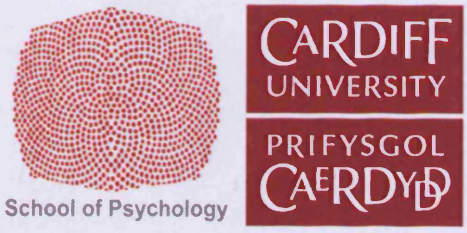
CARDIFF UNIVERSITY

Help seeking behaviour and risk in the context of female fertility

Laura Elizabeth Bunting
BSc (Hons) Psychology
Cardiff University

A thesis submitted
for the degree of Doctor of Philosophy

School of Psychology
Cardiff University
2008



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

I dedicate this thesis to the memory of

Ewaryst Wojcikiewicz

DECLARATION

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

Signed ..... (candidate) Date 09/02/09

STATEMENT 1

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

Signed ..... (candidate) Date 09/02/09

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 ..... (candidate) Date 09/02/09

STATEMENT 3

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 ..... (candidate) Date 09/02/09

STATEMENT 4: PREVIOUSLY APPROVED BAR ON ACCESS

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

Signed ..... (candidate) Date .....

Acknowledgements

My first and foremost thanks go to my supervisor Dr Jacky Boivin. I am indebted to her invaluable advice, support and encouragement throughout the past three years. I have benefited greatly from her wealth of knowledge, enthusiasm for research, and her ability to actively exercise positive reappraisal strategies at all the appropriate times.

Thank you to everyone in the Cardiff fertility lab for listening to talks and ideas and providing me with vital feedback and advice. A special thanks to Laura P for the initial encouragement to apply for the PhD and for continual support throughout. Huge thanks to Natasha for all her assistance, time and effort in getting it all completed.

I would like to thank all the staff involved at the websites and clinics used for data collection. Specifically I thank Mary James and Susan Jose at the Cardiff and Vale Antenatal Clinic, Dr Caroline Scherf and Carolyn Alport at the Cardiff and Vale Sexual and Reproductive Health Unit, Dr Janet Evans at IVF Wales, Hannah Maundrell at askbaby.com, and Hattie Davies at gettingpregnant.co.uk. Thank you for all your time, effort and advice in the development and distribution of the surveys. In addition I thank Laura Brighton and Andrew Thomas for data collection, and last but not least all the participants who have taken the time and effort to complete the studies.

Thank you to Professor John A. Collins for his expert knowledge and help with data analysis for Chapter 2. Further, I am very grateful to all the experts and members of ACT involved in the discussions about the factors associated with female infertility, especially, Professor Karl Nygren for his invaluable knowledge, advice and input into this work.

A special thanks to all the staff involved in the development of the projects. In particular I thank Lorraine Woods and Louise Blackburn for graphic design, Laura Morris, Phillip Fayers, Paul Allen and Emma Wadsworth for web support and enormous assistance with Survey Tracker, and finally Hilmar, Dave, Val, Jeff, Kevin and Andy for endless help with IT and all other work issues.

My final thanks go to my family and friends for their never-ending support and encouragement throughout the past three years. To Suzie, Tom, Rose and Adam, my office buddies, for support, advice, help and endless conversations. To my mum and dad for always listening to me expounding on my many moments of stress and (few) moments of elation. Last but by no means least I thank Lloyd for absolutely everything.

Thesis Summary

Parenthood is a life goal desired by the majority of young people. However, not all couples who desire a pregnancy will achieve one spontaneously and a proportion of couples will need medical help to resolve underlying fertility problems. However previous research has highlighted a lack of fertility awareness in the general population. The aim of the studies to be presented in this thesis was to better understand help seeking behaviour in the context of fertility problems, establish risk factors associated with fertility potential, and identify targets for public health campaigns to improve fertility health related behaviour.

The results from the current set of studies demonstrated that infertility is a prevalent problem in society with around 9% of the adult population affected. Given that parenthood is a desired goal by the majority of adults, it was therefore surprising to find that on average just over 50% of people with fertility problems seek any medical advice or care; with an even smaller number receiving treatments. A key factor associated with fertility self-care and the initiation of treatment (when needed) was knowledge about fertility and the potential for successful treatment because such knowledge helps people take care of their fertility and reduces fear of diagnosis if a problem conceiving arises. Although young people (future parents) know that negative lifestyle factors can reduce fertility, they falsely believe in fertility myths and the power of being healthy.

Finally, the risk factors associated with reduced female fertility potential were established. The majority of these risk factors have the ability to be modified and even prevented and thus offer the opportunity to develop a tool for women to assess their own fertility potential, and take more responsibility and control over their fertility health. Overall, the work presented in this thesis demonstrates that raising public awareness about fertility health issues is key in helping women understand that their current actions can impact on their future life goals and to help those experiencing fertility problems to act in a timely manner to seek the medical advice and help they may require.

Publications

Papers

Chapter 2:

Boivin, J., Bunting, L., Collins, J.A., & Nygren, K. (2007). An international estimate of infertility prevalence and treatment-seeking: Potential need and demand for infertility medical care. *Human Reproduction, 22(6),* 1506-1512: doi:10.1093/humrep/dem046.

Chapter 3:

Bunting, L., & Boivin, J. (2007). Decision-making about seeking medical advice in an internet sample of women trying to get pregnant. *Human Reproduction, 22(6),* 1662-1668: doi:10.1093/humrep/dem057.

Chapter 4:

Bunting, L., & Boivin, J. (2008). Knowledge about infertility risk factors, fertility myths and illusory benefits of healthy habits in young people. *Human Reproduction, 23(8),* 1858-1864: doi: 10.1093/humrep/den168.

Talks

Boivin, J., & Bunting, L. (2006). Decision making about seeking medical advice in a community sample of women trying to get pregnant. In: Program and Abstracts of the 22nd Annual Meeting of the European Society for Human Reproduction and Embryology. June 2006. Prague: *Human Reproduction, 21 (Supplement 1)*, i163.

Bunting, L., & Boivin, J. (2008). Need and demand for fertility treatment and the importance of raising public awareness about fertility health issues. In: Program and Abstracts of the 22nd Annual Conference of the European Health Psychology Society and the 11th Annual Conference of the BPS Division of Health Psychology. September 2008. Bath: *Psychology & Health, 23 (Supplement 1)*, i49.

Posters

Bunting, L., & Boivin, J. (2008). Fertility knowledge in young people; more work needs to be done. In: Program and Abstracts of the 23rd Annual Meeting of the European Society for Human Reproduction and Embryology. July 2008. Barcelona: *Human Reproduction, 23 (Supplement 1)*, i225.

Index of Tables

Table **Page**

Chapter 2

Chapter 3

Index of Tables (*continued*)

Table **Page**

Chapter 4

Chapter 5

Study 5.1

Study 5.2

Index of Figures

Figure **Page**

Chapter 4

Chapter 5

Study 5.2

Glossary of Abbreviations

ASRM.....American Society for Reproductive Medicine

ESHRE.....European Society of Human Reproduction and Embryology

FAFS.....Factors Affecting Fertility Scale

FRFS.....Fertility Risk Factors Survey

HBM.....Health Belief Model

HFEA.....Human Fertilisation and Embryology Authority

IVF.....*in vitro* Fertilisation treatment

NHS.....National Health Service

NICE.....National Institute for Health and Clinical Excellence

ONS.....Office of National Statistics

PID.....Pelvic Inflammatory Disease

STD/I.....Sexually Transmitted Disease/Infection

TDMQ.....Treatment Decision Making Questionnaire

TPB.....Theory of Planned Behaviour

TTM.....Transtheoretical Model of Behaviour Change

WHO.....World Health Organisation

Chapter 1
General Introduction and Thesis Overview

Taking Responsibility for Ones Own Fertility

In 2006 the British Government and Department of Health published a White paper detailing their future strategies and goals for building a world-class national health service (NHS) and social care system (Department of Health, 2006). Critically, the paper focused on how the individual, that is, the potential patient, can be involved in the choices surrounding his or her health. A wider ambition of this approach is to engage people into making healthier choices about all parts of their lives, from their day-to-day lifestyle habits to the decisions they make when faced with illnesses. To better enforce, encourage and maintain these changes the paper further proposed the introduction of a series of 'LifeCheck' tools for people to assess their lifestyle risks and to take the right steps to make healthier choices.

The NHS Choices is a website containing online assessment tools for people to complete providing them with their personalised risk of certain illnesses (e.g., diabetes) and more generally issues regarding their current health and lifestyles habits (e.g., diet, exercise). As well as providing people with a personalised assessment, the tools offer advice and support about how risks can be reduced (e.g., reduction in smoking) and how these changes can be maintained (e.g., local support groups, free prescriptions for nicotine replacement treatment).

Thus, the future of the health care system in the United Kingdom appears to centre on personalising and empowering people to take charge of their own health and well-being. Through this more personalised approach the ultimate aim of these strategies is to provide better prevention (e.g., reduction in smoking reduces risk of

smoking related illness) and earlier intervention services (e.g., getting people to realise when, and how to, seek help; Department of Health, 2006). Such a strategy is supported by the World Health Organisation (WHO, 2002), who proposed that the most effective way of preventing diseases from occurring in the first place is the systematic assessment of the factors that cause the disease (i.e., what are the risk factors for disease A) and the implementation of effective strategies for the reduction of these causes.

All the NHS Choices tools aim to assess important and current health issues, such as, diabetes, obesity, cancer. The Choices website does cover a few issues with regard to fertility. Namely, issues surrounding trying to get pregnant (e.g., timing of sexual intercourse to maximise conception), when conception does not occur (e.g., what tests will the doctor do) and issues surrounding pregnancy (e.g., confirming a pregnancy, preparing for labour). As yet however, the information provided is very general and not personalised like the tools associated with risk of diabetes or cancer.

In accordance with current Government policies for the future of health care, that is, empowering people to take charge of their own health this thesis will explore these issues with regard to fertility health, namely the choices and motivations surrounding individuals when fertility difficulties occur. Further, it will establish the factors associated with a detrimental impact on fertility that could potentially be addressed in effective interventions (e.g., personalised risk assessment of fertility difficulties) targeting men and women who wish to become parents now (or in the future), with the aim of preventing (i.e., reduce risk) and intervening (i.e., guidance of when to seek help) to help couples achieve their parenting goals. Current research suggests that fertility issues are indeed an important health area worthy of further

investigation and the following sections present an overview of the issues examined in the present thesis.

Need and Demand for Fertility Medical Services (Chapter 2)

Parenthood is a desired goal by the majority. A number of studies have revealed that around 95% of young women and men surveyed stated that they intended to have children in the future (Kemkes-Grottenthaler, 2003; Lampic, Svanberg, Karlström, & Tydén, 2006; Skoog Svanberg, Lampic, Karlstöm, & Tydén, 2006). Most societies around the world are pro-natalist, whereby the experience of parenthood is central to individual and group identity and the life plan of most people within the community (Whiteford & Gonzalez, 1995). This is further supported by the low prevalence of men and women who remain voluntarily childless when assessed at their end of their reproductive lives, less than 5% (Chancey, 2006). Indeed childlessness can be a discrediting attribute for both those childless by choice and by chance (Lampman & Downing-Guyer, 1995). Therefore any factor that may impact on achieving the goal of parenting applies to the vast majority of people.

Not everyone who tries to get pregnant will be successful in their natural attempts and in order to better help people achieve parenting goals one needs to know both prevalence of fertility problems and demand for fertility medical services. It is estimated that the average conception rate per month is about 30% (Zinaman, Clegg, Brown, O'Connor, & Selevan, 1996; Gnoth, Godehardt, Godehardt, Frank-Herrmann, & Freundl, 2003), with a cumulative conception rate of around 75% after six months and 90% after one year (A. Taylor, 2003). Consequently, around 10% of couples that have regular unprotected sexual intercourse for 12 months will not achieve a pregnancy and these couples are considered infertile (National Institute for Health and

Clinical Excellence, NICE, 2004). The prevalence of infertility has been estimated in many national surveys (e.g., in Denmark: Schmidt, Münster, & Helm, 1995; United Kingdom: Buckett & Bentick, 1997; China: Che & Cleland, 2002) but worldwide comparisons have not yet been carried out and the full extent of this problem is not fully known. Therefore the first aim of Chapter 2 was to assess the number of couples affected by infertility in more and less developed nations by conducting a comprehensive literature review of population based surveys. Establishing such information will gauge the extent of the problem.

Treatment provides infertile couples with the chance of achieving their parenthood goal, yet demand for fertility treatment has not adequately been assessed. Assisted reproductive technology (ART) began to develop during the 1970's (Hammond & Stillman, 1999) culminating in the birth of Louise Brown in 1978 conceived with in vitro fertilization (IVF, Steptoe & Edwards, 1978). IVF involves the fertilisation of an egg outside of the woman's body, i.e., 'fertilisation in glass' (HFEA, 2007/2008) by means of a series of pharmacologic (i.e., hormonal) and physical interventions. Treatments such as IVF have been shown to have good success rates, with the majority of couples (69.4%) who initiate treatment achieving their goal of parenthood with about 3.7 treatments within five years (Pinborg, Schmidt & Nyboe Andersen, 2007). Further, in the United Kingdom alone, the Human Fertilisation and Embryology Authority (HFEA) estimate that one baby in every 80 is born as a result of IVF treatment (The HFEA guide to infertility, 2007/2008). This data clearly demonstrates that treatment can enable people to realise a major life goal when natural attempts to conceive have failed. There are a number of studies that have reported the demand for fertility medical services, but as yet there has been no comprehensive review of these studies, assessing whether people faced with a fertility difficulty seek

and receive medical help, therefore a second aim of Chapter 2 was to assess the demand for fertility medical services using available worldwide data.

Factors Influencing the Decision to Seek Medical Advice for Fertility Problems (Chapter 3)

When faced with any illness or health related issue people are faced with a number of choices surrounding how to effectively (or ineffectively) deal with the situation. For example, the detection of a new lump in the breast or testicle may be dealt with in a number of ways. The person may ignore the lump, they may monitor the lump to see if it goes away or increases in size, or the person may immediately seek medical advice as to what the lump is. Any one of these decisions will have required people to think about the lump and make a decision about what to do (or what not to do). Depending on the diagnosis of the lump, these decisions can have major implications on the outcome. If the lump is cancerous, the person who ignored the lump or delayed seeking treatment will have risked due to inaction greater disease progression than those seeking more timely advice. Indeed, a delay of three months or more between the time when a lump in the breast is detected and the initial medical consultation has been found to decrease the potential for breast cancer survival (Facione, 1993; Richards, Westcombe, Love, Littlejohns, & Ramirez, 1999).

An extensive amount of literature has focused on the decision making processes when people are faced with the detection of a new lump and has identified factors that can facilitate or hinder seeking timely medical advice (Facione, 1993; Oliveria, Christos, Halpern, Fine, Barnhill & Berwick, 1999; Carney, Fitzsimons, & Dempster, 2002; Grunfeld, Ramirez, Hunter, & Richards, 2002; Bish, Ramirez, Burgess & Hunter, 2005; Smith, Pope, & Botha, 2005; Facione & Facione, 2006). These factors may also be important to couples faced with an inability to conceive.

The aim of Chapter 3 was to establish the critical factors associated with the initiation of fertility treatment when a fertility problem occurs. In Chapter 3 the empirical and theoretical literature on decision making about fertility difficulties was reviewed and a cross-sectional study was conducted to assess the decision making strategies of women who were currently trying to conceive, some of which had already sought medical advice or treatment about a potential fertility problem. A better understanding of these factors may help to facilitate effective advice and guidance to enable people to receive the medical help they may require and reduce unnecessary delay, to further aid them in their goals of becoming a parent.

Knowledge of Fertility Risk Factors in Young People (Chapter 4)

Current research suggests people are not behaving optimally when it comes to factors that impact on fertility potential. For example, there has been a steady increase in the age at first pregnancy in Western societies. In the UK, the proportion of babies with mothers aged 35 years or more increased markedly from 6.5% in 1976 to 22.5% in 2000 (Bakeo, 2004) and in the US this rate has more than doubled since 1978 (Hamilton, Martin, & Sutton, 2004). This is alarming considering female fertility rapidly declines after the age of 35 (Menken, Trussell, & Larsen, 1986; Dunson, Colombo, & Baird, 2004), with women aged 35-39 years having half the chance of conceiving compared to women aged 19 – 26 years (A. Taylor, 2003). Further, a number of negative lifestyle factors are on the rise in more and less developed countries (e.g., obesity, sexually transmitted diseases/infections [STD/STI]), all of which have been negatively associated with female fertility potential. These figures are made all the more alarming when one considers that many of these factors are preventable and modifiable.

