	.31**	.27**	1.00	.07	.45**	.33**	.54**
5. Change in perceived cost of influenza vaccination	-.10	.13	.15*	.07	1.00	.00	.05	.17*
6. Self-efficacy in coping with vaccine side-effects	.08	.18*	.26**	.45**	.00	1.00	.72**	.51**
7. Self-efficacy for arranging time and transportation	.09	.16*	.27**	.33**	.05	.72**	1.00	.54**
8. Intention	.13	.17*	.20**	.54**	.17**	.51**	.54**	1.00

Note: ** p = 0.01 (two-tailed); * p = 0.05 (two-tailed)

Subsequently, a linear regression analysis was conducted with change in intention score as the outcome variable and change in perceived risk of developing influenza, perceived severity of influenza, perceived benefits from influenza vaccination, perceived costs of vaccination, self-efficacy for coping with vaccine side-effects, and self-efficacy in arranging time and transportation scores as the independent variables. Results from the linear regression analysis showed that the change in all independent variables accounted for 43 per cent of the variance in change in intentions, and changes in three variables: perceived benefit from influenza vaccination (Beta =. 38, p <.001), perceived costs of vaccination (Beta=.13, p = .01), and perceived self-efficacy in arranging time and transportation (Beta =.34, p <.001), were significantly related to the change in intentions (Table 7.7.5).

Table 7.7.5 Prediction of change in intentions from the changes in the risk perception, outcome expectancies, and self–efficacy subscales

Predictor variable	**Beta**	***t***	***p* value**
Change in perceived risk of developing influenza	-.03	-.42	0.68
Change in perceived severity of influenza	-.03	-.47	0.64
Change in perceived benefits from influenza vaccination	.38	6.23	< .001
Change in perceived costs of vaccination	.13	2.45	.01
Change in self-efficacy for coping with vaccine side effects	.11	1.33	.184
Change in self-efficacy in arranging time and transportation	.34	4.41	< .001
Adj. $R^2 = .43$, $F = 27.0$, $p < .001$			

Finally, a logistic regression was conducted to test whether the risk perception, outcome expectations, self-efficacy, intention, and action planning at T2 would be able to predict actual vaccination behaviour. Overall, the model had an adequate fit to the data; the model yielded a nagelkerke R^2 of 0.49 and the Hosmer and Lemeshow was not significant ($\chi^2 = .38$, df = 8, $p = 0.87$). The results revealed that self-efficacy for arranging time and transportation and behavioural intention was significantly correlated with vaccination behaviour (Odds ratio= 1.51, $p = .028$; Odds ratio = 3.47, $p = .001$, respectively) (Table 7.7.6).

Table 7.7.6 Summary of logistic regression analysis predicting actual vaccination behaviour among high-risk Thai adults (n = 201)

Predictor Variable	***B***	***S.E.***	***Wald statistic***	***p* value**	**Odds ratio (95%CI)**
Perceived risk of influenza	.11	.10	1.14	.27	1.1 (.91-1.36)
Perceived severe of influenza	-.06	.09	.45	.50	0.94 (.78-1.13)
Perceived benefit of influenza vaccination	-.08	.12	.41	.52	0.93 (.73-1.17)
Perceived cost of vaccination	-.14	.42	.12	.73	.86 (.38-1.97)
Self-efficacy in coping with vaccine side-effects	.05	.32	.03	.87	1.05 (.57-1.96)
Self-efficacy for arranging time and transportation	.54	.23	5.61	.028	1.51 (1.1-2.67)
Intention	1.24	.36	11.85	.001	3.47 (1.71-7.06)
Planning	-.51	.66	.61	.43	0.59 (0.16-2.17)

7.8 Discussion

This randomised-controlled pilot study had two objectives: (1) to determine the effects of a HAPA-based educational leaflet intervention on influenza vaccination behaviours in a sample of high-risk Thai adults; and (2) to test the utility of the HAPA model in predicting both intention and subsequence vaccination behaviour among this high-risk group. In relation to the first objective, the intervention based on the HAPA model showed significant differences between groups in changes over time in key mediator variables such as knowledge, risk perception, self-efficacy, outcome expectancies, and intention in obtaining influenza vaccination. This was evidenced by series of analyses of covariance (ANCOVA) with baseline score on each variable as a covariate, indicating that there was a significant main effect for both time and group on any of the HAPA variables. Accordingly, the leaflet achieved its first goal; to increase the strength of intentions to seek influenza vaccination. Unfortunately, its second goal, to translate these motivational differences into behavioural differences was not achieved. Between conditions vaccination rates did not differ.

7.8.1 Measuring the impact of the intervention: changes in key mediators

In this study, knowledge of influenza symptoms and vaccine side-effects was assessed by presenting participants with a list of 13 symptoms and eight potential vaccine side-effects. At time 1, participants in both groups mistakenly associated seizure, common cold symptoms (watery eyes and itching in nose, throat or eyes) and gastrointestinal symptoms with influenza. These results confirm the finding of our previous qualitative study regarding insufficient knowledge about influenza symptoms among high-risk Thai people. In Thai, common cold is referred to as *khai wat,* while influenza is referred to as *khai wat yai.* This suggests an explicit indication that "influenza" is more serious than "a cold". This may partly explain why the fever and upper respiratory infection symptoms were seen as major symptoms of influenza among our participants, at T1. Interestingly, approximately one fifth of participants included diarrhoea and nausea as symptoms of the influenza. Elsewhere, researchers have also found that lay people recognised gastrointestinal symptoms (nausea, diarrhea, and stomach ache) as a characteristic of influenza (McCombie, 1987; Pachter, Niego, & Pelto, 1996; Baer, Weller, Pachter et al., 1999). For example, in

Tampa, the symptoms of influenza recognised by the participants included nausea, diarrheoa, stomach ache (gastrointestinal symptoms), body aches and pains, fatigue, fever, and upper respiratory symptoms (Baer, Weller, Pachter et al., 1999). Gastrointestinal symptoms reported by the Americans living in Tampa appear to be the same symptoms as "folk flu" identified by McCombie (1987) in southern Arizona, as mentioned in Chapter 4. According to McCombie (1987), "folk flu" was characterised by nausea, vomiting and diarrhoea. The concept of "folk flu" does not accord with the biomedical knowledge about the clinical symptoms of influenza; influenza illness in adults is typically characterised by abrupt onset of fever, headache, muscles ache and pain, fatigue, sore throat, and a dry cough (Jennings & Read, 2002; Cunha, 2004; Eccles, 2005; Treanor, 2005).

A lack of knowledge of influenza symptoms may not be specific to our samples. The study conducted in the US. by Santibanez, Nowalk, Zimmerman et al. (2002) found that although there was no difference in accurately describing the symptoms of influenza between vaccinated and unvaccinated older people, overall only 44 per cent (448/1007) of the participants correctly described one or more of the typical influenza symptoms, including headache, myalgia, cough, sore throat, and fever. Furthermore, a significantly greater proportion of those who had not been vaccinated reported that they did not know the symptoms of influenza than those who received vaccination (17 per cent vs. 7 per cent). The lack of knowledge and misinformation among high-risk older people about the symptoms of influenza underscores the need for education efforts about the influenza symptoms to these individuals because lack of this information may lead to confusion about the effectiveness of influenza vaccine; older people might think that the influenza vaccine did not work if they got influenza-like symptoms despite being vaccinated against influenza (Santibanez, Nowalk, Zimmerman et al., 2002; Zimmerman, Nowalk, Raymund et al., 2003). However, in this study, following the implementation of intervention, participants in the intervention group had greater improvements in knowledge about influenza symptoms; a significant increase in accurately describing the typical influenza symptoms (fever, muscle aches, extreme tiredness, dry cough, headache, and sore throat), whereas a significant increase in accurately describing only two typical influenza symptoms (fever and muscle aches) was observed among those in the control group.

Additionally, the results of this study showed that participants in the intervention group were less likely to describe difficult breathing or swelling of the face as side-effects after taking the influenza vaccine than those in the control group. These findings support the contention that our educational leaflet provided some clarification with regard to influenza symptoms and vaccine side-effects. This is consistent with the previous studies that have demonstrated the effectiveness – and specific effect - of tailored messages in changing knowledge, beliefs related to severity of influenza, vaccine safety and its effectiveness among high-risk groups (LaVela, Cameron, Priebe et al., 2008; Wray, Buskirk, Jupka et al., 2009). Wray, Buskirk, Jupka et al. (2009), for example, carried out a randomised controlled trial comparing the effectiveness of two influenza vaccine leaflets (vaccine safety messages [VSM] based on the Health Belief Model (Becker, 1974) and vaccine information statement [VIS]) in 111 African Americans aged 50 years or older. The study showed that the participants in the VSM group had a higher level of beliefs related to the safety and efficacy of influenza vaccine than those exposed to the vaccine information statement [VIS]. However, the VSM had no effects on changing intentions to obtain the influenza vaccination among people in this group. Similar results were obtained in a pre-and post-intervention study conducted by LaVela, Cameron, Priebe et al. (2008) who found that individuals with spinal cord injuries and disorders had greater improvements in knowledge and beliefs related severity of influenza after viewing an educational message based on the Theory of Planned Behaviour (TPB: Ajzen, 1991; Ajzen, 2005) and the Extended Parallel Process Model (EPPM: Witte, 1992), although no change in perceptions of susceptibility to influenza infection was observed.

In the present study, intervention participants were more likely to believe that "Flu can kill people in poor health", and they disagreed with the belief that "Flu is not serious enough to interfere with my daily activities, and "Flu is a very minor health problem". Other significant differences in risk perceptions of influenza between the intervention and control groups included: "I have a good health, so I don't need to get a flu shot", and "My body could fight off the flu because I have a strong immune system". Results also revealed that there were more statistically significant changes in beliefs about the consequences (outcome expectancies) related to influenza vaccine among intervention participants compared to those in the control group. In particular,

significant positive changes in mean scores between T1 and T2 were shown in beliefs that "If I get the flu shot, it can prevent me from getting a more severe case of flu", I could protect my family and friends from flu". This study also found some significant differences in negative perception of the influenza vaccine between the two groups, including "If I get the flu shot, I will be more likely to get other illnesses", and that "If I get the flu shot, it will weaken my immune system".

Knowledge, attitude towards, and beliefs about influenza and the influenza vaccine have been shown to have a significant influence on the decision to receive the influenza vaccine. Previous studies revealed that negative perceptions of influenza and influenza vaccination were found to be associated with low vaccination acceptance (Zimmerman, Nowalk, Raymund et al., 2003; Takahashi, Noguchi, Rahman et al., 2003; Chi & Neuzil, 2004; Brunton, Weir, & Jennings, 2005). A survey study conducted by Chi and Neuzil (2004) showed that thirty-six per cent of the 324 respondents had at least one negative attitude towards influenza vaccination, and 61 per cent of these individuals had been immunised against influenza, compared with 93 per cent of those who did not have the negative beliefs.

Additionally, the result of the present study also showed that significant positive changes in perceived self-efficacy in obtaining influenza vaccination were found between the two groups such as "I can cope with side-effects after receiving the flu vaccine", "I can find the time to get vaccinated against the flu", "Receiving a flu shot will not interfere with my daily routine", and "I will get a flu shot even though I am quite busy during the vaccination period". Furthermore, intervention participants held more positive intentions in receiving influenza vaccine in the forthcoming vaccination period than those in the control group at T2.

One explanation for the positive changes in cognitive-motivational variables in the present study is the specific content of the HAPA-based educational leaflet. It was designed primarily to target people with chronic diseases requiring influenza vaccination and to motivate them to obtain vaccination against influenza by using tailored educational message. In addition, the leaflet sought to enhance confidence in obtaining the influenza vaccination. The content of the educational leaflet highlighted the susceptibility and severity of influenza, modes of transmission, the symptoms and

complications, the positive and negative consequences (outcome expectancies) of receiving influenza vaccine, potential side-effects, the effectiveness of influenza vaccine, and self-efficacy to get vaccinated against influenza.

A major difference between the HAPA-based educational leaflet and the standard government information leaflet was that the HAPA-based leaflet more fully addressed the risk of developing a severe case of influenza in high-risk people with chronic medical conditions, the benefits of influenza vaccination in preventing hospitalisation or serious influenza-related complications (such as pneumonia, bloodstream infections) among these individuals and more discussion about common misperceptions regarding influenza vaccination (e.g. the flu vaccine does not contain any live virus, so it will **NOT** give you the flu). In addition, the personal accounts of people who had been injected with influenza vaccine was added in this educational leaflet to increase in participants' efficacy in their ability to both benefit from and cope with the vaccination.

While behaviour change techniques such as providing information about the behaviour-health link, providing information on the consequences of a recommended behaviour, prompt specific goal setting, and prompt barrier identification (Abraham & Michie, 2008), as well as the inclusion of personal accounts attempting to raise normative beliefs favouring vaccination were addressed in the HAPA-based leaflet, the standard government information leaflet provided the reader general information about influenza and general benefits of influenza vaccination; there was no specific detail regarding the complications of influenza in high-risk individuals and other benefits of influenza vaccination. These differences may have contributed to the significant gains in knowledge, risk perception, outcome expectancies, self-efficacy and intention to be immunised against influenza by the intervention group over the control group. Also, the HAPA-based leaflet was pretested with patients with chronic renal disease. The patients' feedback was positive; these patients felt the massage was clear and easy to understand. Furthermore, these patients felt that it was very persuasive and informative, and they reported that the leaflet would be useful to high-risk people.

Our findings are also in line with the theoretical assumptions of the HAPA model (Schwarzer, 1992, 2001, 2008), showing that providing participants about their personal risk and the consequence of receiving the influenza vaccine, as well as increasing their perceived self-efficacy in getting vaccinated against influenza can enhance their intentions to receive influenza vaccine in the next vaccination period. The fact that changes in key HAPA variables of outcome expectancies and self-efficacy were independently associated with changes in strength of intentions suggests that these variables are both susceptible to change following relatively brief and simple interventions and have a critical and mediating role in shaping intentions.
A possible explanation for these observations may be that the present study targeted middle-aged and older people with chronic disease. These individuals experienced a major health crisis; thus, they may be more likely to be motivated to adopt preventive health behaviour than younger individuals. It is expected that motivation to change will be high in the context of major life events (Schwarzer & Lusczcnska, 2008). Other studies applying the HAPA to older patients in orthopaedic rehabilitation and cardiac rehabilitation have shown the usefulness of the model in explaining behaviour and in the design of interventions for the sample of middle-aged and older individuals (Ziegelmann, Lippke, & Schwarzer, 2006; Renner, Spivak, Kwon et al., 2007; Scholz, Sniehotta, Dipl-Psych et al., 2007).

However, it should be noted that the HAPA, like many social cognitive models, focuses on intra-individual factors without taking into consideration other factors, such as social, environmental and economic factors, that may affect influenza vaccination. In addition, the model does not incorporate the effects of social norms and peer influences on an individual's decision-making about health behaviours. In the previous qualitative study, we found that participants' vaccination decisions were influenced by family members and peers, healthcare providers' recommendations and the availability of free vaccine. Others studies have also shown that the decision to vaccinate or not was significantly affected by the influence of healthcare providers, family members and friends (e.g. CDC, 1988; Zimmerman, Santibanez, Janosky, 2003; Evans, Prout, Prior et al., 2007), and the costs and convenience of obtaining the vaccination (e.g. Kroneman, Paget, & van Essen, 2003; Burns, Ring, & Carroll, 2005). This suggests the presence of other factors (e.g. social and economic factors), in addition to those included in this study (psychological factors), influences influenza

vaccination behaviour. Thus, in future study, those factors should also be taken into consideration when designing interventions to increase influenza vaccine uptake.

7.8.2 Measuring the impact of the intervention: vaccination behaviour

In addition to testing the effectiveness of a HAPA-based leaflet on changing in key mediator variables, this study also investigated the efficacy of a HAPA-based leaflet on influenza vaccination behaviour. Taking into consideration the importance of post-intentional phase of behaviour change in which an intention is translated into behaviour, action planning (implementation intentions) manipulation was included in the leaflet used in this study. Forming implementation intentions facilitate goal attainment through increasing the activation of the anticipated situational cue and automating the goal-directed response to that cue (Gollwitzer, 1999; Gollwitzer & Sheeran, 2006). Thus, individuals who form action planning are more likely to recognise their intentions and perform the recommended behaviour when the specified situation is encountered (Gollwitzer, 1999, Schwarzer, 1992, 2001).

In contrast to the findings in relation to intentions, this study was unable to show a significant effect of the HAPA leaflet on influenza vaccination behaviour. Although the number of participants who received influenza vaccine in the intervention group appeared higher than the comparison group, there was no significant difference in vaccination rates between the two groups.

Unfortunately, a number of factors may have limited the effects of our intervention on influenza vaccination rate. Firstly, the rates of vaccination were unprecedentedly high even in the standard intervention condition, making gains in vaccination rates particularly difficult to achieve. Previous vaccination rates were as low as 38 per cent (Sriwongpan P., personal communication, March 6, 2009), in comparison to the 84 per cent found in the standard condition of the study. Clearly, factors other than the planned interventions may have affected these rates. The most obvious confounding factor was that the vaccination period coincided with a global outbreak of H1N1 influenza. Although the standard influenza vaccination did not immunise against this disease (information which was given in the leaflet), the high levels of awareness and concern related to this outbreak may have led to the spontaneous and unplanned

behaviours (in this case, vaccination) that can be triggered by high-risk situations (Gollwitzer & Brandstatter, 1997). Thus, the global outbreak of H1N1 influenza may partly account for increasing in influenza vaccine uptake among high-risk Thai adults. Evidence in support of this hypothesis can be found in two recent studies conducted in Hong Kong which found that beliefs that 'influenza vaccine was efficacious in preventing bird-to-human avian influenza transmission', and that 'there is a need to receive influenza vaccination following the Severe Acute Respiratory Syndrome (SARS) and avian influenza' were strongly associated with influenza vaccination behaviour (Lau, Kim, Tsui et al., 2008; Lau, Lau, & Lau, 2009).

A second explanation for the relatively weak behavioural effects of our intervention may involve confounding as a result of all participants, regardless of condition, receiving an appointment letter from the public health staff, detailing when and where they could get the influenza vaccination. Participants had to take this letter to the clinic in order to identify themselves as in a "high-risk group" and to receive a free vaccine at the hospital. This may have triggered some goal planning among participants in the comparison condition.

A third possible explanation for the lack of difference between the groups is that all participants in this study had relatively strong intentions to obtain the influenza vaccine, and were being asked to engage in a relatively simple behaviour. In this context, it is possible that action planning added little to the likelihood of them taking up the influenza vaccine (see, for example, Sheeran & Orbell, 1999; Sheeran & Orbell, 2000; Sniehotta, Soares, & Dombrowski, 2007). The only variable we found to predict vaccination in addition to intention was self-efficacy in relation to transport to the clinic to receive the vaccination, and this relationship was relatively modest. Thus, while this variable may be affected by planning, the key driver to vaccination appears to have been the individual's intention to the attend vaccination clinic. This may not provide a full explanation for the lack of between group differences in vaccination rates, as intentions were stronger in the HAPA condition than the standard one. However, it is possible that there is a threshold of intention above which higher levels of intention add little to the likelihood of engagement in a particular behaviour. Thus, it is possible that both groups were sufficiently motivated to seek vaccination,

and differences in relatively high intention scores had only a marginal impact on behaviour.

Despite these potential confounds, a 5 per cent difference in vaccination rates between the HAPA and standard leaflet groups was found. While this was not significant in our sample (arguably due to the study being underpowered to detect differences of this low magnitude), if this finding were to generalise to a wider population, then the HAPA leaflet could result in significantly more people seeking vaccination despite this behavioural prompt. This conclusion is clearly speculative, and requires further large scale research to verify. However, given the potential no cost benefit of using a HAPA-based leaflet, this would seem the leaflet of choice, even before more definitive data is obtained.

7.8.3 Testing the predictive utility of the HAPA model: predicting intention to receive the influenza vaccine

In relation to the second objective (to evaluate theoretical links proposed by the HAPA), however, the HAPA variables provided good predictions of intention to get vaccinated against influenza and of subsequent influenza vaccination behaviour. Risk perceptions, outcome expectancies, and self-efficacy accounted for 56 per cent of the variance in intention at T1.

Prediction of change in intention provided a similar pattern of results. A linear regression analysis indicated that approximately 46 per cent of the variance in the change in intentions could be explained by the change in risk perception, outcome expectancies, and self-efficacy. This is comparable with previous research using the HAPA model in other health behaviours, which found that the model was able to explain between 30-69 per cent of the variance in intentions (e.g. Schwarzer & Renner, 2000; Garcia & Mann, 2003; Luszczynska & Schwarzer, 2003; Sniehotta, Scholz, & Schwarzer, 2005; Chow & Mann, 2010). Outcome expectancies and self-efficacy were significantly correlated with intention to obtain influenza vaccine. A similar pattern of results was seen for the change in intention scores, a linear regression analysis indicated that only outcome expectancy change and self-efficacy change were found to be an independent predictor of change in intentions.

Our findings lend support to the HAPA, suggesting an important role for outcome expectancies and self-efficacy in the formation of behavioral intentions (Luszczynska & Schwarzer, 2003; Schwarzer & Luszczynska, 2008). This study also showed the predictive superiority of self-efficacy over outcome expectancies in the motivation phase. The HAPA suggests that outcome expectancies can be seen as precursors of self-efficacy. While people need to know the possible consequences of a particular behaviour, they also need to feel confident in their ability to perform a desired behaviour. Self-efficacy is therefore considered to be the most powerful predictor of behavioural intentions (Lippke, Ziegelmann, & Schwarzer, 2005; Luszczynska & Schwarzer, 2003; Schwarzer, Luszczynska, Ziegelmann et al., 2008).

The finding that risk perception was not a significant predictor of vaccination intention is consistent with those of previous studies applying the HAPA model (e.g. Schwarzer, Schüz, Ziegelmann et al., 2007; Schwarzer & Luszczynska, 2008). Luszczynska and Schwarzer (2003) found that intention to perform breast self-examination was predicted by outcome expectancies and action self-efficacy, but not risk perception. Similarly, Schwarzer, Schüz, Ziegelmann et al. (2007) conducted four studies to investigate the applicability of the model across four preventive behaviours (dental flossing, seat belt use, dietary behaviour, and physical activity. The findings showed that action planning and recovery self-efficacy significantly predicted all four of the investigated preventive health behaviours. By contrast, risk perception was not significantly associated with any of the variables under study.

Our findings are also in line with the HAPA model (e.g. Schwarzer & Renner, 2000; Luszczynska & Schwarzer 2003; Schwarzer, Schüz, Ziegelmann et al., 2007), which states that risk perception is a relatively weak predictor of behaviour, as its key role is to lead people to deliberate about changing high-risk behaviours and thereby stepping them into the stage of awareness of a health threat (Weinstein, 2000; Schwarzer, 2001; Schwarzer, Schüz, Ziegelmann et al., 2007; Schwarzer & Luszczynska, 2008). Recent study that examined stage-specific predictors of stage transitions between non-intenders, intenders, and actors in relation to physical activity confirmed that risk perceptions were important in forming an intention for people in the pre-intention stage who have no pre-existing intention, but did not appear to exert much influence

on those who already set their goal intentions to start an activity (Lippke, Ziegelmann, & Schwarzer, 2005).

7.8.4 Testing the predictive utility of the HAPA model: predicting vaccination behaviour

Influenza vaccination behaviour was predicted by self-efficacy and intention in obtaining influenza vaccine in the forthcoming vaccination period (89.6 per cent of participants correctly classified into vaccinated and non-vaccinated groups). Self-efficacy predicted both intention and subsequent influenza vaccination behaviour. These findings are consistent with other studies and provide support the HAPA model in that intention and self-efficacy appear to be key factors influencing on behavioural change (Schwarzer & Renner, 2000; Luszczynska, Mazurkiewicz, Ziegelmann et al., 2007; Scholz, Keller, & Perren, 2009). Clearly, these results suggest that individuals with strong self-efficacy and intention to get vaccinated are more likely to have had influenza vaccination. It has been argued that self-efficacy beliefs were crucial to successful change of health behaviours. Self-efficacious persons believed that they had the capacity to exercise control, even in the face of difficulties or barriers and tended to set higher goals for themselves and committed to their goals more strongly, which in turn influenced actual behaviour (Bandura, 1989; Locke & Latham, 1990).

Nevertheless, contrary to our expectations, action planning did not contribute to the prediction of influenza vaccination among high-risk Thai adults. In previous studies applying the HAPA, action planning was found to mediate the relations between intentions and behaviour, implying that individuals with strong intention will be more likely to engage in planning, and those who do an action plan will be more likely to perform the desired behaviour (Sniehotta, Scholz, & Schwarzer, 2005; Schwarzer, 2008; Reuter, Ziegelmann, Lippke et al., 2009). Action planning was also found to account for more variance in the prediction of health behaviours (Lippke, Dipl-Psych, Ziegelmann et al., 2009). The study investigating whether action planning and coping plan would improve the prediction of physical exercise conducted by Scholz, Schuz, Ziegelmann et al. (2008) showed that the inclusion of action planning and coping planning increased the amounts of explained variance in vigorous physical activity from 17 per cent to 23 per cent. Other studies have also reported that action planning was a good predictor of behaviour change (e.g. Luszczynska & Schwarzer, 2003;

Sniehotta, Scholz, & Schwarzer, 2005; Schwarzer, Luszczynska, Ziegelmann et al., 2008).

Our findings are not consistent with those of previous studies; action planning was not found to be a predictor of vaccination behaviour. However, it has been suggested that behaviour is governed either by intentions or by perceived and actual environment (Schwarzer, 2009). In the present study, it is likely that influenza vaccination behaviour may not only involve cognitive processes, but was also influenced by external situation such as the outbreak of H1N1 influenza during the vaccination period. This may have attenuated the effect of action planning on predicting vaccination behaviour. In addition, the study was likely underpowered to detect a true association between action planning and vaccination behaviour. Further studies with larger samples are needed to better elucidate the relationship between these two variables.

7.9 Strengths and Limitations

The strengths of this study include its randomised controlled design, and the application of theoretical framework. However, potential limitations need to be addressed. In this study, the questionnaires were read out loud to some participants with limited literacy by a trained researcher. These participants were then asked to score their own responses. This method of data collection may positively affect participants' scores. Another limitation is that the study was conducted in two urban communities. The findings of this study may not be generalisable to high-risk people living in suburban and rural communities. However, this randomised-controlled pilot study showed that our intervention was feasible and acceptable to promote influenza vaccination to high-risk people with chronic medical conditions. Thus, it can be implemented in other settings and may have potential to raise influenza vaccination rates among these high-risk individuals.

7.10 Conclusion

In summary, the study demonstrated the effectiveness of a HAPA-based leaflet in enhancing intention to be immunised against influenza among high-risk Thai adults. The intervention also improved vaccination rate although the difference in vaccination rates between the two groups did not approach statistical significance. Further larger trials should test whether action planning (implementation intentions) works in increasing influenza vaccination rates among high-risk people, as well as its efficacy in enhancing the likelihood of performing other single behaviours such as mammography screening and dental check-up visit. Additionally, the results of the study provide support for the application of the HAPA model in the context of vaccination behaviour and highlight that the HAPA is a useful model in predicting intention to obtain influenza vaccine and subsequent influenza vaccination behaviour. Self-efficacy and intention were significantly associated with influenza vaccination behaviour. Based on these findings, a HAPA-based leaflet may serve as a useful tool for motivating a group of people who are at risk for influenza-related complications and severe disease to get vaccinated against influenza. It is a cost-and time-effective intervention that helps to reduce the workload to the public health staff or health promotion practitioners. The findings provide valuable information to public health staff for modifying and improving the content of the standard influenza leaflet that is currently available for the high-risk people, as well as designing other effective interventions in order to achieve a greater impact in increasing vaccination rates of high-risk people with chronic diseases.

Chapter 8: General discussion and Conclusion

8.1 Introduction

The 2004 outbreak of influenza A H5N1 and the WHO's recommendation for a national pandemic plan has led the Thai Ministry of Public Health to develop an influenza vaccination programme. Free influenza vaccine for high-risk older people was initially provided in 2008. However, the overall immunisation rate in this high-risk group for the first year of the project was relatively low, particularly in Chiang Rai province. Accordingly, this research aims to addresses these issues and considers how to motivate high-risk individuals to get vaccinated against influenza.

As shown in chapter 4, a broad range of factors have been postulated to be associated with the uptake of influenza vaccination. These include demographic factors, cognitive, psychological, social support, health beliefs, economic, and health system factors (e.g. Telford & Rogers, 2003; Zimmerman, Nowalk, Raymund et al., 2003; Chi & Neuzil, 2004; Kohlhammer, Schnoor, Schwartz et al., 2007; Evans, Prout, Prior et al., 2007; Ward & Draper, 2007; Blank, Freiburghaus, Schwenkglenks et al., 2008). In order to increase influenza vaccine uptake among high-risk Thai people, these factors need to be addressed. It has been suggested that before initiating a complex intervention, pleliminary work (such as qualitative research, surveys, or case study) is essential to improve an understanding of the intervention components, and to provide the detailed information on the context in which the trial would take place (Campbell, Fitzpatrick, Haines et al., 2000; MRC, 2000).

Therefore, in the present reseach, a qualitative study exploring high-risk individual's understandings influenza and factors associated with influenza vaccine uptake was conducted first in order to provide crucial information about people's beliefs regarding influenza, the influenza vaccine and factors influencing influenza vaccination, as well as information on diverse population characteristics in which the trial (study 2) would to be implemented. This contributes to decision making about the planning and design of an intervention.

A number of specific implications were drawn from the first study, and they were significant in shaping the educational intervention programme that was implemented and evaluated in study two. These include the need for the development of an appropriate educational intervention programme and the need for designing a questionnaire that is clear and easy to understand for older Thai people. Additionally, the qualitative research also helped to identify the potential barriers to influenza vaccination among our participants. Apart from this, the personal accounts of people who had received the influenza vaccination (study 1) were used as part of the intervention materials to increase participants'efficacy in relation to their ability to get vaccinated against influenza in study 2.

Findings from an interview study indicated that most participants had insufficient knowledge about influenza and influenza vaccination. Salience of risk, influence of others, perception of the need for preventive health care, and the availability of influenza vaccine played a major role in the decision making about receiving influenza vaccine in high-risk Thai adults. These findings provide valuable insight into what interventions may be appropriate for promoting influenza vaccine acceptance among these individuals.

Having identified the intervention components that should be targeted, the next step was to create an appropriate intervention to promote the influenza vaccination uptake in this high-risk group. Among several factors, cognitive factors are considered to be the important proximal determinants that mediate the effects of others factors upon the performance of health behaviours. Furthermore, they are more likely to be amenable to change than other factors (Conner & Norman, 1998, 2005), providing an impetus to design an intervention to improve influenza vaccination rate in high-risk Thai adults. In addition, the current study is designed as a pilot randomised pragmatic trial. Accordingly, study 2 focuses only on the intra-individual factors affecting the decision making about obtaining influenza vaccine, and the HAPA model was used as a theoretical framework for the present study.

Like other social cognitive models, the HAPA emphasises the rationality of human action (Schwarzer, 2001). In changing the behaviour, an individual is believed to make a deliberate decision to comply, and to weigh up the costs and benefits of the

likely outcomes of different courses of action (Conner & Norman, 1998, 2005; Schwarzer, 2001). The aim of study 2 was to examine the effect of a HAPA-based leaflet and action planning intervention on influenza vaccination behaviour among high-risk urban dwelling Thai adults. In addition to assessing the effects of intervention, this study also provided an opportunity to examine the predictive utility of the HAPA model in explaining behavioural intentions and vaccination behaviour in a sample of high-risk Thai adults.

As the HAPA model is considered to be an appropriate theoretical approach to conceptualise the important factors and their relations for the current study; thus, the the choices of study outcome and the selection of constructs to measure were guided by the model. In this study, the outcome measures include the psychosocial determinants (HAPA variables) of influenza vaccination behaviour and immunisation rates. Although no single theoretical model can encompass all the elements for behaviour change, it helps to understand factors underlying decisions whether or not to engage in a particular behaviour, to identify mechanisms of change and, perhaps most importantly, guide us to design effective prevention programme to change health-related behaviours (Weinstein, 1993; Abraham, Sheeran, & Johnston., 1998; Conner & Norman, 1998; Fishbein & Yzer, 2003; Morrison & Bennett, 2006; Lippke & Ziegelmann, 2008; Michie, Johnston, Francis et al., 2008). While the HAPA focuses on the proximal psychological influences on behaviour (in this case, vaccination), we have to recognise that in the broader social environment, there are a number of factors influencing influenza vaccination acceptance among high-risk people. In this chapter, a brief summary of the research findings is presented, highlighting what the results showed. Following this, the theoretical implications, methodological implications, limitations and directions for future research are discussed. Finally, implications for clinical practice and a conclusion are provided.

8.2 Summary of major research findings

This section briefly revisits findings from the research project. As indicated in Chapter 5, to date there has been limited research on influenza vaccine acceptance in high-risk individuals and factors underlying people's vaccination decision in

Thailand. Major findings from this research revealed that high-risk Thai adults had low levels of knowledge about influenza and influenza vaccination. Many were unsure about the cause and symptoms of influenza, mode of transmission, the seriousness of influenza and its complications. Moreover, they believed that influenza infection was no worse than a "bad cold", and very few participants thought that it could cause death. Most participants reported that they knew little or nothing about the influenza vaccination. Unlike other studies (e.g. Burns, Ring, & Carroll, 2005; Evans, Prout, Prior et al., 2007), we found that side-effects following vaccination were not a major concern among our participants. Their decisions whether or not to get vaccinated against influenza were based on a number of factors, including salience of risk, influence of others, perception of the need for preventive health care, and the availability of influenza vaccine.

Subsequently, a controlled before and after trial was conducted in Muang district, an urban community of Chiang Rai province, Thailand. Two geographically separated communities were chosen to limit contamination between trial arms. The intervention participants received a HAPA-based leaflet (Schwarzer, 1992, 2001) which was designed to motivate them to get vaccinated against seasonal influenza. Additionally, they were asked to form a specific plan (Gollwitzer, 1999) detailing where, when and how they would obtain the influenza vaccination. Those in the control group received a standard government information leaflet. The study showed that there were significant changes in knowledge regarding influenza symptoms at T2 in the intervention group. Also, participants in the intervention group were less likely to describe difficult breathing or swelling of the face as side-effects of influenza vaccination than the control group; thus, demonstrating significantly greater gains in knowledge of vaccine side-effects. Additionally, the intervention had positive effects in changing risk perceptions, outcome expectancies, self-efficacy, and intentions relative to the comparison condition. Stronger intentions to become vaccinated against influenza in the intervention group than the comparison group were explained by change in outcome expectancies (perceived benefits of vaccination and perceived costs of vaccination) and self-efficacy in arranging time and transportation. No significant difference in vaccination rates was observed between two groups. In addition, influenza vaccination was predicted by self-efficacy and intention.

Overall, study 2 provided evidence that an intervention based on the HAPA model is feasible and acceptable to promote influenza vaccination to high-risk Thai adults. A HAPA-based leaflet may be a useful and resource-effective tool to enhance individual's vaccination intention, but larger trials are required to confirm these findings and to examine further the impact of similar interventions on influenza vaccination rates.

8.3 Theoretical implications

8.3.1 The HAPA model: predicting intention and vaccination behaviour

Results from the qualitative data analyses revealed that perceived risk of contracting influenza and participants' beliefs about costs, risks, and benefits of influenza vaccination did appear to play an important role in determining the acceptance or rejection of influenza vaccination. These findings attest to the important role of risk perception and outcome expectancies in shaping an individual's vaccination intention, and this is consistent with the assumption of the HAPA model, which proposes that risk perceptions and outcome expectancy are important in forming an intention to perform a behaviour (Schwarzer, 1992, 2001).

Previous studies have focused on using social cognition models to predict intention to receive influenza vaccine, including Health Belief Model (Lau, Yang, & Tsui et al., 2006; Mok, Yeung, & Chan, 2006; Lyn-cook, Halm, & Wisnivesky, 2007), Health Belief Model and the Multidimensional Locus of Control Theory (Nexøe, Kraqstrup, & Sogaard, 1999), Theory of Reasoned Action (Bosompra, Ashikaga, & Ruby, 2004), and Theory of Planned Behaviour (Gallagher & Povey, 2006). Thus, in those studies, change in health behaviour is focused on motivational factors. In contrast, the present research has taken one step forward by assessing both motivational and post-intentional predictors (action planning). This is because the recent developments in social cognition models suggest that intentions alone are not sufficient to drive behaviour change (Weinstein, 1993; Abraham, Sheeran, & Johnston, 1998; Sheeran, 2002).

The HAPA model which proposes both motivation and volition processes of behaviour change was chosen as the theoretical framework. This model allows for a

test of both the predictors of intentions and actual behaviour within the same framework. The HAPA has been shown to predict intention and behaviour in a range of behaviours (Schwarzer & Renner, 2000; Schwarzer & Luszczynska, 2003; Schwarzer, Schüz, Ziegelmann et al., 2007; Schwarzer, 2008, Chow & Mullan, 2010). This is the first time that the model has been used in the context of vaccination behaviour. The HAPA represents a parsimonious modelling style, and the model fits the data well overall; HAPA variables were able to explain 56 per cent of the variance of intentions to get vaccinated against influenza among our participants. In other words, the HAPA appears to be an appropriate theoretical model for predicting intention to obtain influenza vaccination and subsequent vaccination behaviour. In the formation of intention, risk perception was found to make a minor contribution as compared with outcome expectancies and self-efficacy. This finding is consistent with the assumption of the model, which posits that the role of cognitive variables may be different within the two processes of behaviour change; risk perceptions generally play a crucial role in the fist step on the road to behaviour change; they encourage people to consider behavioural change (Schwarzer, 1992, 2001, 2008).

Additionally, this research has examined the role of outcome expectancies and self-efficacy in predicting intentions to receive influenza vaccine and subsequent vaccination behaviour, which have not been fully explored by previous studies (e.g. Nexøe, Kraqstrup, & Sogaard, 1999; Lau, Yang, & Tsui et al., 2006; Mok, Yeung, & Chan, 2006; Lyn-cook, Halm, & Wisnivesky, 2007). The results of study 2, as described in Chapter 7, provided evidence that outcome expectancies and self-efficacy were stronger in predicting intentions than risk perceptions. Also, self-efficacy was found to predict both intentions and vaccination behaviour. For predicting actual behaviour, the findings showed that perceived self-efficacy and intentions emerged as predictors of influenza vaccination behaviour. The important role played by self-efficacy and intentions in predicting health behaviours have been shown by several previous studies (e.g. Sniehotta, Scholz, & Schwarzer, 2005; Luszczynska, Mazurkiewicz, Ziegelmann et al., 2007; Scholz, Keller, & Perren, 2009). Thus, the findings from this research lend support to existing evidence, and add evidence of the predictive efficacy of the HAPA model in the domain of vaccination behaviour. In addition, the present research extends previous research by providing the evidence to support the applicability of the HAPA in non-western

sample. However, it is difficult to draw definitive conclusions on the universal applicability of the HAPA model based on only one high-risk Thai sample and one target behaviour. Thus, further studies are required to explore the validity of the theory under other cultural settings.

8.3.2 The HAPA model: designing intervention to promote influenza vaccination

There is evidence that theoretical models have been useful in designing effective behaviour change interventions, including those aimed at increasing the uptake of influenza vaccine (e.g. LaVela, Cameron, Priebe et al., 2008; Wray, Buskirk, Jupka, et al., 2009). To design effective behaviour change interventions, this research takes into consideration the importance of the volitional process through which individuals translated their intentions into action; thus, the HAPA model was chosen as the theoretical framework for study two because it suggests both pre-intentional and post-intentional factors relating to behaviour change (Schwarzer, 1992, 2001, 2008). Accordingly, the interventions described in Chapter 7 were based on this model. A HAPA-based leaflet highlighted the key details about susceptibility and severity of influenza, the benefits of influenza vaccination, and participants' efficacy in relation to their ability to both benefit from and cope with the vaccination. In addition to the basic constructs of the HAPA, the leaflet included a specific plan template and encouraged participants to plan in advance how they were going to obtain the influenza vaccination. The results of this research showed that, following the intervention, changes in outcome expectancies and self-efficacy were significantly related to changes in strength of intentions to obtain influenza vaccination. This suggests that brief and simple interventions used in this study had positive effects in enhancing individual's vaccination intention. However, this research was unable to show a significant effect of a HAPA-based leaflet on vaccination behaviour. A number of factors may have contributed to the non-significant effect of our interventions, as discussed in chapter 7. Although the results showed that there was a trend towards higher rates of influenza vaccination in the intervention group (a 5 per cent difference in vaccination rates between the HAPA and standard leaflet groups was observed following the intervention), the present thesis brings the research forward by attempting to use both motivational and volitional interventions to

improve the uptake of influenza vaccine in high-risk individuals, and future research may reveal more positive results.

8.4 Methodological implications

In terms of the study design and methodology, the present research builds on previous studies (Nexøe, Kraqstrup, & Sogaard, 1999; Lau, Yang, & Tsui et al., 2006; Mok, Yeung, & Chan, 2006; Gallagher & Povey, 2006; Lyn-cook, Halm, & Wisnivesky, 2007). Firstly, for predicting intention and subsequent vaccination behaviour, study 2 was the longitudinal study with two measurement points assessed key components of HAPA variables (risk perceptions, outcome expectancies, and self-efficacy). Most previous studies have used cross-sectional designs (Nexøe, Kraqstrup, & Sogaard, 1999; Armstrong, Berlin, Schwartz et al., 2001; Gallagher & Povey, 2006; Lau, Yang, & Tsui et al., 2006; Mok, Yeung, & Chan, 2006; Kwong, Lam, & Chan, 2009); thus, the results of those of previous studies do not reflect changes over time.

Secondly, the important point in terms of the methodology is that this research used a controlled before and after trial to investigate behaviour change, which is advantageous in establishing cause-and-effect relationships between an intervention programme and outcome. There are no known prior studies assessing volitional interventions by using a controlled before and after trial in the context of vaccination promotion. Despite the lack of significant effects of intervention on influenza vaccination behaviour (89.90 per cent vs. 84.31 per cent), the author regards this study as encouraging the development of a larger trial to test the efficacy of a HAPA-based leaflet. The intervention is relatively simple, inexpensive to implement, and requiring no assistance once the leaflet is distributed to the target group. Moreover, this intervention can reach large populations. The findings of this research suggest that the overall intervention is at least effective in enhancing individual's vaccination intentions, and has the potential to change behaviour.

The non-significant effects of our intervention may have been confounded by the global outbreak of a new strain of H1N1 influenza A virus, as discussed in chapter 7. Although it is expected that another influenza pandemic will occur, this is difficult to

predict when it will appear (Taubenberger, Morens, & Fauci, 2007). Alternatively, in future research, monitoring trends in immunisation coverage over time can be used to assess the effect of our intervention on vaccination behaviour among high-risk individuals.

8.5 Limitations of the research and future directions

While the present thesis provides a number of interesting findings, it also has certain limitations. For the qualitative study, the findings are limited to the participants involved in the study. Since this study focused only on high-risk adults living in urban community of Chiang Rai province, a further study with a different and larger sample size is necessary to better understand the beliefs and perceptions about influenza and influenza vaccination in Thailand, where large-scale influenza vaccination programmes have yet to be undertaken. Another limitation is that the participants in this qualitative study were selected from one health centre's database. These participants were health service users, and therefore their views might not reflect the views of non-users. In any future study, increasing the diversity of the participants (both health service users and non-users) can add the depth and accuracy of the findings regarding beliefs and perceptions about influenza and influenza vaccination among high-risk individuals.

In study 2, some limitations also need to be addressed. First, as a pilot trial investigating the effects of a HAPA-based educational leaflet on influenza vaccination, only two communities (intervention and comparison areas) were involved in the study; thus, this restriction clearly limits the generalisability of the results. In future study, testing the intervention in a larger population of communities will provide more confident interpretation of the findings and possibly greater generalisability. Second, since there was no intervention group which implemented only motivational intervention (a HAPA-based leaflet without action planning manipulation); therefore it can not be investigated whether the marginal effects of our interventions are the result of motivational intervention or the result of the interaction of forming an action plan (volitional intervention) and a motivational intervention.

Future research should seek to replicate and extend this research by investigating action planning intervention independent from a HAPA-based educational leaflet.

In addition, matching intervention to the HAPA stages of change has been found to be effective in changing health behaviours (e.g. Lippke, Ziegelmann, & Schwarzer, 2004; Schüz, Sniehotta, & Schwarzer, 2007; Schwarzer, 2008). Therefore, further investigation should also focus on designing and testing stage-matched intervention in the context of vaccination promotion. Third, it should be noted that in this trial, outcome assessors were not fully blinded to the treatment assignment during follow-up assessment. Because blinding of outcome assessors can prevent bias; therefore, for further studies, assessor blinding should be maintained throughout the trial.

With regard to the predictive utility of the HAPA model, although the results of this research provide support for the HAPA model in predicting intention and subsequent vaccination behaviour in high-risk Thai adults, larger studies need to be carried out in different settings with different samples. Also, more research is required to continue investigating its applicability to other health behaviours and to other cultural settings. In particular, the results of this research showed that action planning did not contribute to the prediction of influenza vaccination among high-risk Thai adults. This finding is inconsistent with previous studies applying the HAPA model (e.g. Luszcznska & Schwarzer, 2003; Sniehotta, Scholz, & Schwarzer, 2005; Schwarzer, Schüz, Ziegelmann et al., 2007). However, in the present research, it is likely that vaccination behaviour is influenced by the global outbreak of H1N1 influenza during the vaccination period. This may have attenuated the effects of action planning on predicting vaccination behaviour. Also, our study was likely underpowered to detect expected associations between these two variables. Thus, future studies are warranted to clarify the lack of predictive power of action planning in predicting vaccination behaviour.

8.6 Implications for clinical practice

Vaccination for seasonal influenza remains the best preventive measure available (WHO, 2005). It has been suggested that increasing influenza vaccination rates to more than 90 per cent in all recommended groups should substantially reduce the

impact of annual influenza epidemic (Couch, 2000). In this respect, all health care workers need to take every opportunity to encourage influenza vaccination among individuals in high risk groups. To achieve this goal, and develop more effective vaccination programmes, there needs to be a better understanding of the factors underlying people's vaccination decisions. The results of current research showed that most participants had insufficient knowledge about influenza and influenza vaccination (study 1). This clearly underlines the need for providing information on influenza and influenza vaccine to the public before and during any vaccination programme.

Previous studies have shown that knowledge and attitude towards and beliefs about influenza and influenza vaccine have a significant influence on the decision to obtain influenza vaccination (Honkanen, Keistinen, & Kivela, 1996; Gosney, 2000; Santibanez, Nowalk, Zimmerman et al., 2002; Chi & Neuzil, 2004; Brunton, Weir, & Jennings, 2005). Education efforts need to address the need for influenza vaccination in all high-risk persons, regardless of their general health status and the severity of their underlying disease, in order to counter perceptions that only seriously ill person requires to obtain influenza vaccination. Recently, one study evaluating the effectiveness of influenza vaccine in persons aged 18-64 years with high-risk medical conditions showed that influenza vaccination prevented 87 per cent of hospitalisation among this high-risk group (Hak, Buskens, van Essen et al., 2005). Based on the results of this research (study 2), key beliefs that need to be encouraged include: (1) high-risk individuals are susceptible to get a more severe case of influenza, (2) influenza infection can cause severe complications, (3) getting vaccinated against influenza can reduce its severity if contracted, (4) vaccination against influenza also protects family and friends from influenza.

Health care workers should also be prepared and encouraged to discuss vaccination with their patients. According to this suggestion, they need to supply solid information about influenza and its complications, as well as discuss the safety and efficacy of influenza vaccine. Also, most participants in this research (study 1) stated that they had never heard about influenza vaccination from their healthcare providers. Armed with solid information about influenza and influenza vaccine, healthcare workers will be able to provide clear information regarding influenza vaccination to

the high-risk target individuals. This will lead to increased acceptance of influenza vaccine among these groups. A number of studies have shown that advice from health care workers was strongly associated with influenza immunisation (e.g. CDC, 1988; Honkanen, Keistinen, & Kivela, 1996; Perenboom & Davidse, 1996; Zimmerman, Nowalk, Raymund et al., 2003; Nowalk, Zimmerman, Shen et al., 2004; Tabbarah, Zimmerman, Nowalk et al., 2005). The information received from health care workers can help to increase vaccination rate, even among those with a negative attitude toward vaccination. Chi and Neuzil (2004) found that among people with negative attitudes towards influenza vaccination, the vaccination rate was 75 per cent among those whose healthcare providers recommended the vaccine, whereas vaccination rate of 20 per cent was observed among those whose healthcare providers did not recommend it. The results of the present research also suggest that improving vaccination uptake may be more successful if influenza vaccine is recommended by healthcare workers. Efforts to improve influenza vaccination uptake should broaden its focus to include not only high-risk older people but also younger people as the opinion of them plays a dominant role in encouraging older people to receive the annual vaccine. Other strategies include offering free influenza vaccine and improving access.

In the current research, the findings that a HAPA-based leaflet had positive effects on changing knowledge, risk perception, self-efficacy, outcome expectancies, and intentions in obtaining influenza vaccination among intervention participants, have practical significance. This research suggests that the theory-based educational leaflet may serve as a useful tool to encourage high-risk people to be immunised against influenza. A HAPA-based leaflet can be available in waiting rooms in healthcare settings. High-risk older people can gainfully spend their time reading the leaflet while waiting for their healthcare providers. Furthermore, if these individuals can discuss with their healthcare providers (such as nurses) about the contents of the leaflet and influenza vaccination, this may increase the rate of vaccination among this high-risk group. Clearly, it is very important that people' beliefs about vaccination need to be taken into consideration in that discussion. In particular, for those who do not consider themselves to be at high risk for serious complications of influenza, healthcare workers will need more time with these individuals to explore their beliefs;

this will help them fully understand their susceptibility to influenza and their risk for serious influenza-related complications.

Additionally, a HAPA-based leaflet can also be sent to high-risk older individuals living in the community, together with a reminder letter from healthcare workers. In this way, healthcare workers can convey their recommendations and provide information about the risks of influenza and the benefits of the influenza vaccine, as well as encourage their patients to form an action plan to obtain influenza vaccination. It is a cost-and time-effective intervention that helps reduce the workload of healthcare workers. Although in the current research, a HAPA-based leaflet is aimed at high-risk older persons living in urban community, the same approach may also be applied to older people who are residents of nursing homes and other chronic care facilities. In addition, public health authorities may consider recommending the use of a HAPA-based leaflet for promoting influenza vaccination on a large scale.
Although there are a number of intervention studies that have been carried out to improve influenza vaccination, many of the interventions were atheoretical (Molloy, 2010; Thomas, Russell, & Lorenzetti, 2010). For such interventions, the specific components (key active ingredients) of an intervention programme have not been identified. This makes them difficult to design and to determine why interventions are effective or ineffective. By contrast, the intervention programme used in the current research is based on the HAPA model, and identifies the variables that cause a change in intentions (outcome expectancy and self-efficacy), and vaccination behaviour (self-efficacy and intention). Thus, the study findings offer an understanding of factors that influence behavioural intentions and actual vaccination behaviour. Public health staff and other healthcare professionals can gain insight from these findings in creating effective strategies to promote influenza vaccination to high-risk individuals.

8.7 Conclusions

The findings of this research have provided valuable information regarding beliefs about influenza and influenza vaccination and factors that influence urban-dwelling Thai adults' decisions whether or not to receive influenza vaccine. The results of this

research suggest that it is essential to provide information on influenza and influenza vaccination to the public before the vaccination programme will be implemented in a large scale or nation-wide. Salience of risk, influence of others, perception of the need for preventive health care and the availability of influenza vaccine emerged as an influential factors in the decision whether or not to obtain influenza vaccination among high-risk people. These factors provide a number of targets for any health programme designed to promote influenza vaccination. However, such programmes are more likely to be successful if individuals' beliefs about influenza and influenza vaccination are taken into account in developing interventions to increase influenza vaccination of high-risk people.

Theoretical models also provide target variables to be addressed within any behaviour change intervention. They help determine the focus and content of any educational programme, and can be utilised to explain how intervention works to promote behaviour change (Fishbein & Yzer, 2003). The HAPA (Schwarzer, 1992, 2001) provides one such explanatory model. Thus, the model has been used as a theoretical background of the intervention content in study 2. The study demonstrated the efficacy of a HAPA-based educational leaflet in enhancing intention to obtain the influenza vaccination among high-risk Thai adults. Also, the results of this research showed that there was a trend towards higher influenza vaccination rate in the intervention group. However, further studies are needed to determine the actual effects of a HAPA-based leaflet in raising the rate of influenza immunisation among this high-risk group.

Additionally, the findings highlight that the HAPA appears to be an appropriate theoretical model in predicting intention to receive the influenza vaccine and subsequent vaccination behaviour. Self-efficacy and intention were found to predict vaccination behaviour. However, the use of HAPA constructs that provide a clear theoretical framework for predicting influenza vaccination may lead to overlooking of other variables such as social, environmental, and economic factors; these factors are not incorporated as a variable in the model, but may play an important role in the prediction of vaccination behaviour, as indicated by previous studies (e.g. Nichol, Korn, Margolis, 1990; Humair, Buchs, & Stalder, 2002; Luthi, Mean, Ammon et al., 2002; Kroneman, Paget, & van Essen, 2003; Tabbarah, Zimmerman, Nowalk et al.,

2005; Damiani, Federico, Visca et al., 2007; Endrich, Blank, & Szucs, 2009). There is no single approach to predict or change health behaviour. Despite the limitations of the HAPA, the findings offer valuable information for the public health staff or health promotion practitioners for modifying and improving the content of the currently available influenza leaflet, as well as designing of other effective interventions in order to achieve a greater impact on uptake rates. The HAPA-based leaflet can be integrated into routine practice. It is inexpensive to reproduce and disseminate. There is no difference in the cost, length, and complexity of printing process between a HAPA-based leaflet and a standard government information leaflet. Nevertheless, the findings suggest that a HAPA-based leaflet goes further than a standard one in changing cognitive-motivational variables. Considering these findings and the interventions used in this study, psychological interventions may be one useful means for encouraging older people to seek influenza vaccination, and perhaps increasing the use of influenza vaccine among these high-risk individuals.

References

Abraham, C., Sheeran, P., Spears, R., & Abrams, D. (1992). Health beliefs and promotion of HIV-preventive intentions among teenagers: A Scottish perspective. *Health Psychology, 11*, 363-370.

Abraham, C., Sheeran, P., & Johnston, M. (1998). From health bliefs to self regulation: theoretical advances in the psychology of action control. *Psychology and Health, 13*, 569-591.

Abraham, C., & Michie, S. 2008. A taxonomy of behaviour change techniques used in interventions. *Health Psychology* 27, pp. 379-387.

Abraham, C., & Michie, S. (2008). A taxonomy of behaviour change techniques used in interventions. *Health Psychology, 27*, 379-387.

Abraham, C., & Sheeran, P. (2005). The Health Belief Model. In M. Conner & P. Norman (Eds.), *Predicting health behaviour* (pp. 28-80). Glasgow: Bell & Bain Ltd.

Abramson, Z. H., & Cohen-Naor, V. (2000). Factors associated with performance of influenza immunisation among the elderly. *The Israel Medical Association Journal, 2*, 902-907.

Adonis-Rizzo, M. T. & Jett, K. F. (2006). Health beliefs of Haitian elders related to influenza prevention. *Public Health Nursing, 24*, 18-25.

Ahmed, A. H., Nicholson, K. G., Nguyen-Van Tam, J. S., & Pearson, J. C. G. (1997). Effectiveness of influenza vaccine in reducing hospital admissions during the 1989-90 epidemic. *Epidemiology and Infection, 118*, 27-33.

Ajzen, I., & Fishbein, M. (1980). *Understanding attitudes and predicting social behavior*. Englewood-Cliff, NJ: Prentice-Hall.

Ajzen, I. (1991). The Theory of Planned Behavior. *Organizational Behavior and Human Decision Processes, 50*, 179-211.

Ajzen, I. (2005). *Attitudes, personality and behavior* (2 nd ed.): Open University Press.

Akazawa, M., Sindelar, J. L., & Palteil, D. (2003). Economic costs of influenza-related work absenteeism. *Value in Health, 6*, 107-115.

Al-Mazrou, A., Scheifele, D. W., Soong, T., & Bjornson, G. (1991). Comparison of adverse reactions to whole-virion and split-virion influenza vaccines in hospital personnel. *Canadian Medical Association Journal 145*, 213-218.

Ampofo, K., Gesteland, P. H., Bender, J., Mills, M., Daly, J., Samore, M., Byington, C., Pavia, A. T., Srivastava, R. (2006). Epidemiology, complications, and costs of hospitalisations in children with laboratory-confirmed influenza infection. *Pediatrics, 118*, 2409-2417.

Anderson, E. S., Winett, R. A., & Wojcik, J. R. (2000). Social-cognitive determinants of nutrition behavior among supermarket food shoppers: a structural equation analysis. *Health Psychology, 19*, 479-486.

Andrew, M. K., McNeil, S., Merry, H., & Rockwood, K. (2004). Rates of influenza vaccination in older adults and factors associated with vaccine use: a secondary analysis of the Canadian study of health and aging. *BMC Public Health, 4*(36), 1-8.

Aoki, F. Y., Yassi, A., Cheang, M., Math, M., Murdzak, C., Hammond, G. W., Sekla, L. H., Wright, B. (1993). Effects of acetaminophen on adverse effects of influenza vaccination in health care workers. *Canadian Medical Association Journal, 149*, 1425-1430.

Aoki, F. Y., Macleod, M. D., Paggiaro, P., Carewicz, O., El Sawy, A., Wat, C., Griffiths, M., Walberg, E., Ward, P. (2003). Early administration of oral oseltamivir increases the benefits of influenza treatment. *Journal of Antimicrobial Chemotherapy, 51*, 123-129.

Armitage, C. J., & Conner, M. (2000). Social cognition models and health behaviour: a structured review. *Psychology and Health, 15*, 173-189.

Armitage, C. (2004). Evidence that implementation intentions reduce dietary fat intake: a randomized trial. *Health Psychology, 23*, 319-323.

Armitage, C. J. (2007). Efficacy of a brief worksite intervention to reduce smoking: the roles of behavioral and implementation intentions. *Journal of Occupational Health Psychology, 12*, 376-390.

Armstrong, K., Berlin, M., Schwartz, S., Propert, K., & Ubel, P. A. (2001). Barriers to influenza immunization in a low-income urban population. *American Jounal of Preventive Medicine, 20*, 21-25.

Ashley, J., Smith, T., & Dunnell, K. (1991). Deaths in Great Britain associated with the influenza epidemic of 1989/90. *Population Trends, 65*, 16-20.

Baer, R. D., Weller, S. C., Pachter, L., Trotter, R., de Alba Garcia, J. G., Glazer, M., Klein, R., Deitrick, L., Baker, D. F., Brown, L., Khan-Gordon, K., Martin, S. R., Nichols, J., Ruggiero, J. (1999). Cross-cultural perspectives on the common cold: data from five populations. *Human Organization, 58*, 251-260.

Baer, R. D., Weller, S. C., de Alba Garcia, J. C., & Rocha, A. S. (2008). Cross-cultural perspectives on physician and lay models of the common cold. *Medical Anthropology Quarterly, 22*, 148-166.

Bakker, A. B., Buunk, B. P., & Siero, F. W. (1997). Application of a modified Health Belief Model to HIV preventive behavioral intentions among gay and bisexual men. *Psychology and Health, 12*, 481-492.

Bandura, A. (1977). Self-efficacy: toward a unifying theory of behavioural change. *Psychological Review, 84*, 191-215.

Bandura, A. (1986). *Social foundations of thought and action: a social cognitive theory*. Englewood Cliffs, New Jersy Prentice-Hall.

Bandura, A. (1989). Human agency in Social Cognitive Theory. *American Psychologist, 44*, 1175-1184.

Bandura, A. (1997). *Self-efficacy: the exercise of control*. New York: W.H. Freeman and Company.

Bandura, A. (2004). Health promotion by social cognitive means. *Health Education & Behaviour, 31*, 143-164.

Baranowski, T., Baranowski, J., Cullen, K. W., Marsh, T., Islam, N., & Zakeri, I. (2003). Squire's Quest!: dietary outcome evaluation of a multimedia game. *American Journal of Preventive Medicine, 24*, 52-61.

Bean-Mayberry, B., Yano, E. M., Mo, M. K., Bayliss, N. K., Xu, X., & Fine, M. J. (2009). Does sex influence immunization status for influenza and pneumonia in older Veterans? *Journal of American Geriatrics Society, 57*, 1427-1432.

Beck, K. H., & Lund, A. K. (1981). The effects of health threat seriousness and personal efficacy upon intentions and behavior. *Journal of Applied Social Psychology, 11*, 401-415.

Becker, M. H. (1974). *The Health Belief Model and preventive health behaviour*. New Jersey: Charles B. Slack, Inc.

Beigel, J. H. (2008). Influenza *Critical Care medicine, 36*, 2660-2666.

Belshe, R. B., Gruber, W. C., Mendelman, P. M., Mehta, H. B., Mahmood, K., Reisinger, K., Teanor, J., Zangwill, K., Hayden, F. G., Bernstein, D. I., Kotloff, K., King, J., Piedra, P. A., Block, S. L., Yan, L., Wolff, M. (2000). Correlates of immune protection induced by live, attenuated, cold-adapted, trivalent, intranasal influenza virus vaccine. *The Journal of Infectious Disease, 181*, 1133-1137.

Belshe, R. B., Nichol, K. L., Black, S. B., Shinefield, H., Cordova, J., Walker, R., Hessel, C., Cho, I., Mendelman, P. M. (2004). Safety, efficacy, and effectiveness of live, attenuated cold-adapted influenza vaccine in an indicated population aged 5-49 years. *Clinical Infectious Disease, 39*, 920-927.

Bernstein, e., Kaye, D., Abrutyn, E., Gross, P., Dorfman, M., & Murasko, D. M. (1999). Immune response to influenza vaccination in a large healthy elderly population. *Vaccine, 17*, 82-94.

Beyer, W. E. P., Palache, A. M., Baljet, M., & Masurel, N. (1989). Antibody induction by influenza vaccines in the elderly : a review of the literature. *Vaccine, 7*, 385-394.

Beyer, W. E. P., Palache, A. M., de Jong, J. C., & Osterhaus, A. D. M. E. (2002). Cold-adapted live influenza vaccine versus inactivated vaccine: systemic vaccine reactions, local and systemic antibody response, and vaccine efficacy. *Vaccine, 20*, 1340-1353.

Blank, P. R., Freiburghaus, A. U., Schwenkglenks, M., & Szucs, T. D. (2008). Trends in influenza vaccination coverage rates in the United Kingdom over six seasons from 2001-2002 to 2006-2007. *Eurosurveillance, 13*, 498-504.

Blank, P. R., Schwenkglenks, M., & Szucs, T. D. (2009a). Disparities in influenza vaccination coverage rates by target group in five European countries: Trends over seven consecutive seasons. *Infection 37*, 390-400.

Blank, P. R., Schwenkglenks, M., & Szucs, T. D. (2009b). Vaccination coverage rates in eleven European countries during two consecutive influenza seasons. *Journal of Infection, 58*, 446-458.

Block, S. L., Yogev, R., Hayden, F. G., Ambrose, C. S., Zeng, W., & Walker, R. E. (2008). Shedding and immunogenicity of live attenuated influenza vaccine virus in subjects 5-49 years of age. *Vaccine, 26*, 4940-4946.

Boivin, G., Hardy, I., Tellier, G., & Maziade, J. (2000). Predicting influenza infections during epidemics with use of a clinical case definition. *Clinical Infectious Disease, 31*, 1166-1169.

Bohmer, P.D.,Jennings, L. C., Smith, L. B., Medlicott, R. H. (2004). The national influenza immunisation strategy group: A New Zealand model for influenza vaccination promotion. *International Congress Series, 1263*, 799–804.

Boni, M. F. (2008). Vaccination and antigenic drift in influenza. *Vaccine* 26S, C8-C14.

Bonito, A. J., Lenfestey, N. F., Eicheldinger, C., Iannacchione, V. G., & Campbell, L. (2004). Disparities in immunisations among elderly medicare beneficiaries, 2000 to 2002. *American Journal of Preventive Medicine, 27*, 153-160.

Boone, S. A., & Gerba, C. P. (2005). The occurrence of influenza A virus on household and day care center fomites. *Journal of Infection, 51*, 103-109.

Booth, L. V., Coppin, R., Dunleavey, J., & Smith, H. (2000). Implementation of influenza immunisation policy in general practice: 1997 to 1998. *Communicable Disease and Public Health, 3*, 39-42.

Bosompra, K., Ashikaga, T., & Ruby, A. (2004). Attitudes, Perceived norms, and intentuions: a needs assessment study of the influenza immunisation intentions of elderly citizens in Vermont. *The Journal of Rural Health 20*, 125-130.

Bourgeois, F. T., Valim, C., Wei, J. C., McAdam, A. J., & Mandl, K. D. (2006). Influenza and other respiratory virus-related emergency department visits among young children. *Pediatrics, 118*, e1-e8.

Bouvier, N. M., & Palese, P. (2008). The biology of influenza viruses. *Vaccine, 26S*, D49-D53.

Boyce, T. G., Gruber, W. C., Coleman-Dockery, S. D., Sannella, E. C., Reed, G. W., Wolff, M., Wright, P. F. (2000). Mucosal immune response to trivalent live attenuated intranasal influenza vaccine in children. *Vaccine, 18*, 82-88.

Brandstatter, V., Lengfelder, A., & Gollwitzer, P. M. (2001). Implementation intentions and efficient action initiation. *Journal of Personality and Social Psychology, 81*, 946-960.

Brankston, G., Gitterman, L., Hirji, Z., Lemieux, C., & Gardam, M. (2007). Transmission of influenza A in human beings. *Lancet Infectious Disease, 7*, 257-265.

Brewer, N. T., Chapman, G. B., Gibbons, F. X., Gerrard, M., & McCaul, K. D. (2007). Meta-analysis of the relationship between risk perception and health behaviour: the example of vaccination. *Health Psychology, 26*, 136-145.

Bridges, C. B., Thompson, W. W., Meltzer, M. I., Reeve, G. R., Talamonti, W. J., Cox, N. J., Lilac, H. A., Hall, H., Klimov, A., Fukuda, K. (2000). Efectiveness and cost-benefit of influenza vaccination of healthy working adults: a randomized controlled trial. *Journal of American Medical Association, 284*, 1655-1663.

Bridges, C. B., Kuehnert, M. J., & Hall, C. B. (2003). Transimission of influenza: implications for control in health Care Settings. *Clinical Infectious Disease, 37*, 1094-1101.