It may well be that people are unaware of the factors detrimental to their fertility since fertility is not yet part of the mainstream public health issues. A number of studies have highlighted a lack of general understanding of fertility health issues. For example, participants have been found to have a poor understanding of the biology of reproduction (e.g., when ovulation occurs, Lampic et al., 2006; World Fertility Awareness Month, 2006), a general lack of understanding about infertility, such as a definition and its prevalence within the general population (Blake, Smith, Bargiacchi, France, & Gudex, 1997; Adashi et al., 2000), and a lack of awareness about risk factors associated with a detrimental impact on fertility potential (e.g., older age, Lansac, 1995; Lampic et al., 2006; Skoog Svanberg et al., 2006). The aim of Chapter 4 was to assess knowledge of factors associated with female fertility in young women and men. To assess knowledge about fertility health issues participants were asked to rate the impact that known risk factors (e.g., smoking, alcohol consumption), known myths (e.g., adopting a child) and healthy habits (e.g., being of normal weight) would have on the chances of 100 women getting pregnant.

Foundational Research for a Personalised Fertility Status Tool (Chapter 5)

Past research has shown that even if people are aware of risk factors, they may not apply them to their own situation and therefore may not feel at risk, even when they are. For example, research suggests that most people are aware of the detrimental effect of smoking (Hay, Shuk, Cruz, & Ostroff, 2005), yet nearly 30% of British women still smoke (Goddard, 2006). Indeed what underpins the NHS Choices is the fact that it provides people with a personalised score, enabling them to assess their own risk with regard to specific illnesses. Research suggests that personalising risk may be a more effective way of enabling behaviour change (Fischhoff, Bostrom, & Quadrel, 1993; Elton, Ryman, Hammer, & Page, 1994; NHS centre for reviews and

dissemination, 1998; Strychar, Champagne, Ghadirian, Bonin, Jenicek, & Lasater, 1998; McClure, 2002). Therefore what may be important in helping people understand and realise the factors associated with reduced fertility potential is to develop a tool that assesses an individual's risk of fertility impairment. Consequently, the aim of Chapter 5 was to generate foundational research to develop a fertility assessment tool. The implications surrounding raising awareness about health issues and the development of a personalised risk assessment tool were explored. Study 5.1 reviewed the current literature on factors associated with female infertility and Study 5.2 examined whether these factors could differentiate between pregnant and non-pregnant women.

General Discussion and Conclusions (Chapter 6)

The chapter will focus on the overall aims of the thesis, presenting the main findings for the studies conducted. Further, the clinical implications of such findings and future research goals will be discussed.

Chapter 2
Prevalence of infertility and demand for infertility medical care

Introduction

Most adults have life plans that include children. In a large survey (n = 2057) carried out in Sweden, 95 % of childless women and men aged 23-25 years stated that they wanted to have children in the future (Lampic et al., 2006), with most considering it to be a major life goal to fulfil (Tyden, Svanberg, Karlstrom, Lihoff, & Lampic, 2006; Virtala, Kunttu, Huttunen, & Virjo, 2006). However, not all couples that desire a pregnancy will achieve one spontaneously and for a proportion of couples medical help will be needed to resolve underlying fertility problems. Despite a strong desire for children in the population there is evidence to show that couples do not necessarily seek medical help when experiencing fertility difficulties for various reasons (e.g., psychological, socio-demographic: Schmidt et al., 1995; Wulff, Hogberg, & Stenlund, 1997; Langdridge, Connolly, & Sheeran, 2000; Stephen & Chandra, 1998, 2000; Wyshak, 2001) but as the data on the prevalence of infertility and the use of fertility medical services is as yet not reviewed it is difficult to ascertain to what extent low treatment seeking behaviour is a problem that warrants further psychological investigation.

Infertility has been recognised as a public health issue worldwide by the World Health Organisation (WHO) and in his opening lecture of a WHO international meeting Dr Mahmoud Fathalla focused on accessibility as a key millennium challenge for those involved in the delivery of infertility treatment and assisted reproduction (see Vayena, Rowe, & Griffin, 2001). In order to set up adequate fertility services (both medical and psychological) to meet this challenge one must know both the potential need and demand for medical services. In this chapter the existing literature

will be reviewed to assess the potential need for infertility medical care as indicated by the prevalence of infertility in world populations and ascertain the actual proportion of couples that seek and/or receive medical care for fertility difficulties.

Definition of Fertility and Infertility

There are two ways of looking at reproduction, one that focuses on the capacity to have children (e.g., fertility, fecundity) and one on the incapacity (e.g., infertility, subfertility, childlessness). The current chapter will focus on the latter. Infertility is broadly defined as a delay in conception for a given period of time and has been a major medical and social preoccupation (Morice, Josset, Chapron, & Dubuisson, 1995). Research often categorises infertility into primary and secondary. Primary infertility refers to the non-achievement of any conception whether it results in a live birth or not, whereas secondary infertility is the non-achievement of a subsequent pregnancy or live birth (Schmidt & Münster, 1995). Subfecundity describes any form of reduced fertility (Gnoth, Godehardt, Frank-Herrmann, Friol, Tigges & Freundl, 2005), for example, a reduced probability of conception, or difficulties carrying a pregnancy to term (Nguyen & Wilcox, 2005). Finally, childlessness refers to whether a woman has ever had a child in a given period of marriage (Larsen, 2005).

Definition of Prevalence

According to the World Health Organisation (WHO, Global InfoBase from http://www.who.int/infobase, retrieved February 28, 2008) the prevalence of a disease/risk factor is defined as the ratio of the number of cases of a disease/risk factor present and the number of individuals in the population at a designated time. With regards to infertility prevalence it is often distinguished by current or lifetime

occurrence. Current prevalence is measured as the individual experiencing the disorder at the present time while lifetime prevalence is the probability that an individual will have had the disease/risk factor at some point in their life (up to the time of assessment) (Last, 1995).

Issues Surrounding the Use of Different Definitions

In order to determine the need for infertility treatment it is essential to know the prevalence of infertility within the population (Larsen, 2005). However there are a number of methodological issues that need to be taken into consideration when reviewing population studies that may impact on the prevalence ratings reported.

Defining infertility.

Within the reproductive health literature infertility is frequently defined in a number of varying ways. Infertility can cover disorders ranging from sterility to (nearly) normal fertility and is often used synonymously with other terms such as subfertility, which may lead to misinterpretation, errors in communication and confusion (Habbema, Collins, Leriodn, Evers, Lunenfeld, & te Velde, 2004). For example, Marchbanks, Peterson, Rubin, and Wingo (1989) found that the definition of infertility can influence research findings associated with the age at infertility classification, which women are classified as infertile, the number of women classified as infertile, and the probability of future conception. In an attempt to overcome these issues the generally agreed definition refers to infertility as an inability to conceive (American Society for Reproductive Medicine: ASRM, 2006; National Institute for Clinical Excellence: NICE, 2004). The WHO further clarifies infertility as the inability to achieve a spontaneous pregnancy (Rowe, Comhaire, Hargreave, & Mellows, 1993).

Exposure time.

Exposure refers to the time period during which the woman has been exposed to unprotected regular sexual intercourse, that is, the time interval when conception was theoretically possible. Historically the exposure times most frequently used in research establishing the prevalence of infertility have been 12 and 24 months (Habbema et al., 2004). Overall there is an 84% conception rate following 12 months unprotected intercourse (te Velde, Eijkemans, & Habbema, 2000), and 95% after 24 months of exposure (Joffe, Villard, Plowman, & Vessey, 1995). The discrepancy in intervals occurs because in clinical practice a 12 month interval is used due to the desirability of initiating fertility treatment as soon as infertility is suspected to avoid decrements in fertility due to disease progression or increasing age (Larsen, 2005). However, in theory many have argued to use a threshold of 12 months may be too soon to intervene medically if the success rates of achieving a pregnancy and the probability of future success is still considerably high, as shown by further increases in fertility for those exposed for 24 months (te Velde et al., 2000; Habbema et al., 2004; Larsen, 2005).

Thus in epidemiological research it is important to reduce the number of false positives by allowing more time for fertile people to conceive (using the definition of a failure to conceive after 24 months of unprotected intercourse) (Habbema et al., 2004; Larsen, 2005). Using different exposure times does impact on the prevalence reported; with the 24 months exposure showing lower prevalence rates (due to the larger denominator; Schmidt & Münster, 1995). While there is no clear distinction between which exposure time (12 or 24 months) is more appropriate for the definition of infertility, according to the current guidelines in the United Kingdom (NICE, 2004)

and the United States (ASRM, 2006) infertility is defined as inability to conceive after 1 year of regular unprotected intercourse.

In addition to the discrepancy in the use of different exposure intervals, studies also use different time frames when reporting prevalence. For example one may look at the prevalence of current infertility/subfecundity ("Are you now experiencing a delay in conception/difficulty carrying a child?", Larsen, 2005), while others may report cumulative or lifetime infertility/subfecundity ("Have you ever experienced a delay in conception/carrying a child?", Larsen, 2005). Finally, some may report a period of childlessness after marriage ("After being married for [specified number] years do you have a child?", Larsen, 2005). The use of different points in time will impact on the prevalence rate reported, with lifetime childlessness reporting higher rates when compared to current (Schmidt & Münster, 1995), and must be taken into account when interpreting the rates drawn from the present review of the literature.

Demand for Fertility Services

Couples can follow several pathways once they suspect they have a fertility problem. They could do nothing; they could seek medical advice (e.g., general practitioner, gynaecologist) and, depending on the outcome of this consultation, they could go on to seek fertility treatment. They could also seek non-medical pathways for example adoption. It is also possible that couples will seek medical advice and decide against undergoing fertility treatment. For example, dropout in the early phase of diagnosis, before the start of fertility treatment can be as high as 40% (Gleicher, Vanderlaan, Karande, Morris, Nadherney, & Prat, 1996; Malcolm & Cummings, 2004). In addition, couples may be unable to access the fertility services they require. For example, in sub-Saharan Africa formal public health care provides very limited

treatment options and private health care is often too expensive for couples experiencing problems conceiving (Sundby, Mboge, & Sonko, 1998; Barden-O'Fallon, 2005; Dyer, 2008).

Fertility treatment encompasses a broad range of services that could range from medical advice about sexual relations to state-of-the-art assisted reproductive technologies and establishing the need for fertility medical services depends to some extent on the definition used for 'infertility medical services'. There are practice guidelines for couples contacting medical General Practitioners (GPs) about suspected fertility treatment and these provide a more or less standard approach. For example, the NICE (2004) clinical guidance indicates that couples should first undergo a thorough medical history (including lifestyle habits and general health), followed by a series of diagnostic tests and then specific treatments to address the cause of the infertility. Thus surgery might be used to remove adhesions caused by endometriosis, injection of sperm directly into oocytes (i.e., intracytoplasmic sperm injection) to by-pass infertility due to poor sperm motility or ovarian stimulation to restore ovulation for anovulatory disorders. Each treatment could be repeated more than once so that couples can, in theory, be in fertility treatment for many years (NICE, 2004). It is also the case that more conventional treatments will be used before more high technological (and costly) treatments so that there is a progression of treatments. For example, insemination will be used before in vitro fertilization and ovulation induction will be used before ovarian stimulation (e.g., NICE, 2004; ESHRE, 2008). How long couples spend in treatment is not known, and the success of being in treatment varies depending on diagnosis, age and other prognostic factors.

Infertility Across More and Less Developed Nations

Infertility is an issue for men and women across all countries regardless of their developmental status (i.e., more or less developed countries). Previous research has however highlighted differences between more and less developed nations regarding the prevalence of infertility and the demand for fertility medical services. For example, as already mentioned, in less developed countries such as sub-Saharan Africa access to formal medical care for fertility difficulties is sparse and can often include irrelevant and even potentially damaging methods (Sundby et al., 1998). This is in stark contrast to more developed countries where a variety of the most up-to-date, high-tech treatments are available, with some countries such as Demark providing them for free. Such differences may impact on the reported up-take for medical treatments. One may also expect to find differences in the prevalence of infertility between more and less developed nations. Previous research has reported that the prevalence rate of infertility in more developed countries such as America ranges from 8-15% (Mosher & Bachrach, 1996), however in less developed countries such as sub-Saharan African the prevalence rates are estimated to be as high as 30% or more (Frank, 1983; Meheus, Reniers, & Colletet, 1986).

The Present Study

The aim of the present study was to determine the prevalence of infertility and demand for medical services by conducting a thorough literature review taking into account the methodological issues regarding the different uses and definitions of infertility. Given the diversity in definitions for infertility, exposure intervals, time frames, and specific details for each study were documented in order to determine the comparability of prevalence rates. Further, and where available, the percentage of couples that had sought medical advice and/or treatment for fertility problems was

also recorded. Finally, all countries were categorised according to developmental status (e.g., more or less developed) in order to establish any differences in prevalence rates and the demand for fertility services due to economic differences.

Materials and Methods

Materials

Prevalence of infertility.

In order to establish the prevalence of infertility, population surveys were examined. Citations eligible for the present study were those based on population surveys published since 1990. That is, estimates that defined infertility prevalence within a hospital or medical practice were excluded. According to Gunnell and Ewings (1994) many of those with infertility do not seek help, and of those who do, many are not referred for specialist advice. Therefore studies reporting prevalence ratings based on clinical and medical samples may be underestimating the true number of couples faced with fertility difficulties. PubMed was used for peer reviewed scientific reports. A specific PubMed search used the terms infertility [MeSH] (Medical Subject Headings) and epidemiological studies. The 85 citations since 1990 were scanned for relevance, full reports were obtained as necessary and other citations were identified in the reference lists of the relevant citations (see Appendix A for PubMed search history). The 28 studies selected for review involved populations from different countries and defined different reproductive states: infertility, subfecundity and childlessness. Distinctions were made between current and lifetime prevalence of infertility.

Demand for infertility medical care.

In order to assess demand for infertility, medical services literature searches were directed at identifying publications concerned with the take-up of any infertility

medical services. Demand for infertility medical care was defined as the proportion of couples that decide to seek any medical advice or care to resolve their fertility problem. A specific PubMed search used the terms Infertility [MeSH] AND *Patient Acceptance of Health Care [MeSH] producing 141 records and 15 reviews since 1990 (see Appendix A for PubMed search history). A further search used Infertility [Title/abstract] AND treatment-seeking (9 citations since 1990). All were scanned for relevance, full reports were obtained as necessary and other citations were identified in the reference lists of the relevant citations. In total 17 studies provided information on demand for medical care.

Procedure

Development status.

All empirical reports (prevalence, seeking medical care) were categorised according to development status using the United Nations listing of development status by country or region (http://unstats.un.org/unsd/methods/m49/m49regin.htm, last accessed April 10 2006). These guidelines take into consideration three criteria in order to assess the development status of each country: low-income status, economic vulnerability and human resources weakness (Sallam, 2008). Data extraction was conducted by two people (Author & John A. Collins).

Prevalence of infertility.

A percent infertile was calculated for each study based on the proportion of women reported as infertile (or childless) compared to total number of women reported in the study population. For one report of 28 countries in sub-Saharan Africa (Larsen, 2000), a single averaged percent infertile score was calculated from available data in the report.

Demand for infertility medical care.

An overall percentage that included seeking any type of medical care (e.g., general advice, diagnostic testing, treatment advice, actual treatment) was calculated for each study reporting treatment seeking behaviour ([total seeking medical care/total infertile]*100) and, where available, breakdowns according to the percentage seeking treatment advice versus percentage receiving treatment.

Deriving international estimates of infertility prevalence and treatment seeking.