Bright, R. A., Medina, M., Xu, X., Perez-Oronoz, G., Wallis, T. R., Davis, X. M., Povinelli, L., Cox, N. J., Klimov, A. L. (2005). Incidence of adamantane resistance among influenza A (H3N2) viiruses isolated worldwide from 1994 to 2005: a cause for concern. *Lancet, 366*, 1175-1181.

Bright, R. A., Shay, D. K., Shu, B., Cox, N. J., & Klimov, A. L. (2006). Adamantane resistance among influenza A viruses isolated early during the 2005-2006 influenza season in the United Strates. *The Journal Of the American Medical Association, 295*, 891-894.

Brownstein, J. S., Wolfe, C. J., & Mandl, K. D. (2006). Empirical evidence for the effect of airline travel on inter-regional influenza spead in the United Strates. *PLoS Medicine, 3*, 1826-1835.

Brunton, C., Weir, R., & Jennings, L. (2005). Knowledge and attitudes about influenza vaccination amongst general practitioners, practice nurses, and people aged 65 and over. *The Newzealand Medical Journal, 118*, 1-11.

.

Bryant, W. K., Ompad, D. C., Sisco, S., Blaney, S., Glidden, K., Phillips, E., Vlahov, D., Galea, S. (2006). Determinants of influenza vaccination in hard-to-reach urban populations *Preventive Medicine, 43*, 60-70.

Brydak, L. B., & Machala, M. (2000). Humoral Immune Response to influenza vaccination in patients from high risk groups. *Drugs, 60*, 35-53.

Brydak, L. B., Machala, M., Mysliwska, J., Mysliwska, A., & Trzonkowski, P. (2003). Immune response to influenza vaccination in an elderly. *Journal of Clinical Immunology, 23*, 214-222.

Brydak, L. B., Machala, M., Centkowski, P., Warzocha, K., & Bilinski, P. (2006). Humoral response to hemagglutinin components of influenza vaccine in patients with non-Hodgkin malignant lymphoma. *Vaccine, 24*, 6620-6623.

Budd, R. J., Hughes, I. C. T., & Smith, J. A. (1996). Health beliefs and compliance with antipsychotic medication. *British Journal of Clinical Psychology, 35*, 393-397.

Burns, V. E., Ring, C., & Carroll, D. (2005). Factors influencing influenza vaccination uptake in an elderly, community-based sample. *Vaccine, 23*, 3604-3608.

Cameron, K. A., Song, J., Manheim, L. M., & Dunlop, D. D. (2010). Gender disparities in health and healthcare use among older adults. *Journal of Women's Health, 19*, 1643-1650.

Campbell, D., & Rumley, M. (1997). Cost-effectiveness of the influenza vaccine in a healthy, working-age population. *Journal of Occupational & Environmental Medicine, 39*, 408-414.

Campbell, M., Fitzpatrick, R., Haines, A., Kinmonth, A. L., & Sandercock, P. (2000). Framework for design and evaluation of complex interventions to improve health. *British Medical Journal, 32*, 694-695.

Campos-Outcalt, D. (2004). Influenza vaccine: new recommendations for infants and children aged 6 to 23 months. *Journal of Family Practice, 53,* 874-877.

Carrat, F., & Valleron, A., J. (1995). Influenza mortality among the elderly in France, 1980-90: how many deaths may have been avoided through vaccination? *Journal of Epidemiology and Community Health, 49*, 419-425.

Carson, J. A. S., Gillham, M. B., Kirk, L. M., Reddy, S. T., & Battles, J. B. (2002). Enhancing self-efficacy and patient care with cardiovascular nutrition education. *American Jounal of Preventive Medicine, 23*, 296-302.

Carver, C., & Scheier, M. F. (1990). Origins and Functions of positive and negative affect: a control-process view. *Psychological Review, 97*, 19-35.

Carver, C. S., & Scheier, M. F. (1996). Self-regulation and its failures. *Psychological Inquiry, 7*, 32-40.

Cates, C. J., Jefferson, T., & Rowe, B. (2008). Vaccines for preventing influenza in people with asthma. *Cochrane Database of Systematic Reviews 2007*(2), 1-9.

Catz, S. L., Kelly, J. A., Bogart, L. M., Benotsch, E. G., & McAuliffe, T. L. (2000). Patterns, correlates and barriers to medication adherence among persons prescribed new treatments for HIV disease. *Health Psychology, 19*, 124-133.

CDC. (1988). Adult immunization: knowledge, attitudes, and practices--Dekalb and Fulton counties, Georgia, 1988. *Morbidity and Mortality Weekly Report, 37*(43), 657- 661.

CDC. (1993). Final results: medical influenza vaccine demonstration; selected states, 1988-1992. *Morbidity and Mortality Weekly Report, 42*, 601-604.

CDC. (1999). Reasons reported by Medicare beneficiaries for not receiving influenza and pneumococcal vaccinations--United States, 1996. *Morbidity & Mortality Weekly Report, 43*, 886-889.

CDC. (2001). Influenza and pneumococcal vaccination levels among persons aged 65 or older years--United States, 1999. *Morbidity and Mortality Weekly Report, 50*, 532-537.

CDC. (2003). *Influenza and pneumococcal immunisation: a qualitative assessment of the beliefs of physicians and older Hispanic Americans and African Americans.* Retrieved 8 October 2007, from http:// www.health.gov/communication/db/FileDownload.asp?ID=171

CDC. (2005). Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP). *Morbidity and Mortality Weekly Report,* 54(No.RR-8), 1-40.

CDC. (2006). Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP). *Morbidity and Mortality Weekly Report* ,55, 1-41.

CDC. (2007). Prevention and control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP). *Morbidity and Mortality Weekly Report,* 56 (No. RR-6), 1-53.

CDC. (2008). Prevention and Control of influenza: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2008. *Morbidity and Mortality Weekly Report,* 57, 1-61.

CDC. (2009a). *Role of laboratory diagnosis of influenza.* Retrieved 15 May 2010, from http://www.cdc.gov/influenza/professionals/diagnosis/labrole.htm

CDC. (2009b). Prevention and control of seasonal influenza with vaccines: Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2009. *Morbidity and Mortality Weekly Report* 58, pp. 1-51.

CDC. (2010a). Update: Influenza Activity---United States, august 30, 2009-March 27, 2010, and composition of the 2010-2011 influenza vaccine. *Morbidity and Mortality Weekly Report* 59, pp. 423-430.

CDC. (2010b). Prevention and control of influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2010. *Morbidity and Mortality Weekly Report* 59, pp. 1-62.

Cha, T., Kao, K., Zhao, J., Fast, P. E., Mendelman, P. M., & Arvin, A. (2000). Genotypic stability of cold-adapted influenza virus vaccine in an efficacy clinical trial. *Journal of Clinical Microbiology, 38, 839-845.*

Champion, V., & Miller, T. (1996). Predicting mammography utilization through model generation. *Psychology, Health & Medicine, 1,* 273-283.

Chan, G. C., & Tang, S. F. (2006). Parental knowledge, attitudes and antibiotic use for acute upper respiratory tract infection in children attending a primary healthcare clinic in Malaysia. *Singapore Medical Journal, 47*, 266-270.

Chan, K. H., Maldeis, N., Pope, W., Yup, A., Ozinskas, A., Gill, J., Seto, W. H., Shortridge, K. F., Peiris, J. S. M. (2002). Evaluation of the directigen FluA+B test for rapid diagnosis of influenza virus type A and B infections. *Journal of Clinical Microbiology, 40*(5), 1675-1680.

Chan, M. (2009). *World now at the start of 2009 influenza pandemic.* Retrieved 08 August 2009, from http://www.who.int/mediacentre/news/statements/2009/h1n1_pandemic_phase6_20090611/en/index.html.

Chapman, J., Armitage, C. J., & Norman, P. (2009). Comparing implementation intention inteventions in relation to young adults' intake of fruit and vegetables. *Psychology and Health, 24*, 317-332.

Charmaz, K. (2006). *Constructing Grounded Theory: a practical guide through qualitative analysis*. London: sage Publications.

Chen, Y., Yi, Q. L., Wu, J., & Li, F. (2007). Chronic disease status, self-perceived health and hospital admissions are important predictors for having a flu shot in Canada. *Vaccine, 25*, 7436-7440.

Chew, F. T., Doraisingham, S., Ling, A. E., Kumarasinghe, G., & Lee, B. W. (1998). Seasonal trends of viral respiratory tract infections in the tropics. *Epidemiology of Infection, 121*, 121-128.

Chi, R. C., & Neuzil, K. M. (2004). The association of sociodemographic factors and patient attitudes on influenza vaccination rates in older persons. *The American Journal of Medical Sciences, 327*, 113-117.

Chiatti, C., Rosa, M. D., Barbadoro, P., Lamura, G., Stanislao, F. D., & Prospero, E. (2010). Socioeconomic determinants of influenza vaccination among older adults in Italy. *Preventive Medicine, 51*, 332-333.

Choowattanapakorn, T. (1999). The social situation in thailand: the impact on elderly people. *International Journal of Nursing Practice, 5*, 95-99.

Chow, A., Ma, S., Ling, A. E., & Chew, S. K. (2006). Influenza-associated deaths in tropical Singapore. *Emerging Infectious Disease, 12*, 114-121.

Chow, S., & Mullan, B. (2010). Predicting food hygiene: an investigation of social factors and past behaviour in an extended model of the Health Action Pocess Approach. *Appetite, 54*, 126-133.

Christenson, B., & Lundbergh, P. (2002). Comparison between cohorts vaccinated and unvaccinated against influenza and pneumococcal infection. *Epidemiology and Infection, 129*, 515-524.

Christiansen, M., Vik, P. W., & Jarchow, A. (2002). College student heavy drinking in social contexts versus alone. *Additive Behaviors, 27*, 393-404.

Chunsuttiwat, S. (2002). *Thai Ministry of Public Health.* Nonthaburi: Ministry of Public Health Publications.

Ciszewski, A., Bilinska, Z. T., Brydak, L. B., Kepka, C., Kruk, M., Romanowska, M., Ksiezycka, E., Przyluski, J., Piotrowski, W., Maczynska, R., Ruzyllo, W. (2008). Influenza vaccination in secondary prevention from coronary ischaemic events in coronary artery disease: FLUCAD study. *European Heart Journal, 29*, 1350-1358.

Clague, B., Chamany, S., Burapat, C., Wannachaiwong, Y., Simmeman, J. K., Dowell, S. F. & Olsen, S. J. (2006). A household survey to assess the burden of influenza in rural Thailand. *Southeast Asian Journal of Tropical Medicine & Public Health, 37*, 488-493.

Clements, M. L., O' Donnell, S., Levine, M. M., Chanock, R. M., & Murphy, B. R. (1983). Dose response of A/Alaska/6/77 (H3N2) cold-adapted reassortant vaccine virus in adult volunteers: role of local antibody in resistance to infection with vaccine virus. *Infection and Immunity, 40*, 1044-1051.

Clements, M. L., & Murphy, B. R. (1986). Development and persistence of local and systemic antibody responses in adults given live attenuated or inactivated influenza A virus vaccine. *Journal of Clinical Microbiology, 23*, 66-72.

Clements, M. L., Betts, R. F., Tierney, E. L., & Murphy, B. R. (1986). Serum and nasal wash antibodies associated with resistance to experimental challenge with influenza A wild-type virus. *Journal of Clinical Microbiology, 24*, 157-160.

Cohen, J. (1988). *Statistical power analysis for the behavioral sciences*. Hillsdale, New Jersey: Erlbaum.

Collier, L. & Oxford, J. (2006). *Human virology*. Oxford: Oxford University press.

Colley, E. (2008). Influenza vaccination in adults with a long-term condition. *Community Practitioner, 81*, 25-28.

Colquhoun, A. J., Nichol, K. L., Botha, J. L., & Raymond, N. T. (1997). Effectiveness of influenza vaccine in reducing hospital admissions in people with diabetes. *Epidemiology and Infection, 119*, 335-341.

Comstock, G. W. (1994). Evaluating vaccination effectiveness and vaccine efficacy by means of case-control studies. *Epidemiologic Reviews, 16*, 77-89.

Conner, M., & Norman, P. (1998). Social Cognition Models in health psychology. *Psychology and Health, 13*, 179-185.

Conner, M., & Norman, P. (2005). Predicting health behaviour: a social cognition approach. In M. Conner & P. Norman (Eds.), *Predicting health behaviour.* London: Bell & Bain Ltd.

Conner, M. (2008). Initiation and maintenance of health behaviors. *Applied Psychology: An International Review, 57*, 42-50.

Corbin, J. (1986). Qualitative data analysis for Grounded Theory. In W. C. Chenitz & J. M. Swanson (Eds.), *From practice to Grounded Theory* (pp. 91-120). Carifornia: Addison-Wesley Publishing Company.

Corbin, J., & Strauss, A. (2008). *Basics of qualitative research.* Los Angeles: Sage Publications.

Cornford, C. S., & Morgan, M. (1999). Elderly people's beliefs about influenza vaccination. *British Journal of General Practice, 49*, 281-284.

Couch, R. B. (2000). Influenza; prospects for control. *Annals of Internal Medicine, 133*, 992-998.

Couch, R. B., & Kasel, J. A. (1983). Immunity to influenza in man. *Annual Review of Microbiology, 37*, 529-549.

Cox, N. J., & Bender, C. A. (1995). The molecular epidemiology of influenza viruses. *Seminars in Virology, 6*, 359-370.

Cox, N. J., & Sabbarao, K. (1999). Influenza. *Lancet, 354*, 1277-1282.

Cox, N. J., & Sabbarao, K. (2000). Global epidemiology of influenza: past and present. *Annual Review of Medicine, 51*, 407-421.

Cox, S., Posner, S. F., McPheeters, M., Jamieson, D., Kourtis, A. P., & Meikle, S. (2006). Hospitalisations with respiratory illness among pregnant women during influenza season. *Obstetrics & Gynecology, 107*, 1315-1322.

Creswell, J. W. (1998). *Qualitative inquiry and research design: choosing among five traditions*. Thousand oaks: Sage Publications.

Cunha, B. A. (2004). Influenza: historical aspects of epidemics and pandemics. *Infectious Disease Clinics of North America, 18*, 141-155.

Damiani, G., Federico, B., Visca, M., Agostini, F., & Ricciardi, W. (2007). The impact of socioeconomic level on influenza vaccination among Italian adults and elderly; a cross-sectional study. *Preventive Medicine, 45*, 373-379.

Davis, J. W., Fujimoto, R. Y., Chan, H., & Juarez, D. T. (2009). Factors affecting the influenza vaccination of high risk adults in Hawaii. *Hawaii Medical Journal, 68*, 50-54.

Davies, R., & Pepys, J. (1976). Egg allergy, influenza vaccine, and immunoglobulin E antibody. *Journal of Allergy and Clinical Immunology 57*, 373-383.

de Andres, A. L., Carrasco-Garrido, P., Hernandez-Barrera, V., Vazquez-Fernandez del Pozo, S., de Miguel, A. G., & Jimenez-Garcia, R. (2006). Influenza vaccination among the elderly Spanish population: trend from 1993 to 2003 and vaccination-related factors. *European Journal of Public Health, 17*, 272-277.

Demicheli, V., Jefferson, T., Rivetti, D., & Deeks, J. (2000). Prevention and early treatment of influenza in healthy adults. *Vaccine, 18*, 957-1030.

Demicheli, V., Pietrantonj, C. D., Jefferson, T., Rivetti, A., & Rivetti, D. (2007). Vaccines for preventing influenza in healthy adults. *Cochrane Database of Systematic Reviews 2007*(2), 1-7.

Denzin, N. K., & Lincoln, Y. S. (2005). Introduction: the disciplin and practice of qualitative research. In N. K. Denzin & Y. S. Lincoln (Eds.), *The Sage handbook of qualitative research* (3rd ed., pp. 1-32). Thousand oaks: Sage Publicatiobs.

De Vet, E., Oenema, A., Sheeran, P., & Brug, J. (2009). Should implementation intentions interventions be implemented in obesity prevention: the impact of if then plans on daily physical activity in Dutch adults. *International Journal of Behavioral Nutrition and Physical Activity, 6*, 1-9.

Dewitte, S., Verguts, T., & Lens, W. (2003). Implementation intentions do not enhance all types of goals: the moderating role of goal difficulty. *Current Psychology, 22*, 73-89.

Dijkstra, A., & Vries, H. (2000). Self-efficacy expectations with regard to different tasks in smoking cessation. *Psychology and Health, 15*, 501-511.

Dishman, R. K., & Buckworth, J. (1996). Increasing physical activity: a quantitative systhesis. *Medicine and Science in Sports and Execise, 28*, 706-719.

Dishman, R. K., Motl, R. W., Saunders, R., Felton, G., Ward, D. S., Dowda, M., Pate, R. R. (2004). Self-efficacy partially mediates the effect of a school-based physical-activity intervention among adolescent girls. *Preventive Medicine, 38*, 628-636.

Dodds, L., McNeil, S. A., Fell, D. B., Allen, V. M., Coombs, A., & Scott, J. (2007). Impact of influenza exposure on rates of hospital admissions and physician visits because of respiratory illness among pregnant women. *Canadian Medical Association Journal, 176*, 463-468.

Doing, K. M., Jerkofsky, M. A., Dow, E. G., & Jellison, J. A. (1998). Use of fluorescent-antibody staining of cytopcentrifuge-prepared smears in combination with cell culture for direct detection of respiratory viruses *Journal of Clinical Microbiology, 36*(7), 2112-2114.

Donovan, J. (1991). Patient education and the consultation: the importance of lay beliefs. *Annals of the Rheumatic Disease, 50*, 418-421.

Dorrell, L., Hassan, I., Marshall, S., Chakraverty, P., & Ong, E. (1997). Clinical and serological responses to an inactivated influenza vaccine in adults with HIV infection, diabetes, obstructive airways disease, elderly adults and healthy volunteers. *International Journal of STD & AIDS, 8*, 776-779.

Dosseh, A., Ndiaye, K., Spiegel, A., Sagna, M., & Mathiot, C. (2000). Epidemiological and virological inflienza survey in Dakar, Senegal: 1996-1998. *The American Journal of Tropical Medicine and Hygiene, 62*, 639-643.

Dowdle, W. R., Coleman, M. T., Mostow, S. R., Kaye, H. S., & Schoenbaum, S. C. (1973). Inactivated influenza vaccine. *Postgraduate Medical Journal 49*, 159-163.

Dowell, S. F. (2001). Seasonal variation in host susceptibility and cycles of certain infectious disease. *Emerging Infectious Disease, 7*, 369-374.

Eccles, R. (2002). An explanation for the seasonality of acute upper respiratory tract viral infections. *Acta Otolaryngol 122*, 183-191.

Eccles, R. (2005). Understanding the symptoms of the common cold and influenza. *The Lancet Infectious Diseases 5*, 718-725.

Edwards, K. M., Dupont, W. D., Westrich, M. K., Plummer, W. D., Palmer, P. S., & Wright, P. F. (1994). A randomized controlled trial of cold-adapted and inactivated vaccines for the prevention of influenza A disease. *The Journal of Infectious Disease, 169*, 68-76.

Edwards, W. (1954). The Theory of decision making. *Psychological Bulletin, 51*, 380-417.

Ellickson, P. L., & Hays, R. D. (1992). On becoming involved with drugs: modeling adolescent drug use over time. *Health Psychology, 11*, 377-385.

Ellickson, P. L., Bell, R. M., & McGuigan, K. (1993). Preventing adolescent drug use: long-term results of a junior high program. *American Jounal of Public Health 83*, 856-861.

Endrich, M. M., Blank, P. R., & Szucs, T. D. (2009). Influenza vaccination uptake and socioeconomic determinants in eleven European countries. *Vaccine, 27*, 4018- 4024.

Ennis, F. A., Yi-Hua, Q. I., & Schild, G. C. (1982). Antibody and cytotoxic T lymphocyte responses of humans to live and inactivated influenza vaccines. *Journal of General Virology 58*, 273-281.

Ershler, W. B. (1988). Influenza vaccination in the elderly: can efficacy be enhanced? *Geriatrics, 43*, 79-83.

Esposito, S., Gasparini, R., Bosis, S., Marchisio, C., Crovari, P., & Principi, N. (2005). Clinical and socio-economic impact of influenza and respiratory syncytial virus infection on healthy children and their households. *Clinical Microbiology and Infection, 11*, 925-936.

Evans, M. R., & Watson, P. A. (2003). Why do older people not get immunised against influenza? a community survey. *Vaccine, 21*, 2421-2427.

Evans, M. R., Prout, H., Prior, L., Tapper-Jones, L. M., & Butler, C. C. (2007). A qualitative study of lay beliefs about influenza immunisation in older people. *British Journal of General Practice, 57*, 352-358.

Fedson, D. S. (2005). Preparing for pandemic vaccination: an international policy agenda for vaccine development. *Journal of Public Health Policy, 26*, 4-29.

Feise, R.J. (2002). Do multiple outcome measures require p-value adjustment? *BMC Medical Research. Methodology* 2, 8.

Ferguson, N. M., Galvani, A. P., & Bush, R. M. (2003). Ecological and immunological determinants of influenza evolution. *Nature, 428-433.*

Fiebach, N. H., & Viscoli, C. (1991). Patient acceptance of influenza vaccination. *The American Journal of Medicine, 91*, 393-400.

Figaro, M. K., & Belue, R. (2005). Prevalence of influenza vaccination in a high-risk population: impact of age and race. *Journal of Ambulatory Care Management, 28*, 24-29.

Findlay, P. F., Gibbons, Y. M., Primrose, W. R., Ellis, G., Downie, G. (2000). Influenza and pneumococcal vaccination: patient perceptions. *Postgraduate Medical Journal*, *76*, 215-217.

Fishbein, M., & Yzer, M. C. (2003). Using theory to design effective health behavior interventions. *Communication Theory, 13*, 164-183.

Fischera, S. D., & Frank, D. I. (1994). The Health Belief Model as a predictor of mammography screening. *Health Values, 18*, 3-9.

Fleiss, J. L., Levin, B. and Paik, M.C. (2003). *Statistical Methods for Rates and Proportions (3rd ed.)*. New York: John Wiley & Sons.

Fleming, D. M., Watson, J. M., Nicholas, S., Smith, G. E., & Swan, A. V. (1995). Study of the effectiveness of influenza vaccination in the elderly in the epidemic of 1989-90 using a general practice database. *Epidemiology and Infection, 115*, 581-589.

Fleming, D. M., Zambon, M., & Bartelds, A. I. M. (2000). Population estimates of persons presenting to general practitioners with influenza-like illness, 1987-96: a study of the demography of influenza-like illness in sentinel practice networks in England and Wales, and in The Netherlands. *Epidemiology and Infection, 124*, 245-253.

Floyd, D. L., Prentice-Dunn, S., & Rogers, R. W. (2000). A meta-analysis of research on protection Motivation Theory. *Journal of Applied Social Psychology, 30*, 407-429.

Foster, D. A., Talsma, A., Furumoto-Dawson, A., Ohmit, S. E., Margulies, J. R., Arden, N. H., Monto, A.S. (1992). influenza vaccine effectiveness in preventing hospitalization for pneumonia in the elderly. *American Journal of Epidemiology, 136*, 296-307.

Francis, T., & Magill, T. P. (1937). The antibody response of human subjects vaccinated with the virus of human influenza. *Journal of Experimental Medicine, 65*, 251-259.

Frank, J. W., Henderson, M., & McMurray, L. (1985). Influenza vaccination in the elderly. *Canadian Journal of Physiology and Pharmacology, 15*, 371-375.

Frank, A. L., Taber, L. H., & Wells, J. M. (1985). Comparison of infection rates and severity of illness for influenza A subtypes H1N1 and H3N2. *The Journal of Infectious Disease, 151*(1), 73-80.

Friedman, L. C., Hoffman, L. P., Nelson, D. V., Baer, P. E., & Webb, J. A. (1994). Dispositional optimism, self-efficacy, and health beliefs as predictors of breast self-examination. *American Jounal of Preventive Medicine, 10*, 130-135.

Fujimoto, S., Kobayashi, M., Uemura, O., Iwasa, M., Ando, T., Katoh, T., Nakamura, C., Maki, N., Togari, H., & Wada, Y. (1998). PCR on cerebrospinal fluid to show influenza-associated acute encephalopathy or encephalitis. *The Lancet, 352*, 873-875.

Gallagher, S., & Povey, R. (2006). Determinants of older adults'intentions to vaccinate against influenza: a theoretical application. *Journal of Public Health, 28*, 139-144.

Garcia, K., & Mann, T. (2003). From "I wish" to "I will": social-cognitive predictors of behavioral intentions. *Journal of Health Psychology, 8*, 347-360.

Gatherer, D. (2009). The 2009 H1N1 influenza outbreak in its historical context. *Journal of Clinical Virology, 45*, 174-178.

Gavin, P. J., & Thomson, R. B. (2003). Review of rapid diagnostic tests for influenza. *Clinical and Applied Immunology Reviews, 4*, 151-172.

Gerdil, C. (2003). The annual production cycle for influenza vaccine. *Vaccine, 21*, 1776-1779.

Gianella, A., Walter, A., Revollo, R., Loayza, R., Vargas, J., & Roca, Y. (2009). Epidemiological analysis of the influenza A (h1N1) outbreak in Bolivia, May August 2009. *Eurosurveillance, 14*, 1-4.

Gill, T. K., Taylor, A. W., & Watson, M. (2007). Trends in influenza immunisation amongst an elderly Australian community. *Vaccine, 25*, 5428-5432.

Glaser, B. G. (1978). *Theoretical sensitivity: advances in the methodology of Grounded Theory*. San Francisco: The Sociology Press.

Godin, G., & Shephard, R. J. (1990). Use of Attitude-Behaviour Models in exercise promotion. *Sports Medicine, 10*, 103-121.

Godin, G., & Kok, G. (1996). The theory of planned behaviour: a review of its applications to health-related behaviours. *American Journal of Health Promotion, 11*, 87-97.

Gollwitzer, P. M., & Brandstatter, V. (1997). Implementation intentions and effective goal pursuit. *Journal of personality and social psychology, 73*, 186-199.

Gollwitzer, P. M., & Oettingen, G. (1998). The emergence and implementation of health goals. *Psychology and Health, 13*, 687-715.

Gollwitzer, P. M., & Schaal, B. (1998). Metacognition in action: the importance of implementation intentions. *Personality and Social Psychology Review, 2*(2), 124-136.

Gollwitzer, P. M. (1999). Implementation intentions: strong effects of simple plans. *American Psychologist, 54*, 493-503.

Gollwitzer, P. M., & Sheeran, P. (2006). Implementation intentions and goal achievement: a meta-analysis of effects and processes. *Advances in experimental Social Psychology, 38*, 69-119.

Gorse, G. J., Belshe, R. B., Munn, N. J. (1986). Safety of and serum antibody response to cold-recombinant influenza A and inactivated trivalent influenza virus vaccines in older adults with chronic diseases. *Journal of Clinical Microbiology* 24, pp. 336-342.

Gorse, J. G., Belshe, R. B., & Munn, N. J. (1988). Local and systemic antibody responses in high-risk adults given live-attenuated and inactivated influenza A virus vaccines. *Journal of Clinical Microbiology, 1988*, 911-918.

Gorse, J. G., & Belshe, R. B. (1990). Enhance of anti-influenza A virus cytotoxicity following influenza A virus vaccination in older, chronically ill adults. *Journal of Clinical Microbiology, 28*, 2539-2550.

Gosney, M. (2000). Factors affecting influenza vaccination rates in older people admitted to hospital with acute medical problems. *Journal of Advanced Nursing, 32*, 892-897.

Govaert, T. M. E., Dinant, G. J., Aretz, K., Masurel, N., Sprenger, M. J. W., & Knottnerus, J. A. (1993). Adverse reactions to influenza vaccine in elderly people: randomised double blind placebo controlled trial. *British Medical Journal, 307*, 988-990.

Govaert, T. M. E., Thijs, C. T. M. C. N., Masurel, N., Sprenger, M. J. W., Dinant, G. J., & Knottnerus, J. A. (1994). The efficacy of influenza vaccination in elderly individuals: a randomized double-blind placebo-controlled trial. *Journal of American Medical Association, 272*, 1661-1665.

Govaert, T., Dinant, G. J., Aretz, K., Knottnerus, J. A. (1998). The predictive value of influenza symptomatology in elderly people. *Family Practice* 15, pp. 16-22.

Gravenstein, S., Miller, B. A., & Drinka, P. (1992). Prevention and controlof influenza A outbreaks in long-term care facilities. *Infection Control and Hospital Epidemiology, 13*, 49-54.

Greenberg, S. B., Allen, M., Wilson, J., & Atmar, R. L. (2000). Respiratory viral infections in adults with and without chronic obstructive pulmonary disease. *American Journal of Respiratory and Critical Care Medicine 162*, 167-173.

Gross, P. A., Weksler, M. E., Quinnan, G. V., Douglas, G., Gaerlan, P. F., & Denning, C. R. (1987). Immunization of elderly people with two doses of influenza vaccine. *Journal of Clinical Microbiology, 25*, 1763-1765.

Gross, P. A., Hermogenes, A. W., Sacks, H. S., Lau, J., & Levandowski, R. A. (1995). The efficacy of influenza vaccine in elderly persons : a meta-analysis and review of the literature. *Annals of Internal Medicine, 123*, 518-527.

Gross, P. A., Russo, C., Dran, S., Cataruozolo, P., Munk, G., & Lancey, S. C. (1997). Time to earliest peak serum antibody response to influenza vaccine in the elderly. *Clinical and Diagnostic Laboratory Immunology, 4*, 491-492.

Guarner, J., & Falcon-Escobedo, R. (2009). Comparison of the pathology caused by H1N1, H5N1, and H3N2 influenza viruses. *Archives of Medical Research, 40*, 655-661.

Gubareva, L. V., Kaiser, L., & Hayden, F. G. (2000). Influenza virus neuraminidase inhibitors. *The Lancet, 355*, 827-835.

Gurfinkel, E. P., Leon de la Fuente, R., & Mendiz, O. (2004). Flu vaccination in acute coronary syndromes and planned percutaneous coronary interventions (FLUVACS) study. *European Heart Journal, 25*, 25-31.

Haber, P., DeStefano, F., Angulo, F. J., Iskander, J., Shadomy, S. V., Weintraub, Chen, R. T. (2004). Guillain-Barre Syndrome following influenza vaccination. *Journal of American Medical Association, 292*, 2478-2481.

Hak, E., Nordin, J., Wei, F., Mullooly, J., Poblete, S., Strikas, R., Nichol, K. (2002). Influence of high-risk medical conditions on the effectiveness of influenza vaccination among elderly members of 3 large managed-care organizations. *Clinical Infectious Disease, 35*, 370-377.

Hak, E., Wei, F., Nordin, J., Mullooly, J., Poblete, S., & Nichol, K. L. (2004). Development and validation of a clinical prediction rule for hospitalization due to pneumonia or influenza or death during influenza epidemics among community-dwelling elderly persons. *The Journal of Infectious Disease, 189*, 450-458.

Hak, E., Buskens, E., van Essen, G. A., de Bakker, D. H., Grobbee, D. E., Tacken, M. A. J. B., van Hout, B. A., Verheij, T. J. M. (2005). Clinical effectiveness of influenza vaccination in persons younger than 65 years with high-risk medical conditions. *Archives of Internal Medicine, 165*, 274-280.

Hak, E., Buskens, E., Nichol, K. L., & Verheij, T. J. M. (2006). Do recommended high-risk adults benefit from a first influenza vaccination? *Vaccine, 24*, 2799-2802.

Hall, C. B., Dolin, R., Gala, C. L., Markovitz, D. M., Zang, Y. Q., Madore, P. H., Disney, F. A. (1987). Children with influenza A infection: treatment with rimantadine. *Pediatrics, 80*, 275-282.

Hannoun, C., Megas, F., & Piercy, J. (2004). Immunogenicity and protective efficacy of influenza vaccination. *Virus Research, 103*, 133-138.

Harrison, J. A., Mullen, P. D., & Green, L. W. (1992). A meta-analysis of studies of the Health Belief Model with adults. *Health Education Research, 7*, 107-116.

Hartert, T. V., Neuzil, K. M., Shintani, A. K., Mitchel, E. F., Snowden, M. S., Wood, L. B., Dittus, R. S., Griffin, M. R. (2003). Maternal mortality and perinatal outcomes among pregnant women with respiratory hospitalizations during influenza season. *American Journal of Obstetrics & Gynecology 189*, 1705-1712.

Harwood, A. (1971). The Hot-Cold theory of disease: implications for treatment of Puerto Rican Patients. *The Journal of the American Medical Association, 216*, 1153-1158.

Hayden, F. G., Osterhaus, A. D. M. E., Treanor, J. J., Fleming, D. M., Aoki, F. Y., Nichol, K. G., Bohnen, A. M., Hirst, H. M., Keene, O. N., Wightmam, K. (1997). Efficacy and safety of the neuraminidase inhibitor zanamivir in the treatment of influenza virus infections. *The New England Journal of Medicine, 337*, 874-880.

Hayden, F. G., Fritz, R. S., Lobo, M. C., Alvord, W. G., Strober, W., & Straus, S. E. (1998). Local and systemic cytokine responses during experimental human influenza A virus infection. *The Journal of Clinical Investigation, 101*(3), 643-649.

Hayden, F. G., Treanor, J. J., Fritz, R. S., Lobo, M. C., Miller, M., Kinnersley, N., Mills, R. G., Ward, P., & Straus, S. E. (1999). use of the oral neuraminidase inhibitor oseltamivir in experimental human influenza. *The Journal of the American Medical Association, 282*, 1240-1246.

Hayden, F. G., Larisa, G., Monto, A. S., Klein, T. C., Elliott, M., Hammond, J. M., Sharp, S. J., & Ossi, M. J. (2000). Inhaled zanamivir for the prevention of influenza in families. *The New England Journal of Medicine, 343*, 1282-1289.