In order to obtain the necessary population values for the international estimates, data from several sources were consulted:

i. The world population current (i.e., 6.508 billion) at the time of the review was obtained from the web site of the United States Census Bureau: http://www.census.gov/ipc/www/world.html (last accessed April 06 2006).

ii. The proportion of women age 15-49 who were in a married or consensual union was estimated from the World Contraceptive Use Report available on the web site of the Population Division, Department of Economic and Social Affairs, United Nations, New York, NY 10017, USA in the report: http://www.un.org/esa/population/publications/contraceptive2003/wcu2003.htm (last accessed April 06 2006). The most recent estimates on this website were for 2000 and these were updated to 2006 by applying the 1.706% average population increase in less developed and 0.277% in more developed countries from 1993 to 2003 reported in the most recent World Health Report http://www.who.int/whr/2005/en/index.html (last accessed April 06 2006).

iii. Since estimates of infertility prevalence usually have as their denominator women aged 20-44, the population of women aged 20-44 years in married and

consensual unions was derived from the population aged 15-49 using the age structure of global populations reported by the U.S. Census Bureau: http://census.gov/ipc/prod/wp02/wp-02004.pdf (page 33, last accessed April 06 2006).

iv. The calculation of international estimates of prevalence began with the number of women aged 20-44 married or living in a consensual union in more developed and less developed countries. Each of the population estimates from more and less developed countries was multiplied by the corresponding proportion of women with infertility to get estimates of infertile women in more and less developed countries.

v. The estimated number of infertile women in more and less developed countries was then multiplied by the proportion of women seeking infertility medical care to get estimates of the number of infertile women seeking medical care in more and less developed countries.

Results

Prevalence of Infertility

Table 2.1 shows data from population surveys reporting on prevalence of current and lifetime infertility.

Table 2.1
Prevalence of infertility according to developmental status (see page 28 for notes).

Authors (Year of survey)	Country or region	Women sampled	Age of sample	Exposure time	Sample Size	Percent infertile	Sample characteristics	Sample used for prevalence estimate	Definition(s) used
More Developed countries									
Current Infertility									
Philippov et al. 1998 (1998)	Russia	Married	18-45	12	2,000	16.7	General population, selected at random from polling station lists of the electorate. Every 7th women was included in the selection, questionnaire	No information available	Infertility: not conceived after 12 months or more of unprotected intercourse
Royal Commission 1993 (1991)	Canada	Married >1 yr	18-44	12	1,412	8.5	Randomly selected from general population, questionnaire	No information available	Infertility: cohabiting for 2 years without contraception
Royal Commission 1993 (1991)	Canada	married >1 yr	18-44	24	1,412	7.0	Randomly selected from general population, questionnaire	No information available	Infertility: cohabiting for 2 years without contraception
Stephen & Chandra 2006 (2002)[f]	United States	Married	15-44	12	15,303	7.4	Nationally represented survey, interview	No information available	Infertility: problems conceiving for more than 12 months Subfecundity: difficulties in carrying a pregnancy to term. The former was made up from a number of answers to questions about contraceptive use and coital frequency

Table 2.1
Prevalence of infertility according to developmental status (continued, see page 28 for notes).

Authors (Year of survey)	Country or region	Women sampled	Age of sample	Exposure time	Sample Size	Percent infertile	Sample characteristics	Sample used for prevalence estimate	Definition(s) used
More Developed countries *(continued)*									
Current Infertility (continued)									
van Balen et al. 1997b (1992)	Netherlands	All	25-49	12	3,295	10.7	National survey of households, randomly selected from all population, interview	Trying to conceive	Infertility: 12 months of unprotected regular intercourse without getting pregnant with a first child
Webb & Holman 1992 (1988)	Australia	Married	16-44	12	1,495	3.5	Sample selected from women residing in the Perth metropolitan area, sample drawn using a cluster, multistage method, interview	Trying to conceive	Infertility: > 12 months of unprotected intercourse
Lifetime Infertility									
Buckett & Bentick 1997 (1995)	United Kingdom	All	45-54	12	728	17.3	Randomly selected from Shropshire FHSA primary care register, questionnaire	Trying to conceive	Infertility: > 12 months trying to conceive
Dick et al. 2003 (1991-3)	Australia	All	15-50	12	1,638	18.4	Population based case control study, interview	Trying to conceive	Infertility: some stage during reproductive lives, were unable to conceive despite attempts for >12 consecutive months

Table 2.1
Prevalence of infertility according to developmental status (continued, see page 28 for notes).

Authors (Year of survey)	Country or region	Women sampled	Age of sample	Exposure time	Sample Size	Percent infertile	Sample characteristics	Sample used for prevalence estimate	Definition(s) used
More Developed countries *(continued)*									
Lifetime Infertility (continued)									
Ducot et al. 1991 (1988)	France	All	18-49	12	3,181	12.2	Representative national sample	Trying to conceive	Infertility: had to wait at one time longer than would have wished to become pregnant (>12 months)
Greil & McQuillan 2004 (2002)	United States	All	25-50	12	580	21.2	Randomly selected, interviews through computerised phone calls.	Trying to conceive	Infertility: ever tried unsuccessfully to get pregnant for >12 months Infertility: ever tried for 12 months or more to conceive any of their pregnancies
Gunnell & Ewings 1994 (1993)	United Kingdom	All	36-50	12	2,377	26.4	Randomly selected from the Somerset Family Health Services Authority population register, questionnaire	Includes voluntary & involuntary infertility	Infertility: Failure to become pregnant after 12 months of regular unprotected intercourse
Olsen, Basso et al. 1998 (1991-3)[a]	Europe	All	25-44	12	6,630	11.3	Population based survey from five European countries. Survey conducted through personal interviews and structured questionnaires translated into each national language	Trying to conceive	Infertility: > 12 months trying to conceive

Prevalence of infertility according to developmental status (continued, see page 28 for notes).

Authors (Year of survey)	Country or region	Women sampled	Age of sample	Exposure time	Sample Size	Percent infertile	Sample characteristics	Sample used for prevalence estimate	Definition(s) used
More Developed countries *(continued)*									
Lifetime Infertility (continued)									
Rostad et al. 2006 (1985-95)	Norway	All	50-69	12	9,983	6.6	Cross sectional population-based health surveys, questionnaire	Trying to conceive	Infertility: inability to conceive within a year of unprotected intercourse, regardless of later pregnancy
Schmidt et al. 1995 (1995)	Denmark	All	15-44	12	2,865	15.7	Randomly selected, postal questionnaire	Trying to conceive	Infertility: A woman having attempted to become pregnant for > 12 months without achieving pregnancy
Templeton et al. 1990 (1988)	United Kingdom	All	46-50	24	766	14.1	Randomly selected from an age cohort of women through the Grampian Health Board's primary care register, postal questionnaire	Trying to conceive	Infertility: having difficulty in becoming pregnant for > 24 months
Webb & Holman 1992 (1988)	Australia	Married	16-44	12	1,495	19.1	Sample selected from women residing in the Perth metropolitan area, sample drawn using a cluster, multistage method, interview	Includes voluntary & involuntary infertility[c]	Infertility: > 12 months of unprotected intercourse
					52,253[d]				

Table 2.1
Prevalence of infertility according to developmental status (continued, see page 28 for notes).

Authors (Year of survey)	Country or region	Women sampled	Age of sample	Exposure time	Sample Size	Percent infertile	Sample characteristics	Sample used for prevalence estimate	Definition(s) used
Less Developed countries									
Current Infertility									
Che & Cleland 2002 (1988-95)[b]	China	Newly Married	25-45	12	7,872	9.3	All couples marrying for the first time identified through the marriage licence offices of two districts. All couples who had the intention of delaying the first conception were enrolled, and those without such intention were randomly selected, interview	No information available	Infertility: inability to conceive a live birth after a specified duration (12 months) of regular unprotected intercourse
Larsen 2005 (2003)	Northern Tanzania	All	20-44	24	2,019	6.9	Cross sectional study, random ally selected, first marital union, interview	Trying to conceive	Infertility: tried to conceive for at least 24 months: "how long have you tried to get pregnant"
Sundby et al. 1998 (1994)	Gambia	Married	15-49	12	2,918	9.2	Random selection of 24 out of 1847 Enumeration Areas (EA). All households in each of the 24 EA were interviewed	Trying to conceive	Primary infertility: no pregnancy or live children born despite being married and not having used family planning for at least 12 months

Table 2.1
Prevalence of infertility according to developmental status (continued, see page 28 for notes).

Authors (Year of survey)	Country or region	Women sampled	Age of sample	Exposure time	Sample Size	Percent infertile	Sample characteristics	Sample used for prevalence estimate	Definition(s) used
Less Developed countries *(continued)*									
Lifetime Infertility									
Barden-O'Fallon 2005 (2000-2)	Rural Malawi	All	15-34	12	678	19.6	Population based survey, interviewed once a week for 6 weeks, and at one and two years later	Trying to conceive	Infertility: whether an individual reports ever experiencing a difficult time in getting pregnant (>12 months) Infertility: whether they consider themselves or their partner to be infertile
Fuentes & Devoto 1994 (1993)	Santiago, Chile	Married	15-45	12	474	25.7	Randomly selected from newly married wives using the National Electoral Registry, interview	No information available	Infertility: having unprotected sexual intercourse ≥ 12 months at some time in their lives disregarding whether they are currently infertile or not

Table 2.1
Prevalence of infertility according to developmental status (continued, see page 28 for notes).

Authors (Year of survey)	Country or region	Women sampled	Age of sample	Exposure time	Sample Size	Percent infertile	Sample characteristics	Sample used for prevalence estimate	Definition(s) used
Less Developed countries *(continued)*									
Lifetime Infertility (continued)									
Geelhoed et al. 2002 (1999)	Rural Ghana	All	15-44	12	1,073	11.8	Community based survey. A probability sample was obtained though systematic random sampling of houses, one person of appropriate age and sex in each house selected, interview	No information available	Infertility: no pregnancy has been achieved after ≥ 12 months of unprotected intercourse. Women were regarded to have had infertility when they were ≥ 35 years and had fewer than three children. Men were assumed to have experienced infertility if they were ≥ 45 years and had fewer than two children.
Zargar et al. 1997 (1997)[b]	Indian Kashmir	Married >1 yr	15-44	12	10,063	15.1	Random selection of 30 villages from each tehsil (administrative subunits) interview	Trying to conceive	Primary infertility: Failure to conceive after 12 months of unprotected sexual intercourse in a couple trying to achieve a pregnancy who had not previously conceived.

Table 2.1
Prevalence of infertility according to developmental status (continued, see page 28 for notes).

Authors (Year of survey)	Country or region	Women sampled	Age of sample	Exposure time	Sample Size	Percent infertile	Sample characteristics	Sample used for prevalence estimate	Definition(s) used
Less Developed countries *(continued)*									
Lifetime Infertility (continued)									
Che & Cleland 2002 (1988-95)[b]	Shanghai, China	Newly Married	25-45	24	7,872	3.0	All couples marrying for the first time identified through the marriage licence offices of two districts. All couples who had the intention of delaying the first conception were enrolled, and those without such intention were randomly selected, interview	No information available	Infertility: inability to conceive a live birth after a specified duration (24 months) of regular unprotected intercourse
Lifetime childlessness									
Unisa 1999 (1998)	India (Pradesh)	Married >3 yrs	20-49	36	6,640	5.0	Random selection of 30 villages in district, interview	No information available	Childlessness: inability to deliver a live born child (trying for >12 months)
Ericksen & Brunette 1996 (1977-92)[c]	sub-Saharan Africa	Newly Married	20-41	60	WFS & DHS	14.5	28 nations using the DHS and WFS surveys, interview	No information available	A women is considered infertile at last observation if she has had no live births during the last 5 years before censoring, otherwise she is considered fertile.

Table 2.1
Prevalence of infertility according to developmental status (continued).

Authors (Year of survey)	Country or region	Women sampled	Age of sample	Exposure time	Sample Size	Percent infertile	Sample characteristics	Sample used for prevalence estimate	Definition(s) used
Less Developed countries *(continued)*									
Lifetime childlessness (continued)									
Larsen 2000 (1977-97)	sub-Saharan Africa	Newly Married	20-44	60	66,453	16.4	28 nations using the DHS and WFS surveys, interview	No information available	A woman is considered infertile at last observation if she has had no live births during the last 5 years before censoring, otherwise she is considered fertile.
Liu et al. 2005 (2005)	China (national)	Newly Married	15-57	84	21,970	1.3	Analysis was based on the National Two-Per-Thousand Sample Survey on Fertility and Contraception (NSSFC), interview	Trying to conceive	A non-contracepting and sexually active woman who had not reported a recognised pregnancy after at least seven years of marriage.
					120,160				

[a]Information from the European Study of Infertility and Subfecundity. Five countries included: Denmark, Germany, Italy, Poland, Spain. Data also used by Olsen et al. (1996), and Karmaus and Juul (1999). [b]Primary Infertility only. [c]DHS: Demographic and Health Surveys. WFS: World Fertility Survey; Lifetime: in pre-menopausal women this means lifetime to date of interview. [d]Total does not include duplicate current and lifetime. [e] In the calculations for lifetime prevalence no distinctions were made between voluntary and involuntary childlessness. [f]Prevalence based on subfecundity and infertility.

More developed countries.

Fourteen studies provided estimates of infertility prevalence in 13 more developed countries, on the basis of surveys involving 52,253 women. In total, four estimates were for current infertility of 12 month duration (3.5% - 16.7%), one was for current subfecundity and infertility of 12 month duration (7.4%) and one was for current infertility of 24 month duration (7.0%). The prevalence of current infertility ranged from 3.5% to 16.7%. The estimate of current infertility for this range was the median figure of 9% for 12 months delay.

Nine estimates were for lifetime infertility lasting 12 months (6.6% - 26.4%) and one was for lifetime infertility lasting 24 months (14.1%). The prevalence of lifetime infertility ranged from 6.6% to 26.4%. The estimate of lifetime infertility for this range was the median figure of 17% for 12 months delay.

Of the 14 studies reporting prevalence in more developed countries all studies used the definition infertility (see Table 2.1, pages 20-28). Five studies reported a definition of infertility that included an exposure time (e.g., 12 months), unprotected intercourse and outcome measured (i.e., lack of conception, pregnancy). A further two studies reported an exposure time and unprotected intercourse but provided no information on the outcome measured. The remaining six studies reported infertility with information on an exposure time (e.g., 12 months) but no information on contraceptive use. Finally, one study (Stephen & Chandra, 2006) used subfecundity and infertility in their calculations for prevalence of infertility, defining subfecundity as difficulties carrying a pregnancy to term and infertility as problems conceiving.

Ten studies reported that the prevalence rate documented was estimated using only women trying to conceive, two studies included women with voluntary and

involuntary infertility, and the remaining three studies provided no information on intentions to conceive within the women sampled (total equals 15 studies as Webb & Holman, 1992 calculated lifetime prevalence making no distinctions between voluntary and involuntary childlessness and current infertility using only women trying to conceive).

Less developed countries.

Eleven studies provided estimates of infertility prevalence in less developed countries in surveys involving 120,160 women. There were only three studies for prevalence of current infertility showing a range from 6.9% for a 24 month delay in northern Tanzania to 9.2% and 9.3% for 12 month delay in Gambia and Shanghai, respectively. The median estimate of current infertility for this range was 9% for 12 months delay.

Five estimates were for lifetime occurrence of periods of infertility lasting 12-36 months (3.0% - 25.7%). A further four studies examined infertility prevalence for a period between 5 and 7 years after marriage (1.3% - 16.4%). The lowest estimated rate of childlessness in the first 5 - 8 years of marriage was 1.3% in China, whereas the highest estimated rate was 16.4% using the weighted average for sub-Saharan African countries (the range was 8 - 28% for the 28 countries as reported in the original report: Larsen, 2000). The prevalence of lifetime infertility ranged from 3.0% to 25.7%. The estimate of lifetime infertility for this range was the median figure of 17% for 12 months delay.

Of the 11 studies reporting prevalence in less developed countries seven studies used the definition infertility, and four used the definition childlessness (see Table 2.1, pages 20-28). Of those that used infertility five studies included an

exposure time (e.g., 12 months), unprotected intercourse and outcome measured (i.e., lack of conception, pregnancy). A further two studies reported infertility with information on exposure time (e.g., 12 months) and the outcome measured but no information on contraceptive use. Finally, four studies reported childlessness as the reproductive state defined. Of these four studies, one referred to childlessness as an inability to deliver a live born child, two defined childlessness as the presence of no live births over a period of time (5 years of marriage) and one defined childlessness as no recognised pregnancy over a period of time (7 years of marriage).

Five studies reported that the prevalence rate recorded was based only on women trying to conceive and the remaining six studies provided no information on intentions to conceive within the women sampled.

Demand for Infertility Medical Care

Table 2.2 shows the proportion of women who sought and/or received medical care in more and less developed countries.

More developed countries.

Twelve studies provided estimates of seeking behaviour from six countries and one of these (Olsen, Basso, Spinelli, & Kuppers-Chinnow, 1998) provided an average estimate from a further five European countries. In total these surveys concerned 4,810 infertile women. The proportion of infertile couples seeking any infertility medical care ranged from 42% to 76.3%, with an average of 56.1%. It was also possible to examine the proportion of infertile women who underwent infertility medical care. An average of 42.0% of women sought medical advice (six studies) and 22.4% underwent treatment (four studies).

Table 2.2
Demand for infertility medical care according to developmental status.

Authors	Country or Region	Number infertile	Percent seeking any medical care (%)	Percent overall seeking different types of treatment (%)		Percent not seeking care (%)
				Treatment advice	Received treatment	
More developed countries						
Buckett & Bemtick 1997	United Kingdom	126	61 (48.4)	43 (34.1)	26 (20.6)	65 (51.6)
Dick et al. 2003[a]	Australia	302	198 (65.6)	–	–	104 (34.4)
Ducot et al. 1991	France	387	240 (62.0)	118 (30.0)	44 (11.4)	147 (38.0)
Greil & McQuillan 2004	United States	123	64 (52.0)	–	32 (26.0)	59 (48.0)
Gunnell & Ewings 1994	United Kingdom	618	310 (50.2)	170 (27.5)	–	308 (49.8)
Olsen, Basso et al. 1998[ab]*	Europe	751	349 (49.0)	–	–	363 (51.0)
Philippov et al. 1998	Russia	333	254 (76.3)	186 (55.6)	–	79 (23.7)
Schmidt et al. 1995[c]	Denmark	448	198 (44.2)	–	–	250 (55.8)
Stephen & Chandra, 2000[d]	United States	1,210	508 (42.0)	–	380 (31.4)	702 (58.0)
Templeton et al. 1990	United Kingdom	108	75 (69.4)	67 (62.0)	–	33 (30.6)
van Balen et al. 1997b[ae]	Netherlands	351	85 (65.6)	–	–	46 (35.1)
Webb & Holman 1992[f]	Australia	53	23 (48.9)	20 (42.6)	–	24 (51.1)
			56.1[g]	*42.0*[g]	*22.4*[g]	*43.9*[g]
Less developed countries						
Barden-O'Fallon 2005[a]	Rural Malawi	133	77 (57.9)	–	–	56 (42.1)
Che & Cleland 2002[a]	China	732	417 (57.0)	–	–	315 (43)
Fuentes & Decoto 1994[a]	Chile	122	33 (27.0)	–	–	89 (73.0)
Sundby et al. 1998	Gambia	281	112 (40.0)	98 (34.9)	–	169 (60.0)
Unisa 1999	India (Pradesh)	332	246 (74.1)	–	193 (58.0)	86 (26.0)
			51.2[g]	*34.9*[g]	*58.0*[g]	*48.8*[g]
			55.7[h]			45.3[h]

[a]No information was provided on the type of medical care sought. [b]Information from the European Study of Infertility and Subfecundity. Five countries included: Denmark, Germany, Italy, Poland, Spain. Data also used by Olsen et al. 1996, and Karmaus & Juul (1999). [c]26 participants who sought treatment did not meet definition for infertility so were excluded from further analysis. [d]Most recent paper (Stephen & Chandra 2006) did not include information regarding type of treatment sought [e]Calculations based on number of people who responded to the final questionnaire (n = 131). [f]Current infertility. Calculations based on reproductive disability sample (n = 47). [g]Averaged total percent per development status. [h]Averaged total percent across more and less developed countries. *Calculations based on the number of infertile people who participated in the treatment seeking section (n = 712).

- No data reported.

Less developed countries.

From less developed countries, five studies provided estimates from five countries, involving 1,600 infertile women. The proportion of infertile couples seeking any infertility medical care ranged from 27.0% to 74.1% with an average of 51.2%. Only one study in less developed nations provided the proportion of women who sought treatment advice (34.9%), and only one study gave the percentage who received infertility treatment (58.0%).

Care-seeking appears to follow a similar pattern in more and less developed countries, with slightly more couples seeking care in developed countries (mean 56.1%) than in less developed countries (mean 51.2%). The average proportion of women not seeking treatment in all countries was 45.3%.

Estimated Number of Couples Needing and Demanding Infertility Medical Services

Table 2.3 shows population values overall and according to age and marital status. An estimated 1.139 billion women aged 15 - 49 are currently in married or consensual unions in 2006 and they represent 17.5% of the 6.508 billion world population. The 804 million women aged 20-44 in married or consensual unions are 12.4% of the 6.508 billion total, and this category includes 122 million women in more developed countries and 682 million women in less developed countries.

Table 2.3
World estimate of potential need and demand for infertility medical care.

	World	More Developed countries	Less Developed countries
(i) World population 09:44 GMT (EST+5) Apr 06, 2006	6,508,032,884		
(ii) Population data Number of women of reproductive age (15-49 years) who are in a marital or consensual union: 2006	1,139,394,885	172,888,758	966,506,127
(iii) Number of women age 20-44 years who are in a marital or consensual union	804,278,743	122,039,123	682,239,619
(iv) Potential Need (Prevalence of infertility) Number of women 20-44 years in marital or consensual union currently not conceiving in one year (while not using a contraceptive method) Estimate (9%)	72,385,087	10,983,521	61,401,566
(v) Demand for treatment Number of infertile couples seeking medical care Estimate (56%)	40,535,648	6,150,771	34,384,876
Number of infertile couples not seeking medical care Estimate (44%)	32,573,289	4,942,584	27,630,705

Note. See Methods section for notes on (i) to (v).

There are 72.4 million women aged 20-44 and living in married or consensual relationships who have infertility defined as currently experiencing >12 month delay in conception while not using contraception. Of these women, on average 40million are likely to seek medical health care and 32.6 million will not seek health care for the management of the infertility.

Discussion

Infertility is a prevalent problem in society with around 9% of the adult population affected. Given that parenthood is a desired goal by the majority of adults, it is therefore surprising to find that on average only 56% of infertile couples are

seeking any medical advice or care, with an even smaller number receiving treatment. There are a number of possibilities to account for the discrepancy between desire to have children and actually seeking treatment when a fertility problem occurs. The possible methodological, population and cultural issues will be explored here and the further psychological determinants that may facilitate or hinder engagement in the medical process will be discussed in Chapter 3.

Prevalence of Infertility

Perhaps unexpectedly the results indicate that there may not be as much difference in the prevalence of infertility according to development status as has previously been assumed. The prevalence estimates produced are valid insofar as these were based on all population surveys of current infertility published since 1990, totalling a sample of approximately 170,000 women, with almost all studies (88%) sampling at least 1000 women. Although current prevalence from less developed countries was based on only three reports, these sampled approximately 13,000 women. Lifetime prevalence of infertility, which was based on many more studies (n = 19), was remarkably similar in more (10 studies = 6.6% - 26.4%) and less (nine studies = 5.0% - 25.7%) developed countries, suggesting that similarity in the current prevalence was not just an artefact of a smaller number of studies.

A number of possibilities could account for such similarities. One explanation is that the countries most affected by the factors that reduce fertility, which include for example curable sexually transmitted diseases (STDs), were not those sampled in the surveys reported. A WHO report showed that the number of adults per 1,000 population infected with curable STDs was 19 in North America and 20 in Western Europe (WHO, 2001), which was comparable to the rates for less developed countries

contributing to the review (see Table 2.1, pages 20-28), that is, 21 and 18 in North Africa and East Asia, respectively. By comparison the number infected in Sub-Saharan Africa was 119 and was 50 in Southeast Asia, which did not contribute to the estimate of current infertility. However, even with this consideration the results show that lifetime prevalence of infertility is similar in more and less developed countries even in those countries that have demonstrated higher exposure to infectious disease (e.g., Chile, sub-Saharan Africa).

Another possibility is that the course of infertility over time may show convergence of prevalence according to development status. For example, Stephen and Chandra (2006) recently reported from the National Survey of Family Growth (NSFG) that prevalence of 12-month infertility stayed more or less the same in the United States from 8.5% in 1982 to 7.4% in 2002. In contrast, in some African countries (e.g., Central African Republic, Cameroon, Nigeria) prevalence has dropped dramatically from an exceptionally high level reaching 30 - 40% in the 1950s and 1960s compared to a national estimate of only 6% in 1994 (Larsen, 2005; WHO 1991). This decline in the prevalence of infertility may be due to significant decreases of 30 - 40% in the prevalence of some STDs in African nations (WHO, 2001).

Similarities in prevalence rates between more and less developed countries could also be due to the category of women sampled in some of the studies, restricting the criteria to only ever-married or cohabiting women. This is problematic if a woman has to prove her fertility before she can get married (i.e., a pregnancy or birth is part of the process of getting married) as is customary in many West African societies (Larsen, 2005). Only three out of the 11 studies in the less developed countries sampled all women irrespective of marital status (prevalence range of 6.9% - 19.6%),

therefore the remaining 9 studies (prevalence range of 1.3% - 25.7%) sampling married or cohabiting women may not represent a true reflection of the number of women with fertility problems in less developed nations.

A further sampling issue is whether the study included all women, or a subset of women who stated trying to conceive currently or at some point in their reproductive life. The WHO (Rowe et al., 1993) recommends that in order to accurately represent involuntary childlessness researchers must include intentions to conceive in their questioning of couples. Within the current review, two studies reported including all women regardless of voluntary or involuntary infertility in more developed countries. However, in 10 studies (four from more developed and six from less developed countries) the intentions of the women sampled were unknown. By including all women one is removing the intention of those sampled, which may lead to distortion of the prevalence rating (Schmidt & Münster, 1995). Not knowing a couple's intention to conceive may further impact on conclusions drawn about the need and demand for infertility medical care. One may find that prevalence may be reported as high (as it includes all women regardless of intention), yet the uptake of treatment low, as the treatment seeking behaviour only includes the women who actually intended to achieve a pregnancy. However, the rate of voluntary childlessness is generally low, about 5% (Chancey, 2006) and therefore would not necessarily produce significant bias. It would be imperative to consider these issues when developing future cross-country population studies on the prevalence of infertility.

Equally important to consider is the possibility that the similarity in prevalence of infertility between more and less developed countries is genuine but that the mechanism(s) contributing to that prevalence differs according to country. W. Cates,

Farley, & Rowe (1985) reported that most cases of infertility in Africa were due to infection, which is very low in more developed countries. In the latter however, there is a steady increase in age-related infertility which is not found in less developed nations (Lunenfeld & Van Steirteghem, 2004). In the United Kingdom, the proportion of babies with mothers aged 35 years or more increased markedly from 6.5% in 1976 to 22.5% in 2000 (Bakeo, 2004) and in the United States this rate has more than doubled since 1978 (Hamilton et al., 2004). This is in stark contrast to countries such as sub-Saharan Africa where women marry at young ages (average age = 19.03; Harwood-Lejeune, 2000) and the average age at first birth is 19.9 years (average based on data from the Demographic Health Survey conducted in Central African Republic, Mali and Eritrea, Population Council, 1997a, 1997b, 1997c).

In Western society the increase in age-related infertility is thought to be due to a number of demographic, social and lifestyle factors, leading people to spend more time than ever in education and in the so-called period of 'emerging adulthood' that focuses on education and individual growth and development (Arnett, 2000). For example people are taking longer to find a suitable romantic partner (age at first marriage in Europe has increased by more than 4 years since the 1980s, Chappell, Pearce, Carlos-Bovagnet, & Till, 2005), and are spending more time in the early years of partnership on non-parenting couple activities (e.g., 'enjoying life', travel, van Balen, 2005) made easier by highly effective contraception. Further, economic uncertainty and affordability of children is also of more concern now (ESHRE Capri workshop, 2001) than in previous decades as is female career aspiration and development (Bewley, Davies, & Braude, 2005) though interference with occupational goals is still more of an issue for men than women (Langdridge, Connolly, & Sheeran, 2005).

It would be important to establish the impact such factors (e.g., STDs, age) have on infertility rates in more and less developed countries, for it may be that these factors can be readily modifiable (e.g., via increased awareness about age related decline in fertility) and preventable (condom use to prevent transmission of STD: W. Jr. Cates & Stone 1992), which in turn may impact on future fertility rates in both societies.

Previous studies have found that the use of different definitions of infertility can lead to problems in the interpretation of results on prevalence rates (Marchbanks et al., 1989). In the current review the majority of the studies (96%) referred to infertility as an inability or difficulty in conceiving, which is generally the most agreed definition according to NICE, ASRM and the WHO. In addition the majority of studies (72%) reported using 12 months as the exposure time for infertility, again in accordance with the most agreed definition. Therefore one can be confident that the majority of the studies used in the current review to estimate the prevalence of infertility were using the most agreed definition, thus reducing the chances of any misinterpretation due to methodological issues impacting on the prevalence ratings.

Need and Demand for Treatment

As already mentioned parenting surveys have revealed that the vast majority of those surveyed wish to have children at some point in their lives (Virtala et al., 2006, Lampic et al., 2006, Tyden et al., 2006) and one would therefore expect that most people would seek medical care when faced with fertility difficulties. However, demand for infertility treatment was unexpectedly low in more and less developed countries with just over half of the people who experienced fertility problems

deciding to seek any infertility medical care, and an even lesser number of couples (<25%) receiving treatment.

Why are there inconsistencies between desire to have children and treatment seeking behaviour when faced with problems conceiving? One possible factor is the period of exposure in a given study; with a current 12 month reported period of trying to conceive, perhaps the studies are underestimating the percentages of couples that, after a prolonged period of natural attempts, say two years, eventually do seek medical treatment. However, the average for engagement in medical services in the current studies was 58% (Webb & Holman, 1992; van Balen, Verdurmen & Ketting, 1997b; Philippov, Radionchenko, Bolotova, Voronovskaya, & Potemkina, 1998; Stephen & Chandra, 2000) compared with 54% in the remaining lifetime surveys, suggesting that too short an exposure time was not the main cause of low treatment-seeking.

A lack of consensus for a definition of infertility may also obscure true estimate of the number of couples that seek treatment. Gunnell and Ewings (1994) found that many infertile couples who do seek help are not referred for specialist medical advice and therefore do not access the medical help they need. They concluded that this was primarily due to a lack of concrete referral guidelines for General Practitioners (GP) to use when couples present with difficulties conceiving. If the majority of population surveys use 12 months as a definition of infertility but the medical practice within the country is delaying and sending couples for further investigations at a later stage, treatment up-take and use may be underestimated in the surveys.

The mechanisms for why treatment seeking behaviour is low may be different according to development status even if the rate is the same; one possibility is due to cultural differences surrounding infertility. Firstly, in many developing countries there is a perception of infertility as being due to evil forces, and as a result many infertile couples often first seek traditional and religious treatments in an attempt to ward off the evil (Okonofua, Harris, Odebiyi, Kane, & Snow, 1997). In addition infertility may lead to divorce, or the husband taking on another partner who can produce children, thus reducing the need for medical care (Okonofua, 2003). In more developed countries van Balen et al. (1997b) found in a sample of 131 infertile couples that another way to cope with infertility was to pursue other life goals like a professional career, activities in voluntary associations or taking up educational/further study rather than seek medical help for the infertility problem, and this may reflect the changing importance of children as a developmental life goal. One third of the sample in that study believed that having children did not constitute the only pursuit that makes life meaningful (van Balen et al., 1997b).

Secondly, people may not be motivated to seek treatment if fertility services are known to be limited or unavailable. For example, in less developed countries medical treatment is not readily available, and when it is, it is often expensive and relatively ineffective. Often the couples that can afford treatment seek it overseas (Okonofua, 2003), paradoxically reinforcing limited availability in the less developed country because the demand decreases. Conversely, in more developed countries such as the USA treatment is a very expensive process and can only be obtained by those that have the appropriate insurance policies or the wealthy. However, it must be mentioned that although these are important implications for access to treatment seeking, even in the countries that provide generous access to treatment, for example

Denmark, the rate of seeking medical care was about the same as that reported for Gambia where access is much more restricted (Sundby et al., 1998).

This discussion has highlighted a number of factors associated with the prevalence of infertility and the demand for medical treatment across the World. A number of the causes of prevalence and demand were common to both more and less developed nations (e.g., accessibility to medical care) while some were unique to developmental status (e.g., increasing change in age at first birth in Western societies). In addition, the results suggest that information on the prevalence and demand of fertility treatment is much more limited from the less developed countries. Cross-cultural epidemiological data is now needed to further explore and resolve the issues noted here. This is of great importance as all these factors will have an impact on decision making when couples are faced with fertility difficulties.

Notwithstanding the social and methodological implications cited in this chapter to explain the current findings, it is also important to establish the psychological factors associated with the reported low uptake of treatment. Together this may help to disentangle why people are not seeking treatment and what can be done to enable people (if they wish) to seek the medical help that may make their desired goal of parenthood more achievable.