Heckhausen, H., & Gollwitzer, P. M. (1987). Thought contents and cognitive functioning in motivation versus volitional stages of mind. *Motivation & Emotion, 11*, 101-120.

Hedrick, J. A., Barzilai, A., Behre, U., Henderson, F. W., Hammond, J., Reilly, L., Keene, O. (2000). Zanamivir for treatment of symptomatic influenza A and B infection in children five to twelve years of age: A randomized controlled trial. *The Pediatric Infectious Disease Journal, 19*, 410-417.

Helman, C. G. (1978). "Feed a cold, Starve a fever"- Folk models of infection in an English suburban community, and their relation to medical tratment. *Culture, Medicine and Psychiatry, 2*, 107-137.

Herrera, G. A., Iwane, M. K., Cortese, M., Brown, C., Gershman, K., Shupe, A., Averhoff, F., Chaves, S. S., Gargiullo, P., & Bridges, C. B. (2007). Influenza vaccine effectiveness among 50-64-year-old persons during a season of poor antigenic match between vaccine and circulating influenza virus strains: Colorado, United States, 2003-2004. *Vaccine, 25*, 154-160.

Hill, D., Gardner, G., & Rassaby, J. (1985). Factors predisposing women to take precautions against breast and cervix cancer. *Journal of Applied Social Psychology, 15*, 59-79.

Hilleman, M. R. (1998). Six decades of vaccine development--a personal history. *Nature Medicine Vaccine Supplement, 4*, 507-514.

Hilleman, M. R. (2000). Vaccines in historic evolution and perspective: a narrative of vaccine discoveries. *Vaccine, 18*, 1436-1447.

Holloway, I. (2005). *Qualitative research in health care*: Open University Press.

Honkanen, P. O., Keistinen, T., & Kivela, S-L. (1996). Factors associated with influenza vaccination coverage among the elderly: role of health care personnel. *Public Health, 110*, 163-168.

Horby, P. W., Williams, A., Burgess, M. A., & Wang, H. (2005). Prevalence and determinants of influenza vaccination in Australians aged 40 years and over--a national survey. *Australian and Newzealand Journal of Public Health, 29*, 35-37.

Hughes, I., Hill, B., & Budd, R. (1997). Compliance with antipsychotic medication: from theory to practice. *Journal of Mental Health, 6*, 473-489.

Humair, J.P, Buchs, C. R., Stalder, H. (2002). Promoting influenza vaccination of elderly patients in primary care. *Family Practice* 19, pp. 383-389.

Hurt, A. C., Allexander, R., Hibbert, J., Deed, N., & Barr, I. G. (2007). Performance of six influenza rapid tests in detecting human influenza in clinical specimens. *Journal of Clinical Virology, 39*, 132-135.

Hurwitz, E. S., Haber, M., Chang, A., Shope, T., Teo, S., Ginsberg, M., Waecker, N., & Cox, N. J. (2000). Effectiveness of influenza vaccination of day care children in reducing influenza-related morbidity among household contacts. *Journal of American Medical Association, 284*, 1677-1682.

Irving, W. L., James, D. K., Stephenson, T., Laing, P., Jameson, C., Oxford, J. X., Chakraverty, P., Brown, D. W.G., Boon, A. C. M., & Zambon, M. (2000). Influenza virus infection in the second and third trimesters of pregnancy: a clinical and seroepidemiological study. *British Journal of Obstetrics and Gynaecology, 107*, 1282-1289.

Izurieta, H. S., Haber, P., Wise, R. P., Iskander, J., Pratt, D., Mink, C., Chang, S., Braun, N.M., & Ball, R. (2005). Adverse events reported following live, cold adapted, intranasal influenza vaccine. *Journal of American Medical Association, 294*, 2720-2725.

Jackson, L. A., Holmes, S. J., Mendelman, P. M., Huggins, L., Cho, I., & Rhorer, J. (1999). Safety of a trivalent live attenuated intranasal influenza vaccine, FluMist, administered in addition to parenteral trivalent inactivated influenza vaccine to seniors with chronic medical conditions. *Vaccine, 17*, 1905-1909.

Jackson, C., Lawton, R., Knapp, P., Raynor, D. K., & Conner, M. (2005). Beyond intention: do specific plans increase health behaviours in patients in primary care? a study of fruit and vegetable consumption. *Social Science & Medicine, 60*, 2383-2391.

Jackson, C., Lawton, R., Raynor, D. K., Knapp, P., Conner, M. T., Lowe, C. J., & Closs, S. J. (2006). Promoting adherence to antibiotics: a test of implementation intentions. *Patient Education and Counselling, 61*, 212-218.

Jackson, L. A., Jackson, M. L., Nelson, J. C., Neuzil, K. M., & Weiss, N. S. (2006). Evidence of bias in estimates of influenza vaccine effectiveness in seniors. *International Journal of Epidemiology, 35*, 337-344.

Jain, S., Kamimoto, L., Bramley, A., Schmitz, A. M., Benoit, S. R., Louie, J., Sugerman, D. E., Druckenmille, J. K., Ritger, K. A., & Chugh, R. (2010). Hospitalized patients with 2009 H1N1 influenza in the United States, April-June 2009. *New England Journal of Medicine, 361*, 1935-1944.

Janz, N. K., & Becker, M. H. (1984). The Health Belief Model: a decade later. *Health Education Quarterly, 11*, 1-47.

Jefferson, T., Rivetti, D., Rivetti, A., Rudin, M., Pietrantonj, C. D., & Demicheli, V. (2005). Efficacy and effectiveness of influenza vaccines in elderly people: a systematic review. *Lancet, 366*, 1165-1174.

Jefferson, T., Demicheli, V., Pietrantonj, D., & Rivetti, D. (2009). Amantadine and rimantadine for influenza A in adults (review). *Cochrane Database of Systematic Reviews* (2), 1-10.

Jennings, R. & Read, R. C. (2002). *Influenza in practice* Oxford: The Alden Group.

Jimenez, R., Larrauri, A., Carrasco-Garrido, P., Esteban, J., Gomez-Lopez, L. I., & Gil, A. (2003). Influenza coverages in Spain and vaccination-related factors in the subgroup aged 50-64 years. *Vaccine, 21*, 3550-3555.

Jimenez-Garcia, R., Carrasco-Garrido, P., Maya-Montero, E., Martinez-Hennandez, D., Hernandez-Barrera, V., & de Miguel, A. G. (2005). Influenza vaccination among diabetic adults. *Diabetes Care, 28*, 2031-2033.

Jimenez-Garcia, R. Mayo-Montero, E., Hernandez-Barrera, V., Sierra-Moros, M. J., Bachon del Amo, I., Carrasco-Garri do, P., Martinez-Hernandez, D. & de Miquel, A. G. (2005). Evolution of anti-influenza vaccination coverage in Spain from 1993 to 2001. *Vaccine* 23, pp. 2844-2850.

Jimenez-Garcia, R., Hernandez-Barrera, v., Carrasco-Garrido, P., Vazquez-Fernandez del Pozo, S., & de Miguel, A. G. (2006). Influenza vaccination among cardiovascular disease sufferers in Spain: related factors and trend, 1993-2003. *Vaccine, 24*, 5073-5082.

Jimenez-Garcia, R., Jimenez, I., Carrasco-Garrido, P., Hernandez-Barrera, v., de Andres, A. L., del Barrio, J. L., & de Miguel, A. G. (2008). Coverage and predictors of influenza vaccination among adults with diabetes in Spain. *Diabetes Research and Clinical Practice, 79*, 510-517.

Jimenez-Garcia, R., Hernandez-Barrera, V., Carrasco-Garrido, P., de Andres, A. L., & de Miguel, A. G. (2009). Predictors of influenza vaccination in adults withchronic bronchitis. *Respiratory Medicine, 103*, 1518-1525.

Jimenez-Garcia, R., Hernandez-Barrera, V., de Andres, A. L., Jimenez-Trujillo, I., Esteban-Hernandez, J., & Carrasco-Garrido, P. (2010). Gender influence in influenza vaccine uptake in Spain: time trends analysis (1995-2006). *Vaccine, 28*, 6169-6175.

Johansen, H., Sambel, C., & Zhao, W. (2006). Flu shots--national and provincial/ territorial. *Health Reports, 17*, 43-48.

Jones, S. (1985). Depth interviewing. In R. Walker (Ed.), *Applied qualitative research* (pp. 45-55). London: Gower.

Julkunen, I., Melen, K., Nygvist, M., Pirhonen, J., Sareneva, T., & Matikainen, S. (2001). Inflammatory response in influenza A virus infection. *Vaccine, 19*, S32-S37.

Kaiser, L., Wat, C., Mills, T., Mahoney, P., Ward, P., & Hayden, F. (2003). Impact of oseltamivir treatment on influenza-related lower respiratory tract complications and hospitalizations. *Archives of Internal Medicine, 163*, 1667-1672.

Kamps, B. S., Hoffmann, C., & Preiser, W. (2006). Influenza Report 2006. Retrieved 06 June 2010, 2010, from http://www.influenzareport.com/influenzareport.pdf

Kee, S. Y., Lee, J. S., Cheong, H. J., Chun, B. C., Song, J. Y., Choi, W. S., Jo, Y. M., Seo, Y. B., & Kim, W.J. (2007). Influenza vaccine coverage rates and perceptions on vaccination in South Korea. *Journal of Infection, 55*, 273-281.

Keech, M., Scott, A. J., & Ryan, P. J. J. (1998). The impact of influenza and influenza-like illness on productivity and healthcare resource utilization in a working population. *Occupational Medicine, 48*, 85-90.

Keech, M., & Beardsworth, P. (2008). The impact of influenza on working days lost: A review of the literature. *Pharmacoeconomics, 26*, 911-924.

Keenan, H., Campbell, J., & Evans, P. H. (2007). Influenza vaccination in patients with asthma: why is the uptake so low? *British Journal of General Practice, 57*, 359-363.

Keitel, W. A., Cate, T. R., Couch, R. B., Huggins, L. L., & Hess, K. R. (1997). Efficacy of repeated annual immunization with activated influenza virus vaccine over a five year period. *Vaccine, 15*, 1114-1122.

Keren, G., Segev, S., Morag, A., Zakay-Rones, Z., Barzilai, A., & Rubinstein, E. (1988). Failure of influenza vaccination in the aged. *Journal of Medical Virology, 25*, 85-89.

Keren, R., Zaoutis, T. E., Saddlemire, S., Luan, X. Q., & Coffin, S. E. (2006). Direct medical cost of influenza-related hospitalizations in children. *Pediatrics, 118*, e1321-e1327.

Kilbourne, E. D., Laver, W. G., Schulman, J. L., & Webster, R. G. (1968). Antiviral activity of antiserum specific for an influenza virus neuraminidase. *Journal of Virology, 2*, 281-288.

Kilbourne, E. D., Couch, R. B., Kasel, J. A., Keitel, W. A., Cate, T. R., Quarles, J. H., Grajower, B., Pokorny, B. A., & Johanson, B. E. (1995). Purified influenza A virus N2 neuraminidase vaccine is immunogenic and non-toxic in humans. *Vaccine, 13*, 1799-1803.

Knight, R. A., & Hay, D. A. (1989). The relevance of the Health Belief Model to Australian smokers. *Social Science & Medicine, 28*, 1311-1314.

Kohlhammer, Y., Schnoor, M., Schwartz, M., Raspe, H., & Schafer, T. (2007). Determinants of influenza and pneumococcal vaccination in elderly people: a systematic review. *Public Health, 121*, 742-751.

Koningsveld, R. V., Steyerberg, E. W., Moghes, R. A., Swan, A. V., van Doorn, P., & Jacobs, B. (2007). A clinical prognostic scoring system for Guillain-Barre' syndrome. *Lancet Neurology, 6*, 589-594.

Kremers, S. P. J., Mesters, I., Pladdet, I. E., & van den Borne, B. (2000). Partcipation in a sigmoidoscopic colorectal cancer screening program: a pilot study. *Cancer Epidemiology, Biomarkers & Prevention, 9*, 1127-1130.

Kroneman, M., Paget, W. J., & van Essen, G. A. (2003). Influenza vaccination in Europe: an inventory of strategies to reach target populations and optimise vaccination uptake. *Eurosurveillance, 8*(6), 130-138.

Kuiken, T., & Taubenberger, J. K. (2008). Pathology of human influenza revisited. *Vaccine, 26S*, D59-D66.

Kumar, A., Zarychannski, R., Pinto, R., Cook, D. J., Marshall, J., Lacroix, J., Stelfox, T. , bagshaw, S., & Choong, K. (2009). Critically ill patients with 2009 influenza A (H1N1) infection in Canada. *Journal of American Medical Association, 302*, 1872-1879.

Kvale, S. (1996). *Interviews: An Introduction to qualitative research interviewing.* Thousand Oaks: Sage Publications.

Kwong, E. W., & Lam, I. O. (2008). Chinese older people in Hong Kong: health beliefs about influenza vaccination. *Nursing Older People, 20*, 29-33.

Kwong, E. W., Lam, I. O., & Chan, T. M. (2009). What factors affect influenza vaccine uptake among community-dwelling older Chinese people in Hong Kong general outpatient clinics? *Journal of Clinical Nursing, 18*, 960-971.

LaForce, F. M., Nichol, K. L., & Cox, N. J. (1994). Influenza: virology, epidemiology, disease, and prevention. *American Journal of Preventive Medicine, 10*, 31-44.

Lalezari, J., Campion, K., Keene, O., & Silagy, C. (2001). Zanamivir for the treatment of influenza A and B infection in high-risk patients. *Archives of Internal Medicine, 161*, 212-217.

Landi, F., Onder, G., Carpenter, I., Garms-Homolova, V., & Bernabei, R. (2005). Prevalence and predictors of influenza vaccination among frail, community-living elderly patients: an international obsevational study. *Vaccine, 23*, 3896-3901.

Lasky, T., Terracciano, G. J., Magder, L., Koski, C. L., Ballesteros, M., Nash, D., Clark, S., Haber, P., Stolley, P. D., Schonberger, L. B., & Chen, R. T. (1998). The Guillain-Barre syndrome and the 1992-1993 and 1993-1994 influenza vaccines. *New England Journal of Medicine, 339*, 1797-1802.

Lau, J. T. F., Yang, X., & Tsui, H. Y. (2006). Prevalence of influenza vaccination and associated factors among community-dwelling Hong Kong residents of age 65 or above. *Vaccine, 24*, 5526-5534.

Lau, J. T., Kim, J. H., Choi, K. C., Tsui, H. Y., & Yang, X. (2007). Changes in pevalence of influenza vaccination and strength of association of factors predicting influenza vaccination over time--results of two population-based surveys. *Vaccine, 25*, 8279-8289.

Lau, J.T, Kim, J. H., Tsui, H. Y., Griffiths, S. (2008). Perceptions related to bird-to-human avian influenza, influenza vaccination, and use of face mask. *Infection*, 36, 434-443.

Lau, L., lau, Y., & Lau, Y. H. (2009). Prevalence and correlates of influenza vaccination among non-institutionalized elderly people: an exploratory cross-sectional survey. *International Journal of Nursing Studies, 46*, 768-777.

LaVela, S. L., Cameron, K. A., Priebe, M., & Weaver, F. M. (2008). Development and testing of a vaccination message targeted to persons with spinal cord injuries and disorders. *The Journal of Spinal Cord Medicine, 31*, 44-52.

Leonard, G. P., Leib, H., Birkhead, G. S., Smith, C., Costello, P., & Conron, W. (1994). Comparison of rapid detection methods for influenza A virus and their value in health-care management of institutionalized geriatric patients. *Journal of applied Microbiology, 32*(1), 70-74.

Lerner, B. W. & Lerner, K. L. (2008). *Infectious Disease: In context.* The Gale Group.

Levine, M., Beattie, B. L., & Mclean, D. M. (1987). Comparison of one-and two-dose regimens of influenza vaccine for elderly men. *Canadian Medical Association Journal, 137*, 722-726.

Lewis-Parmar, H., & McCann, R. (2002). Achieving national influenza vaccine targets-an investigation of the factors affecting influenza vaccine uptake in older people and people with diabetes. *Communicable Disease and Public Health, 5*, 119-126.

Li, Y. C., & Liu, C. M. (2009). Threat-responsiveness and the decision to obtain free influenza vaccinations among the older adults in Taiwan. *BMC Public Health, 9* (275), 1-6.

Lieberman, L. S. (1979). Medico-nutritional practices among Puerto Ricans in a small urban northeastern community in the United States. *Social Science & Medicine, 13B*, 191-198.

Linde, A. (2001). The importance of specific virus diagnosis and monitoring for antiviral treatment. *Antiviral Research, 51*, 81-94.

Lippke, S., Ziegelmann, J. P., & Schwarzer, R. (2004). Initiation and maintenance of physical exercise: stage-specific effects of a planning intervention. *Research in Sports Medicine, 12*, 221-240.

Lippke, S., Ziegelmann, J. P., & Schwarzer, R. (2005). Stage-specific adoption and maintenance of physical activity: testing a three-stage model. *Psychology of Sport and Exercise, 6*, 585-603.

Lippke, S., & Ziegelmann, J. P. (2008). Theory-based health behaviour change: developing, testing, and applying theoies for evidence-based interventions. *Applied Psychology: An International Review, 57*, 698-716.

Lippke, S., Dipl-Psych, A. U. W., Ziegelmann, J. P., Dipl-Psych, T. R., & Schwarzer, R. (2009). Self-efficac moderates the mediation of intentions into behavior via plans. *American Jounal of Health Behavior, 33*, 521-529.

Lipsitch, M., & Viboud, C. (2009). Influenza seasonality: lifting the fog. *Proceedings of the National Academy of Sciences 106*, 3645-3646.

Locke, E. A., & Latham, G. P. (1990). *A theory of goal setting & task performance*. New Jersey: Prentice-Hall, Inc.

Lofgren, E., Fefferman, N. H., Naumov, Y. N., Gorski, J., & Naumova, E. N. (2007). Influenza seasonality: underlying causes and modeling theories. *Journal of Virology, 81*, 5429-5436.

Longini, I. M., Koopman, J. S., Monto, A. S., & Fox, J. (1982). Estimating household and community transmission parameters for influenza. *American Journal of Epidemiology, 115*, 736-751.

Looijmans-Van den akker, I., Nichol, K. L., Verheij, T. J. M., Rutten, G. E. H. M., Buskens, E., & Hak, E. (2006). Clinical effectiveness of first and repeat influenza vaccination in adult and elderly diabetic patients. *Diabetes Care, 29*, 1771-1776.

Lowen, A. C., Mubareka, S., Steel, J., & Palese, P. (2007). Influenza virus transmission is dependent on relative humidity and temperature. *PloS Pathogens, 3*, 1470-1476.

Lowen, A. C., Steel, J., Mubareka, S., & Palese, P. (2008). High temperature (30C) blocks aerosal but not contact transmission of influenza virus. *Journal of Virology, 82*, 5650-5652.

Luszczynska, A. (2004). Change in breast self-examination behaviour: effects of intervention on enhancing self-efficacy. *International Journal of Behavioral Medicine, 11*, 95-103.

Luszczynska, A., & Schwarzer, R. (2003). Planning and self-efficacy in the adoption and maintenance of breast self-examination: a longitudinal study on self-regulatory cognitions. *Psychology and Health, 18*, 93-108.

Luszczynska, A., & Schwarzer, R. (2005). Social Cognitive Theory. In M. Conner & P. Norman (Eds.), *Predicting health behaviour* (pp. 127-169). Glasgow: Bell & Bain Ltd.

Luszczynska, A., Sobczyk, A., & Abraham, C. (2007). Planning to lose weight: randomised controlled trial of an implementation intention prompt to enhance weight reduction among overweight and obese women. *Health Psychology, 26*, 507-512.

Luszczynska, A., Mazurkiewicz, M., Ziegelmann, J. P., & Schwarzer, R. (2007). Recovery self-efficacy and intention as predictors of running or jogging behavior: a cross-lagged panel analysis over a two-year period. *Psychology of Sport and Exercise, 8*, 247-260.

Luthi, F. C., Mean, F., Ammon, C., & Burnand, B. (2002). Evaluation of a population-based prevention program against influenza among Swiss elderly people. *Swiss Medical Weekly, 132*, 592-597.

Lyn-cook, R., Halm, E. A., & Wisnivesky, J. P. (2007). Determinants of adherence to influenza vaccination among inner-city adults with persistent asthma. *Primary Care Respiratory Journal, 16*, 229-235.

Mac Donald, R., Baken, L., Nelson, A., & Nichol, K. L. (1999). Validation of self-report of influenza and pneumococcal vaccination status in elderly outpatients. *American Journal of Preventive Medicine, 16*, 173-177.

Maciosek, M. V., Solberg, L. I., Coffield, A. B., Edwards, N. M., & Goodman, M. J. (2006). Influenza vaccination: health impact and cost effectiveness among adults aged 50-64 and 65 and older. *American Journal of Preventive Medicine, 31*, 72-79.

Maddux, J. E., & Rogers, R. W. (1983). Protection motivation and self-efficacy; a revised theory of fear appeals and attitude change. *Journal of Experimental Social Psychology, 19*, 469-479.

Maddux, J. E. (1993). Social Cognitive Models of health and exercise behavior: an introduction and review of conceptual issues. *Journal of Applied Sport Psychology, 5*, 116-140.

Makela, M. J., Pauksens, K., Rostila, T., Fleming, D. M., Man, C. Y., Keene, O. N., & Webster, A. (2000). Clinical efficacy and safety of the orally inhaled neuraminidase inhibitor zanamivir in the treatment of influenza: A randomised, double-blind, placebo-controlled European study. *Journal of Infection, 40*, 42-48.

Maiman, L. A., & Becker, M. H. (1974). The Health Belief Model: origins and correlates. In M. H. Becker (Ed.), *The Health Belief Model and personal health behaviour*. New Jersey: Charles B. Slack, Inc.

Mangtani, P., Breeze, E., Kovats, S., Ng, E. S. W., Roberts, J. A., & Fletcher, A. (2005). Inequalities in influenza vaccine uptake among people aged over 74 years in Britain. *Preventive Medicine, 41*, 545-553.

Margolis, K. L., Nichol, K. L., Poland, G. A., & Pluhar, R. E. (1990). Frequency of adverse reactions to influenza vaccine in the elderly. *Journal of American Medical Association, 264*, 1139-1141.

Masurel, N. & Laufer, J. (1984). A one year study of trivalent influenza vaccines in primed and unprimed volunteers: immunolgenicity, clinical reaction and protection. *Journal of Hygiene Cambridge , 92*, 263-276.

Mayo-Montero, E., Hernandez-Barrera, V., Carrasco-Garrido, P., de Miguel, A. G., & Jimenez-Garcia, R. (2007). Influenza vaccination among persons with chronic respiratory diseases: coverage, related factors and time-trend, 1993-2001. *Public Health, 121*, 113-121.

McCombie, S. C. (1987). Folk flu and viral syndrome: an epidemiological perspective. *Social Science & Medicine, 25*, 987-993.

McCullers, J. A., Wang, G. C., He, S., & Webster, R. G. (1999). Reassortment and insertion-deletion are strategies for the evolution of influenza B viruses in nature. *Journal of Virology, 73*, 7343-7348.

McCullers, J. A., Facchini, S., Chesney, P. J., & Webster, R. G. (1999). Influenza B virus encephalitis. *Clinical Infectious Disease, 28*, 898-900.

Meltzer, M. I., Cox, N. J., & Fukuda, K. (1999). The economic impact of pandemic influenza in the United Strates: priorities for prevention. *Emerging Infectious Disease, 5*, 659-671.

Menec, V. H., Black, C., MacWilliam, L., & Aoki, F. Y. (2003). The impact of influenza-associated respiratory illness on hospitalisations, physician visits, emergency room visits, and mortality. *Canadian Journal of Public Health, 94*, 59-63.

Michie, S., & Abraham, C. (2004). Interventions to change health behaviours: evidence-based or evidence-inspired? *Psychology and Health, 19*, 29-49.

Michie, S., Dormandy, E., & Marteau, T. M. (2004). Increasing screening uptake amongst those intending to be screened: the use of action plans. *Patient Education and Counselling, 55*, 218-222.

Michie, S., Johnston, M., Francis, J., Hardeman, W., & Eccles, M. (2008). From theory to intervention: mapping theoretically derived behavioural determinants to behaviour change techniques. *Applied Psychology: An International Review, 57*, 660-680.

Michie, S., & Prestwich, A. (2010). Are interventions theory-based? Development of a theory coding scheme. *Health Psychology, 29*, 1-8.

Millar, M. G. (1997). The effects of emotion on breast self-examination: another look at the Health Belief Model. *Social Behavior and Personality, 25*, 223-232.

Miller, E. K., Griffin, M. R., Edwards, K. M., Weinberg, G. A., Szilagyi, P. G., Staat, M. A., Iwane, M. K., Zhu, Y., Hall, C. B., Fairbrother, G., Seither, R., & Erdman, D. (2008). Influenza burden for children with asthma. *Pediatrics, 121*, 1-8.

Milne, S., Sheeran, P., & Orbell, S. (2000). Prediction and intervention in health-related behavior: a meta-analytic review of Protection Motivation Theory. *Journal of Applied Social Psychology, 30*, 106-143.

Milne, S., Orbell, S., & Sheeran, P. (2002). Combining motivational and volitional interventions to promote exercise participation: protection motivation theory and implementation intentions. *British Journal of Health Psychology, 7*, 163-184.

Ministry of Public Health. (2008). *Promoting influenza vaccination in high-risk elderly Thai people*. Retrieved 11 March 2008, from http:// www.moph.go.th

Ministry of Public Health. (2009). *Situations, policy, strategy, and guideline for prevention and control of pandemic influenza (H1N1) 2009*. Retrieved 11 July 2010, from http://beid.ddc.moph.go.th/eng/images/stories/Newpercent202010/3percent20Situation_strategy30percent20Decpercent2009.pdf

MIV study group. (2005). The macro epidemiology of influenza vaccination in 56 countries, 1997-2003. *Vaccine , 23*, 5133-5143.

Mok, E., Yeung, S. H., & Chan, M. F. (2006). Prevalence of influenza vaccination and correlates of intention to be vaccinated among Hong Kong Chinese. *Public health Nursing, 23*, 506-515.

Molinari, N. A. M., Ortega-Sanchez, I. R., Messonnier, M. L., Thompson, W. W., Wortley, P. M., Weintraub, E., & Bridges, C. B. (2007). The annual impact of seasonal influenza in the US: measuring disease burden and costs. *Vaccine, 25*, 5086-5096.

Molloy, G. J. (2010). Increasing influenza vaccination rates: where is the behaviour change theory? *Vaccine, 28*, 3632.

Montano, D. E. (1986). Predicting and understanding influenza vaccination behavior : alternatives to Health Belief Model. *Medical Care, 24*, 438-453.

Monto, A. S., & Kendal, A. P. (1973). Effect of neuraminidase antibody on Hong Kong influenza. *Lancet, 301*, 623-625.

Monto, A. S., Robinson, D. P., Herlocher, M. L., Hinson, J. M., Elliott, M. J., & Crisp, A. (1999). Zanamivir in the prevention of influenza among healthy adults: A randomized controlled trial. *The Journal Of the American Medical Association, 281*, 31-35.

Monto, A. S., Gravenstein, S., Elliott, M., Colopy, M., & Schweinle, J. (2000). Clinical signs and symptoms predicting influenza infection. *Archives of Internal Medicine, 160*, 3243-3247.

Monto, A. S., Hornbuckle, K., & Ohmit, S. E. (2001). Influenza vaccine effectiveness among elderly nursing residents; a cohort study. *American Journal of Epidemiology, 154*, 155-160.

Monto, A. S., Pichichero, M. E., Blanckenberg, S. J., Ruuskanen, O., Cooper, C., Fleming, D. M., & Kerr, C. (2002). Zanamivir prophylaxis: An effective strategy for the prevention of influenza types A and B within households. *The Journal of Infectious Disease, 186*, 1582-1588.

Monto, A. S. (2008). Epidemiology of influenza. *Vaccine, 26S*, D45-D48.

Monto, A. S., Ohmit, S. E., Petrie, J. G., Johnson, E., Truscon, R., Teich, E., Rotthoff, J., Boulton, M., & Victor, J. C. (2009). Comparative efficacy of inactivated and live attenuated influenza vaccines. *New England Journal of Medicine, 361*, 1260-1267.

Morishima, T., Togashi, T., Yokota, S., Okuno, Y., Miyazaki, C., Tashiro, M., & Okabe, N. (2002). Encephalitis and encephalopathy associated with an influenza epidemic in Japan. *Clinical Infectious Disease, 35*, 512-517.

Morrison, V. & Bennett, P. (2006). *An introduction to health psychology*. London: Pearson Education Limited.

Moscona, A. (2005). Drug therapy: neuraminidase inhibitors for influenza. *The New England Journal of Medicine, 353*, 1363-1373.

Moscona, A. (2008). Medical management of influenza infection. *Annual Review of Medicine, 59*, 397-413.

Moss, S. E., Klein, R., & Klein, B. E. K. (1991). Cause-specific mortality in a population-based study of diabetes. *American Journal of Public Health, 81*, 1158-1162.

Moura, F. E. A., Perdigao, A. C. B., & Siqueira, M. M. (2009). Seasonality of influenza in the tropics: A distinct pattern in Northeastern Brazil. *The American Journal of Tropical Medicine and Hygiene, 81*, 180-183.

Medical Research Council. (2000). *A framework for development and evaluation of RCTs for complex interventions to improve health.* Retrived 10 January 2009, from http://www.mrc.ac.uk/Utilities/Documentrecord/index.htm?d=MRC003372

Mullen, P. D., Hersey, J. C., & Iverson, D. C. (1987). Health behavior models compared. *Social Science & Medicine, 24*, 973-981.

Mullooly, J. P., Barker, W. H., & Nolan, T. F. (1986). Risk of acute respiratory disease among pregnant woman during influenza A epidemics. *Public Health Reports, 101*, 205-211.

Mullooly, J., Bennett, M. D., Hornbrook, M. C., Barker, W. H., Williams, W. W., Patriarca, P. A., & Rhodes, P. H. (1994). Influenza vaccination programs for elderly persons: cost-effectiveness in a health maintenance organization. *Annals of Internal Medicine, 121*, 947-952.

Mullooly, J. P., Bridges, C. B., Thompson, W. W., Chen, J., Weintraub, E., Jackson, L., Black, S., & Shay, D. K. (2007). Influenza-and RSV-associated hospitalisations among adults. *Vaccine, 25*, 864-855.

Murata, Y., Walsh, E. E., & Falsey, A. R. (2007). Pulmonary complications of interpandemic influenza A in hospitalized adults. *The Journal of Infectious Disease, 195*, 1029-1037.

Murgraff, V., McDermott, M. R., & Walsh, J. (2003). Self-efficacy and behavioral enactment: the application of Schwarzer's Health Action Process Approach to the prediction of Low-risk, single-occasion drinking. *Journal of Applied Social Psychology, 33*, 339-361.

Murphy, B. R., & Clements, M. L. (1989). The Systemic and mucosal immune response of humans to influenza A virus. *Current Topics in Microbiology and Immunology, 146*, 107-116.

Murphy, K. R., Eivindson, A., Pauksens, K., Stein , W. J., Tellier, G., Watts, R., Leophonte, P., Sharp, S. J., & Loeschel, E. (2000). Efficacy and safety of inhaled zanamivir for the treatment of influenza in patients with asthma or chronic obstructive pulmonary disease: A double-blind, randomised, placebo-controlled, multicentre study. *Cinincal Drug Investigation, 20*(5), 337-349.

Musana, K. A., Yale, S. H., Mazza, J. J., & Reed, K. D. (2004). Practical considerations to influenza vaccination. *Clinical Medicine & Research, 2*, 256-259.

National Statistical Office. (2006). *Thailand multiple indicator cluster survey: Chiang Rai province*. Bangkok: Ministry of Information and Communication Technology.

Nayak, J., & Treanor, J. J. (2009). Antiviral treatment and prophylaxis of influenza virus in children. *Pediatric Annals, 38*, 667-674.

Neuzil, K. M., Reed, G. W., Mitchel, E. F., Simonsen, L., & Griffin, M. R. (1998). Impact of influenza on acute cardiopulmonary hospitalizations in pregnant women. *American Journal of Epidemiology, 148*, 1094-1102.

Neuzil, K. M., Mellen, B. G., Wright, P. F., Mitchel, E. F., & Griffin, M. R. (2000). The effect of influenza on hospitalisations, outpatient visits, and courses of antibiotics in children. *The New England Journal of Medicine, 342*, 225-231.

Neuzil, K. M., Dupont, W. D., Wright, P. F., & Edwards, K. M. (2001). Efficacy of inactivated and cold-adapted vaccines against influenza A infection, 1985 to 1990: the pediatric experience. *Pediatric Infectious Disease Journal, 20*, 733-740.

Neuzil, K. M., Zhu, Y., Griffin, M. R., Edwards, K. M., Thompson, J. M., Tollefson, S. J., Wright, P. F. (2002). Burden of interpandemic influenza in children younger than 5 years: A 25-year prospective study. *The Journal of Infectious Disease, 185*, 147-152.

Newall, A. T. & Scuffham, P. A. (2008). Influenza-related disease: The cost to the Australian healthcare system. *Vaccine , 26*, 6818-6823.

Nexøe, J., Kraqstrup, J., & Sogaard, J. (1999). Decision on influenza vaccination among the elderly: A questionnaire study based on the Health Belief Model and the Multidimensional Locus of Control Theory. *Scandinavian Journal of Primary Health Care, 17*, 105 – 110.

Ng, T. P., Pwee, K. H., Niti, M., & Goh, L. G. (2002). Influenza in Singapore: assessing the burden of illness in the community. *The Annals, Academy of Medicine, Singapore 31*, 182-188.

Nguyen, H. L. K., Saito, R., Ngiem, H. K., Nishikawa, M., Shobugawa, Y., Nguyen, D. C., Shobugawa, Y., Nguyen, D. C., & Hoang, L. T. (2007). Epidemiology of influenza in Hanoi, Vietnam, from 2001 to 2003. *Journal of Infection, 55*, 58-63.

Nguyen-Van-Tam, J. S., & Hampson, A. W. (2003). The epidemiology and clinical impact of pandemic influenza *Vaccine, 21*, 1762-1768.

Nichol, K. L., Korn, J. E., Margolis, K. L., Poland, G. A., Petzel, R. A., & Lofgren, R. P. (1990). Achieving the national health objective for influenza immunisation: success of an institution-wide vaccination programme. *American Journal of Medicine, 89*, 156-160.

Nichol, K. L., Lofgren, R. P., & Gapinski, J. (1992). Influenza vaccination: knowledge, attitudes, and behaviour among high-risk outpatients. *Archives of Internal Medicine, 152*, 106-110.

Nichol, K. L., Lind, A., Margolis, K. L., Murdoch, M., McFadden, R., Hauge, M., Magnan, S. & Drake, M. (1995). The effectiveness of vaccination against influenza in healthy, working adults. *New England Journal of Medicine 333*, 889-893.

Nichol, K. L., Wuorenma, J., & Sternberg, T. V. (1998). Benefits of Influenza vaccination for low-intermediate-, and high-risk senior citizens. *Archives of Internal Medicine, 158*, 1769-1776.

Nichol, K. L., Mendelman, P. M., Mallon, K. P., Jackson, L. A., Gorse, G. J., Belshe, R. B., Glezen, W. P., & Wittes, J. (1999). Effectiveness of live, attenuated intranasal influenza virus vaccine in healthy, working adults: a randomised control trial. *Journal of American Medical Association, 281*, 137-144.

Nichol, K. L., Baken, L., & Nelson, A. (1999). Relation between influenza vaccination and outpatient visits, hospitalization, and mortality in elderly persons with chronic lung disease. *Annals of Internal Medicine, 130*, 397-403.

Nichol, K. L. (2001). Live attenuated influenza virus vaccines: new options for the prevention of influenza. *Vaccine, 19*, 4373-4377.

Nichol, K. L., & Zimmerman, R. (2001). Ceneralist and subspecialist physicians'knowledge, attitudes, and practices regarding influenza and pneumococcal vaccinations for elderly and other high-risk patients. *Archives of Internal Medicine, 161*, 2702-2708.

Nichol, K. L., Nordin, J., Mullooly, J., Lask, R., Fillbrandt, K., & Iwane, M. (2003). Influenza vaccination and reduction in hospitalizations for cardiac disease and stroke among the elderly. *New England Journal of Medicine, 348*, 1322-1332.

Nichol, K. L. & Treanor, J. J. (2006). Vaccines for seasonal and pandemic influenza. *The Journal of Infectious Disease, 194*, S111-118.

Nichol, K. L., Nordin, J., Nelson, D. B., Mullooly, J. P., & Hak, E. (2007). Effectiveness of influenza vaccine in the community-dwelling elderly. *New England Journal of Medicine, 357*, 1373-1381.

Nicholson, K. G., Kent, J., & Hammersley, V. (1999). Influenza A among community-dwelling elderly persons in Leicestershire during winter 1993-1994; cigarette smoking as a risk factor and the efficacy of influenza vaccination. *Epidemiology and Infection, 123*, 103-108.

Nicholson, K. G., Aoki, F. Y., Osterhaus, A. D. M. E., Trottier, S., Carewicz, O., Mercier, C. H., Rode, A., Kinnersley, N., & Ward, P. (2000). Efficacy and safety of oseltamivir in treatment of acute influenza: a randomised controlled trial. *The Lancet, 355*, 1845-1850.

Nicholson, K. G., Wood, J. M., & Zambon, M. (2003). Influenza. *Lancet, 362*, 1733-1745.

Noar, S. M., Benac, C. N., & Harris, M. S. (2007). Does tailoring matter? Meta-analytic review of tailored print health behaviour change interventions. *Psychological Bulletin, 133*, 673-693.

Nordin, J., Machala, M., Poblete, S., Strikas, R., Petrucci, R., Wei, F., Rush, B., Safirstein, B., Wheeler, D., & Nichol, K. (2001). Influenza vaccine effectiveness in preventing hospitalizations and deaths in persons 65 years or older in Minnesota, New York, and Oregon: data from 3 health plans. *The Journal of Infectious Disease, 184*, 665-670.

Norman, P., & Conner, M. (1993). The role of Social Cognition Models in predicting attendance at health checks. *Psychology and Health, 8*, 447-462.

Norman, P., Boer, H., & Seydel, E. R. (2005). Protection Motivation Theory. In M. Conner & P. Norman (Eds.), *Predicting health behaviour* (pp. 170-222). Glasgow: Bell & Bain, Ltd.

Nowalk, M. P., Zimmerman, R. K., Shen, S., Jewell, I. K., & Raymund, M. (2004). Barriers to pneumococcal and influenza vaccination in older community-dwelling adults (2000-2001). *Journal of the American Geriatrics Society 52*, 25-30.

Nowalk, M. P., Zimmerman, R., Tabbarah, M., Raymund, M., & Jewell, I. K. (2006). Determinants of adult vaccination at inner-city health centers: a descriptive study. *BMC Family Practice, 7*(2), 2-7.

Obenauer, J. C., Denson, J., Mehta, P. K., Su, X., Mukatira, S., Finkelstein, D. B., Xu, X., Wang, J. (2006). Large-scale sequence analysis of avian influenza isolates. *Sciene, 311*, 1576-1580.

Ohmit, S. E., & Monto, A. S. (1995). Influenza vaccine effectiveness in preventing hospitalization among the elderly during influenza type A and type B seasons. *International Journal of Epidemiology, 24*, 1240-1248.

Ohmit, S. E., victor, J. C., Rotthoff, J. R., Teich, E. R., Truscon, R. K., Baurn, L. L., Rangarajan, B., Newton, D. W., Boulton, M. L., & Monto, A. S. (2006). Prevention of antigenically drifted influenza by inactivated and live attenuated vaccines. *The New England Journal of Medicine, 355*, 2513-2522.

O'Leary, A., Shoor, S., Lorig, K., & Holman. (1988). A cognitive behavioral treatment for rheumatoid arthritis. *Health Psychology, 7*, 527-544.

Oliveira, E. C., & Marik, P. E. C., G. (2001). Influenza pneumonia: A descriptive study. *Chest, 119*, 1717-1723.

Onitsuka, H., Imamura, T., Miyamoto, N., Shibata, Y., Kashiwagi, T., Ayabe, T., Kawagoe, J., Matsuda, J., Ishikawa, T., Unoki, T., Takenaga, M., Gukunaga, S., Koiwaya, Y., & Eto, T. (2001). Clinical manifestations of influenza A myocarditis during the influenza epidemic of winter 1998-1999. *Journal of Cardiology, 37*, 315-323.

Orbell, S. (1996). Social cognition and social structure in the prediction of cervical screening uptake. *British Journal of Health Psychology, 1*, 35-50.

Orbell, S., & Sheeran, P. (1998). "Inclined abstainerss" : a problem for predicting health-related behaviour. *British Journal of Social Psychology, 37*, 151-165.

Pachter, L., Niego, S., & Pelto, P. (1996). Differences and similarlities between health care providers and parents regarding symptom lists for childhood respiratory illnesses. *Ambulatory Child Health, 1*, 196-204.

Pachucki, C. T. (2005). Rapid tests for influenza. *Current Infectious Disease Reports, 7*, 187-192.

Pallant, J. (2005). *SPSS: survival manual*. Berkshire, England: Open University Press.

Parenboom, R. J. M., & Davidse, W. (1996). Increasing the coverage of vaccination against influenza by general practitioners. *Journal of Public Health Medicine, 18*, 183-187.

Parent, N., & Fortin, F. (2000). A randomized, controlled tial of vicarious experience through peer support for male first-time cardiac surgery patients: impact on anxiety, self-efficacy expectation, and self-reported activity. *Heart & Lung, 29*, 389-400.

Parkman, P. D., Galasso, G. J., Top, F. H., & Noble, G. R. (1976). From the National Institute of Allergy and Infectious Disease of the National Institutes of Health, the Center for Disease Control, and the Bureau of Biologics of the Food and Drug Administration. *The Journal of Infectious Disease* 134, pp. 100-107.

Parks-Stamm, E. J., Gollwitzer, P. M., & Oettingen, G. (2007). Action control by implementation intentions: effective cue detection and efficient response initiation. *Social Cognition, 25*, 248-266.

Patriarca, P. A., Weber, J. A., Parker, R. A., Orenstein, W. A., Hall, W. N., Kendal, A. P., & Schonberge, L. B. (1986). Risk factors for outbreaks of influenza in nursing homes: a case-control study. *American Journal of Epidemiology, 124*, 114-119.

Patton, M. Q. (1987). *How to use qualitative methods in evaluation*. California: Sage Publications.

Patton, M. Q. (2002). *Qualitative research and evaluation methods*. (3rd ed). Thousand Oaks: Sage Publication.

Payaprom, Y., Bennett, P., Burnard, P., Alabaster, E., & Tantipong, H. (2010). Understandings of influenza and influenza vaccination among high-risk urban dwelling Thai adults: a qualitative study. *Journal of Public Health Policy, 32*, 26-31.

Petric, M., Comanor, L., & Petti, C. A. (2006). Role of the laboratory in diagnosis of influenza during seasonal epidemics and potential pandemics *The Journal of Infectious Disease, 194*, S98-S110.

Pinto, B. M., Friedman, R., Marcus, B. H., Kelley, H., Tennstedt, S., & Gillman, M. W. (2002). Effects of a computer-based, telephone-counseling system on physical activity. *American Jounal of Preventive Medicine, 23*, 113-120.

Plusa, T., Brydak, L., Jahnz-Rozyk, K., Targowski, T., & Machala, M. (2004). Effect of influenza vaccinations on humoral response in patients with bronchial asthma or chronic obstructive pulminary disease. *International Congress Series, 1263*, 563-567.

Poehling, K. A., Edwards, K. M., & Weinberg, G. A. (2006). The underrecognized burden of influenza in young children. *The New England Journal of Medicine, 355*, 31-40.

Poole, P., Chacko, E. E., Wood-Baker, R., & Cates, C. J. (2006). Influenza vaccine for patients with chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews 2007*(1), 1-11.

Potter, C. W., & Oxford, J. S. (1979). Determinants of immunity to influenza in man. *British Medical Bulletin, 35*, 69-75.

Potter, C. W. (2001). A history of influenza. *Journal of applied Microbiology, 91*, 572-579.

Pregliasco, F., Sodano, L., Mensi, C., Selvaggo, M. T., Adamo, B., D'Arginio, P. G., F., et al. (1999). Influenza vaccination among the elderly in Italy. *Bulletin of the World Health Organisation, 77*, 127-131.

Prentice-Dunn, S., & Rogers, R. W. (1986). Protection Motivation Theory and preventive health: beyond the Health Belief Model. *Health Education Research, 1*, 153-161.

Prestwich, A., Ayres, K., & Lawton, R. (2008). Crossing two types of implementation intentions with a protection motivation intervention for the reduction of saturated fat intake: a randomized trial. *Social Science & Medicine, 67*, 1550-1558.

Prior, L., & Evans, M. R. P., H. (2010). Talking about colds and flu: the lay diagnosis of two common illnesses among older British people. *Social Science & Medicine*, doi:10.1016/j.socscimed.2010.09.054

Prislin, R., Dyer, J. A., Blakely, C. H., & Johnson, C. D. (1998). Immunisation Status and sociodemographic characteristics: the mediating role of beliefs, attitudes, and perceived control. *Public Health, 88*, 1821-1826.

Prochaska, J. O., DiClemente, C. C., & Norcross, J. C. (1992). In search of how people change: applications to additive behaviors. *American Psychologist, 47*, 1102-1114.

Prochaska, J. O., & DiClemente, C. C. (1983). Stages and processes of self-change of smoking: Toward an integrative model of change. *Journal of Consulting and Clinical Psychology, 51*, 390-395.

Raftopoulos, V. (2007). Beliefs, knowledge and attitudes of community-dwelling Greek elders towards influenza and pneumococcal vaccination. *The Internet Journal of Epidemiology* [Online] 4. Retrieved 20 October 2007, from http://www.ispub.com/ostia/index.php?xmlFilePath=journals/ije/vol4n1/influenza.xml

Randall, D. M., & Wolff, J. A. (1994). The time interval in the intention-behaviour relationship: meta-analysis. *British Journal of Social Psychology, 33*, 405-418.

Raude, J., & Setbon, M. (2009). Lay perceptions of the pandemic influenza threat. *European Journal of Epidemiology, 24*, 339-342.

Ray, C. G., Icenogle, T. B., Minnich, L. L., Copeland, J. C., & Grogan, T. M. (1989). The use of intravenous ribavirin to treat influenza virus-associated acute myocaditis. *The Journal of Infectious Disease, 159*(5), 829-836.

Rehmet, S., Ammon, A., Pfaff, G., Bocter, N., & Petersen, L. R. (2002). Cross-sectional study on influenza vaccination,Germany, 1999-2000. *Emerging Infectious Disease, 8*, 1442-1447.

Reichert, T. A., Sugaya, N., Fedson, D. S., Clezen, W. P., Simonsen, L., & Tashiro, M. (2001). The Japanese experience with vacinating schoolchildren against influenza. *New England Journal of Medicine, 344*, 889-896.

Renner, B., Spivak, Y., Kwon, S., & Schwarzer, R. (2007). Does age make a difference? predicting physical activity of South Koreans. *Psychology and Aging, 22*, 482-493.

Reuter, T., Ziegelmann, J. P., Lippke, S., & Schwarzer, R. (2009). Long-term relations between intentions, planning, and exercise: a 3-year longitudinal study after orthopedic rehabilitation. *Rehabilitation Psychology, 54*, 363-371.

Rippetoe, P. A., & Rogers, R. W. (1987). Effects of components of Protection-MotivationTheory on adaptive and maladaptive coping with a health threat. *Journal of personality and Social psychology, 52*, 596-604.

Rodgers, W. M., Hall, C. R., Blanchard, C. M., McAuley, E., & Munroe, K. J. (2002). Task and scheduling self-efficacy as predictors of exercise behavior. *Psychology and Health, 17*, 405-416.

Rohde, G., Wiethege, A., Borg, I., Kauth, M., Bauer, T. T., Gillissen, A., Bufe, A., & Schultze-Werninghaus, G. (2003). Respiratory viruses in exacerbations of chronic obstructive pulmonary disease requiring hospitalisation: a case-control study. *Thorax, 58*, 37-42.

Rogers, R. (1975). A Protection Motivation Theory of fear appeals and attitude change. *Journal of Psychology, 91*, 93-114.

Rogers, R. W. (1983). Cognitive and physiological processes in fear-based attitude change: a revised theory of protection motivation. In T. Cacioppo & R. Petty (Eds.), *Social psychology: a sourcebook.* New York: Guilford Press.

Rosenstock, I. M. (1974). The Health Belief Model and preventive health behaviour. In M. H. Becker (Ed.), *The Health Belief Model and personal health behaviour.* New Jersey: Charles B. Slack, Inc.

Rosenstock, I. M., Strecher, V. J., & Becker, M. H. (1988). Social Learning Theory and the Health Belief Model. *Health Education Quarterly, 15*, 175-183.

Rothberg, M. B., Haessler, S. D., & Brown, R. B. (2008). Complications of viral influenza. *The American Journal of Medicine, 121*, 258-264.

Rothman, K. (1990). No adjustments are needed for multiple comparisons. *Epidemiology* , 1, 43–46.

Ruben, F. L., Potter, C. W., & Stuart-Harris, C. H. (1975). Humoral and secretory antibody responses to immunization with low and high dosage split influenza virus vaccine. *Archives of Virology, 47*, 157-166.

Ruiter, R. A .C., Abraham, C., & Kok, G. (2001). Scary warnings and rational precautions: a review of the psychology of fear appeals. *Psychology and Health, 16*, 613-630.

Russell, M. L., & Maxwell, C. J. (2000). The prevalence and correlates of influenza vaccination among a Home Care population. *Canadian Journal of Public Health, 91*, 441-444.

Rutledge, D. N. (1987). Factors related to women's practice of breast self-examination. *Nursing Research, 36*, 117-121.

Rutter, D. R., & Quine, L. (2002). Social cognition models and changing health behaviours. In D. R. Rutter & L. Quine (Eds.), *Changing health behaviour* (pp. 1-27). Buckingham: Open University Press.

Rutter, D. R., Steadman, L., & Quine, L. (2006). An implementation intentions intervention to increase uptake of mammography *Annals of Behavioral Medicine, 32*, 127-134.

Santibanez, T. A., Mootrey, G. T., Euler, G. L., & Janssen, A. P. (2010). Behaviour and beliefs about influenza vaccine among adults aged 50-64 years. *American Journal of Health Behaviour, 34*, 77-89.

Santibanez, T. A., Nowalk, M. P., Zimmerman, R. K., Jewell, I. K., Bardella, I. J., Wilson, S. A., & Terry, M. A. (2002). Knowledge and beliefs about influenza, pneumococcal disease, and immunizations among older people. *Journal of American Geriatrics Society, 50*, 1711-1716.

Sarria-Santamera, A. T., J. (2003). Influenza vaccination in old adults in Spain. *European Journal of Public Health, 13*, 133-137.

Savulescu, C., Valenciano, M., de Mateo, S., & Larrauri, A. (2010). Estimating the influenza vaccine effectiveness in elderly on a yearly basis using the Spanish influenza surveillance network--pilot case-control studies using different control groups, 2008-2009 season, Spain. *Vaccine, 28*(16), 2903-2907.

Scheifele, D. W., Bjornson, G., & Johnston, j. (1990). Evaluation of adverse events after influenza vaccination in hospital personnel. *Canadian Medical Association Journal, 142*, 127-130.

Schirmer, P., & Holodniy, M. (2009). Oseltamivir for treatment and prophylaxis of influenza infection. *Expert Opinion on Drug Safety, 8*(3), 357-371.

Schnoll, R., & Zimmerman, B. J. (2001). Self-egulation training enhances dietary self-efficacy and dietary fiber consumption. *Journal of the American Dietetic Assosiation, 101*, 1006-1011.

Scholz, U., Sniehotta, F. F., Dipl-Psych, S. B., & Schwarzer, R. (2007). Increasing physical exercise levels: age-specific benefits of planning. *Journal of Aging and Health, 19*(5), 851-866.

Scholz, U., Schuz, B., Ziegelmann, J. P., Lippke, S., & Schwarzer, R. (2008). Beyond behavioural intentions: planning mediates between intentions and physical activity. *British Journal of Health Psychology, 13*, 479-494.

Scholz, U., Keller, R., & Perren, S. (2009). Pedicting behavioural intentions and physical exercise: a test of the Health Action Pocess Approach at the intrapersonal level. *Health Psychology, 28*, 702-708.

Scholz, U., Nagy, G., Gohner, W., Luszczynska, A., & Kiliegel, M. (2009). Changes in self-regulatory cognitions as predictors of changes in smoking and nutrition behaviour. *Psychology and Health, 24*, 545-561.

Schonberger, L. B., Bregman, D. J., Sullivan-Bolyai, J. Z., Keenlyside, R. A., Ziegler, D. W., Retailliau, H. F., Eddins, D. L., & Bryan, J. (1979). Guillain-Barre syndrome following vaccination in the national influenza immunization program, United States, 1976-1977. *American Journal of Epidemiology, 110*, 105-123.

Schüz, B., Sniehotta, F. F., & Schwarzer, R. (2007). Stage-specific effects of an action control intervention on dental flossing. *Health Education Research, 22*, 332-341.

Schüz, B., Sniehotta, F. F., Mallach, N., & Wiedemann, A. U. (2009). Predicting transitions from preintentional, intentional and actional stages of change. *Health Education Research, 24*, 64-75.

Schwarzer, R. (1992). The Health Action Process Model (HAPA). Retrieved 10 March 2008, from http://userpage.fu-berlin.de/~health/model.htm

Schwarzer, R. (1992). Self-efficacy in the adoption and maintenance of health behaviours: theoretical approaches and a new model In R. Schwarzer (Ed.), *Self-efficacy: though control of action* (pp. 217-243) . Washington: Hemisphere Publishing Corporation.

Schwarzer, R. (1999). Self-regulatory processes in the adoption and maintenance of health behaviors. *Journal of Health Psychology, 4*, 115-127.

Schwarzer, R., & Renner, B. (2000). Social-cognitive predictors of health behaviour: action self-efficacy and coping self-efficacy. *Health Psychology, 19*, 487-495.

Schwarzer, R. (2001). Social-cognitive factors in changing health-related behaviours. *Current Directions in Psychological Science, 10*, 47-51.

Schwarzer, R., Sniehotta, F. F., & Lippke, S. (2003). On the assessment and analysis of variables in the Health Action Process Approach: conducting an investigation. Retrieved 8 March 2008, from http://web.fu-berlin.de/gesund/hapa_web.pdf

Schwarzer, R., Schuz, B., Ziegelmann, J. P., & Lippke, S. (2007). Adoption and maintenance of four health behaviours: theory-guided longitudinal studies on dental flossing, seat belt use, dietary behaviour, and physical activity. *Annals of Behavioral Medicine, 33*, 156-166.

Schwarzer, R. (2008a). Modeling health behaviour change: how to predict and modify the adoption and maintenance of health behaviors. *Applied Psychology: An International Review, 57*, 1-29.

Schwarzer, R., Luszczynska, A., Ziegelmann, J. P., & Scholz, U. (2008). Social cognitive predictors of physical exercise adherence: three longitudinal studies in rehabilitation. *Health Psychology, 27*, S54-S63.

Schwarzer, R. (2008b). Some burning issues in research on health behaviour change. *Applied Psychology: An International Review, 57*, 84-93.

Schwarzer, R., & Luszczynska, A. (2008). How to overcome health-compromising behavious; the Health Action Process Approach. *European Psychologist, 13*, 141-151.

Schwarzer, R. (2009). HAPA model. Retrieved 21 November 2010, from http://www.hapa-model.de/

Scuffham, P. A. (2004). Estimating influenza-related hospital admissions in older people from GP consultation data. *Vaccine, 22*, 2853-2862.

Sengupta, S., & Strauss, R. P. (2004). African American elders' perceptions of the influenza vaccine in Durham, North Carolina. *North Carolina Medical Journal, 65*, 194-199.

Seydel, E., Taal, E., & Wiegman, O. (1990). Risk-apprasal, outcome and self-efficacy expectancies: cognitive factors in preventive behaviour related to cancer. *Psychology and Health, 4*, 99-109.

Sheeran, P. (2002). Intention-behavior relations: a conceptual and empirical review. *European Review of Social Psychology, 12*, 1-36.

Sheeran, P., & Orbell, S. (1998). Do intentions predict condom use? meta-analysis and examination of six moderator variables. *British Journal of Social Psychology, 37*, 231-250.

Sheeran, P., & Orbell, S. (1999). Implementation intentions and repeated behaviour: augmenting the predictive validity of the theory of planned behaviour. *European Journal of Social Psychology, 29*, 349-369.

Sheeran, P., & Orbell, S. (2000). Using implementation intentions to increase attendance for cervical cancer screening. *Health Psychology, 19*, 283-289.

Sheeran, P., Milne, S., Webb, T., & Gollwitzer, P. M. (2005). Implementation intentions and health behaviour. In M. Conner & P. Norman (Eds.), *Predicting health behaviour: research and practice with social cognition models* (pp. 276-323). Glasgow: Open University Press.

Shek, L. P., & Lee, B. W. (2003). Epidemiology and seasonality of respiratory tract virus infections in the tropics. *Paediatric Respiratory Reviews, 4*, 105-111.

Shephard, R. J., & Shek, P. N. (1998). Cold exposure and immune function. *Canadian Journal of Physiology and Pharmacology, 76*, 828-836.

Sheppard, B. H., Hartwick, J., & Warshaw, P. R. (1988). The theory of reasoned action: a meta-analysis of past research with recommendations for modifications and future research. *Journal of Consumer Research, 15*, 325-343.

Shieh, W. J., Blau, D. M., Denison, A. M., Delcon-Carnes, M., Adem, P., Bhatnaqur, J., Sumner, J., Liu, L., Patel, M., Batten, J., Greer, P., Jones, T., Smit, C., Bartlett, J., Montaque, J., White, E., Rollin, D., Gao, R., Seales, C., Jost, H., Metcalfe, M., Goldsmith, C.S., Humphrey, C., Schmitz, A., Drew, C., Paddock, C., Uyeki, T. M. & Zaki, S. R. (2010). 2009 pandemic influenza A (H1N1): pathology and pathogenesis of 100 fatal cases in the United States. *The American Journal of Pathology* , *177*, 166-175.

Sigelman, C. K. (2011). Age and Ethnic differences in cold weather and contagion theories of colds and flu. *Health Education & Behaviour,* doi: 10.1177/1090198111407187

Simmerman, J. M., Thawatsupha, P., Kingnate, D., Fukuda, K., Chaising, A., & Dowell, S. F. (2004). Influenza in Thailand: a case study for middle income countries. *Vaccine, 23*, 182-187.

Simmerman, J. M., Lertiendumrong, J., Dowell, S. F., Uyeki, T. M., Olsen, S. J., Chittaganpitch, M., et al. (2006). The cost of influenza in Thailand. *Vaccine, 24*, 4417-4426.

Simmerman, J. M. & Uyeki, T. M. (2008). The burden of influenza in East and South-East Asia: a review of the English language literature. *Influenza and Other Respiratory Viruses* , *2*, 81-92.

Simmerman, J. M., Chittaganpitch, M., Levy, J., Chantra, S., Maloney, S., Uyeki, Thamthitiwat, S., Olsen, S., Fry, A., Ungchusak, K., Baggett, H. C., & Chunsuttiwat, S. (2009). Incidence, seasonality and mortality associated with influenza pneumonia in Thailand: 2005-2008. *PloS One, 4*, 1-8.

Simon, P. M., Morse, E. V., Balson, P. M., Osofsky, H. J., & Gaumer, H. R. (1993). Barriers to human immunodeficiency virus related risk reduction among male street prostitutes. *Health Education Quarterly, 20*, 261-273.

Simonsen, L., Clarke, M. J., Williamson, D., Stroup, D. F., Arden, N. H., & Schonberger, L. B. (1997). The impact of influenza epidemics on mortality: introducing a severity index. *American Journal of Public Health, 87*, 1944-1950.

Simonsen, L. (1999). The global impact of influenza on morbidity and mortality. *Vaccine, 17*, S3-S10.

Simonsen, L., Fukuda, K., Schonberger, L. B., & Cox, N. J. (2000). The impact of influenza epidemics on hospitalizations. *The Journal of Infectious Disease, 181*, 831-837.

Simonsen, L., Taylor, R., Viboud, C., Miller, M. A., & Jackson, L. A. (2007). Mortality benefits of influenza vaccination in elderly people: an ongoing controversy. *Lancet Infectious Disease, 7*, 658-666.

Sivadon-Tardy, V., Orlikowski, D., Porcher, R., Sharshar, T., Durand, M. C., Enouf, V., & Rozenberg, F. (2009). Guillain-Barr'e syndrome and influenza virus infection. *Clinical Infectious Disease, 48*, 48-56.

Smith, W., Andrewes, C. H., & Laidlaw, P. P. (1933). A virus obtained from influenza patients. *The Lancet*, 66-68.

Smit, M., Beynon, K. A., Murdoch, D. R., & Jennings, L. C. (2007). Comparison of the NOW influenza A & B, NOW flu A, NOW flu B, and directigen flu A+B assays, and immunofluorescence with viral culture for the detection of influenza A and B viruses. *Diagnostic Microbiology and Infectious Disease, 57*, 67-70.

Sniehotta, F. F., Scholz, U., Schwarzer, R., Fuhrmann, B., Kiwus, U., & Voller, H. (2005). Long-term effects of two psychological interventions on physical exercise and self-regulation following coronary rehabilitation. *International Journal of Behavioral Medicine, 12*(4), 244-255.

Sniehotta, F. F., Schwarzer, R., Scholz, U., & Schuz, B. (2005). Action planning and coping planning for long-term lifestyle change: theory and assessment. *European Journal of Social Psychology, 35*, 565-576.

Sniehotta, F. F., Scholz, U., & Schwarzer, R. (2005). Bridging the intention-behaviour gap: planning, self-efficacy, and action control in the adoption and maintenance of physical exercise. *Psychology and Health, 20*(2), 143-160.

Sniehotta, F. F., Scholz, U., & Schwarzer, R. (2006). Action plans and coping plans for physical exercise: a longitudinal intervention study in cardiac rehabilitation. *British Journal of Health Psychology, 11*, 23-37.

Sniehotta, F. F., Soares, V. A., & Dombrowski, S. U. (2007). Randomized controlled trial of a one-minute intervention changing oral self-care behavior. *Journal of Dental Research, 86*, 641-645.

Sniehotta, F. F. (2009). Towards a theory of intentional behaviour change: plans, planning, and self-regulation. *British Journal of Health Psychology, 14*, 261-273.

Stanley, M. A., & Maddux, J. E. (1986). Cognitive processes in health enhancement: investigation of a combined protectionmotivation and self-efficay model. *Basic and Applied Social Psychology, 7*, 101-113.

Stanton, B. F., Li, X., Ricardo, I., Galbraith, J., Feigelman, S., & Kaljee, L. (1996). A randomised, controlled effectiveness trial of an AIDS prevention program of low-income African-American youths. *Archives of Pediatrics & Adolescent Medicine, 150*, 363-372.

Stehr-Green, P. A., Sprauer, M. A., Williams, W. W., & Sullivan, K. M. (1990). Predictors of vaccination behaviour among persons ages 65 years and older. *American Jounal of Public Health, 80*, 1127-1129.

Steinhauer, D. A., & Skehel, J. J. (2002). Genetics of influenza viruses. *Annual Review of Genetics, 36*, 305-332.

Steininger, C., Kundi, M., Aberle, S. W., & Aberle, J. H., Popow-Kraupp, T. (2002). Effectiveness of reverse transcription-PCR, virus isolation, and enzyme-linked immunosorbent assay for diagnosis of influenza A virus infection in different age groups. *Journal of Clinical Microbiology, 40*(6), 2051-2056.

Stephenson, I., & Nicholson, K. G. (2001). Influenza: vaccination and treatment. *European Respiratory Journal, 17*, 1282-1293.

Stephenson, I., & Zambon, M. (2002). The epidemiology of influenza. *Occupational Medicine, 52*(5), 241-247.

Straits-Troster, K. A., Kahwati, L. C., Kinsinger, L. S., Orelien, J., Burdick, M. B., & Yevich, S. J. (2006). Racial/ethnic differences in influenza vaccination in the eterans Affairs Healthcare System. *American Jounal of Preventive Medicine, 31*, 375-382.

Strauss, A., & Corbin, J. (1998). *Basics of qualitative research: techniques and procedures for developing Grounded Theory*. Thousand Oaks: Sage Publications.

Strecher, V. J., DeVellis, B. M., Becker, M. H., & Rosenstock, I. M. (1986). The role of self-efficacy in achieving health behaviour change. *Health Education Quarterly, 13*, 73-91.

Strickler, J. K., Hawksworth, A. W., Myers, C., Irvine, M., Ryan, M. A. K., & Russell, K. L. (2007). Influenza vaccine effectiveness among US military basic trainees, 2005-06 season. *Emerging Infectious Disease, 13*, 617-619.

Studahl, M. (2003). Influenza virus and CNS manifestations. *Journal of Clinical Virology, 28*, 225-232.

Sutherland, S. (2002). Influenza virus. In: Greenwood, D. et al. eds. *Medical microbiology* (pp. 468-474). London: Churchill Livingstone,

Sutton, S. (2005). Stage Theories of health behaviour. In M. Conner & P. Norman (Eds.), *Predicting health behaviour* (pp. 324-371). Glasgow: Bell & Bain Ltd.

Sutton, S. (2008). How does the Health Action Process Approach (HAPA) bridge the intention-behavior gap? an examination of the model's causal structure. *Applied Psychology: An International Review, 57*, 66-74.

Sweet, C., & Smith, H. (1980). Pathogenicity of influenza virus. *Microbiological Reviews, 44*(2), 303-330.

Szucs, T. D. (1999). Influenza: The role of burden-of-illness research. *Pharmacoeconomics, 16 Suppl.*(1), 27-32.

Szucs, T. D., & Muller, D. (2005). Influenza vaccination coverage rates in five European countries--a population-based cross-sectional analysis of two consequtive influenza seasons. *Vaccine, 23*, 5055-5063.

Tabbarah, M., Zimmerman, R., Nowalk, M. P., Janosky, J. E., Troy, J. A., Raymund, M., & Jewell, I. K. (2005). What predicts influenza vaccination status in older Americans over several years? *Journal of American Geriatrics Society, 53*, 1354-1359.

Takahashi, O., Noguchi, Y., Rahman, M., Shimbo, T., Goto, M., Matsui, K., Asai, A., Onishi, M., Koyama, H., & Sawada, I. (2003). Influence of family on acceptance of influenza vaccination among Japanese patients. *Family Practice, 20*, 162-166.