Chapter 3
Decision-making about seeking medical advice in an internet sample of women trying to get pregnant

Introduction

Given the importance of parenthood as a central life goal, it is surprising to find from the results in Chapter 2 that on average just over 50% of couples who are faced with fertility problems actually seek medical care. Considering the current high success rates of treatment (Pinborg et al., 2007) it would be important to better understand this paradox in order to establish whether couples desiring to use medical intervention can be aided in their decision-making to help them better realise this goal. The aim of the present study was to identify demographic, fertility and psychological factors that differentiated those who had sought or not sought medical advice or treatment for fertility difficulties in order to identify factors that might facilitate or hinder treatment-seeking. Table 3.1 summarises the constructs in the theoretical framework reviewed in the next section.

Table 3.1
Description of the constructs in each theoretical framework and those assessed in the present study.

Theory and Constructs	Description of Construct
Theory of Planned Behaviour	
External variables	Demographic, socioeconomic, education
Personality traits	Optimism, neuroticism etc.
Behavioural attitude	Evaluations of the behaviour
Subjective norms, normative beliefs & motivation to comply	Persons belief about whether significant others think he or she should engage in the behaviour
Perceived behavioural control	Individual's perception of the extent to which the behaviour is easy or difficult to perform
Behavioural intention	Intentions to perform the behaviour
Transtheoretical Model of Change	
Precontemplation	No intention of behaviour change, unaware of any problems
Contemplation	Awareness that a problem exists no commitment to take action. Weighing of the pros and cons of resolving problem
Preparation	Intention to perform the behaviour shortly, involve other people (e.g., spoke to family doctor, friends or family)
Action	Modify behaviour to attempt to deal with problem
Maintenance*	Continue behaviour change to achieve goal
Health Belief Model	
Demographic, socioeconomic, personality variables	Demographic, socioeconomic, personality variables (e.g., optimism)
Perceived susceptibility	Awareness of a problem and seriousness of problem
Perceived threat	Concerns about seriousness & consequences of problem
Cues to action	Perception of symptoms, social influence
Barrier identification	Perceived benefits versus barriers to behaviour
Help-Seeking Model for Infertility	
Symptom salience	Awareness of a problem
Life course factors	Age, marital status, parity
Individual and social cues	Importance of motherhood, partner's desires
Enabling and predisposing factors	Socioeconomic, demographic, education, general perception of health, knowledge of a problem

Note. *Stage not assessed in present study.

Help-seeking Theory and Empirical Literature

Medical help-seeking (hereafter help-seeking) refers to the efforts and/or actions used to assist individuals to seek and use health services when a behaviour or manifestation (i.e., symptom) is out of the ordinary or new (e.g., occurrence of a new lump in the breast) (Pescosolido, 2007). Patient delay in help-seeking refers to the time between an individual's first awareness of a sign or symptom of illness and the initial medical consultation, and has been studied in numerous areas of health (Bish et al., 2005). Many people have mixed feelings about undergoing medical treatment (van Balen & Verdurmen, 1999). On the one hand, medical treatment may result in an improvement of health or even in saving one's life; on the other hand treatments may be unpleasant and may even carry risks. Past research has highlighted the existence of two main reasons given by patients that delayed seeking help (Ristvedt & Trinkaus, 2005). The first suggested a lack of awareness of the importance of potential dangers; the person believed that their symptoms were minor and would clear up without any medical intervention. The second suggested a delay in seeking treatment due to avoidance of the situation; the person was concerned that their symptoms were serious but became immobilised by fear, embarrassment or denial (Ristvedt & Trinkaus, 2005). In addition, several theoretical models have been proposed in order to describe and explain how people form intentions and take action, and these can be applied to help-seeking behaviour.

Theoretical Literature

The Theory of Planned Behaviour.

The theory of planned behaviour (TPB) (Ajzen, 1991) states that a person's intention to perform a certain act (e.g. seek treatment) is determined largely by his/her attitude toward the act and the subjective norm about the act. Subjective norms consist

of a person's beliefs about whether significant others think he or she should engage in the behaviour. In the application of the TPB to help-seeking for suspected fertility problems attitudes (i.e., women's evaluations of the treatment process), would be predictors of their behavioural intentions. The TPB also includes perceived behavioural control, which is the individual's perception of the extent to which seeking treatment, for example, is easy or difficult. Control is seen as a continuum with easily executed behaviours at one end and behavioural goals demanding high resources, opportunities and specialised skills, at the other (Conner & Norman, 1996).

In support of the application of the theory to fertility, studies have highlighted that most women rely on the advice of friends and family to decide on the appropriate treatment before consulting a doctor (White, McQuillan, & Greil, 2006). Further, Callan, Kloske, Kashima, and Hennessey (1988) used the TPB toward better understanding of women's decisions to drop out of fertility treatment. Those who did not continue with treatment (Discontinuers) were less optimistic that another attempt would make them mothers, make their marriages happier, or improve the quality of their lives, and in terms of their perceptions of social pressures, discontinuers also believed that their husbands, family, friends and doctors did not think that they should have another IVF attempt. However, it was not a prospective study therefore one does not know whether negative attitudes and unsupportive environments were a cause or consequence of the decision not to pursue further treatment. Further, the study focused on decision making once already engaged in the treatment process (i.e., having more treatment or discontinuing) and the factors shown to be important could differ in women deciding whether or not to initiate seeking medical help.

The Transtheoretical Model of Behaviour Change.

Another approach to understanding treatment-seeking suggests that decision-making is a process involving specific stages (Prochaska, DiClemente, & Norcross, 1992). At the Precontemplation stage individuals have no intention of changing their behaviour in the near future. Many individuals in this stage are unaware of their problems (e.g., fertility difficulties). Resistance to recognising or modifying the situation (e.g., seeking advice from the family doctor) is the main characteristic of precontemplation. Contemplation is the stage in which people are aware that a problem exists and are seriously thinking about overcoming it but have not yet made a commitment to take action. People can remain in the contemplation stage for long periods (DiClemente & Prochaska, 1985). An important aspect of the contemplation stage is the weighing of the pros and cons of the problem and the solution to the problem. Contemplators appear to struggle with positive evaluations of the situation (e.g., treatment may make me pregnant) and the amount of effort and energy it will cost to overcome the problem (e.g., treatment may be expensive or is unnatural) (DiClemente, Fairhurst, Velasquez, Prochaska, Velicer, & Rossi, 1991; Velicer, Prochaska, DiClemente, & Brandenburg, 1985). Serious consideration of problem resolution is the central element of contemplation.

The Preparation stage combines intention and behavioural criteria. Individuals in this stage are intending to take action shortly and may have taken some minor actions in the past (e.g., spoke to the family doctor). The Action stage is where individuals modify their behaviour, experiences, or environment in order to overcome effectively and deal with the situation (e.g., seeking treatment). Finally, in the Maintenance stage people work towards achieving their goal. (e.g., seek treatment until pregnancy is achieved). Traditionally, maintenance was viewed as a static stage.

However, maintenance is a continuation of change (e.g., the continuation of treatment when it is uncomfortable or costly, or when it fails).

According to the transtheoretical model (TTM) successful behaviour change, that is, success in moving from one stage to another until behaviour has changed, is driven by a series of ten process (consciousness raising, self-re-evaluation, self-liberation, counter-conditioning, stimulus control, reinforcement management, helping relationships, dramatic relief, environmental re-evaluation & social liberation). There has been some debate as to whether all ten processes are important in behaviour change (Lamb & Joshi, 1996), for example, Bowen, Meischke, and Tomoyasu (1994) reported that people in the later stages of the model (e.g., Action and Maintenance) were more likely to endorse items for eight of these processes proposed than people in earlier stages (e.g., Precontemplation). Nevertheless, in an attempt to better understand these processes in determining a person's transition from no behaviour change (e.g., still smoking) to behaviour change (e.g., quit smoking) many studies have developed sets of 'staging' questions to ascertain progress towards change . For example, "I have not given the matter of quitting smoking a thought at all" (Precontemplation) to "I have been consciously avoiding smoking for longer than the last six months" (Maintenance: Lamb & Joshi, 1996). These studies have been successful in establishing support for the model (e.g., Prochaska, DiClemente, Velicer, Ginpil, & Norcross, 1985; Curry, Kristal, & Bowen, 1992; Lamb & Joshi, 1996).

However, a number of authors have highlighted potential issues with the model, questioning the actual existence of the stages (Povey, Conner, Sparks, James, & Shepherd, 1999; DeNooijer, Van Assema, De Vet, & Brug, 2005; Etter, 2005;

West, 2005). Some studies have reported that there were no differences between people in early stages compared to later stages (Glanz et al.,1994) and that fewer processes than originally proposed by Prochaska and colleagues may be involved for behaviour change in certain contexts (e.g., dietary fat reduction: Lamb & Joshi, 1996). Taking into account these concerns proponents of the model argue that stages are a useful way of addressing the critical tasks involved in the transition to behaviour change, and that stages are considered states and not traits and thus quite unstable allowing individuals to move between them quickly (DiClemente, 2005). Previous research has also found support for a combination of the TPB and TTM, with the TPB providing good discrimination between the stages of change as proposed by the TTM. For example, people in the maintenance stage had more positive attitudes, perceived greater social pressure, more control, and had stronger intentions to maintain the behaviour change (e.g., continuing to eat a low-fat diet, continuing to stop smoking) compared to those in the precontemplation stage (Armitage & Arden, 2002). It is clear that while there are still some controversies over the existence of the stages and whether they can be applied effectively to decision making the TTM is still popular when discussing and attempting to understand behaviour change in health.

The Health Belief Model.

The Health Belief Model postulates that individuals will take action (e.g. seeking treatment) if they regard themselves as susceptible to the disease in question (e.g., unable to conceive) and if they believe it to have potentially serious consequences (e.g., children central to their life plan). Action is also dependent on the belief that the anticipated barriers to (or costs of) taking the action are outweighed by its benefits (e.g., the success of having a child outweighing the financial or emotional costs of seeking treatment, Rosenstock 1990).

The health belief model (HBM) is based on several beliefs and attitudes categorised into perceived susceptibility, perceived threat and perceived benefits and barriers. Perceived susceptibility refers to one's own perception of the seriousness of the potential health condition, including personal estimates about one's own susceptibility to illness in general (e.g., how likely one is to have a fertility problem). Perceived threat encompasses feelings of concern about the seriousness of an illness/disease and the consequences of not seeking help to attempt to overcome it (e.g., how childlessness would impact on one's life). Perceived benefits and barriers of actively taking up health behaviours are also predictors of action (e.g., financial costs, invasiveness of treatment versus achieving parenthood, peace of mind that everything had been tried). In a review of 13 studies using the HBM, the best predictors of an outcome such as seeking medical treatment for an illness were the barriers associated with taking a course of action (Janz and Becker, 1984). The potential negative aspects of a particular health action, or perceived barriers, may act as impediments to undertaking the recommended behaviour. Other variables such as demographic, socio-psychological, personality and level of knowledge may also affect the individual's perception and thus indirectly influence health-related behaviour. Research has found that such factors influence the perception of susceptibility, benefits and barriers (Rosenstock 1990).

The model also proposes that cues to action can trigger health behaviour when appropriate beliefs are held. These 'cues' include a diverse range of triggers such as individual perceptions of symptoms, social influence and health education campaigns (Sheeran and Abraham, 1996). A main cue in the case of infertility would be lack of conception after a long period of exposure to unprotected sexual intercourse.

There has been some criticism of the model regarding the lack of definitions of the formulated components (Armitage & Conner, 2000) and the weak correlations of the variables with behaviour (Sheeran & Abraham, 1996). However, a plethora of research exists supporting the HBM. Perceived barriers and benefits, perceived susceptibility, and cues to action have been found to be the most influential factors in predicting intention in a number of health settings, such as the uptake of cervical cancer screening (Agurto, Bishop, Sánchez, Betancourt, & Robles, 2004), use of birth control in adolescents (S. L. Wang, Charron-Prochownik, Sereika, Siminerio, & Kim, 2006), condom use in adolescents (Mahoney, Thombs, & Ford, 1995), uptake of testicular self-examination (McClenahan, Shevlin, Adamson, Bennett, & O'Neill, 2007), uptake of breast self-examination (Garcia & Mann, 2003), and increased calcium intake to prevent osteoporosis (Tussing & Chapman-Novaofski, 2005). Given these results it would be important to assess the model in the context of intentions to seek medical help for fertility difficulties, an area which to the author's knowledge, has not previously been examined.

Model of helpseeking for infertility.

Drawing on a number of theories of help-seeking White et al. (2006) proposed a help-seeking model specific to infertility, whereby action is dependent on inter-relationships amongst personal and social cues, as well as on enabling (e.g. financial resources) and predisposing (e.g. a priori knowledge of symptoms) conditions. White et al. (2006) found that less than half of the infertile (defined as no conception after 12 months of sexual intercourse without contraception) women (40%) sought medical help, results similar to those reported in Chapter 2. White et al. (2006) concluded that perceiving a fertility problem existed (e.g., via the realisation that persistent attempts at conceiving have failed) was central to a woman's treatment seeking behaviour. The

main barrier to perceiving that a fertility problem existed was having the perception of good overall health.

Empirical and Psychological Literature

In addition to the theoretical frameworks other factors accounting for variation in treatment-seeking have emerged from empirical work in comparing people who had sought/not sought fertility treatment. Firstly, treatment seekers were in better social and economic situations. They were older, more likely to be currently married, have a higher income (Stephen & Chandra, 1998, 2000), and be educated to a higher level (school education > 9 years) (Schmidt et al., 1995; Wulff et al., 1997; Wyshak, 2001). Secondly, treatment seekers were more aware of their fertility and health. They had clearer intentions to get pregnant, were more likely to seek information on their own and were more likely to self-define as having fertility problems (Greil & McQuillan, 2004). Thirdly, they had a higher need for parenthood with stronger desires to have children (Langdridge et al., 2000), and were less likely to have previously delivered a child (Templeton, Fraser, & Thompson, 1990; Ducot, Spira, Thonneau, Toulemon, & Leirdon, 1991; Gunnell & Ewings, 1994; Schmidt et al., 1995). Fourthly, they had more favourable attitudes toward treatment. Previous research has found that those who seek treatment for a fertility problem have a lower score on a medical anxiety questionnaire compared to non-treatment seekers (van Balen & Verdurmen, 1999).

Finally personality styles (e.g., optimism, neuroticism) have been shown to influence health and help-seeking behaviours through coping (Scheier & Carver, 1985). Dispositional optimism refers to a personality characteristic involving expectations that good as opposed to bad outcomes will generally occur (Scheier &

Carver, 1987) and has been associated with less delay in seeking help in a variety of diseases (e.g., breast cancer symptoms: Lauver & Tak, 1995).

Research suggests that people high in optimism will deal with stressful events in ways that are more adaptive (Scheier & Carver, 1987). For example, optimistic individuals may use more problem-focused coping, namely manage or come up with effective solutions to the problem (e.g., making a plan of action to seek medical advice if not pregnant within 12 months and following it), whereas pessimists (high expectations that bad events will occur more than good events) may utilize more emotion-focused coping strategies brought about by the distress aroused by their negative expectations, that is, become disengaged from the situation (e.g., avoid talking about the persistent failed attempts at trying to conceive) (Lancastle & Boivin, 2005). Indeed studies exploring women's coping styles with failed IVF attempts have highlighted that escapism and/or avoidance coping styles are associated with poor adaptation to failure (Litt, Tennen, & Affleck, 1992; Terry & Hynes, 1998). Further, in the Callan et al. (1988) study exploring decision-making after a failed IVF attempt women who deterred from another treatment cycle were less optimistic about future treatment outcomes. However, Verhaak, Smeenk, van Minnen, Kremer, and Kraaimaat (2005) found that while personality factors such as neuroticism were important to emotional adjustment to infertility, coping styles such as problem management, emotion approach and cognitive avoidance were not. It could be that dealing with infertility requires a number of coping strategies that change in nature over time as failed attempts to conceive accumulate and reassessment of the parenthood goal occurs (Verhaak et al., 2005).