Talbot, T. R., Crocker, D. D., Peters, J., Doersam, J. K., Lkizler, M. R., Sannella, E., Wright, P. F., & Edwards, K. M. (2005). Duration of virus shedding after trivalent intranasal live attenuated influenza vaccination in adults. *Infection Control and Hospital Epidemiology, 26*, 494-500.

Talbot, H. K., & Falsey, A. R. (2010). The diagnosis of viral respiratory disease in older adults. *Clinical Infectious Disease, 50*, 747-751.

Tam, C. C., O' Brien, S. J., & Rodrigues, L. C. (2006). Influenza, campylobacter and Mycoplasma infections, and hospital admissions for Guillain-Barr'e syndrome, England. *Emerging Infectious Disease, 12*(12), 1880-1887.

Tan, E. K., Lim, L. H., Teoh, Y. L., Ong, G., & Bock, H. L. (2010). Influenza and seasonal influenza vaccination among diabetics in Singapore: knowledge, attitudes and practices. *Singapore Medical Journal, 51*, 623-630.

Taubenberger, J. K., & Layne, S. P. (2001). Diagnosis of influenza virus: coming to grips with the molecular era. *Molecular diagnosis, 6*(4), 291-305.

Taubenberger, J. K., Morens, D. M., & Fauci, A. S. (2007). The next influenza pandemic: can it be predicted? *The Journal Of the American Medical Association, 297*, 2025-2027.

Taubenberger, J. K., & Morens, D. M. (2008). The pathology of influenza virus infections. *Annual Review of Pathology: Mechanisms of disease, 3*, 499-522.

Taylor, M. C. (2005). Interviewing. In I. Holloway (Ed.), *Qualitative research in health care* (pp. 39-54). Berkshire, England: Open University Press.

Telford, R., & Rogers, A. (2003). What influences elderly peoples'decisions about whether to accept the influenza vaccination? a qualitative study. *Health Education Research, 18*, 743-753.

Thomas, R. E., Russell, M. L., & Lorenzetti, D. L. (2010). Systematic review of interventions to increase influenza vaccination rates of those 60 years and older. *Vaccine, 28*, 1684-1701.

Thompson, W. W., Shay, D. K., Weintraub, E., RBrammer, L., Cox, N. J., Anderson, L. J., & Fukuda, K. (2003). Mortality associated with influenza and respiratory syncytial virus in the United Strates. *The Journal Of the American Medical Association, 259*, 179-186.

Thompson, W. W., Shay, D. K., Weintraub, E., Brammer, L., Bridges, C. B., Cox, N. J., & Fukuda, K. (2004). Influenza-associated hospitalizations in the United States. *Journal of American Medical Association, 292*, 1333-1340.

Tiensin, T., Chaitaweesub, P., Songserm, T., Chaisigh, A., Hoonsuwan, W., Buranathai, C., Parakamawongsa, T., Amonsin, A., Gilbert, M., Nielen, M., & Stegeman, A. (2005). Highly pathogenic avian influenza H5N1, Thailand 2004. *Emerging Infectious Diseases 11*, pp. 1664-1672.

Tomoda, T., Morita, H., Kurashige, T., & Maassab, H. F. (1995). Prevention of influenza by the intranasal administration of cold-recombinant, live-attenuated influenza virus vaccine: importance of interferon-y production and local IgA response. *Vaccine, 13*, 185-189.

Toovey, S. (2008). Influenza-associated central nervous system dysfunction: A literature review. *Travel Medicine and Infectious Disease, 6*, 114-124.

Treanor, J. J., Hayden, F. G., Vrooman, P. S., Barbarash, R., Bettis, R., Riff, D., Singh, S., Kinnersley, N., Ward, P., & Mills, R. G. (2000). Efficacy and safety of the oral neuraminidase inhibitor oseltamivir in treating acute influenza. *The Journal of the American Medical Association, 283*(8), 1016-1024.

Treanor, J. J. (2004). Weathering the influenza vaccine crisis. *New England Journal of Medicine, 351*, 2037-2040.

Treanor, J. J. (2005). Influenza virus. In: Mandell, G.L. et al. eds. *Principles and Practices of infectious disease* (pp. 2060-2085). Vol. 2. Philadelphia: Elsevier Inc., USA,

Treanor, J. J. (2010). Influenza virus. In: Mandell, G.L.B., J. E., Dolin, R. ed. *Principles and practices of infectious disease* (pp. 2265-2288). Philadelphia: Churchill Livingstone.

Tsolia, M. N., Logotheti, I., Papadopoulos, N. G., Mavrikou, M., Spyridis, N. P., Drossatou, P., Kafetzis, D., & Konstantopoulos, A. (2006). Impact of influenza infection in healthy children examined as outpatients and their families. *Vaccine, 24*, 5970-5976.

van Elden, L. J. R., Nijhuis, M., Schipper, P., Schuurman, R., & van Loon, A. M. (2001). Simultaneous detection of influenza viruses A and B using real-time quantitative PCR. *Journal of Clinical Microbiology, 39*(1), 196-200.

van Elden, L. J. R., van Kraaij, M. G. J., Nijhuis, M., Hendriksen, K. A. W., Dekker, A. W., Rozenberg-Arska, M., & van Loon, A. M. (2002). Polymerase chain reaction is more sensitive than viral culture and antigen testing for the detection of respiratory viruses in adults with hematological cancer and pneumonia. *Clinical Infectious Disease, 34*, 177-183.

Van der Velde, F. W. and Van der Pligt, J. (1991). AIDS-related health behaviour: coping, protection motivation and previous behaviour. *Journal of Behavioural Medicine, 14*, 429-451.

van Essen, G. A., Kuyvenhoven, M. M., & de Melker, R. A. (1997). Why do healthy elderly people fail to comply with influenza vaccination? *Age and Aging, 26*, 275-279.

van Essen, G. A., Palache, A. M., Forleo, E., & Fedson, D. S. (2003). Influenza vaccination in 2000: recomendations and vaccine use in 50 developed and rapidly developing countries. *Vaccine, 21*, 1780-1785.

van Osch, L., Reubsaet, A., Lechner, L., & de Vries, H. (2008). The formation of specific action plans can enhance sun protection behavior in motivated parents. *Preventive Medicine, 47*, 127-132.

Vellozzi, C., Burwen, D. R., Dobardzic, A., Ball, R., Walton, K., & Haber, P. (2009). Safety of trivalent inactivated influenza vaccines in adults: background for pandemic influenza vaccine safety monitoring. *Vaccine, 27*, 2114-2120.

Vesikari, T., Karvonen, A., Korhonen, T., Edelman, K., Vainionpaa, R., Salmi, A., Saville, M. K., Cho, I., Razmpour, A., Rappaport, R., O'Neill, R., Georgiu, A., Gruber, W. C., Mendelman, P. M., & Forrest, B. (2006). A radomized, double-blind study of the safety, transmissibility and phenotypic and genotypic stability of cold-adapted influenza virus vaccine. *The Pediatric Infectious Disease Journal, 25*, 590-595.

Viboud, C., Alonso, W. J., & Simonsen, L. (2006). Influenza in tropical regions. *PLoS Medicine, 3*, 468-471.

Wang, Z., Tobler, S., Roayaei, J., & Eick, A. (2009). Live attenuated or inactivated influenza vaccines and medical encounters for respiratory illnesses among US military personnel. *Journal of American Medical Association, 301*, 945-953.

Ward, L., & Draper, J. (2007). A review of the factors involved in older people's decision making with regard to influenza vaccination: a literature review. *Journal of Clinical Nursing*, 5-16.

Webb, T., & Sheeran, P. (2006). Does changing behavioral intentions engender behaviour change? : a meta-analysis of the experimental evidence. *Psychological Bulletin, 132*, 249-268.

Webb, T. L., & Sheeran, P. (2007). How do implementation intentions promote goal attainment? a test of component processes. *Journal of Experimental Social Psychology, 43*, 295-302.

Weinstein, N. D. (1993). Testing four competing theories of health protection behaviour. *Health Psychology, 12*, 324-333.

Weinstein, N. D., Rothman, A. J., & Sutton, S. (1998). Stage theories of health behaviour: conceptual and methodological issues. *Health Psychology, 17*, 290-299.

Weinstein, N. D. (2000). Perceived probability, perceived severity, and health-protective behaviour. *Health Psychology, 19*, 65-74.

Weinstein, N. D., Kwitel, A., McCaul, K. D., Magnan, R. E., Gerrard, M., & Gibbons, F. X. (2007). Risk perceptions: assessment and elationship to influenza vaccination. *Health Psychology, 26*, 146-151.

Welliver, R., Monto, A. S., Carewicz, O., Schatteman, E., Hassman, M., Hedrick, J., Jackson, H. C., Huson, L., Ward, P., & Oxford, J. S. (2001). Effectiveness of oseltamivir in preventing influenza in household contacts: A randomised controlled trial. *The Journal of the American Medical Association, 285*, 748-754.

Whitley, R. J., Hayden, F. G., Reisinger, K. S., Young, N., Dutkowski, R., Ipe, D., Milis, R. G., & Ward, P. (2001). Oral oseltamivir treatment of influenza in children. *The Pediatric Infectious Disease Journal, 20*(2), 127-133.

Whittaker, G. R. (2001). Intracellular trafficking of influenza virus: clinical implications for molecular medicine. *Expert Reviews in Molecular medicine* Retrieved 16 April 2010, from http://www-ermm.cbcu.cam.ac.uk

WHO. (1980). A revision of the system of nomenclature for influenza viruses: a WHO memorandum. *Bulletin of the World Health Organization , 58*, 585-591.

WHO. (2000). Influenza vaccines: recomendations for the use of inactivated influenza vaccines and other preventive measures. *Weekly epidemiological record, 75*, 281-288.

WHO. (2003). *Influenza ,Fact sheet N°211 revised March 2003.* Retrieved 16 October 2007, from http://www.who.int/mediacentre/factsheets/2003/fs211/en/

WHO. (2004). Global distribution of influenza vaccine, 2000-2003. *Weekly epidemiological record, 40*, 366-367.

WHO (2005a). *WHO global influenza preparedness plan: the role of WHO and recommendations for national measures before and during pandemic.* Retrieved 23 June 2008, from http://www.who.int/csr/resources/publications/influenza/GIP_2005_5Eweb.pdf

WHO. (2005b). WHO recommendations on the use of rapid testing for influenza diagnosis. Retrieved 19 April 2010, 2010, from http://www.who.int/csr/disease/avian_influenza/guidelines/RapidTestInfluenza_web.pdf

WHO. (2009). The five-six month timetable for influenza vaccine production from isolation of vaccine strain to release first vaccine lots. Retrieved 03 June 2010, from http://www.who.int/vaccine_research/The5-6month.pdf

WHO. (2010a). WHO Global influenza surveillance network. Retrieved 24 March 2010, from http://www.whoo.int/csr/disease/influenza/surveillance/en/print.html

WHO. (2010b). Pandemic (H1N1) 2009-update 94. Retrieved 1 April, 2010, from http://www.who.int/csr/don/2010_04_01/en/index.html

WHO. (2010c). Recommended viruses for influenza vaccines for use in the 2010-2011 northern hemisphere influenza season. Retrieved 27 May 2010, from http://www.who.int/csr/disease/influenza/recommendations2010_11north/en/ndx.html

Wiedemann, A. U., Lippke, S., Reuter, T., Schuz, B., Ziegelmann, J. P., & Schwarzer, R. (2009). Prediction of stage transitions in fruit and vegetable intake. *Health Education Research, 24*, 596-607.

Willig, C. (2001). *Introducing qualitative research in psychology*. Buckingham: Open University Press.

Williams, K. E., & Bond, M. J. (2002). The roles of self-efficacy, outcome expectancies and social support in the self-care behaviours of diabetics. *Psychology, Health & Medicine, 7*, 127-141.

Wise, T. G., Dolin, R., Mazur, M. H., Top, F. H., Edelman, J. R., & Ennis, F. A. (1977). Serologic responses and systemic reactions in adults after vaccination with Bivalent A/Victoria/75-A/New Jersey/76 and Monovalent B/Hong Kong/72 Influenza vaccines. *The Journal of Infectious Disease, 136*, S507-S517.

Witte, K. (1992). Putting the fear back into fear appeals: the extended parallel process model. *Commnication Monographs, 59*, 329-349.

Wong, C. M., Chan, K. P., Hedley, A. J., & Peiris, J. S. M. (2004). Influenza-associated mortality in Hong Kong. *Clinical Infectious Disease, 39*, 1611-1617.

Wong, C. M., Yang, L., Chan, K. P., Leung, G. M., Chan, K. H., Guan, Y., Lam, T. H., Hedley, A. J., & Peiris, J. S. M. (2006). Influenza-associated hospitalization in a subtropical city. *PLoS Medicine, 3*, 485-492.

Wray, R. J., Jupka, K., Ross, W., Dotson, D., Whiworth, A. R., & Jacobson, H. (2007). How can you improve vaccination rates among older African Americans? *The Journal of Family Practice, 56*, 925-929.

Wray, R. J., Buskirk, T. D., Jupka, K., Lapka, C., Jacobsen, H., & Pakpahan, R. (2009). Influenza vaccination concerns among older blacks: A randomised controlled trial. *American Journal of Preventive Medicine, 36*, 429-434.

Wright, P. F., Thompson, J., & Karzon, D. (1980). Differing virulence of H1N1 and H3N2 influenza strains. *American Journal of Epidemiology, 112*, 814-819.

Wrosch, C., Miller, G., Scheier, M. F., & de Pontet, S. B. (2007). Giving up on unattainable goals: benefits for health? *Personality and Social Psychology Bulletin, 33*, 251-265.

Wulfert, E., & Wan, C. K. (1993). Condom use: a self-efficacy model. *Health Psychology, 12*, 346-353.

Wurtele, S. K., & Maddux, J. E. (1987). Relative contributions of protection motivation theory components in predicting exercise intentions and behavior. *Health Psychology, 6*, 453-466.

Wurtele, S. K. (1988). Increasing women's calcium intake: the role of health beliefs, intentions, and health value. *Journal of Applied Social Psychology, 18*, 627-639.

Wyper, M. A. (1990). Breast self-examination and the Health Belief Model: variationns on a theme. *Research in Nursing & Health, 13*, 421-428.

Yap, F. H. Y., Ho, P. L., Lam, K. F., Chan, P. K. S., Cheng, Y. H., & Peiris, J. S. M. (2004). Excess hospital admissions for pneumonia, chronic obstructive pulmonary disease, and heart failure during influenza seasons in Hong Kong. *Journal of Medical Virology, 73*, 617-623.

Yap, K. L., & Ada, G. L. (1978). Transfer of specific cytotoxic T lymphocytes protects mice inoculated with influenza virus. *Nature, 273*, 238-239.

Yin, R. K. (2010). *Qualitative research from start to finish.* New York: The Guiford Press.

Young, J., & Garro, L. (1994). *Medical choice in a Maxican village*. Prospect Heights, IL: Waveland Press.

Yzer, M. C., Fisher, J. D., Bakker, A. B., Siero, F. W., & Misovich, S. J. (1998). The effects of information about AIDS risk and self-efficacy on women's intentions to engage in AIDS preventive behavor. *Journal of Applied Social Psychology, 28*, 1837-1852.

Zambon, M. (2001). The pathogenesis of influenza in humans. *Reviews in Medical Virology, 11*, 227-241.

Zhang, P., Tao, G., & Irwin, K. L. (2000). Utilization of preventive medical services in the United States: a comparison between rural and urban populations. *The Journal of Rural Health, 16*, 349-356.

Ziegelmann, J. P., Lippke, S., & Schwarzer, R. (2006). Adoption and maintenance of physical activity: planning interventions in young, middle-aged, and older adults. *Psychology and Health, 21*, 145-163.

Zimmerman, R. K., Nowalk, M. P., Raymund, M., Tabbarah, M., Hall, D. G., Wahrenberger, J. T., Wilson, S. A., & Ricci, E. M. (2003). Tailored interventions to increase influenza vaccination in neighborhood health centers serving the disadvantaged. *American Jounal of Public Health, 93*, 1699-1705.

Zimmerman, R. K., Raymund, M., Janosky, J. E., Nowalk, M. P., & Fine, M. J. (2003). Sensitivity and specificity of patient self-report of influenza and pneumococcal polysaccharide vaccinations among elderly outpatients in diverse patient care strata. *Vaccine, 21*, 1486-1491.

Zimmerman, R., Nowalk, M. P., Tabbarah, M., Hart, J. A., Fox, D. E., & Raymund, M. (2009). Understanding adult vaccination in urban, lower-socioeconomic settings: influence of physician and prevention system. *Annals of Family Medicine, 7*, 534-541.

Zwar, N., Hasan, I., Harris, M., & Traynor, V. (2007). Barriers and facilitators to influenza vaccination among high-risk groups aged less than 65 years—views from general practitioners and practice nurses. *Australian and New Zealand Journal of Public Health, 31*, 558-561.

Appendix

Appendix 1: Consent Form

Version 1: 16/2/2009
Study Number:
Participant Identification Number:

The uptake of Influenza vaccination among high-risk urban dwelling Thai adults: a controlled before and after study

CONSENT FORM

Instructions: Please read each section carefully before you complete this consent form, if you wish to give consent, please tick the box provided and sign this consent form, and return the signed and completed form to the research assistant.

1. I confirm that I have read and understand the information sheet for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	☐
3. I understand that relevant sections of any of my medical notes and data collected during the study may be looked at by responsible individuals from the Health Centre or from Chiang Rai Hospital, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	☐
4. I agree to take part in the above study	☐

.....	.....	.....
Name of Participant	Date	Signature
.....	.....	.....
Name of Person taking consent (if different from researcher)	Date	Signature
.....	.....	.....
Researcher	Date	Signature

Appendix 2: Participant Information Sheet

Version 1 16 Feb 2009

PARTICIPANT INFORMATION SHEET

The uptake of Influenza vaccination among high-risk urban dwelling Thai adults : a controlled before and after study

You are being invited to take part in a research project. This study will examine whether an information leaflet will help people understand more about the flu and the flu vaccination, and whether they are more likely to have the vaccine if they have read the leaflet.

Before deciding whether to take part, it is important that you understand why the research is being done and what it will involve. So please read the following information carefully and discuss the study with your family, friends, and the public health staff if you want to.

Why have I been asked to take part?

You have been chosen to take part because we are recruiting from people aged 45- 65 years with chronic diseases like asthma, heart disease, chronic lung diseases, chronic kidney diseases, and diabetes mellitus; this because current evidence suggests that these people will benefit greatly from receiving the flu vaccine.

Do I have to take part?

No! It is up to you to decide whether or not you want to take part.

If you decided to take part,

- the research assistant will ask you to sign a form giving your consent
- you will be given a copy of this information sheet and your signed form to keep.

What if I change my mind and want to stop my participation?

Your decisions will be treated with respect, so you are free to withdraw from the study at any time without giving a reason, and this will not affect your medical care or treatment that is received now or in the future.

What will happen to me if I take part?

If you agree to take part in the study, the Village Health Volunteers will arrange date and time for you to meet with a research assistant, either in your home or at a health centre depending on your preference. The study will involve filling in two questionnaires (at the start of the project and two weeks after the first time), and this will last for approximately 45 minutes to 1 hour of each questionnaire.

After filling out the first questionnaire, you will receive an educational leaflet. It will be sent to you by post. This leaflet provides important information influenza and the flu vaccine.

What will I have to do?

We hope that you will be willing to fill out two questionnaires, and we also hope the leaflet will answer the questions you have about influenza and the flu vaccine and help you to make the decision about getting the flu vaccine.

What are the possible disadvantages and risks of taking part?

There are no risks involved in taking part but it is possible that you may consider the time spent filling questionnaires is one disadvantage of taking part in the study.
In total, the study will require approximately 2 hours of your time.

What are the possible benefits of taking part?

There are no direct benefits for the individuals who take part in the study but we hope the results will provide useful information for the public health staff in developing an effective influenza vaccination programme for people with chronic diseases who would benefit most from the flu vaccination.

What if there is a problem?

If you have a concern about any aspect of the study, you should ask to speak with the principal researcher who will do her best to answer any questions you may have. Telephone Yupares Payaprom on 08-61623326 or 053-718745. You can also contact the head of the health centre on 08-38608624.

Will my taking part in this study be kept confidential?

Yes. All information that is collected about you during the course of this study will be kept strictly confidential. We will not include your name or any other information that might identify you, so you cannot be recognised from it.

What will happen to the results of the research study?

The results of the study may be published in scientific papers. The findings will also be shared with the public health staff and other healthcare professionals through workshops and conferences. No individual who took part in this study will be identifiable.

Who has reviewed the study?

The study has been reviewed and approved by the Research Review and Ethics Screening Committee (School of Nursing and Midwifery Studies, Cardiff University) and the Local Research Ethics Committee in Chiang Rai province.

*****Thank you for taking the time to read this information and/or choosing to participate******

Appendix 3: Ethical Approval

Ref. no. CR 0027.102/9346

The Internal Ethical Committee for Research in Human Subject
Chiang Rai Regional Hospital

Title of Project: The uptake of Influenza vaccination among high-risk urban dwelling Thai adults

Principle Investigator: Yupares Payaprom
Institute: CARDIFF UNIVERSITY

Reviewed Document:
Protocol "The uptake of Influenza vaccination among high-risk urban dwelling Thai adults : A pilot randomesed controlled study"

The Internal Ethical Committee for Research in Human Subject, Chiang Rai Regional Hospital in ethical concern, reviewed the protocol and approved for implementation of the research mentioned above. Therefore Thai version of the protocol will be mainly conducted.

Issued date: March 20, 2009
Expiration date: March 19, 2010

.....
(SUPUK PITIPAKORN, MD.)
Chairman, Internal Ethical Committee

.....
(SUPUK PITIPAKORN, MD.)
Director in charge, Chiang Rai Region Hospital

Appendix 4: HAPA-based Educational Leaflet

Is there anyone who should not be vaccinated?

Some people should not be vaccinated. They include:

- People who are allergic to egg or egg products.
- Individuals who have had an allergic reaction to an influenza vaccination in the past.
- People who have a fever should wait to get vaccinated until their symptoms lessen.

When should I have the flu shot?

The best time to have the vaccine is between June and July before the main flu season. Don't wait until there's a flu epidemic. The vaccine will be free, if you have at least one chronic disease — asthma, diabetes, heart disease, chronic lung disease, and kidney disease.

Where do I get vaccinated against the flu?

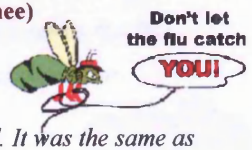
The public health staff will send a letter to inform you of the appointment date and place where you can get the flu shot.

Are you going to get the influenza shot this year?

If you are still in two minds, here are some people's experiences of their vaccination.

"When I caught flu, I felt so weak and so painful that I can barely get up. I had fever and muscle pain. It was serious. After I got the shot, I have not caught Influenza. I have a running nose and catch a cold some time though" **(Mr. Tongdee Somrat)**

"I have underlying disease, which is asthma. I have to protect myself. At first I had not agreed to get the flu shot because I was afraid of allergies and breathing difficulty, but I was fine after the injection. **(Mrs. Sangjun Boonmee)**



"I felt little pain where I was injected. It was the same as common injection, and my muscles ached on the first night, but not much. I only felt for a day. Then I was okay. After the vaccination, I have not been ill with influenza." **(Mr. Amaroj Na Lampang)**

Getting a influenza vaccination: Plan Ahead!

You are more likely to go for having the flu shot, If you decide now about where, when and how you will go. Please write in below when, where and how you plan to get a flu vaccine.

"If I get an appointment letter to have the flu vaccine, then I will……(please write down **what you plan to do**, e.g. go for taking the flu vaccine) at……(please write down **Where**, e.g. Chiang Rai hospital, private clinic), and I'm going to get there by…… ……(please write down **How** you go to that place, e.g. walking, taking a bus or asking son/daughter/ relatives to take you to get the flu vaccine*)."*

The FLU & YOU

Don't let Flu knock you out – make sure you're getting the flu vaccine this year!

Flu immunisation Information

Chiang Rai Regional Hospital,
Ministry of Public Health

Why do I need to worry about the flu?

Influenza is commonly called "the flu". It is a very contagious illness caused by a virus. This virus is different from a cold virus. Having flu is much worse than a cold particularly if you have a chronic disease. You are at high risk for severe complications such as bronchitis, pneumonia, blood infections and ear infections. This may put you in hospital. Unfortunately, some people with chronic disease die from influenza complications every year, **so why risk it?**

How do I catch the flu?

The flu is easily passed from one person to another by the coughs and sneezes of people who are already infected. Anyone living in or visiting a home where someone has influenza can become infected. Sometimes you can get the flu by touching something that has the flu virus on it (door knobs, table, telephone receivers), and then touching your mouth or nose.

What are the flu symptoms?

The flu usually starts **suddenly and severely with some or all** of these symptoms: * Fever * Headache * Severe muscle aches * Tiredness/extreme fatigue * Dry cough * Sore throat * Runny or stuffy nose

Can the flu be prevented?

Yes! The best way to prevent the flu is to get the flu vaccine each year to protect yourself. You will also be protecting your beloved ones, especially any children, by not spreading the flu. However, the seasonal flu vaccine cannot prevent the bird flu and swine flu.

What are the benefits of influenza vaccination?

The flu vaccine can be very useful to people with chronic diseases like asthma, diabetes, heart disease, chronic lung disease, and kidney disease. Catching the flu can worsen chronic medical conditions or cause serious complications in these individuals. Most people who have been vaccinated will not get the flu. But if you do catch flu, it's most likely to be milder than if you had not been vaccinated. Taking the influenza shot will help you a lot through the flu season:

Don't get flu! Don't spread Flu!,
Don't have serious complications,
Reduce the risk of going into hospital, and
Stay Healthy during the Flu season!

What are the side effects from the flu vaccine?

The flu vaccine is very safe. It does not contain any live virus, so it will **NOT** give you the flu. The most common side effect of the flu vaccine is soreness where you were injected. Occasionally, some people experience a mild fever and aching muscles. This usually goes away after a day or two. Any other reactions are very rare.

I've never had the flu. Do I need to be vaccinated?

You may look and feel healthy, but anyone can get sick with the flu. It spreads easily from person to person, and most hospitalisations and deaths affect people with chronic diseases. Getting vaccinated is the best protection against the flu.

Appendix 5: A standard Government Leaflet

Precautions: people who should seek medical advice before getting the flu shot

- Anyone with a serious allergy to any of the components in the vaccine such as eggs, egg products, neomycin and formaldehyde.

- Anyone who has had reactions to a previous dose of influenza vaccine.

- A patient with a history of neurological disease or weakness muscle.

Adverse reactions after influenza vaccination

People can have a low-grade fever, soreness at injection site after receiving the flu vaccine. These symptoms are usually mild and last 1-2 days. Severe allergic reactions to the flu vaccine are very rare.

Department of Disease Control,
Ministry of Public Health, Thailand
National Health Security Office

Seasonal Influenza vaccination service for people with chronic disease

Department of Disease Control, Ministry of Public Health, Thailand

National Health Security Office

Seasonal Influenza vaccination service for people with chronic disease

The Ministry of Public Health in cooperation with the National Health Security Office provides flu vaccine free of charge in the year 2009 to people with chronic disease.

- These include those with chronic obstructive pulmonary disease, asthma, cerebrovascular disease, chronic renal disease, cancer patients receiving chemotherapy, and diabetes mellitus.

Influenza symptoms

People who get the flu have a wide-range of symptoms, including fever, cough, headache, sore throat, muscle aches, chill, and weakness; These symptoms generally last 2 to 4 days.

What's the flu vaccine?

A flu shot is made from killed influenza virus. The vaccine stimulates the immune system to produce antibodies that protect against influenza viruses. However, the seasonal influenza vaccine cannot prevent the bird flu.

After vaccination, it takes about two weeks for antibodies to develop in the body and provide protection. The immunity from the vaccine lasts for a period of about 1 year. However, people who have been vaccinated against influenza can still get the flu, but they will usually get a milder case than people who have not received the vaccine.

The benefits of influenza vaccination

The flu vaccine will help to prevent seasonal influenza and its complications. In particular, the vaccine will help to reduce the chances of developing severe case of influenza in the people with chronic disease which can result in the death.

In Thailand, the studies were conducted to evaluate the effectiveness of influenza vaccination among elderly persons living in the community and among patients with chronic obstructive pulmonary disease. The results showed a 2-fold decrease in the incidence of influenza in elderly people and greater than a four fold decrease in the patients with chronic obstructive pulmonary disease.

Appendix 6: Interview schedule

Interview schedule

1.How would you describe the flu?

Probes:

a. How do you catch flu?

b. What are the signs and symptoms of the flu?

c. Is the "flu" the same as a "cold"?

d. How serious do you think flu is?

e. Do you consider influenza to be a serious illness?
(Why or why not)

f. Can influenza cause death?

2. How have you learned about flu?

Probes:

a. Family/friends/ health professionals/TV/newspaper?

b. Have you or any of your family ever had flu?

3. What you do if you get sick from the flu?

4. How do you protect yourself from getting the flu?

5. Have you ever heard about the influenza vaccination or Flu shot?

Probes:

a. What have you heard about it (benefits and drawbacks)?

b. Where did you hear about it?

c. Do you feel you know enough about the flu shot?

d. Who is recommended to have influenza vaccine?
(Do you know who should get a Flu shot?)

2. How effective do you think that a flu shot will protect you from getting the flu?

3. What sort of side effects would occur to people after getting a flu shot?

4. Do you believe that people would have had the flu after getting a flu shot?
5. Do you think you really need a flu shot?

Probes:

a. Why or Why not?

b. Have you or your family ever received a flu shot?

6. Could you make your own decision to get a flu shot?

7. Has anyone encouraged you to get a flu shot?

8. Who would influence you to get a flu shot?

Probes: Would it be a physician, your family/ friends, a religious leader?

9. Which will help you decide whether you will get a flu shot?

10. Will you get the flu shot this year?

11. What sorts of things would make you decide to get a flu shot?

Probes:

a. Could you afford for a flu shot?

b. Where can you get a flu shot? and Is this convenient?

12. In your opinion, what would make elderly people more willing to get a flu shot?

Appendix 7: Questionnaire

ID Number ☐

Influenza and Influenza Vaccination Questionnaire

Instructions

Please read the following questions carefully and answer each one. If you have any difficulties in completing the questionnaire, you can ask the research assistant for help. We will treat information you give us as confidential.

General information

1. Age.....yrs

2. Sex ☐ Male ☐ Female

3. Marital status

   ☐ Single ☐ Married ☐ Divorced or Separated

   ☐ Widowed ☐ Living with partner

4. Educational Level

   ☐ Primary school

   ☐ Secondary school ☐ Vocational/ Technical

   ☐ Other (specify).....

5. Occupation

   ☐ None ☐ Farmer ☐ Labourer

   ☐ Merchant ☐ Pensioner

   ☐ Other (specify).....

6. Have you ever had a flu shot?

   ☐ Yes ☐ No

   If yes, when.....

7. What are symptoms of flu? **(Please tick the box which corresponds with your answer.)**

Symptoms of the flu	**Definitely Yes**	**Definitely No**	**Not sure**
Fever (usually high) and chills			
Muscle aches and pains			
Seizure			
Extreme tiredness			
Diarrhoea			
Watery eyes			
Runny or stuffy nose			
Itching in nose, throat or eyes			
Sneezing			
Nausea			
Dry cough			
Headache			
Sore throat			

8. What can be the side effects of flu vaccination? **(Please tick the box which corresponds with your answer.)**

Side effects of the flu vaccine	**Definitely Yes**	**Definitely No**	**Not sure**
There are no side-effects			
A slight fever for 8-24 hours after vaccination.			
Soreness, pain at the vaccination spot.			
Swelling around the vaccination spot.			
Vomiting, diarrhea, and being nauseous.			
A fever, runny nose with dark and thick secretions.			
Feeling generally unwell and mild or moderate muscle aches for a couple days.			
Difficult breathing or swelling of the face.			

SECTION ONE

Please indicate **how much you agree or disagree with the following statements by choosing the face that best matches how you feel.** There are no right or wrong answers.

		 Strongly disagree	 Disagree	 Not sure	 Agree	 Strongly agree
1.	Influenza is a serious disease.					
2.	If I get the flu I will become very sick.					
3.	Flu spreads between people very easily.					
4.	I am likely to catch the flu if other people in my District develop it.					
5	Flu is a very minor health problem.					
6.	If someone in my family develops flu, everyone else will.					
7	Flu is not serious enough to interfere with my daily activities.					
8.	Compared to other people, the likelihood that I will get the flu is very large.					
9.	Flu can make my existing illness worse.					
10.	If I catch the flu, I may have to go to hospital.					
11.	Flu can be very serious for people with poor health.					

		Strongly disagree	Disagree	Not sure	Agree	Strongly agree
12.	I do not think that I am personally at risk of contracting the flu.					
13.	My body could fight off the flu because I have a strong immune system.					
14.	Flu can kill people in poor health.					
15.	I have a good health, so I don't need to get a flu vaccine.					

SECTION TWO

In this section, we would like to know about your expectations after getting the flu shot. **Please tick the appropriate box**. There are no right or wrong answers.

		not at all true	a little true	Mostly true	Exactly true
	If I get the flu shot.....				
16.	My chance of getting the flu will be decreased.				
17.	It can prevent me from getting a more severe case of the flu (influenza complications).				
18.	I will feel more confident about not having the flu.				
19.	I will be more likely to get other illnesses.				
20	I could protect my family and friends from flu				

		not at all true	a little true	Mostly true	Exactly true
21.	**If I get the flu shot.....** It will weaken my immune system.				
22	I will be less of a burden to my family.				
23	My family won't worry about my chances of getting a serious case of the flu.				
24.	I will get sick with the flu.				
25.	It will help me stay healthy during the flu season.				