Using Internet Methodology to Access people Trying to Conceive

Research thus suggests clear differences between treatment seekers and non-treatment seekers on a variety of sociodemographic and trait variables. However, a criticism of previous studies is their reliance on using samples recruited from infertility clinics (Greil & McQuillan, 2004) thus potentially by-passing the views of the 45% of couples who are not seeking any medical care for fertility difficulties. In an attempt to overcome these sampling issues a number of studies have employed community designs targeting men and women who are currently trying to conceive or had tried to conceive in the past (van Balen & Verdurmen, 1999; Greil & McQuillan, 2004). However, community studies are expensive and time consuming to setup and run. An alternative is recruitment through online internet studies, which offers inexpensive access to men and women from around the World. The UCLA World Internet Project (Lebo, 2004) has highlighted that while access and the use of the internet varies considerably from country to country, in more developed countries at least half of all people surveyed stated using the internet. In the United Kingdom over 35 million people were active users of the World Wide Web in July 2008 (Nielsen/NetRatings, accessed September 2008). With regard to health related habits, the internet is now frequently used by people to gain information (Bass, 2003; Bundorf, Wagner, Singer, & Baker, 2006) on a number of issues surrounding health habits (e.g., quitting smoking) and help-seeking behaviours (e.g., treatment options, access, availability and success).

The internet affords a number of advantages when conducting questionnaire research both for the researcher and the participant. For example, for the researcher there are low running costs (e.g., questionnaires can be placed on websites for free and there are often low to no participation costs), low maintenance (e.g., data can be

downloaded immediately into analytical software packages reducing the time taken for data entry), and quick turn-around (e.g., response is immediate compared to manually sending out questionnaires to participants and waiting for mailed responses). For the participant, the internet offers its users anonymity (Strecher, 2007), and the convenience of completing research at home or work, at anytime, without having to travel to a specific place (e.g., university research lab) to complete and/or return responses.

However, using the internet as a research tool can be problematic. For example, use in less developed nations is more infrequent in comparison to more developed nations (Strecher, 2007), and within more developed nations access may not be readily available to everyone due to economic situations leading to a bias towards higher socioeconomic users (Weissman, Gotlieb, Ward, Greenblatt, & Casper, 2000). Although studies specific to fertility have found that many couples from all socioeconomic levels are currently using the internet with regard to their fertility (Weissman et al., 2000). Internet use may also be prone to gender differences. With regard to internet use for fertility issues females have been found to be more active in its use than males (Haagen, Tuil, Hendriks, de Bruijn, Braat, & Kremer, 2003). Finally, data may be prone to repeat responders (Gosling et al., 2004), which can be more controlled in paper and pencil questionnaires.

On the whole however, reviews of the use of the internet as a tool in psychological research have been positively appraised, suggesting the quality of the data obtained from such methods are as good as those provided by traditional paper and pencil methods (Gosling, Vazire, Srivastava, & John, 2004; Strecher, 2007).

The Present Study

The main aim of the present study was to determine whether those who seek medical care for a fertility problem are different compared to those who do not seek treatment. In the present study, 426 women completed an online Treatment Decision-Making Questionnaire (TDMQ) posted on a website targeted at couples just starting out in the process of trying to conceive. The sample comprised two groups of women trying to conceive: those who had not yet sought medical advice (Non-consulters, NC) and those who had (Consulters, C).

The variables examined as potential discriminants of consultation status in the TDMQ were drawn from the four theories (i.e., theory of planned behaviour, health belief model, transtheoretical model and the help-seeking model for infertility) and empirical literature on fertility treatment-seeking. Taking a multifactorial approach to understanding decision making by combining elements from a number of help-seeking theories (as White et al., 2006 proposed) can be an effective way of drawing on the individual factors shown by past research to have the most salience influential effect on behaviour change to help better understand decision making. Fishbein and Yzer (2003) recently endorsed this approach by proposing an integrative model of behaviour change that brings together components from the HBM, theory of reasoned action and the social cognitive theory showing past evidence of good predictive abilities in determining behaviour. In line with theory predictions and previous research in other health areas, it was expected that perceptions of one's fertility (e.g., how fertile are you), treatment beliefs, attitudes and knowledge (e.g., treatment is invasive), need for parenthood as well as coping strategies and personality traits would differentiate these two groups of women seeking/not seeking fertility treatment.

Method and Materials

Design

A quasi-experimental cross-sectional between subjects design was employed. The independent variable was consultation status. Group status was determined by whether the participant had had sought (Consulters, C) or not yet sought medical treatment (Non-consulters, NC). The dependent variables were responses to Treatment Decision Making Questionnaire (TDMQ). The Ethics Committee of the School of Psychology, Cardiff University approved the study (for statement of approval see Appendix B).

Participants

Over an eight week period the Treatment Decision Making Questionnaire (TDMQ) was posted on a website targeted at couples just starting out in the process of trying for a child. The final sample consisted of 426 women, of which 48.1% were from the United Kingdom (UK), 38.0% from the United States (US) and 13.8% from the rest of the world. On average women were 28.61 (SD = 5.23) years of age and had been living with their partners for 4.44 (SD = 3.24) years. Of the 426 women 75.1% (n = 320) were educated to college or university level, 8.0% to trade/technical level, 13.1% to secondary, 2.8% to primary and 0.9% stated no educational attainments. Of the sample 15.4% (n = 64) had children with their current or a previous partner (9.2%, n = 39), and 13.4% (n = 57) of male spouses also had children from a previous relationship. Women had been trying to conceive for 12.42 (SD = 15.38) months, with a range of 0 to 132.

Materials

The TDMQ was designed for this study and addressed issues relevant to decision-making as identified in theoretical work and empirical literature. The

questionnaire comprised of 80 questions in four sections (background information, your fertility, engaging in medical treatment and well being). Table A1 (see Appendix C) shows how each question mapped onto theoretical constructs. The wording of the questionnaire was adapted according to whether the participant had (past tense) or had not (present tense) consulted a medical doctor.

The background information section consisted of 11 items. Participants indicated their gender, current country of residence, their age, their partner's age, their and their partner's highest educational qualification (0 = none, 1 = primary, 2 = secondary, 3 = trade/technical, 4 = college/university), how long they had been with their partner and whether they had any children together or separately. For the present research one question from the General Health scale (SF-36: Stewart, Hays, & Ware, 1988) was used to ascertain how healthy the participant currently felt (1 = poor, 2 = fair, 3 = good, 4 = very good, 5 = excellent). This item was taken from the Short Form-36 health survey and has been widely used with past research showing validity with objective measures of health (Stewart et al., 1988). The Short Form 36 Health survey (SF-36: Stewart et al., 1988) is a multipurpose, short-form health survey consisting of eight scales (36 questions) and has been validated in a variety of medical settings (Ware, 2000).

The 'your fertility' section contained three items assessing participants appraisal of their fertility status (e.g., confidence in their success of conception, how fertile they perceived themselves to be, length of time trying). In the 'engagement in medical treatment' section 32 items were used to assess participants involvement in the medical process and the factors that contribute(d) to seeking medical care. Participants were presented with 16 reasons for or against seeking medical advice

developed from the empirical and theoretical literature (1 = contributed not at all – 5 = contributed extremely). For example behavioural attitudes towards treatment derived from the TPB (e.g. medical treatment is successful, invasive etc.), barrier identification derived from the HBM (e.g., complicated to get help), and predisposing and enabling conditions drawn from the help-seeking model for infertility (e.g., financial cost of treatment). In the current study reliability of the 16 item scale was α =0.75. Participants were also presented with 4 positive consequences of seeking medical advice (e.g., become a mother, having a happier relationship) and 5 negative consequences (e.g. friction with spouse, financially worse off) adapted from the Callan et al. (1988) study. Women rated how these consequences would make them feel if they happened to them on a Likert scale from bad (-3) to good (+3).

Network beliefs (i.e., subjective norms) were measured using two items which assessed to what extent the participant felt that 'my partner' or 'most people who are important to me' would want them to seek medical advice. Motivation to comply was measured similarly by two items which assessed the extent to which participants felt they generally wanted to do what 'my partner' or 'most people who are close to me' thought they should do. Participants rated the statements on a Likert scale (+3 "Strongly agree" to -3 "Strongly disagree": adapted from the Callan et al., 1988 study). Additionally, participants indicated how comfortable they were about confiding in family and friends regarding trying for a child (1 = not very comfortable to 5 = very comfortable).

The final section in the TDMQ ('well being') assessed strength of desire to become a parent, personality traits and coping styles. The need for parenthood scale used three items from the Infertility Reaction Scale (Collins, Freeman, Boxer, &

Tureck, 1992) and three items from the Fertility Problem Inventory (Newton, Sherrard, & Glavac, 1999) (six items, higher score is greater need for parenthood). In the present study reliability for the scale was α =0.73.

The Life Orientation Test (LOT) was used to measure dispositional optimism (Scheier & Carver, 1985). The LOT contained 8 items (4 filler items, total = 12 items) assessing general outcome expectancies (e.g., "Good things usually happen to me") with higher scores indicating greater optimism. Scheier and Carver (1985) report α = 0.76 reliability of the scale, with a mean LOT score for a normative sample of female students was 21.41 (*SD* = 5.22; Scheier & Carver, 1985). In the current study reliability of the LOT was α = 0.85 for the 12-item scale and the mean for the whole sample was 18.65 (*SD* = 5.54).

The Ways of Coping questionnaire (Folkman & Lazarus, 1988) was used to assess coping but the original 66-item questionnaire was shortened to 16 items due to time limitations of the length of the TDMQ. In the current study items assessed problem-focused coping (problem management, problem appraisal), and emotion focused coping (emotion focused and escapist) according to Terry & Hynes (1998). Higher scores indicated greater use of the coping strategy. Problem management (four items) referred to effective attempts to manage a situation (e.g., 'thought about what steps to take to deal with the problem'). Problem appraisal (four items) referred to attempts to manage one's own appraisal of how stressful a situation was (e.g., 'tried to see the positive side of the situation'). Emotion focused (four items) referred to one's emotional reaction to a situation (e.g., 'let my feelings out somehow'), and escapist coping (four items) referred to the avoidance or wishful thinking of a situation (e.g.,

'hoped a miracle would happen'). Cronbach's alpha used to assess reliability was α = 0.79, α = 0.56, α = 0.66, α = 0.62 for each subscale respectively.

Questionnaire construction.

The online survey was set up by iPsychExpts (Brand, 2005). Webmasters at 11 websites aimed at couples just 'starting out' in the process of trying to get pregnant were contacted via email to ask whether they would post the TDMQ on their site. It was decided to intentionally avoid sites devoted to people who already had fertility problems. The TDMQ was placed on the only site that replied (i.e., gettingpregnant.co.uk).

Procedure

A sentence about the questionnaire ("Survey for people currently trying to conceive") and an option button was placed at the top of every page on the website. Clicking on the option button took the participants to a consent form and description of the content of the questionnaire (see Appendix D). To continue to complete the questionnaire participants were asked to give their consent by following the instructions, otherwise they could close the page and leave the questionnaire. Questions were presented in specific sections outlined above and once a participant clicked to move to the next page they were unable to go back and change answers. Throughout the questionnaire participants had the option to click out and close the questionnaire with no data being submitted. Once they came to the final page they were given a more detailed explanation of the study and the option to submit their data if they wished. The questionnaire took around 10 – 15 minutes to complete.

Data analysis

Preliminary data screening produced 57 participants that were excluded from analyses due to incomplete (>50% of data missing) or invalid data. In addition, the only 10 male participants were excluded because they were too few to analyse separately. Finally, 5 outliers (>3 standard deviations ± the mean) were identified and excluded, leaving a final sample of 426 female participants.

Multivariate analyses of variance (MANOVA) were carried out to examine differences between Consulters and Non-Consulters on all variables (except demographic characteristics which were compared using t-tests). If the multivariate F-test was significant, then single degree freedom t-tests were examined to determine those variables that maximally discriminated between Consulters and Non-consulters. This approach reduced the risk of alpha inflation associated with multiple testing. In addition, a factor analysis using varimax orthogonal rotation was used to group (and reduce) the 16 reasons that contribute(d) to seeking medical advice (in the 'engagement in medical treatment' section). Factor loadings above .30 were considered significant and presented (Tabachnik & Fidell, 2001). All variables found to be significant at the univariate level were included in a logistic regression to determine factors that were associated with treatment seeking behaviour (coded as 1). Significant variables were entered as blocks in the following order: traits (i.e., coping variables), fertility appraisal (i.e., perception and confidence of fertility), decision making factors (i.e., factors contributing to and consequences of treatment seeking), and accessibility (i.e., treatment cost). The Wald statistic and odds ratio (± 95% confidence interval [CI]) are presented.

Reliability was conducted on all the scales using Cronbach alpha (α). Values between 0.70 – 0.80 indicate acceptable reliability (Field, 2005). A probability value of $p<0.05$ was regarded as statistically significant. All analyses were performed with the software Statistical Package for the Social Sciences (SPSS).

Results

Engagement in the Medical Process

In total 56.57% (n = 241) of women had not consulted a doctor about conceiving (Non-consulters, NC) and 43.43% (n = 185) had already done so (Consulters, C). On average the Consulters had been trying to conceive for 19.14 months (SD = 18.76) and the Non-consulters for 7.24 months (SD = 9.32). The average time since first consultation was 8.79 (SD = 14.32) months for those who had sought advice. Women who had not sought advice said they would do so after a further 10.21 months (SD = 7.06) of trying.

Factors Associated with Decision Making Regarding Treatment Seeking Behaviour

Background information.

As shown in Table 3.2 compared to Consulters, Non-consulters and their partners were younger and had been with their partner for less time. No significant difference was found between groups for country of residence, or level of education, with the majority of the sample (75%) educated to college/university level. There were no differences in the number of previous children (current partner, previous partner or step children) between Non-consulters and Consulters, with 15% of the sample having previously given birth. Finally, there was no difference between groups on the SF-36 General Health question assessing participants overall health ($t(424)$ = 0.21, P = 0.84) with both Consulters and Non-consulters rating their current health as good to very good (sample M = 3.47, SD = 0.88).

Table 3.2
Demographic characteristics according to consultation group.

Background Information	Whole Sample N = 426	Consulter (n = 185)	Non-consulter (n = 241)	t	Degrees of freedom	P value
		Mean (SD)				
Female age	28.61 (5.23)	29.45 (5.22)	27.96 (5.15)	2.95	424	0.003
Partner age	30.89 (5.93)	31.66 (5.98)	30.31 (5.83)	2.35	424	0.019
Years together	4.44 (3.24)	5.11 (3.32)	3.93 (3.09)	3.81	424	0.001
Range	0 - 21					
General health (SF-36)[a]	3.47 (0.88)	3.46 (0.93)	3.48 (0.85)	0.21	424	0.837
Country of residence		**n (%)**		χ^2		
United Kingdom	205 (48.12)	93 (50.27)	112 (46.47)	4.51	2	0.11
United States of America	162 (38.03)	61 (32.97)	101 (41.91)			
Other		31 (16.76)	28 (1.62)			
Education						
College/University	320 (75.12)	140 (75.68)	180 (74.69)	2.32	4	0.68
Trade/technical	34 (7.98)	11 (5.95)	23 (9.54)			
Secondary	56 (13.15)	27 (14.59)	29 (12.03)			
Primary	12 (2.82)	5 (2.70)	7 (2.90)			
None	4 (0.94)	2 (1.08)	2 (0.83)			
Secondary	56 (13.15)	27 (14.59)	29 (12.03)			
Previous children						
Current partner	64 (15.02)	29 (15.68)	35 (14.52)	0.11	1	0.74
Previous partner	39 (9.15)	20 (10.81)	19 (7.88)	1.08	1	0.30
Step children	57 (13.38)	28 (15.14)	29 (12.03)	0.87	1	0.35

[a]Higher scores means more of the attribute.

Fertility characteristics.

A MANOVA comparing Consulters and Non-consulters on fertility perceptions was significant (Pillais = 0.16, Multivariate $F(3, 417) = 26.89$, $P = 0.001$). As shown in Table 3.3 univariate follow-up tests were significant for all variables. Non-consulters had significantly more confidence in their fertility, were more optimistic about their chances of conceiving, and had been trying for fewer months to conceive.

Table 3.3
Fertility characteristics according to consultation group.

Your Fertility	Whole Sample N = 426	Consulter (n = 185)	Non-consulter (n = 241)	t	Degrees of freedom	P value
		Mean (SD)				
Months trying to conceive	12.42 (15.38)	19.14 (18.76)	7.24 (9.32)	8.54	421	0.00
Range	0 - 132					
Confidence in fertility	59.30 (29.51)	52.76 (29.20)	64.32 (28.82)	4.08	424	0.00
Range (0 - 100%)	0 - 99					
Perception of fertility[a]	2.78 (0.83)	2.53 (0.80)	2.97 (0.80)	5.58	422	

[a]Higher scores means more of the attribute (1 = Not at all to 5 = Extremely).