SECTION THREE

The following statements look at how much confidence you would get the flu shot. **Please tick the appropriate box**. There are no right or wrong answers.

		not at all true	a little true	mostly true	Exactly true
26.	**I am confident that.....** I will get the flu shot in the forthcoming vaccination period.				
27.	I can cope with side effects after receiving the flu vaccine (fever, aches, soreness, redness at the injection site).				
28.	I can deal with a fear of needles or shot.				
29.	I can find the time to get vaccinated against the flu.				
30.	Receiving a flu shot will not interfere with my daily routine.				
31.	I will get a flu shot even though I am quite busy during the vaccination period.				
32.	I can arrange the transportation for myself to get vaccinated.				

SECTION FOUR

We are interested in your plan to seek flu vaccine in the next vaccination period. **Please tick the box which corresponds with your answer.**

		Yes	No
33.	I have made a plan **when** I'm going to vaccinate during the next vaccination period.		
34.	I have made a plan **where** I'm going to have the flu shot in the next vaccination period.		
35.	I have made a plan **how** I'm going to get vaccinated against the flu.		

The following statement looks at how much confidence you could use your plan to get the flu vaccine. **Please tick the appropriate box.**

		not at all true	a little true	mostly true	Exactly true
36.	I am confident that I can use this plan.				

SETION FIVE

We would like to know about your intention to receive the flu shot. **Please tick the number that best corresponds to your answer**. There are no correct answers.

		Definitely do not				Definitely do
37.	I intend to receive a flu shot in the forthcoming vaccination period.	□ 1	□ 2	□ 3	□ 4	□ 5
38.	I want to get vaccinated against the flu in the forthcoming vaccination period.	□ 1	□ 2	□ 3	□ 4	□ 5

******Thank you for taking part in this study and for your time. ******

Appendix 8: Published Paper (Study 1)

Journal of Public Health | Vol. 32, No. 1, pp. 26–31 | doi:10.1093/pubmed/fdp086 | Advance Access Publication 25 August 2009

Understandings of influenza and influenza vaccination among high-risk urban dwelling Thai adults: a qualitative study

Y. Payaprom[1,2], P. Bennett[2], P. Burnard[3], E. Alabaster[3], H. Tantipong[4]

[1]Department of Nursing, Chiang Rai Hospital, Chiang Rai, Thailand
[2]Nursing, Health and Social Care Research Centre, Cardiff University, Cardiff, UK
[3]Cardiff School of Nursing and Midwifery Studies, Heath Park Campus, Cardiff University, Cardiff, UK
[4]Department of Medicine, Chiangrai Hospital, Chiang Rai, Thailand
Address correspondence to Y. Payaprom, E-mail: payapromY1@cf.ac.uk

ABSTRACT

Background The 2004 outbreak of influenza A H5N1 and the WHO's recommendation for national pandemic plans has led the Thai Ministry of Public Health to develop an influenza vaccination programme for high-risk adults. To date there is no available information to guide this intervention, and how to maximize the uptake of the vaccine by the Thai population. To address this knowledge gap, this study explored factors influencing urban-dwelling Thai adults' decisions whether or not to have the vaccine. It explored their beliefs about influenza and influenza vaccination, and other influences on their decisions.

Methods In-depth interviews were conducted among 20 high-risk individuals who were aged 65 and over or under 65 years with chronic diseases requiring influenza vaccination. Interviews were tape recorded and analysed following using grounded theory.

Results Most participants had insufficient knowledge about influenza and influenza vaccination. Their decisions in relation to vaccination were based on a number of factors, including salience of risk, influence of others, perception of the need for preventive health care and the availability of influenza vaccine.

Conclusion These findings underscore the need to consider and understand factors underlying people's vaccination decisions to create an effective influenza vaccination programme.

Keywords health promotion, influenza immunization

Introduction

In response to the WHO[1] recommendation that all countries develop influenza preparedness plans and a recent outbreak of influenza resulting in 17 deaths, the Thai government is planning an influenza prevention programme targeting people aged over 65 years with chronic diseases,[2] and extending to those under 65 years in the next following years. Data from studies conducted in western countries indicate that decisions whether or not to receive influenza vaccination are complex, and influenced by several medical and psychosocial factors, including its salience and perceived severity,[3] the influence of healthcare providers, family members and friends[4–6] and the costs and convenience of obtaining the vaccination.[7–9] By contrast, factors influencing vaccine uptake in tropical countries such as Thailand, Vietnam and Indonesia have not been studied. Yet, understanding these issues is critical to the development of effective interventions. In order to begin this process, the present study explored beliefs about influenza and influenza

Y. Payaprom, Registered Nurse, PhD Student
P. Bennett, Professor of Nursing Research
P. Burnard, Professor of Nursing Research
E. Alabaster, Senior Lecturer in Adult Nursing
H. Tantipong, MD Internist, Chiang Rai Hospital, Chiang Rai, Thailand

vaccination, and other factors likely to influence decisions whether or not to accept the influenza vaccination in a sample of urban-dwelling Thai individuals aged 65 years and over or under 65 years with serious chronic health problems. The findings will inform the development of interventions to encourage uptake of influenza vaccination by such individuals.

Methods

Setting and participants

This study was approved by the research ethics committee, Chiang Rai province, Thailand. It was conducted in the Muang district, an urban community of Chiang Rai province with a population of 223 936. Chiang Rai is the northern most province of Thailand and has an adult literacy rate of 93%. It, and the northeast province of Thailand, has similar levels of income (around US$1396 per capita per year, compared to Thailand average income of US$3720) and constitutes about 53% of the total Thai population.[10] As such, the population of Muang district may be considered representative of the poorer half of the Thai population, and they had typical education. The study population were adults who were either aged 65 and over, or under 65 years with chronic diseases, which indicated that they would benefit from the influenza vaccination (e.g. coronary heart or chronic obstructive pulmonary disease). Potential participants were randomly selected from one health centre's database. Their medical records were scrutinized to confirm the suitability of participants for interview. Those with severe chronic conditions (i.e. bed bound or acutely ill), severe mental health problems, or communication difficulties were excluded. Letters of introduction were sent to 30 potential participants: 15 letters in each group.

Interviews

In-depth interviews were conducted between February and March 2008 in participants' homes or at a health centre. Written consent was obtained before the interview. A semi-structured schedule guided the interviews. It explored participants' understandings of influenza and influenza vaccination and factors that may influence their decision whether to accept or decline the influenza vaccination in the forthcoming vaccination period. Interviews lasted between 30 and 60 min, and were tape recorded.

Data analysis

The interviews were transcribed in Thai and analysed following grounded theory tradition.[11] All transcripts were coded by two researchers to increase reliability, with discrepancies resolved through discussion. After extensive data analysis, the transcripts were translated into English and back translated into Thai by an independent translator. The English version of the transcripts is reported here.

Findings

Twenty individuals agreed to participate and were interviewed: 11 aged $\geq$65 years and 9 aged $<$65 years with chronic diseases. Their mean age was 64.9 years, with the oldest participant being 75 years old. Participants were predominantly female and most of them had completed primary school, and were therefore typical of old people in Thailand. All participants lived with others. Five participants reported having had influenza diagnosed by a doctor in the past; there were no laboratory-confirmed cases of influenza. Additionally, six participants reported having had one influenza vaccination: four had been offered the vaccine by their physicians and two reported that their daughters, who were nurses, had advised them to be immunized. All paid for the vaccine and its administration (Table 1). In view of these different vaccine histories, the analysis examined any differences between the transcripts of those who had or had not previously sought or received flu vaccination. They only differed in their perception of the salience of risk for influenza and its severity.

Understanding of influenza and influenza vaccination

Knowledge of influenza and influenza vaccination

Most participants stated they knew little about influenza and did not know how to describe it. A number thought it was associated with the changes of weather, particularly from the rainy to winter season, while only one person stated that influenza was caused by 'germs'. A few participants with chronic diseases thought that these placed them at increased risk of infection.

It's easy for me to catch the flu because my resistance is down. I have lung disease also the changing the weather is a contributing factor. (ID 10)

Most participants confused the symptoms with those of the common cold and other respiratory illnesses.

When you have flu, you have a fever, sneezing, runny nose with watery secretions during the first few days, then these become thick and dark mucus, and you also feel a headache... flu is more serious than a cold. (ID 20)

Table 1 Demographic characteristic of participants

ID	Age	Sex	Marital status	Educational level	Occupation	Living arrangements	Health problems	Had flu in the past	Immunization status
1	72	F	Married	Primary school	None	Children and spouse	None	No	Never
2	60	F	Widowed	Primary school	None	Children	Diabetes	No	Never
3	58	F	Widowed	Primary school	Merchant	Children	Asthma	Yes	Never
4	60	M	Married	Primary school	Farmer	Children and spouse	COPD	No	Immunized
5	75	M	Married	Primary school	None	Children and spouse	None	No	Never
6	69	F	Married	Secondary school	Merchant	Spouse	None	No	Immunized
7	66	M	Married	Primary school	Labourer	Children and spouse	None	No	Never
8	56	M	Married	Primary school	Merchant	Spouse	Diabetes	No	Never
9	54	M	Married	Secondary school	Labourer	Children and spouse	Diabetes	Yes	Never
10	61	M	Married	Primary school	Labourer	Children and spouse	COPD	Yes	Immunized
11	65	M	Married	Vocational/technical	Labourer	Children and spouse	None	No	Never
12	70	F	Widowed	None	None	Children	None	Yes	Never
13	52	F	Married	Primary school	Merchant	Children and spouse	Diabetes	No	Never
14	72	F	Married	Vocational/technical	Pensioner	Children and spouse	None	No	Immunized
15	73	M	Married	Secondary school	Pensioner	Children and spouse	None	Yes	Immunized
16	61	F	Married	Secondary school	Pensioner	Spouse	Asthma	No	Immunized
17	62	F	Widowed	Primary school	None	Children	Diabetes	No	Never
18	74	F	Widowed	None	None	Children	None	No	Never
19	70	M	Married	Primary school	None	Children and spouse	None	No	Never
20	69	F	Widowed	Primary school	None	Children	None	No	Never

Although they considered influenza to be a serious health problem, only a few participants felt that it could cause death.

It's possible that Influenza can make elderly people very ill and even cause death because they have weak immune systems. (ID 4)

If you are not cured in time, you may die of influenza. However, I haven't heard of people dying of it. (ID 8)

Most participants reported that they knew little or nothing about the flu vaccine. A typical comment was:

I had heard about the vaccine for children. Is there the influenza vaccine for elderly people? Well, I have not heard of it. (ID 13)

Additionally, some participants had misconceptions about influenza vaccination, believing that it could either prevent them from catching a cold or may weaken their immune system.

After receiving it [Influenza vaccine], *I have not been ill. Previously, if a person who got cold sneezed or coughed toward me, I would certainly catch a cold.* (ID 10)

In the elderly, immune systems are not as strong as in younger. If I get a flu shot, it may weaken my immune system. (ID 1)

Most participants were not particularly concerned about any vaccine side effects. They thought that these would be the same as for other vaccines. However, a few felt the need to be reassured that the vaccine was safe.

A few people may have [concerns about side effects of vaccine]. *However, if the vaccine comes from the public health staff, and the information is provided on vaccine safety, these should help lessen the people's concerns.* (ID 11)

Source of information

A number of participants reported they had developed influenza at some time in the past. A few others had heard about influenza from others. However, most participants had not been informed about the vaccination by healthcare workers, and only four participants had learned about the vaccine from the mass media,

[I've heard] *from elderly people. Now, less people catch it* [influenza]. *I have rarely heard of someone catching it.* (ID 7)

They've probably heard of influenza for a long time, but they don't understand it. And I think no one in this community remembers what the disease is. (ID 9)

Interviewer: *Have you ever heard about Influenza vaccine from TV?*

Mr. Y: *No, just influenza*
Interviewer: *Do you think you've received enough influenza information from TV?*
Mr. Y: *No, I did not receive any details from it, just got rough information.* (ID 4)

The public health staff... give(s) us a health check-up, but they never mention the influenza vaccine. (ID 13)

Decision-making in influenza vaccination

Salience of risk

Though most participants held generally positive views on influenza vaccination, decisions about the influenza vaccination were based on their perceived risk of contracting influenza. Some reported they would only seek influenza vaccine if there was a local outbreak of influenza.

Even it is free. If we do not have this kind of epidemic [influenza epidemic] *in our community, there is no need to receive the injection.* (ID 7)

Yes, I can wait till there actually is [an influenza epidemic]. *I can have the injection immediately after the outbreak.* (ID 9)

By contrast, those who had previously been vaccinated considered themselves to be at risk of developing influenza and that it would affect them seriously:

I have the underlying disease which is lung disease... I should get a flu shot because I could get the flu easily. (ID 4)

I'm afraid of catching the flu at old age. People my age, once get sick, will get worse and need medical treatment at the hospital. I have to protect myself. (ID14)

Influence of others

A number of participants stated that they would ask their children or other people in the community about whether to have the vaccination.

I have to ask my children before that. If they say I should, I'll receive this injection. If they say no, I will not receive it... I've to ask them whether or not to have a flu shot, it is necessary. (ID 13)

I will talk with my friends... people of the same age and with the same health condition could help us decide whether to get the flu shot or not. If they decide against it, I do not want to do it either. (ID 7)

In addition, a number of participants with chronic medical conditions reported that their decision would rely heavily on their healthcare providers, regardless of their own views.

I've been healthy for about the last 2–3 years, and I've never caught a cold once. So I think it is not necessary to get the flu shot. But if the doctor advised me to have the vaccine, I'll do it. (ID 2)

Availability

Most participants would consider having the vaccination if it was provided free of charge, and preferred to receive it locally.

No, I do not have any money for a vaccine. I will only do it, if it is free. (ID 17)

They should... [get vaccination]. *But what would they do? Elderly people without any income support can only live day by day.* (ID 11)

The health centre is fine. It's near our houses, and it's not crowded. If it's the hospital, you have to spend one day because the hospital service is very slow, and my children have to take me there. (ID 18)

Perception of the need for preventive healthcare

Some participants with chronic medical conditions reported they would consider getting vaccinated because they were concerned that influenza might exacerbate any illness and would make them feel a burden on other people.

I'm afraid of getting sick. I have asthma. I think that my breathing may become difficult. So I have to protect myself. (ID16)

I have lung disease. I feel tired when I breathe, my children bring me to the hospital and they lose their income for one day. I think I will get it [influenza vaccine] (ID 3)

By contrast, several participants who considered themselves to be healthy stated that they would not consider getting vaccinated even though they could afford to pay for it.

I've never caught it, so I am not afraid of it. I'm healthy because I exercise every day. I've a strong immune system. (ID 5)

Interviewer: *Are you afraid of catching influenza if you do not get a flu shot?*
Mrs. V: *I don't know. If I catch it, I will receive the treatment at the hospital.*
Interviewer: *You mean you want to take the chance?*
Mrs. V: *Yes.* (ID 13).

Discussion

Main findings

Overall, the study revealed that high-risk Thai adults had low levels of knowledge about influenza and influenza vaccination. Many were unsure about its cause and symptoms,

mode of transmission, seriousness and complications. Few correctly described the symptoms of influenza, while others confused them with the symptoms of the common cold or other respiratory illnesses. These findings may not be specific to this population: only 44% of a US sample was able to describe typical influenza symptoms.[12] Consistent with previous findings,[13,14] most participants regarded influenza as a relatively serious disease. However, some considered it to be no worse than a 'bad cold, while very few thought that it could cause death. These beliefs appear to have contributed to a reluctance to seek the vaccine among some individuals.

Most participants knew little or nothing about the influenza vaccination, perhaps because the use of influenza vaccine in Thailand has, until recently, been limited to a restricted group of people such as healthcare workers, pilgrims who attend the Hajj and those who are able to afford for it.[15–16] Of note was that side effects following vaccination were not a major concern among our participants, in contrast to some studies that have reported fear of side effects as a significant contributor to decisions not to receive the vaccination.[6,8] By contrast, salience of risk did appear to play an important role in decision-making. Many considered were reluctant to be vaccinated as they considered themselves to be healthy and the risk of developing influenza to be low, or stated they would only seek vaccination if there was a local outbreak of influenza. However, most individuals with pre-existing health conditions were likely to seek vaccination to prevent further health complications. Participants' decisions were also strongly influenced by family members, peers and healthcare providers. This strong social influence is likely to be the result of the close intergenerational ties within Thai families[17] and participants' willingness to accede health decisions to doctors regardless of their own views. Financial barriers also appeared to be an important influence on healthy individuals' immunization decisions, although participants in poor health were more willing to purchase the vaccine.

Our study clearly demonstrated the complexity of personal decision-making in influenza vaccination, particularly in a culture in which there are significant intergenerational influences on such decisions. The results of this study suggest that national and local flu vaccination programmes should be preceded and accompanied by public educational programmes that emphasize the seriousness of influenza, its complications and the specific merits of vaccination for key target groups (such as high-risk individuals). In Thailand such programmes need to be targeted at both potential recipients and significant others, including younger family members, as these individuals appear to be key social facilitators in encouraging high-risk older people to accept vaccination. Finally, the free provision of vaccination is likely to have a marked impact on uptake.

What is already known on this topic

Previous research[6,8,9,13] has shown uptake of influenza vaccine to be influenced by factors including its salience and perceived severity,[3] the influence of healthcare providers, family members and friends,[4–6] and the costs and convenience of obtaining the vaccination.[7,9] However, these findings are restricted to western countries, and data is lacking from tropical countries such as Thailand.

What this study adds

Our data clearly indicate that providing information on influenza and influenza vaccination to the public will be necessary before and during any vaccination programme. Such a programme should both emphasize the symptoms and the severity of influenza as well as explain why the vaccine should be applied to all high-risk groups. It should also be targeted at younger people who will not have the vaccination themselves, but who may influence the vaccination decisions of their parents and others. Maximizing uptake also appears to be predicated on the vaccine being free and available in local healthcare centres or community organizations as well as more centralized hospitals. Doctors and other healthcare workers should also be prepared and encouraged to discuss vaccination with their patients. Although these suggestions are made in application to high-risk urban-dwelling Thai adults, they could be applied to other countries with tropical climates where large-scale influenza vaccination programmes have yet to be undertaken, with further adjustment for differences among countries.

Limitations of this study

The main limitation of this study is its specificity to the population under study. It was conducted in one selected urban community; potentially restricting its implications to high-risk Thai adults living in the Muang district, Chiang Rai, Thailand. Another limitation is that there were 10 potential participants who refused to participate in this study: four felt generally unwell, four did not have enough time for interview and two were not interested. Accordingly, while a good response rate for qualitative research was obtained, it is possible these individuals might have different views on influenza and influenza vaccination from those who participated in the study. Larger, quantitative, studies on representative populations are still necessary to ensure the generalizability of these findings. Despite these cautionary notes, however, our findings provide information relevant to

the development of public health interventions to promote the use of influenza vaccine among high-risk Thai adults.

Acknowledgements

The authors appreciate the staff of the health centre for their help in recruiting potential study participants. We thank Ms. Kanokpan Pancharoen for assistance with note taking, and we appreciate all participants for their active participation in the study. This study forms part of Yupares Payaprom's PhD.

Funding

This study was funded by the Thai government.

References

1 World Health Organization. *WHO Global Influenza Preparedness Plan: The Role of WHO and Recommendations for National Measures Before and During Pandemics.* http://www.who.int/csr/resources/publications/influenza/GIP_2005_5Eweb.pdf (26 June 2008, date last accessed).

2 Ministry of Public Health. *Promoting Influenza Vaccination in High-risk Elderly Thai People.* http://www.moph.go.th (11 March 2008, date last accessed).

3 Cornford CS, Morgan M. Elderly people's beliefs about influenza vaccination. *Br J Gen Pract* 1999;**49**:281–4.

4 Centers for Disease Control and Prevention. Adult immunization: knowledge, attitudes, and practices–Dekalb and Fulton countries, Georgia. *MMWR* 1988;**37**:657–61.

5 Zimmerman RK, Santibanez TA, Janosky JE *et al.* What affects influenza vaccination rates among older patients? An analysis from inner-city, suburban, rural, and veterans affairs practices. *Am J Med* 2003;**114**:31–8.

6 Evan MR, Prout H, Prior L *et al.* A qualitative study of lay beliefs about influenza immunisation in older people. *Br J Gen Pract* 2007;**57**:352–8.

7 Centers for Disease Control and Prevention. Final results: medical influenza vaccine demonstration: selected states, 1988–1992. *MMWR* 1993;**42**:601–4.

8 Burns VE, Ring C, Carroll D. Factors influencing influenza vaccination uptake in an elderly, community-based sample. *Vaccine* 2005;**23**:3604–8.

9 Kroneman M, Paget WJ, van Essen GA. Influenza vaccination in Europe: an inventory of strategies to reach target populations and optimise vaccination uptake. *Euro Surveill* 2003;**8**:130–8.

10 Office of the National Economic and Social Development Board. *Gross Regional and Provincial Product.* Bangkok: NESDB, 2009.

11 Strauss A, Corbin J. *Basic of Qualitative Research: Techniques and Procedures for Developing Grounded Theory.* Thousand Oaks: SAGE, 1998.

12 Santibanez TA, Nowalk MP, Zimmerman RK *et al.* Knowledge and beliefs about influenza, pneumococcal disease, and immunisations among older people. *J Am Geriatr Soc* 2002;**50**:1711–6.

13 Centers for Disease Control and Prevention. *Influenza and Pneumococcal Immunization: A Qualitative Assessment of the Beliefs of Physicians and Older Hispanic Americans and African Americans.* http://www.health.gov/communication/db/FileDownload.asp?ID+171 (8 October 2007, date last accessed).

14 Findlay PF, Gibbons YM, Primrose WR *et al.* Influenza and pneumococcal vaccination: patient perceptions. *Postgrad Med J* 2000;**76**:215–7, 21.

15 Chunsuttiwat S. *Thai Ministry of Public Health.* Nonthaburi: Ministry of Public Health, 2002.

16 Simmerman JM, Thawatsupha P, Kingnate D *et al.* Influenza in Thailand: a case study for middle income countries. *Vaccine* 2004;**23**:182–7.

17 Choowattanapakorn T. The social situation in Thailand: the impact on elderly people. *Int J Nurs Pract* 1999;**5**:95–9.

Appendix 9: Published Paper (Study 2)

Health Psychology

0278-6133/11/$12.00 DOI: 10.1037/a0023580

Using the Health Action Process Approach and Implementation Intentions to Increase Flu Vaccine Uptake in High Risk Thai Individuals: A Controlled Before-After Trial

Yupares Payaprom
Cardiff University

Paul Bennett
University of Swansea

Erica Alabaster
Cardiff University

Hutsaya Tantipong
Chiang Rai Hospital, Chiang Rai, Thailand

Objective: Influenza vaccination rates remain suboptimal in many countries, including Thailand. This study compared the effect of a theory-based educational leaflet, based on the Health Action Process Approach (HAPA), and action planning intervention with a standard government information leaflet designed to increase influenza vaccination uptake among high-risk Thai adults. ***Design:*** A controlled before and after trial was conducted. Participants in the intervention (n = 99) received a leaflet based on the HAPA and asking them to form an action plan identifying where, when, and how they would seek vaccination. Those in the comparison condition (n = 102) received a standard government information leaflet. ***Main Outcomes Measures:*** There are 2 sets of outcome measures: (a) process measures of HAPA related variables taken at T1 and T2, and (b) vaccination rates during the subsequent 2 months. ***Results:*** The HAPA intervention resulted in greater changes on measures of risk perception, outcome expectancies, self-efficacy, and intention than the comparison condition. Stronger intentions to obtain vaccination were explained by changes in outcome expectancies, perceived self-efficacy for arranging time and transportation, and planning. No significant difference in vaccination rates was observed between two groups. Influenza vaccination was directly predicted by self-efficacy and intention. ***Conclusion:*** Results demonstrate that a HAPA-based leaflet may be a useful tool to enhance individual's vaccination intention, but larger trials are required to confirm these findings.

Keywords: before-after study, influenza vaccination, Health Action Process Approach

Each year, influenza epidemics are estimated to cause 3–5 million cases of severe illness, and between 250,000–500,000 deaths throughout the world (World Health Organization [WHO], 2003). In Thailand, an outbreak of the influenza A (H5N1) virus in 2004 resulted in 17 confirmed cases and 12 deaths, while 8.4 million people were infected and 191 died in the 2009 influenza A (H1N1) pandemic (Ministry of Public Health [MOPH], 2009). Together, these highlight the need for the development of an influenza prevention and control program in Thailand. The program has so far made free vaccination available to all health care workers involved in direct patient care and those who have at least one chronic disease (Ministry of Public Health, 2008). Unfortunately, the vaccination rate during the program's first year was relatively low (37.7% in Chiang Rai Province, P. Sriwongpan, personal communication, March 6, 2009): insufficient to provide population protection against the virus.

Factors that influence decisions in relation to vaccination are complex. They include knowledge and beliefs about influenza and the flu vaccine, perceived risk for influenza, health status, concerns about the efficacy and side effects of vaccine, health care providers' recommendations, social influences such as family and friends, and the availability of the vaccine (e.g., Burns, Ring, & Carroll, 2005; Evan, Prout, Prior, Tapper-Jones, and Butler, 2007). These factors provide a number of targets for any public health program designed to increase uptake of influenza vaccine. Theoretical models also help determine the content of any program, and can be utilized to explain how it promotes any behavioral change (Fishbein & Yzer, 2003). The Health Action Process Approach (HAPA; Schwarzer, 2001) provides one such explanatory model, and has been shown to have good predictive utility in relation to a number of health-related intentions and behaviors including diet (Schwarzer & Renner, 2000), alcohol consumption (Murgraff, McDermott, & Walsh, 2003), breast self-examination (Luszczynska & Schwarzer, 2003), physical exercise (Schwarzer, Luszczyn-

Yupares Payaprom and Erica Alabaster, Cardiff School of Nursing and Midwifery Studies, Cardiff University, Cardiff, United Kingdom; Paul Bennett, Department of Psychology, Swansea University, Swansea, United Kingdom; Hutsaya Tantipong, Department of Medicine, Chiang Rai Hospital, Chiang Rai, Thailand.

We thank all the study participants for their cooperation in following all requirements of the study. This research project was partially supported by funds to Yupares Payaprom from the Thai government.

Correspondence concerning this article should be addressed to Yupares Payaprom, Nursing, Health, and Social Care Research Centre, Cardiff University, Eastgate House, 4th floor, 35-43 Newport Road, Cardiff, CF 24 0AB, United Kingdom. E-mail: PayapromY1@Cardiff.ac.uk

ska, Ziegelmann, Scholz, and Lippke, 2008), and food hygiene (Chow & Mullan, 2010).

According to the HAPA, changing health behaviors involves two interacting phases. The *motivation phase* is influenced by risk perception, outcome expectancies, and perceived self-efficacy. Together, these variables influence intentions to perform specific behaviors (e.g., Luszczynska & Schwarzer, 2003; Schwarzer, 2001). After a goal intention has been established, the individual enters the *volition phase*. In this, action planning (Schwarzer, 2001) or the analogous process of developing implementation intentions (Gollwitzer, 1999) play an important role in bridging the intention-behavior gap. Intentions are most likely to be acted on if the individual develops an action plan/implementation intention (Gollwitzer, 1999; Pestwich, Ayres, & Lawton, 2008; Sniehotta, Soares, & Dombrowski, 2007). Summarizing the available data, a meta-analysis of 94 studies conducted by Gollwitzer and Sheeran (2006) indicated that action plans/implementation intentions had an overall effect size of .65 on goal attainment.

The present study investigated whether a leaflet addressing variables identified as relevant by the HAPA and incorporating action planning would result in higher intentions to seek influenza vaccination and vaccination rates than a standard government leaflet among high-risk Thai individuals. The study also investigated the explanatory power of the HAPA in relation to influenza vaccination. It was hypothesized that: (i) implementation of a theory-based leaflet and action planning intervention would lead to greater changes in key mediator variables (knowledge, risk perception, self-efficacy, outcome expectancies, intention to seek vaccination) and higher rates of influenza vaccination than a comparison intervention; (ii) changes in risk perceptions, outcome expectancies, self-efficacy, and establishing an action plan would be associated with changes in intentions to vaccinate over time; and, (iii) establishing an action plan, self-efficacy, and intentions would predict vaccination uptake.

Method

Study Setting

The study was conducted in the Muang district, an urban community in Chiang Rai province, the northernmost province of Thailand, with an adult literacy rate of 93.8% (National Statistical Office, 2006). The Chiang Rai province research ethics committee approved the study. The study was conducted in two geographically separated communities to limit contamination between trial arms. These two areas were similar in overall population size, the number of people with chronic diseases requiring influenza vaccination within them, and the baseline influenza vaccination rate among high-risk people.

Design and Participants

A controlled before and after trial was carried out comparing the effect of a HAPA-based leaflet with a standard government information leaflet on influenza vaccination uptake among high-risk urban dwelling Thai adults. Participants were randomly selected from pools of eligible participants in two geographically separate communities within the Muang district. Participants in one area received a HAPA-based leaflet; those in the other received a standard government leaflet. The study had two sets of outcome measures: (i) process measures of HAPA related variables taken at Time 1(T1) and 2 weeks after the intervention (Time 2: T2); and (ii) vaccination rates during the subsequent 2 months. The study was powered to detect between group differences in vaccination rates of 22% (between the previous year's vaccination rate of 38% and a predicted rate of 60%). This required a sample size of 177 participants with a power of 0.80 at a significance level of 0.05 (Fleiss, Levin, & Paik, 2003). The study was confined to people aged 45–65 years with one or more chronic diseases (including heart disease, diabetes, and asthma) indicating the need for a flu vaccination. Exclusion criteria were: (1) having a known or suspected egg protein allergy; (2) hypersensitivity to any component of the vaccine; (3) severe chronic conditions (i.e., bed bound or acutely ill); (4) dementia or suspected dementia, or (5) an inability to read and write.

Potential participants in each area were identified from the National Health Security Office list. Of the 594 potential participants, 401 met all the eligibility criteria. Of these, 205 were randomly selected to participate in the study using a lottery method without replacement. Four participants withdrew before completing the baseline questionnaire. Accordingly, 201 participants were included in the study (99 in the intervention group and 102 in the comparison group; see Figure 1). The study population had a mean age of 56.24 [SD = 5.86] years, with a range of 45–65 years. The majority of participants (66.67%) were female, most (94.12%) had completed primary school (6 years of schooling), and 88.24% were married. Participants in each group did not differ with regard to age (t = 1.7, df = 199; p = .09), gender (χ^2 = 1.76; p = .18), marital status (χ^2 = 7.05; p = .07), educational level (χ^2 = 4.96; p = .17), occupation (χ^2 = 2.24; p = .53), and prior flu immunization (χ^2 = 3.14; p = .08). Only three people, all of whom were in the HAPA condition, had received one flu vaccination prior to the intervention.

Intervention

Participants in the HAPA condition received a leaflet addressing factors known to influence behavior: risk perception, outcome expectancies, self-efficacy, intentions, and action planning (Schwarzer, 2001). The behavior change techniques used in the leaflet included providing information about the behavior-health link (Abraham & Michie, 2008). This involved highlighting high risk individuals' susceptibility to influenza and its complications (e.g., "You are at high risk for severe complications such as pneumonia, and blood infections. This may put you in the hospital, so why risk it?"). The messages focused on increasing perceptions of personal risk rather than arousing fear of disease (see Ruiter, Abraham, & Kok, 2001).

A second behavior change technique involved providing information on the benefits of vaccination. This involved phrases including "Taking the flu shot will help you a lot through the flu season: Don't get the flu!," "Don't have serious complications," and "Reduce the risk of going into hospital." The leaflet also sought to increase participants' efficacy in relation to their ability to cope with the vaccination by including the personal accounts of people who had received the influenza vaccination (e.g., "I have asthma, I need to protect myself. At first, I had not agreed to get the flu shot because I was afraid of allergies and breathing diffi-

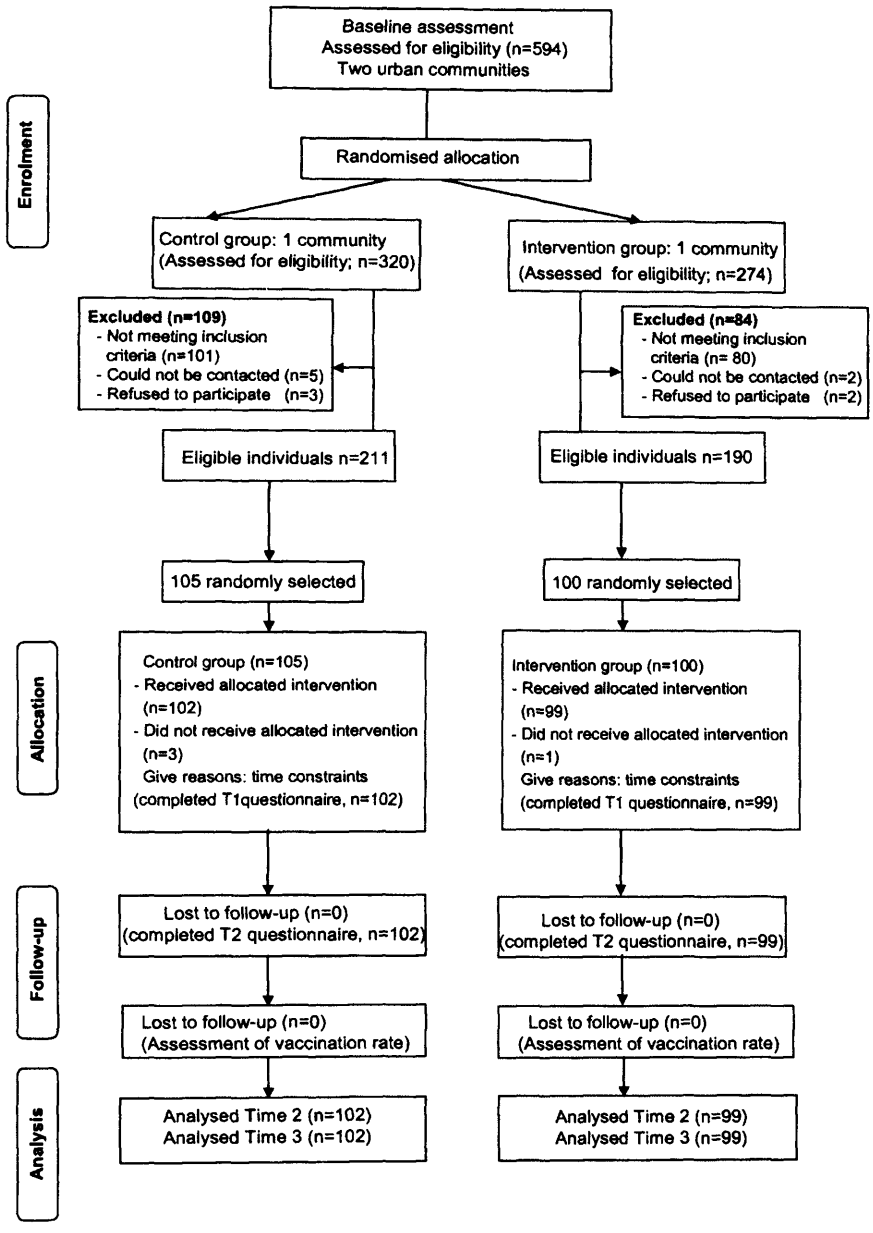


Figure 1. Flow diagram of participants' progress through the trial.

culty, but I was fine after the injection."). These accounts also sought to increase normative beliefs favoring vaccination. Following standard "if-then" protocols (Gollwitzer, 1999), the leaflet also asked participants to develop a specific plan detailing where, when and how they would obtain the vaccination (prompt specific goal setting). Additionally, they were asked to consider how they would get to the clinic to obtain the flu vaccine (prompt barrier identification). The following instructions were included in the leaflet for the intervention group.

"Getting a flu vaccination: Plan ahead! You are more likely to go for having the flu shot, if you decide now about where, when, and how you will go. Please write in below when, where, and how you plan to get a flu vaccine."

"If I get an appointment letter to have the flu vaccine, then I will ..... (please write down what you plan to do, e.g., go for taking the flu shot) at ..... (please write down where, e.g., Chiang Rai Hospital, Private clinic), and I'm going to get there by ..... (please write down how you go to that place, e.g. walking, taking a bus or asking son/daughter/relatives to take you to get the flu vaccine)."

Participants in the comparison group received the standard government information leaflet. This was used in the previous

year's (2009) vaccination program, and provided information about the symptoms of influenza, brief details about the flu vaccine, possible side effects following vaccination, and the general benefits of influenza vaccination, including "flu shots help prevent the flu and its serious complications." No details about the complications of the flu and other benefits of influenza vaccination were addressed. Accordingly, the key techniques in this leaflet were to provide information about the behavior-health link and the consequences of vaccination (Abraham & Michie, 2008). An appointment letter detailing a date and time of vaccination was also sent to all high-risk individuals.

Questionnaires

The questionnaires assessed changes on key HAPA variables. In addition, as information about influenza and the influenza vaccine formed an important element of the leaflet, questions related to influenza symptoms and vaccine side effects were also included. With the exception of three questions addressing planning, asked only at T2, the same questionnaire was given to participants at T1 and T2. A draft questionnaire was pilot tested by 20 Thai adults.

Knowledge

Knowledge of influenza symptoms and vaccine side effects were assessed by presenting participants with a list of 13 symptoms (e.g., fever, watery eyes) and eight potential vaccine side effects (e.g., pain at the vaccination spot, vomiting). There were eight correct influenza symptoms and four correct vaccine side effects. Participants were asked to tick yes, no, or not sure, to the symptom and vaccine side effects checklist.

Risk Perception

For the measure of risk perception, participants were asked to indicate their level of agreement or disagreement with 15 statements referring to (i) the risk of developing influenza and (ii) the consequences of influenza to their lives (e.g., "If someone in my family develops flu, everyone else will," and "Flu can make my existing illness worse"). Items were measured using a 5-point Likert scale from 1 (*strongly disagree*) to 5 (*strongly agree*). Total risk perception scores, ranging from 15 to 75, were calculated by summing the item scores. In addition, separate risk (Cronbach's α T1 = 0.79; T2 = 0.68) and consequence subscales (Cronbach's α T1 = 0.75; T2 = 0.70) were derived.

Outcome Expectancies

Outcome expectations after receiving the vaccine were assessed with seven items, including "If I get the flu shot it can prevent me from getting a more severe case of the flu," and "If I get the flu shot it will help me stay healthy during the flu season." All items were rated on a 4-point Likert scale from 1 (*not at all true*) to 4 (*exactly true*). Item scores were summed to provide a total outcome expectancy score, ranging from 7 to 28 (Cronbach's alpha T1 = .72; T2 = 0.81).

Self-Efficacy

Self-efficacy was measured by asking participants to rate their level of confidence in their ability to obtain and cope with the influenza vaccine in the next vaccination period. The scale comprised seven items, including "I am confident that I can cope with side effects after receiving the flu vaccine," and "I am confident that I can find the time to get vaccinated against the flu." Responses were reported on a 4-point Likert scale from 1 (*not at all true*) to 4 (*exactly true*). Two self-efficacy subscales were derived: self-efficacy in coping with vaccine side effects (Cronbach's α T1 = 0.72; T2 = 0.81) and self-efficacy for arranging time and transportation (Cronbach's alpha T1 = 0.84; T2 = 0.91).

Intention

Participants indicated their level of intention to obtain influenza vaccination with two statements: "I intend to receive a flu shot in the forthcoming vaccination period," and "I want to get vaccinated against the flu in the next vaccination period." Answers were given on a 5-point scale from 1 (*definitely do not*) to 5 (*definitely do*). These items were added to form a sum score of intention, with total scores ranging from 2 to 10 (Pearson's r T1 = 0.61; T2 = 0.67).

Action Planning (T2 Only)

Action planning was measured by responses to three questions: "I have made a plan when I'm going to vaccinate during the next vaccination period," "I have made a plan where I'm going to have the flu shot in the next vaccination period," and "I have made a plan how I'm going to get vaccinated against the flu." The response alternatives were "Yes" and "No." Participants in the HAPA intervention were also required to bring the leaflet to the researcher at the T2 data collection in order to verify whether they had made an action plan. Participants were scored as either completing the planning process (all three issues were addressed) or not completing the process (two or less issues were addressed).

Procedure

Potential participants in both the intervention and comparison areas were approached by village health volunteers who gave them an invitation letter together with a reply slip, indicating their willingness to consider participating in the study. Those who agreed to consider participation were then visited by a research assistant, either in their home or at a health center. At this meeting, participants were given more information about the study and signed a consent form before completing the baseline questionnaire. If participants had limited literacy, the researcher read the statements or questions out loud and asked participants to score their own responses.

After T1 data collection was completed, leaflets enclosed in a plain brown envelope were distributed to participants by the village health volunteers. The HAPA intervention participants received a HAPA-based educational leaflet. The comparison group received a standard influenza leaflet developed by the Ministry of Public Health. Two weeks later, participants were again approached by research assistant, and asked to complete the T2 questionnaires and to show their leaflets verifying their use the implementation intention intervention.

Data Analysis

Analyses were performed on an intention-to-treat basis. Baseline characteristics of participants in the intervention and compar-

ison groups were compared using chi-square test for categorical variables and Student's t test for continuous variables. Within group analyses involved the McNemar's test, comparing the proportions of correct responses on knowledge of influenza symptoms and vaccine side effects at baseline and after the intervention. A series of one-way analyses of covariance (ANCOVAs; with baseline scores as covariates) was conducted on T2 data to identify any significant between group differences on the outcome measures at this time. Relationships between the hypothesized predictor and outcome measures were first analyzed by Pearson's product moment correlations. A linear regression was then used to predict participants' intentions, and a logistic regression was conducted to examine predictors of vaccination behavior. Mediation effects were tested using a bootstrapping procedure for multiple mediator models described by Preacher and Hayes (2008) and using the macros for both linear and dichotomous variables available from their website (http://www.quantpsy.org). The 95% bias-corrected confidence intervals of the estimates of the indirect effects (for both linear and dichotomous outcome variables) were derived with 5,000 bootstrap resamples, with indirect effects interpreted as statistically significant if the 95% confidence interval did not overlap zero.

Results

Measuring the Impact of the Intervention

Adherence to the planning element of the intervention (i.e., full completion of all three planning elements) was high in the intervention group (95/99: 96%) and zero in the control condition.

Knowledge of Influenza Symptoms and Vaccine Side Effects

McNemar tests indicated significant increases in total symptom knowledge scores in both HAPA and standard leaflet groups between T1 and T2 (HAPA leaflet: from 25.25% to 56.56%, $p < .001$; standard leaflet from 21.56% to 37.25%, $p = .002$). Chi-square tests found no significant differences between groups at T1, but significantly higher knowledge of influenza symptoms in the intervention group at T2 (56.56% vs. 37.25%, $\chi^2 = 7.53$, $df = 1$, $p = .006$). Chi-square tests revealed no statistically significant differences in the description of vaccine side effects between the two groups at T1. There were significant increases in knowledge of vaccine side effects in both HAPA leaflet and standard leaflet groups between T1 and T2 (HAPA leaflet group: from 52.0% to 86.3%, $p < .001$; standard leaflet group from 51.5% to 84.4%, $p < .001$). At Time 2, no significant difference in total knowledge of vaccine side effects was observed between the two groups (86.3% vs. 84.8%, $\chi^2 = .08$; $p = .77$). However, more participants in the comparison group incorrectly identified breathing difficulties or swelling of the face as side effects of vaccination than those in the intervention group at T2 (17% vs. 4%, $\chi^2 = 9.54$; $p = .002$).

Changes in HAPA Variables Following the Intervention

The mean scores of all variables (risk perception, outcome expectancy, self-efficacy, and intentions) increased significantly in both groups between T1 and T2. However, participants in the intervention group showed a greater increase than the comparison group on all variables. ANCOVAs indicated significant differences between the groups at T2 on measures of perceived risk of developing influenza [$F(1, 198) = 26.54$, $p < .001$, $\eta_p^2 = .12$]; perceived severity of influenza [$F(1, 198) = 8.44$, $p = .004$, $\eta_p^2 = .04$]; perceived benefits from influenza vaccination [$F(1, 198) = 14.04$, $p < .001$, $\eta_p^2 = .07$]; perceived self-efficacy in coping with vaccine side effects [$F(1, 198) = 11.80$, $p = .001$, $\eta_p^2 = .05$]; perceived self-efficacy in arranging time and transportation to get vaccinated scores [$F(1, 198) = 27.0$, $p < .001$, $\eta_p^2 = .12$]; and intention scores [$F(1, 198) = 33.56$, $p < .001$, $\eta_p^2 = .15$; see Table 1].

Vaccination Behavior

Eighty-nine participants of 99 in the intervention group were vaccinated compared with 86 of 102 in the comparison group. This

Table 1
Mean (SD) for Subscales of Risk Perception, Outcome Expectancies, Self-Efficacy, and Intention to Obtain the Flu Vaccine at Two Time Points (n = 201)

Variables	Total possible score	Group	Time 1 Mean (*SD*)	Time 2 Mean (*SD*)	*p*-value of ANCOVA
Risk perception:					
Risk of developing influenza	35	Comparison	24.51 (3.01)	27.93 (3.63)	<.001
		Intervention	24.09 (3.06)	30.12 (3.33)	
Severity of influenza	40	Comparison	28.51 (3.68)	32.98 (4.56)	.004
		Intervention	28.27 (3.41)	34.59 (4.14)	
Outcome expectancies:					
Perceived benefits from influenza vaccination	28	Comparison	21.25 (3.71)	23.17 (2.93)	<.001
		Intervention	21.13 (3.81)	24.61 (2.97)	
Self-efficacy:					
Coping with vaccine side-effects	12	Comparison	9.78 (2.28)	10.84 (1.50)	.001
		Intervention	9.41 (1.89)	11.36 (1.18)	
Arranging time and transportation	16	Comparison	13.43 (2.75)	14.42 (1.96)	<.001
		Intervention	12.74 (2.58)	15.48 (1.25)	
Intention	10	Comparison	7.34 (1.51)	8.38 (1.36)	<.001
		Intervention	7.21 (1.52)	9.24 (1.20)	

difference was not significant (89.90% vs. 84.31%, respectively; $\chi^2 = 1.39$, $df = 1$, $p = .23$).

Predicting Intentions to Obtain the Flu Vaccine

In order to evaluate the ability of the HAPA model to predict the end-point of the motivational processes (intentions), change scores between T1 and T2 were created for each theoretical predictor variable (risk perception, outcome expectancy, self-efficacy), for all participants. Pearson correlations were then used to identify the association between change in each of the independent variables (and age) and changes in intentions. Changes in risk perceptions, outcome expectancies, and self-efficacy were significantly associated with changes in intentions (see Table 2). To examine whether planning was associated with changes in these mediator variables, a series of t tests was conducted comparing change scores on each variable according to whether or not participants had engaged in planning. These showed planning to be associated with significantly greater changes over time on all the variables (see Table 2).

A linear regression analysis was then conducted including these variables. Together they explained 46% of the variance in intentions (adjusted $R^2 = .46$, $F = 27.823$, $p < .001$). However, only planning ($\beta = 0.17$, $p = .003$), outcome expectancy change ($\beta = 0.40$, $p < .001$), and self-efficacy change in relation to arranging time and transportation, $\beta = 0.31$, $p < .001$) made significant contributions to the final equation (see Table 3). Planning may have contributed to changes in intentions both directly and through its influence on other variables, and in particular self-efficacy in arranging time and transport to vaccination. To test this hypothesis, a test of mediation was conducted using the bootstrap procedure, with intentions as the dependent variable, planning as the independent variable, and self-efficacy in arranging time and transport to vaccination as the mediating variable. As predicted, the direct effect of planning on intentions remained significant ($\beta = 0.483$, $SE = .176$, $t = 2.75$, $p = .006$). However, a significant mediation effect was found (point estimate = .280, 95% bias corrected CI = 0.126–0.510).

Table 3
Prediction of Change in Intentions (n = 201)

Variable	*B*	*SE*	Beta	*t*	*p*
Planning	.52	.17	.17	2.96	.003
Change in:					
Perceived severity of influenza	−.00	.02	−.01	−.15	.878
Outcome expectancy	.15	.02	.40	6.45	<.001
Self-efficacy in coping with vaccine side-effects	.06	.06	.08	1.03	.304
Self-efficacy for arranging time and transportation	.16	.04	.31	3.995	<.001

Note. Adj. $R^2 = .46$, $F = 27.823$, $p < .001$.

Predicting Influenza Vaccination Behavior

A second (logistic) regression, involving all HAPA variables measured at T2 (perceived risk, perceived severity of influenza, outcome expectancies, self-efficacy in coping with vaccine side effects, self-efficacy for arranging time and transportation, intention, and action planning) explored the ability of the HAPA to predict behavioral outcomes. Results summarized in Table 4 showed that overall, the model had an adequate fit to the data; the model yielded a Nagelkerke R^2 of 0.52 and the Hosmer and Lemeshow was not significant ($\chi^2 = 15.12$, $df = 8$, $p = .07$). The results revealed a strong association between vaccination outcome and intention (odds ratio = 3.89, $p < .001$) and a smaller, but still significant, association with self-efficacy for arranging time and transportation (odds ratio = 1.70, $p = .016$). No independent association between planning and vaccination was found. Mediation analysis indicated that self-efficacy for arranging time and

Table 2
Pearson's Correlation Matrix of Change Scores of Social-Cognitive Variables and Between Group T-Tests of Mean Differences According to Use of Planning

Variables	1	2	3	4	5	6	7
Age	1.00	.03	.11	−.04	.07	.10	.13
Changes in:							
Perceived risk of developing influenza	.03	1.00	.49**	.34**	.23**	.16*	.29**
Perceived severity of influenza	.11	.49**	1.00	.35**	.21**	.27**	.32**
Outcome expectancies	−.04	.34**	.35**	1.00	.43**	.33**	.54**
Self-efficacy in coping with vaccine side-effects	.07	.23**	.21**	.43**	1.00	.66**	.49**
Self-efficacy for arranging time and transportation	.100	.16*	.27**	.33**	.66**	1.00	.54**
Intention	.13	.29**	.32**	.54**	.49**	.54**	1.00

	Mean (*SD*) change T1-T2			
	No plan	Plan	*t*	*p*
Perceived risk of developing influenza	1.06 (1.45)	2.05 (1.37)	4.98	<0.001
Perceived severity of influenza	4.48 (4.9)	6.37 (4.35)	2.88	<0.01
Outcome expectancies	2.03 (3.99)	3.41 (3.83)	2.48	0.014
Self-efficacy in coping with vaccine side-effects	1.10 (2.31)	2.24 (1.76)	3.896	<0.001
Self-efficacy for arranging time and transportation	1.00 (2.96)	2.81 (2.45)	4.69	<0.001
Intention	1.06 (1.45)	2.05 (1.37)	4.98	<0.001

* $p = .05$ (two-tailed). ** $p = .01$ (two-tailed).

Table 4
Summary of Logistic Regression Analysis Predicting Actual Vaccination Behavior at Time 2 (n = 201)

Predictor variable	*B*	*SE*	Wald statistic	*p* value	Odds ratio (95% CI)
Perceived risk of influenza	.13	.11	1.62	.203	1.14 (.93–1.39)
Perceived severity of influenza	−.07	.10	.58	.445	.93 (.77–1.12)
Outcome expectancies	−.08	.12	.51	.477	.92 (.72–1.16)
Self-efficacy in coping with vaccine side-effects	.06	.32	.031	.860	1.06 (.57–1.95)
Self-efficacy for arranging time and transportation	.53	.22	5.80	.016	1.70 (1.10–2.62)
Intention	1.36	.35	14.96	<.001	3.89 (1.96–7.76)
Planning	−.94	.65	2.08	.149	.39 (.11–1.40)

transportation to receive the flu vaccination acted as mediator between intentions and vaccination (point estimate = .35, 95% bias corrected CI = 0.077 to 0.629), although the mediation effect was only partial, with intention also still having a strong direct effect on vaccination behavior (β = 1.31, *SE* = .343, Wald = 14.53, $p < .001$).

Discussion

This randomized-controlled study had two objectives: (1) to examine whether an intervention based on the HAPA model would be more effective in changing flu vaccination uptake and related intentions than a standard, atheoretical intervention among high-risk Thai adults; and (2) to test the utility of the HAPA in predicting both intention and subsequent vaccination behavior. In relation to the first objective, the intervention showed significant postintervention differences between the intervention groups on key mediator variables such as knowledge, risk perception, self-efficacy, outcome expectancies, and intention to obtain influenza vaccination. Accordingly, the leaflet achieved its first goal; to increase the strength of intentions to seek flu vaccination relative to a standard intervention. Unfortunately, its second goal, to translate these motivational differences into behavioral differences was not achieved. Between-conditions vaccination rates did not differ.

These findings are consistent with previous studies that have demonstrated the effectiveness of targeted messages in changing beliefs related to severity of influenza, vaccine safety and its effectiveness, self efficacy, and response efficacy among high-risk groups (LaVela, Cameron, Priebe, & Weaver, 2008; Wray et al., 2009). The fact that changes in key HAPA variables of outcome expectancies and self-efficacy were independently associated with changes in strength of intentions suggests that these variables are both susceptible to change following relatively brief and simple interventions and have a critical role in shaping intentions.

In contrast to the findings in relation to intentions, this study was unable to show a significant effect of the HAPA leaflet on influenza vaccination behavior. A number of factors may have attenuated the effects of our intervention on influenza vaccination rates. First, the vaccination rates were unprecedentedly high even in the standard intervention condition, making gains in vaccination rates particularly difficult to achieve. Previous vaccination rates were as low as 38% (P. Sriwongpan, personal communication, March 6, 2009) in the previous year in comparison to the 84% found in the standard condition of the study. Clearly, factors other than the planned interventions may have affected these rates. The most obvious confounding factor was that the vaccination period coincided with a global outbreak of H1N1 influenza. Although the standard flu vaccination did not immunize against this disease (information given in the leaflet), the high levels of awareness and concern related to this outbreak may have led to the spontaneous and relatively unplanned behaviors (in this case, vaccination) that can be triggered by high-risk situations (Gollwitzer & Brandstatter, 1997). Evidence in support of this hypothesis can be found in two recent studies conducted in Hong Kong that found beliefs that "influenza vaccine was efficacious in preventing bird-to-human avian influenza transmission," and that "there is a need to receive influenza vaccination following the Severe Acute Respiratory Syndrome (SARS) and avian influenza" were strongly associated with influenza vaccination uptake (Lau, Kim, Tsui, & Griffiths, 2008; Lau, Lau, & Lau, 2009).

A second explanation for the lack of behavioral impact of our intervention may involve confounding as a result of all participants, regardless of condition, receiving an appointment letter from the public health staff, detailing when and where they could get the influenza vaccination. Participants had to take this letter to the clinic in order to identify themselves as in a "high-risk group" and to receive a free vaccine at the hospital. This may have triggered some goal planning among participants in the comparison condition. A third possible explanation for the lack of difference between the groups is that all participants in this study had relatively strong intentions to obtain the flu vaccine, and were being asked to engage in a relatively simple behavior. In this context, it is possible that action planning added little to the likelihood of them taking up the flu vaccine (see, e.g., Pestwich et al., 2008; Sheeran & Orbell, 1999; Sheeran & Orbell, 2000; Sniehotta et al., 2007): although as noted below, planning may have influenced levels of intention to obtain vaccination.

Despite these potential confounds, a 5% difference in vaccination rates between the HAPA and standard leaflet groups was found. While this was not significant, if this finding were to generalize to a wider population, then the HAPA leaflet could result in significantly more people seeking vaccination despite this behavioral prompt. This conclusion is clearly speculative, and requires further large scale research to verify. However, given the potential no cost benefit of using a HAPA-based leaflet, this would seem the leaflet of choice, even before more definitive data are obtained.

In relation to the second objective (to evaluate theoretical links proposed by the HAPA), changes in risk perceptions, outcome expectancies, and self-efficacy (as well as planning) accounted for 46% of the variance in the change in intentions. This is comparable with previous research using the HAPA model in other health behaviors, which have found that the model to explain between 30

and 69% of the variance in intentions (Chow & Mullan, 2010; Garcia & Mann, 2003; Luszczynska & Schwarzer, 2003; Schwarzer & Renner, 2000; Sniehotta, Scholz, & Schwarzer, 2005). The present results provide further support for the HAPA model, suggesting an important role for outcome expectancies and self-efficacy in the formation of intentions (e.g., Chow & Mullan, 2010; Garcia & Mann, 2003; Schwarzer & Luszczynska, 2008). In contrast, neither the change in perceived risk nor the change in perceived severity of influenza was associated with change in intention to get vaccinated against the flu. The finding that risk perception was not a significant predictor of vaccination intention is consistent with the HAPA model (e.g., Luszczynska & Schwarzer, 2003; Schwarzer & Renner, 2000), which states that risk perception is a relatively weak predictor of behavior, as its key role is to initiate deliberation about the need to change, with other the variables becoming more important subsequently (e.g., Schwarzer, 2001; Weinstein, 2000). Of note also is that while the HAPA considers planning to be a driver of behavior, it may also influence intentions, both directly and indirectly: thinking through and planning how to make time and travel to the vaccination appeared to increase participants' confidence in their ability to do so. This, in turn, increased the strength of their intentions to obtain the vaccination.

Influenza vaccination was predicted by intentions to obtain vaccination, and to a lesser extent by self-efficacy in arranging time and transport to access the vaccine (93% of participants were correctly classified into vaccinated and nonvaccinated groups). This finding is consistent with previous studies and provides support for the proposed links in the HAPA model in that intention and self-efficacy appear to be key factors influencing on behavioral change (e.g., Scholz, Keller, & Perren, 2009; Schwarzer & Renner, 2000). Having said this, despite there being significant between group differences in strength of intention to obtain vaccination, there were no differences in actual vaccination rates between them. This may be attributable to one or more of the factors discussed above. An alternative explanation is that there may be a threshold of intention above which higher levels of intention add little to the likelihood of engagement in a particular behavior. Thus, it is possible that both groups were sufficiently motivated to seek vaccination, and differences in relatively high intention scores had only a marginal impact on behavior.

Contrary to our expectations, action planning did not contribute to the prediction of influenza vaccination uptake. This finding is not consistent with the previous studies applying the HAPA model that have repeatedly reported that action planning was a good predictor of behavior change (e.g., Luszczynska & Schwarzer, 2003; Schwarzer et al., 2008; Sniehotta et al., 2005). However, behavior is governed either by intentions or by the perceived and actual environment (Schwarzer, 2009). In this study, as discussed above, it is possible that influenza vaccination was influenced by the external conditions such as the outbreak of H1N1 influenza during the vaccination period. This may have attenuated the effect of action planning on predicting vaccination behavior. To further elucidate these findings, larger studies need to be performed in different settings with different samples and different behaviors.

The strengths of this study include its controlled design, and the application of theoretical framework. However, potential limitations need to be addressed. The outcome assessors were not fully blinded to treatment group during follow-up assessment. This could have introduced bias to the results: although the researchers were blind until they addressed whether or not participants had completed the planning process. Although a few questionnaires were read out loud to participants with limited literacy by a trained researcher, these participants were asked to score their own responses, without direct input from the assessors. Another limitation is that the study was conducted in two urban communities. The findings of this study may not be generalizable to high-risk people living in suburban and rural communities. However, this controlled before and after study showed that our intervention was feasible and acceptable in promoting influenza vaccination to high-risk people with chronic medical conditions. Accordingly, it can be implemented in other settings. Finally, the study was underpowered to detect the relatively small differences in vaccination rates eventually found. Larger studies would be needed to verify the possibility of significant differences in vaccination rates as a consequence of the HAPA intervention.

Conclusion

The study demonstrated the effectiveness of a theory-based educational leaflet and action planning intervention in enhancing intention to be immunized against the flu among high-risk Thai adults. However, no significant difference in vaccination rates between the two conditions was found. Further, larger, trials should test whether action planning works can increase influenza vaccination rates among high-risk people, as well as its efficacy in enhancing the likelihood of performing other behaviors. Additionally, the results highlight that the HAPA is a useful model in predicting intentions to obtain the flu vaccine and subsequent influenza vaccination behavior. Self-efficacy and intention were found to be a significant predictor of influenza vaccination behavior. The findings provide valuable information to public health/health promotion professionals to allow modification and improve the content of influenza leaflet that are currently available for the high-risk people, as well as designing other effective interventions to achieve a greater impact in increasing vaccination rates of high-risk people with chronic diseases.

References

Abraham, C., & Michie, S. (2008). A taxonomy of behaviour change techniques used in interventions. *Health Psychology, 27,* 379–387.

Burns, V. E., Ring, C., & Carroll, D. (2005). Factors influencing influenza vaccination uptake in an elderly, community-based sample. *Vaccine, 23,* 3604–3608.

Chow, S., & Mullan, B. (2010). Predicting food hygiene: An investigation of social factors and past behaviour in an extended model of the Health Action Process Approach. *Appetite, 54,* 126–133.

Evan, M. R., Prout, H., Prior, L., Tapper-Jones, L. M., & Butler, C. C. (2007). A qualitative study of lay beliefs about influenza immunisation in older people. *British Journal of General Practice, 57,* 352–358.

Fishbein, M., & Yzer, M. C. (2003). Using theory to design effective health behaviour interventions. *Communication Theory, 13,* 164–183.

Fleiss, J. L., Levin, B., & Paik, M. C. (2003). *Statistical methods for rates and proportions* (3rd ed.). New York: Wiley and Sons.

Garcia, K., & Mann, T. (2003). From "I wish" to "I will": Social-cognitive predictors of behavioural intentions. *Journal of Health Psychology, 8,* 347–360.

Gollwitzer, P. M. (1999). Implementation intentions: Strong effects of simple plans. *American Psychologist, 54,* 493–503.

Gollwitzer, P. M., & Brandstatter, V. (1997). Implementation intentions and effective goal pursuit. *Journal of Personality and Social Psychology, 73,* 186–199.

Gollwitzer, P. M., & Sheeran, P. (2006). Implementation intentions and goal achievement: A meta-analysis of effects and processes. *Advances in Experimental Social Psychology, 38,* 69–119.

Lau, J. T. F., Kim, J. H., Tsui, H. Y., & Griffiths, S. (2008). Perceptions related to bird-to-human avian influenza, influenza vaccination, and use of face mask. *Infection, 36,* 434–443.

Lau, L., Lau, Y., & Lau, Y. H. (2009). Prevalence and correlates of influenza vaccination among non-institutionalised elderly people: An exploratory cross-sectional survey. *International Journal of Nursing Studies, 46,* 768–777.

LaVela, S. L., Cameron, K. A., Priebe, M., & Weaver, F. M. (2008). Development and testing of a vaccination message targeted to persons with spinal cord injuries and disorders. *Journal of Spinal Cord Medicine, 31,* 44–52.

Luszczynska, A., & Schwarzer, R. (2003). Planning and self-efficacy in the adoption and maintenance of breast self-examination: A longitudinal study on self-regulatory cognitions. *Psychology and Health, 18,* 93–108.

Ministry of Public Health. (2008). *Promoting influenza vaccination in high-risk elderly Thai people.* Retrieved from http:// www.moph.go.th

Ministry of Public Health. (2009). *Situations, policy, strategy, and guideline for prevention and control of pandemic influenza (H1N1) 2009.* Retrieved from http://beid.ddc.moph.go.th/eng/images/stories/Newpercent202010/3percent 20Situation_strategy30percent20Decpercent2009.pdf

Murgraff, V., McDermott, M. R., & Walsh, J. (2003). Self-efficacy and behavioural enactment: The application of Schwarzer's Health Action Process Approach to the prediction of low-risk, single-occasion drinking. *Journal of Applied Social Psychology, 33,* 339–361.

National Statistical Office. (2006). *Thailand multiple indicator cluster survey: Chiang Rai province.* Bangkok: Ministry of Information and Communication Technology.

Pestwich, A., Ayres, K., & Lawton, R. (2008). Crossing two types of implementation intentions with a protection motivation intervention of the reduction of saturated fat intake: A randomized trial. *Social Science and Medicine, 67,* 1550–1558.

Preacher, K. J., & Hayes, A. F. (2008). Asymptotic and re-sampling strategies for assessing and comparing indirect effects in multiple mediator models. *Behaviour Research Methods, 40,* 879–891.

Ruiter, R. A. C., Abraham, C., & Kok, G. (2001). Scary warnings and rational precautions: A review of the psychology of fear appeals. *Psychology and Health, 16,* 613–630.

Scholz, U., Keller, R., & Perren, S. (2009). Predicting behavioural intentions and physical exercise: A test of the Health Action Process Approach at the intrapersonal level. *Health Psychology, 28,* 702–708.

Schwarzer, R. (2001). Social-cognitive factors in changing health-related behaviours. *Current Directions in Psychology Science, 10,* 47–51.

Schwarzer, R. (2009). *HAPA model.* Retrieved from http://www.hapa-model.de/

Schwarzer, R., & Luszczynska, A. (2008). How to overcome health-compromising behaviors: The Health Action Process Approach. *European Psychologist, 13,* 141–151.

Schwarzer, R., Luszczynska, A., Ziegelmann, J. P., Scholz, U., & Lippke, S. (2008). Social-cognitive predictors of physical exercise adherence: Three longitudinal studies in rehabilitation. *Health Psychology, 27,* S54–S63.

Schwarzer, R., & Renner, B. (2000). Social-cognitive predictors of health behaviour: Action self-efficacy and coping self-efficacy. *Health Psychology, 19,* 487–495.

Sheeran, P., & Orbell, S. (1999). Implementation intentions and repeated behaviour: Augmenting the predictive validity of the theory of planned behaviour. *European Journal of Social Psychology, 29,* 349–369.

Sheeran, P., & Orbell, S. (2000). Using implementation intentions to increase attendance for cervical cancer screening. *Health Psychology, 19,* 283–289.

Sniehotta, F. F., Scholz, U., & Schwarzer, R. (2005). Bridging the intention-behaviour gap: Planning, self-efficacy, and action control in the adoption and maintenance of physical exercise. *Psychology and Health, 20,* 143–160.

Sniehotta, F. F., Soares, V. A., & Dombrowski, S. U. (2007). Randomized controlled trial of a one-minute intervention changing oral self-care behaviour. *Journal of Dental Research, 86.* 641–645.

Weinstein, N. D. (2000). Perceived probability, perceived severity, and health-protective behaviour. *Health Psychology, 19,* 65–74.

World Health Organization. (2003). *Influenza, fact sheet N°211 evised March 2003.* Retrieved from http://www.who.int/mediacentre/factsheets/2003/fs211/en/

Wray, R. J., Buskirk, T. D., Jupka, K., Lapka, C., Jacobsen, H., & Pakpahan, R. (2009). Influenza vaccination concerns among older blacks: A randomized controlled trial. *American Journal of Preventive Medicine, 36,* 429–434.