Engagement in medical treatment.

To group (and reduce) the 16 reasons that contribute(d) to seeking medical treatment a factor analysis was computed. Table 3.4 shows factor loadings for each variable for each component extracted. Four factors were extracted and were labelled as follows; (1) 'fertility and treatment beliefs' consisted of items concerned with fertility awareness and beliefs and attitudes toward treatment and its accessibility, (2) 'discovery threat' consisted of items concerned with being labelled/diagnosed, and its effect (e.g., disrupt marital relationship), (3) 'treatment safety & comfort' consisted of items about the complexity of fertility treatment and being comfortable with

disclosure, (4) 'confidentiality and reassurance' consisted of items concerned with privacy and desired outcomes of medical consultation, and finally; (5) treatment cost.

Table 3.4
Factor loadings for TDMQ items according to exploratory factor analysis.

	Label given to factor				
Engagement in Medical Treatment	**Fertility and Treatment Beliefs**	**Discovery Threat**	**Treatment Safety & Comfort**	**Confidentiality & Reassurance**	**Treatment cost**
Complicated to get help	0.83				
Success of medical treatment	0.80				
How to get help	0.77				
For/against medical interventions	0.69		0.33		
Had a problem	-0.58			0.45	
Being labelled		0.79			
Scared of what doctor might say		0.77			
Told about fertility	0.48	0.56			
Disrupt relationship		0.43			
Medical treatment invasive			0.74		
Worry			0.69		
High-tech procedure		0.33	0.57		
Embarrassment			0.55		
Talk confidentially				0.81	
Reassurance				0.77	
Finance					0.89
Eigenvalue	4.10	2.14	1.56	1.07	1.01
Percent variance	25.62	13.36	9.76	6.68	6.31

Note .Only factor loadings >0.30 presented. Items were assigned to factors with highest loadings.

A MANOVA comparing Consulters and Non-consulters on factor scores was significant (Pillais = 0.79, Multivariate $F(16, 409) = 97.45$, $P = 0.001$). Univariate follow-up tests were significant for most factors. As shown in Table 3.5, 'Fertility and treatment beliefs', 'Discover threat' and 'Treatment safety and comfort' contributed more to decision making for the Consulters compared to the Non-consulters, whereas 'Treatment cost' contributed more for the Non-consulters. No difference between Consulters and Non-consulters was found for the factor 'Confidentiality and reassurance'.

Table 3.5
Means (SD) for TDMQ factors according to consultation group.

Engagement in Medical Treatment	Consulter (n = 185)	Non-consulter (n = 241)	t	Degrees of freedom	P value
	Mean (SD)				
Fertility and treatment beliefs	3.21 (0.73)	2.12 (0.53)	17.98	424	0.001
Discovery threat	2.68 (0.67)	2.25 (1.03)	4.97	424	0.001
Treatment safety & comfort	2.27 (0.83)	1.95 (0.81)	4.07	424	0.001
Confidentiality and reassurance	3.78 (1.02)	3.73 (0.96)	0.53	424	0.598
Treatment cost	2.12 (1.30)	3.18 (1.46)	8.15	424	0.001

Note. For all items higher scores means more of the attribute.

The MANOVA on consequences of seeking treatment was significant (Pillais = 0.07, Multivariate $F(9,416) = 3.61$, $P = 0.001$). Univariate follow-up tests revealed that Non-consulters rated being financially worse off from seeking medical treatment as more negative compared to Consulters ($t(424) = 1.98$, $P = 0.05$) and believed seeking treatment would result in a happier relationship and marriage compared to the Consulters ($t(424) = 3.30$, $P = 0.001$). Finally, Consulters rated talking to someone about fertility concerns as a greater consequence of seeking medical treatment than did the Non-consulters ($t(424) = 2.35$, $P = 0.02$).

The MANOVA on subjective norms and social influence was significant (Pillais = 0.03, Multivariate $F(5,420) = 2.51$, $P = 0.03$). Follow-up tests showed that Non-consulters were less likely to perceive close family and friends to want them to seek advice than Consulters (see Table 3.6). No differences were found between Non-consulters and Consulters for the complying with friends and families wishes to seek medical treatment or any of the partner variables. Consulters scored marginally higher on comfortable confiding in others compared to Non-consulters ($P = 0.06$).

Table 3.6
Means (SD) for network beliefs and motivation to comply according to consultation group.

Normative beliefs and motivations to comply	Consulter (n = 185)	Non-consulter (n = 241)	t	Degrees of freedom	P value
	Mean (SD)				
My partner wants me to seek medical advice	1.76 (1.46)	1.54 (1.50)	1.57	424	0.118
I do what my partner thinks is best	0.96 (1.46)	1.07 (1.55)	0.80	424	0.425
People important want me to seek medical advice	2.22 (1.15)	1.98 (1.28)	2.02	424	0.044
I do what people important to me think I should do	-0.02 (1.71)	0.24 (1.69)	1.56	424	0.120
Comfortable confiding with others	3.48 (1.41)	3.22 (1.49)	1.86	424	0.063

Note. For all items higher scores means more of the attribute.

Well being.

A MANOVA indicated significant multivariate group effects for all the well being questions (Pillais = 0.04, Multivariate $F(6,419) = 2.66$, $P = 0.02$). As shown in Table 3.7, the Non-consulters used problem focused coping (i.e., problem appraisal) more frequently, and were less likely to use emotion-focused (i.e., escapist) coping strategies compared to the Consulters. Both the Consulters and Non-consulters scored highly on the need for parenthood question (sample $M = 21.24$, $SD = 4.24$), and did not differ on this variable. No difference was found for level of optimism with the sample mean 18.56 ($SD = 5.54$).

Table 3.7
Means (SD) for personality and coping according to consultation group.

Well Being	Consulter (n = 185)	Non-consulter (n = 241)	t	Degrees of freedom	P value
	Mean (SD)				
Need for parenthood (6 items, total = 30)	21.44 (4.28)	21.09 (4.22)	0.86	424	0.391
How optimistic are you (Life Orientation Test, 12 items)	18.11 (5.49)	19.06 (5.55)	1.75	424	0.081
Coping style (THWC, 16 items)					
Problem management	7.38 (2.47)	7.30 (2.72)	0.33	424	0.740
Problem appraisal	5.21 (2.12)	5.78 (2.13)	2.76	424	0.006
Escapist	6.04 (2.63)	5.51 (2.61)	2.08	424	0.038
Emotion focused	6.70 (1.90)	6.64 (2.10)	0.323	424	0.747

Note. For all items higher scores means more of the attribute.

Multivariate analysis.

All significant univariate analyses were included in a logistic regression. Table 3.8 shows regression coefficients, Wald statistics, odds ratios and confidence intervals (CI). Variables were entered in the following steps. Personality traits (e.g., coping styles) were entered first, then factors associated with fertility appraisal (e.g., perception of fertility status), then decision making factors (e.g., factors that contributed to decision making about treatment and the consequences of seeking medical help). Finally, accessibility to treatment (e.g., cost of treatment) was the last step.

As Table 3.8 shows all steps were significant, as was the overall model. Using problem appraisal coping was significantly associated with a lower likelihood of seeking medical treatment whereas the opposite was true for women using escapist coping. Women who had been trying for a longer number of months to conceive were 4.46 (CI = 2.74, 7.27) times more likely to have sought medical treatment. In addition being older was associated with a higher likelihood of seeking medical help. However, having a positive perception of one's fertility potential was associated with not seeking treatment.

Table 3.8

Summary statistics for logistic regression (n = 424) examining the associations between significant univariate correlates and the outcome of seeking medical treatment[a].

TDMQ Questions	Coefficient (β)	Standard Error	Wald Statistic	Significance level	Odds ratio (OR)	95% C.I Lower Upper
Traits						
Problem appraisal (THWC)	-0.13	0.05	7.47	0.01	0.88	0.80, 0.96
Escapist (THWC)	0.08	0.04	4.90	0.03	1.09	1.01, 1.17
Block (χ2=12.18, df=2, P=0.002)						
Fertility Appraisal						
Infertile[b]	1.50	0.25	36.03	0.001	4.46	2.74, 7.27
Female age	0.06	0.02	7.89	0.001	1.06	1.02, 1.11
Confidence in fertility	0.00	0.00	0.68	0.41	1.00	0.99, 1.01
Perception of fertility	-0.45	0.18	6.33	0.01	0.64	0.45, 0.91
Block (χ2=77.48, df=42, P=0.002)						
Decision Making Factors						
Factors contributing to decision making						
Fertility and Treatment Beliefs	2.93	0.31	87.26	0.001	18.73	10.13, 34.63
Discovery Threat	-0.05	0.19	0.06	0.81	0.95	0.65, 1.40
Treatment safety & comfort	-0.37	0.22	2.86	0.09	0.69	0.45, 1.06
Confidentiality and reassurance	-0.52	0.18	8.19	0.001	0.59	0.41, 0.85
Consequences of treatment						
Financially worse off	0.14	0.13	1.04	0.31	1.15	0.88, 1.49
Happier relationship and marriage	-0.41	0.14	8.22	0.001	0.66	0.50, 0.88
Talking to someone about fertility concerns	0.31	0.16	3.97	0.05	1.37	1.01, 1.85
People important want me to seek medical advice	0.19	0.13	2.12	0.15	1.21	0.94, 1.56
Block (χ2=204.39, df=8, P=0.001)						
Accessibility						
Treatment cost	-1.34	0.19	52.10	0.001	0.26	0.18, 0.38
Block (χ2=90.08, df=1, P=0.001)						
Overall model (χ2=384.12, df=15, P=0.001)						

Note. For all items higher scores means more of the attribute

[a]Dependent variable was 0 = Not consulted, 1 = Consulted. [b]Infertile refers to trying for more than 12 months to conceive (coded 1 = > 12months trying to conceive).

With reference to the five factors produced from the factor analysis, 'Fertility and treatment beliefs' showed a strong association with treatment seeking behaviour, whereas having concerns with 'Confidentiality and reassurance' was associated with not seeking treatment. In addition concerns about 'Treatment cost' were associated with a lower likelihood of seeking medical treatment. Women who believed treatment allowed one to talk to someone about fertility concerns were 1.37 (CI = 1.01, 1.85) times more likely to seek medical treatment. Conversely, believing treatment would result in a happier relationship and marriage was associated with a lower odds of seeking medical treatment. Being financially worse off as a consequence of seeking treatment was not significant nor was having important people close to you wanting you to seek medical advice in the multivariate model. The factor 'Fertility and treatment beliefs' had the largest odds ratio associated with treatment seeking (OR 18.73, CI = 10.13, 34.63) and 'Treatment cost' the largest odds ratio associated with not seeking treatment (OR 0.26, CI = 0.18, 0.38).

Delayed Help-Seeking

One question raised by the results is whether the women who had not yet consulted a doctor should have been seeking medical advice. According to UK national guidelines, women should seek medical attention after 12 months of regular, unprotected intercourse (or 6 months if the woman is > 35 years) (National Institute of Clinical Excellence [NICE], 2004). The number of women who attained the criterion threshold when medical advice would typically be recommended in practice guidelines was therefore examined. In total 17.43% (n = 42) of NC women met the NICE criteria for referral to specialist fertility services.

In a secondary analysis this sub-group of women were examined to establish whether their scores altered the pattern of results presented by comparing them (labelled Delayers, $n = 42$) to the remaining Non-Consulters ($n = 199$). All significant univariate analysis conducted on the Non-consulters and Consulters were re-analysed in the secondary analysis. As Table 3.9 shows most comparisons were not significant, but a few important differences emerged (after Bonferroni correction, $P < 0.003$). First, Delayers had been trying to conceive for longer, perceived themselves as less fertile and were less confident in their ability to conceive naturally compared to the remaining group of Non-consulters, further 'Discovery threat' was significantly higher for the Delayers compared to the remaining Non-consulters.

Table 3.9
Mean (SD) for significant univariate correlates of decision making for Delayers and Non-consulters.

TDMQ Questions	Delayers (n=42)	Non-consulter (n = 199)	t	P value
	Mean (SD)			
Background Information				
Female age	27.81 (6.42)	27.99 (4.86)	0.21	0.84
Your Fertility				
Months trying to conceive[a]	22.98 (12.07)	3.88 (3.24)	19.30	0.001*
Confidence in fertility	36.93 (28.39)	70.10 (25.44)	7.52	0.001*
Perception of fertility[a]	2.36 (0.79)	3.10 (0.74)	5.81	0.001*
Engagement in Medical Treatment				
What contributes (a)/contributed (b) to seeking medical advice				
Fertility and treatment beliefs	2.32 (0.74)	2.08 (0.47)	2.80	0.01
Discovery threat	2.67 (1.08)	2.16 (1.00)	2.95	0.001*
Treatment safety & comfort	2.21 (0.95)	1.90 (0.76)	2.31	0.02
Confidentiality and reassurance	3.89 (1.17)	3.70 (0.91)	1.21	0.23
Treatment cost	3.67 (1.56)	3.08 (1.42)	2.39	0.02
How does each consequence make you feel				
Financially worse off	-1.02 (1.39)	-1.23 (1.07)	1.08	0.28
Happier relationship and marriage	2.43 (1.25)	2.31 (1.06)	0.66	0.51
Talking to someone about fertility concerns	1.86 (1.59)	1.72 (1.12)	0.67	0.50
How strongly do you agree with the following:				
People important want me to seek medical advice	2.14 (1.24)	1.95 (1.30)	0.91	0.36
Well Being				
Coping style (THWC)				
Problem appraisal	5.74 (2.43)	5.79 (2.07)	0.14	0.89
Escapist	6.05 (2.59)	5.40 (2.61)	1.47	0.14

Note .Degrees of freedom = 239. [a]Degrees of freedom = 237. *Significant after Bonferroni adjustment ($P < 0.003$).

Discussion

The aim of the study was to examine psychological factors associated with decision-making about pursuing medical help for fertility issues. The findings revealed that women's knowledge about their fertility (i.e., awareness that a problem existed) and their emotional reactions to that knowledge (i.e., discovery of a problem, being labelled infertile) were the core motivating forces behind engaging in the medical process.

Previous research has suggested that those who seek treatment for a fertility problem are characteristically different to those who do not, on a variety of socio-demographic and trait variables. The present results lend support to such a statement, and in addition, validate the use of the internet as a valuable tool in accessing women currently trying to get pregnant. The results reveal that those who had sought treatment had positive treatment beliefs, a willingness to know if a problem existed and were more aware of their fertility potential. Consulters were more concerned with factors associated with how to get help, knowing where to get help and the ease of obtaining help. The Non-consulters were more confident about their fertility potential but reported greater worry of the diagnosis that could occur if they sought help. Moreover treatment costs were more of an issue for the Non-consulters than the Consulters.

Detailed analyses of the non-consulters revealed two potential groups of people who had yet to seek medical advice (those who had been trying for more than 12 months [Delayers] and those who had not [rest of the Non-consulters]). For the majority of the Non-consulters their confidence in their fertility and inaction to seek advice may be justified; when the Delayers are removed from this group the Non-

consulters had only been trying to conceive on average for 3.88 months. Given fecundity rates, there were good chances that most of these women would eventually conceive naturally (NICE, 2004). In contrast, the Delayers, who accounted for about 20% of those that had not consulted, had been trying for nearly two years (22.98 months). They were very pessimistic about their chances of getting pregnant naturally yet had never sought any medical advice/treatment, even though seeking advice was clearly warranted. Although many results were similar for the NC versus Delayers, there were some important differences as will be discussed.

Specifically the threat associated with the discovery of a fertility problem was critical to decision making for the Delayers. Specifically, worry about being labelled and diagnosed infertile coupled with not wanting to know that one had a fertility problem were major barriers to seeking help. Feelings of shame to expose a problem have been found in other fertility research (van Balen et al., 1997b). Moreover, fear has been shown to have an effect in decision making in many other health areas (e.g., breast and prostate cancer screening; Consedine, Magai, Krivoshekova, Ryzewicz, & Neugut, 2004; Consedine, Morgenstern, Kudadjie-Gyamfi, Magai, & Neugut, 2006). Research on cancer suggests that those who are most distressed about the possibility of a diagnosis are the slowest to seek help (Bish et al., 2005; Grunfeld, Hunter, Ramirez, & Richards, 2003). Applied to infertility, this suggests that those for whom a diagnosis of infertility would be most threatening, as would seem to the case with Delayers, might postpone (perhaps indefinitely) a visit that could confirm their worst fears (White et al., 2006).

Conversely, previous research has highlighted that those who are over anxious may seek medical advice sooner or more frequently, i.e. seeking medical advice after

2-3 months of trying (White et al., 2006). The current study found a wide range in the number of months before consulting (1 – 47 months, $M = 8.79$, $SD = 14.32$). One cannot however determine why some women sought treatment earlier than others because data was not collected on factors that might have predisposed one to seek treatment early (e.g., known reproductive problems). Personality traits (e.g., monitoring and blunting, S. M. Miller, 1987) might shed light on early treatment seeking as these determine a person's behavioural reaction to everyday health dilemmas. However, in the current study the measured personality variables (e.g., optimism) were not associated with decision-making. This may be because the relevant personality dimensions were not assessed. In order to determine if, and to what extent such variables affect decision making future studies may need to assess a broader range of traits (e.g., monitoring and blunting: S. M. Miller, 1987).

There were unexpected findings for coping variables in that consulters were using less problem appraisal (e.g. saw less the positive side of the situation) and more escapism (e.g. more hoping that a miracle would happen). This is unexpected as prior research suggests problem focused coping (e.g., problem appraisal) is often linked to direct and effective management whereas emotion focused coping (e.g., escapism) is often viewed as inhibiting or delaying effective action. Verhaak et al., (2005) reported that dealing with infertility requires a number of coping strategies whose nature may change over time as failed attempts to conceive and reassessment of the goal (i.e., importance of becoming a parent) occurs (Verhaak et al., 2005). As emotional functioning was not assessed in the present sample one cannot say whether this seemingly ineffective pattern of coping would be associated with poorer mental health outcomes as has been shown in more advanced stages of treatment since variables

were not measured but this is an issue that clearly warrants further investigation (Terry & Hynes, 1998).

Theoretical Implications

Four social cognition models were used to make predictions about help seeking behaviour (see Table 3.1, page 44). Being aware of one's own fertility was found to be a main determinant of seeking medical help, as predicted by all the proposed models/theories. Another key prediction was also supported. Three of the models and theories (TPB, TTM and HBM) postulated that action/behaviour change would occur if one held positive attitudes towards the behaviour (TPB), and beliefs that the benefits of taking action would outweigh the negatives (TTM and HBM). In the present study the women who had consulted were more likely to possess positive treatment beliefs and attitudes surrounding the treatment process, for example, having confidence in medical interventions, believing treatment to be successful and knowing where to get medical help. Further, as predicted by three theories/models (TPB, HBM & Help-seeking model for infertility) sociodemographic and demographic variables differentiated the Consulters to the Non-consulters. For example, Non-consulters were more concerned with the financial burden of seeking treatment.

A few predictions were not supported in the present study. Firstly, limited support for the prediction that social pressures (e.g., subjective norms, and normative beliefs) impact on decision making regarding action/behaviour change was found. In support the Non-consulters were less likely to perceive close family and friends to want them to seek advice than Consulters. However, partner variables, motivation to comply, and comfort disclosing information to close family and friends were not associated with decision making, suggesting that social norms and pressures did not

have as much influence in fertility decision-making as they appear to have in other areas of health. With regards to fertility issues it may be that people feel uncomfortable about discussing their concerns. Adashi et al. (2000) report that infertility is still surrounded by taboos and it is often difficult for couples to address this problem openly. Indeed Consulters reported that a positive consequence of seeking medical treatment would be having someone to talk to about fertility concerns, which may suggest a desire to disclose and talk about a topic that may not be discussed openly among family and friends. In a recent investigation Peronace, Boivin, and Schmidt (2007) found that couples' willingness to speak to family and friends about fertility problems decreased over time as they experienced failed treatments. All the theories propose that social pressures are important in behaviour change so it would be important in future studies to establish in more detail how much of a role family and friends play towards decision making with regards to situations that are usually seen as private, discrete and often embarrassing.

Finally, all the stages of the TTM could not be adequately assessed in the current study due to the design employed (Cross sectional). In the current study the only stages that could be measured were the precontemplation, contemplation, action stage and preparation stage. In this cross-sectional investigation those who had not yet taken action (Non-consulters) were more confident and optimistic that they would eventually conceive, a feeling justified by the fact that they had been trying for few months, and these people could be seen to be in the Pre-contemplation stage. The Delayers might be placed more in the Contemplation stage since they had lost confidence in their ability to conceive after a long period of unsuccessful attempts but had not yet taken action due to fears about the implication of seeking help. In comparison, those who had taken action were clearly more positive about treatment

and more willing to know about a fertility problem, as one would expect in the Action stage. Although the results are in keeping with what might be expected only longitudinal data would be able to test the transition from each stage proposed in the model, assess the time with which people take to move from one stage to another, and study what women do after initial action (consulting a doctor) has occurred.

Taken together the results lend support to all the theories and models proposed especially in relation to the fact that being aware of a problem existing and having adequate knowledge about how to get help are key determinants supported. However these results may lend more support to the HBM, TTM and Help-seeking model for infertility than the TPB as a main prediction of the TPB is that a person's intention to perform a certain act is determined largely by his/her attitude and the attitudes of others in their environment toward the act (Callan et al., 1988). A prediction not fully supported in the current study. On a cautionary note, the aim of the study was to take a multifactorial approach, using a limited number of questions and it may therefore be that each theory/model was not sufficiently covered to test specific model predictions.

Methodological Implications and Limitations

The methodology proved successful. In 8 weeks the study recruited 426 women currently trying to conceive consisting of both those who had and had not previously sought treatment, showing a good representation in terms of critical sample characteristics (e.g., age, month trying, and medical consultation). A criticism of internet studies is that they may consist mainly of women already in treatment that have spent years trying to conceive (Greil & McQuillan, 2004); however while this sample did include women who had been trying for a long time, it also included women at the very early stages of trying to conceive (31.9% of the sample had been

trying for ≤ 3 months, 17.6% for 3 – 6 months, 17.6% for 6 – 12 months and 32.2% more than 12 months) and compared to typical findings in women undergoing in vitro fertilisation, an advanced fertility intervention (e.g., female age, $M = 34$ years, Boivin & Schmidt, 2005) the women in the current study were younger, had been with their partners for less time and, more importantly, had not been trying to conceive for as long. The mean age of the sample ($M = 28.61$, $SD = 5.23$) was also in keeping with the mean age of first birth in the UK ($M = 27.1$, Social Trends 33, 2000: Office for National Statistics). A further benefit is the anonymity that the internet offers, which makes it a useful research tool to access couples who can discuss and relay their opinions on the very private matter of infertility without having the worry of their identity being revealed.

Three other methodological issues warrant comment. First, the current findings provide important information about the nature of variables that might be critical in motivating people to seek medical help. However, cross-sectional designs can only offer information about associations and not cause and effect. For example, positive treatment beliefs were higher in Consulters than the Non-consulters but it cannot be ascertained whether this means that positive treatment beliefs increase treatment seeking behaviour, treatment seeking behaviour increases positive treatment beliefs, or whether both occurs. The results of this study have made an important contribution in identifying that those variables warrant further study, not that they are causal. Only a prospective longitudinal investigation of the same women can provide definitive conclusions about the true causes of seeking medical help. In such a design, psychological assessments would take place when couples started trying to conceive, and would continue periodically until such efforts were discontinued. It would then be possible to examine the pre-consultation psychological processes of those who

subsequently engaged in the medical process, how it changed as a result of their medical experiences and/or how it differed from the profile of those who never subsequently consulted. This methodology would also be an important way to evaluate the predictive value of the models proposed.

A second limitation was the bias potentially introduced by the high level of education of most women in the sample (75.1% educated to college or degree level). Although this could suggest a bias due to internet services being mainly available and/or used by those in higher socioeconomic status it may also be a result of the use of 'college' in the education response scale. In the UK (where 50% of the sample resided) 'College' can encompass a wide selection of qualifications from GCSE (General Certificate of Secondary Education) level to Degree and as only 16% of people of working age do not have qualifications in the UK (see United Kingdom Annual Population Survey, Office of National Statistics, 2004a) using this scale may have therefore lead to more women being classified in the highest educational group. This methodological issue may also explain why the present study did not support previous results showing that level of education is a significant predictor of treatment seeking behaviour (Schmidt et al., 1995; Wulff et al., 1997; Wyshak, 2001). In future it may be of use to ask participants their highest educational qualification.

A final limitation is that only 10 men responded to the survey, which was too few to analyse separately. There could be a number of reasons for this. Men often have a poor knowledge of matters related to health and they are less likely than women to seek help from health care professionals when they are ill (Banks, 2001). With reference to infertility interviews, married infertile couples show that throughout the treatment process, it is the female partner who takes the leadership role, regardless

of who had the reproductive impairment, with the female partner typically the one to suggest new treatment options (Greil, Leitko, & Porter, 1988). Further, many of the websites available to couples who are facing difficulties in getting pregnant are female orientated, therefore when a man searches the internet for information on fertility problems and conception they may not be drawn to look at sites named gettingpregnant.co.uk, babyzone.com or thelaboroflove.com, which were the sites targeted. It may be the case that men would fill out such questionnaires if they were on male oriented health sites (e.g., Men's Health, GQ and FHM), and such sites ought to be targeted in future studies. It would be imperative for future research to assess men's perspectives on fertility decision making.

Clinical Implications and Future Directions

Couples faced with infertility have to cope with a complicated decision making process involving several options for a successful resolution of this crisis (van Balen et al., 1997b). Ultimately, if people do not have the correct information, judgements regarding resolution of a problem will be based on unfounded beliefs. One way to improve decision-making would be to increase knowledge about infertility and the reliable solutions to this health problem, allowing people to be better able to evaluate information they come across and therefore make decisions that will improve their chances of reaching their parenthood goal. The results of the present study affirm the need for practical information about conceiving with medical help and further, support research by Dyer, Abrahams, Hoffman, and van der Spuy (2002) suggesting that interventions that include accurate and valid information and good health education will be the most effective in helping women in accessing medical care, complying with treatment and dealing with the possibility of childlessness.

The results from the current study highlight that women's knowledge about their fertility (i.e., awareness that a problem existed) was a key determinant for seeking medical treatment. In order for people to be able to assess their own fertility and become aware of existing problems they need to possess knowledge about fertility more generally (e.g., how long is too long to be trying to conceive? what are the factors that may impact on fertility potential?). Therefore the next chapter will assess knowledge regarding the factors associated with female infertility.

Chapter 4
Knowledge about infertility risk factors, fertility myths and illusory benefits of healthy habits in young people

Introduction

The results of Chapter 3 highlighted that having an awareness that a problem exists is a key factor associated with the seeking of medical advice and initiation of treatment and that education about fertility issues is needed to prevent fear (i.e., fear of being labelled infertile or fear of what the treatment process entails) and potential unnecessary delay in seeking help when faced with problems conceiving. Knowledge about fertility health issues may also help prevent infertility in the first instance; for example, more information and advice regarding curable sexually transmitted diseases could reduce the number of cases of infertility, particularly in less developed countries, such as Africa where most cases of infertility are due to infection (W. Cates et al., 1985). However, there is a lack of fertility knowledge in the general population. The aim of the current chapter was to assess people's knowledge about factors that may impact on fertility self-care (i.e., knowing and taking care of your own fertility potential).

Fertility Knowledge and Knowledge of Infertility Risk Factors

One would assume that most adults know about human reproduction (e.g., how to get pregnant). Research however would suggest otherwise; a global survey of almost 17,500 people (most of childbearing age) from 10 countries in Europe, Africa, the Middle East and South America, revealed that on the whole level of knowledge regarding fertility and the biology of reproduction was very poor (World Fertility Awareness Month; 2006). Other studies have found that participants overestimate the chances of pregnancy at time of ovulation (Lampic et al., 2006), have little awareness

of when they are most fertile, and lack a general understanding of infertility, such as a definition and its prevalence within the general population (Blake et al., 1997; Adashi et al., 2000). With regards to infertility treatment, although most were aware of in vitro fertilisation (IVF) (Adashi et al., 2000) many overrated the chance of treatment being successful with 39% believing that couples had a success rate of achieving a live birth between 40-100% (Lampic et al., 2006) when in reality the per cycle success rate is closer to 20% (Adamson, de Mouzon, Lancaster, Nygren, Sullivan, & Zegers-Hochschild, 2006).

Knowledge studies to date have primarily focused on knowledge about the biological process of reproduction (e.g., when is a woman fertile, how long sperm survive) and the definition and prevalence of infertility. These are important issues to address as they help people understand when is the best chance of pregnancy (e.g., timing of unprotected intercourse), and the likelihood of having difficulties conceiving (e.g., number of couples affected by infertility). However, equally important is knowledge about the factors that may reduce the chances of conception as a lack of knowledge in these areas may mean that people unintentionally contribute to their own future fertility problems. Scarcely any studies have examined whether people are aware of the main lifestyle (e.g., smoking, alcohol consumption; Roth and Taylor, 2001) and reproductive (e.g., menstrual cycle irregularities; Koff, Rierdan, & Stubbs, 1990) risk factors for infertility. Research focusing on age (Lansac, 1995; Lampic et al., 2006; Skoog Svanberg et al., 2006) and sexually transmitted diseases/infection ([STD/STI's] e.g., increased risk of tubal damage, Mosher and Aral, 1991) also shows a lack of general knowledge. In light of such work it is imperative to assess understanding of the effects of other factors associated with reduced fertility.

Numerous factors have been associated with reduced fertility problems in women that cover demographic information (e.g., age), reproductive history (e.g., menstrual cycle characteristics, history of pelvic surgery), and current lifestyle habits (e.g., alcohol consumption, smoking). The aim of the current study was to establish knowledge regarding risk factors associated with infertility in a young, university-educated sample, who should demonstrate the highest level of fertility knowledge one could expect from young people. Seven risk factors were selected based on their relevance for a young population; age, weight, smoking (tobacco and marijuana), alcohol consumption, stress and sexually transmitted infections (e.g., Chlamydia). There is a plethora of research associating all these factors to reduced fertility (see Chapter 5 for a review). It would therefore be important to ascertain whether young people know the potential influence of these factors. In the present study knowledge about these seven risk factors was examined and compared to knowledge and beliefs about other factors potentially associated with fertility self-care.

Fertility Myths and Illusory Benefits of Healthy Habits

Another important source of misinformation that could impact on fertility self-care is erroneous belief about fertility or the benefits of healthy habits. As a taboo subject people accumulate many misconceptions about reproductive health and factors that affect fertility. For example, one avoids the use of contraception because they falsely believe that a girl cannot get pregnant at first intercourse, or because one believes that condoms reduce pleasure (Wang & Davidson, 2006). Furthermore, people may erroneously perceive themselves to be more fertile simply because they avoid engaging in unhealthy habits. To date knowledge studies have not examined beliefs in fertility myths or perceived associations between healthy habits and fertility potential.

'Old wives tales' describe unusual events occurring due to a person carrying out a relatively normal behaviour (e.g., feed a cold, starve a fever; cracking your knuckles will cause arthritis; Castellanos & Axelrod, 1990; van den Brink, van den Boogaardt, van Deventer, & Peppelenbosch, 2002) and there are a number of tales or fertility myths often repeated in the popular press. For example, women who had given up all hope of conceiving naturally falling pregnant immediately after adopting a child (Lamb & Leurgans, 1979). Other myths concern post coital techniques (e.g., standing on your head, Daniluk, 2001) that would keep the egg and sperm in closer contact and facilitate fertilisation. Although all are relatively harmless in that they do not involve risky behaviour there is no empirical research that these factors have an effect on fertility. To match the number of risk factors examined in the present study seven myths were evaluated (3 regarding post coital behaviours; 2 regarding living area; 1 on healthy eating and 1 about adoption) in the present study.

Many people believe that not engaging in unhealthy habits actually increases health (Blenner, 1990). For example, that never smoking or drinking, or exercising and maintaining a healthy weight is conducive to better fertility. Although such abstinence is a positive way to act the healthy habits typically maintain baseline fertility and do not in and of themselves increase or decrease fertility. Seven healthy habits linked to the risk factors (e.g. never smoking, never drinking alcohol) were examined in this study.

Understanding Risk

In the present study people were asked to evaluate the risk associated with factors known to impact on a woman's chances of becoming pregnant and those with no known associated link with female fertility (e.g., pseudo risk factors and protective

factors). Risk and risk perception is defined in a number of diverse ways and is often interpreted differently by individuals (Sjöberg, 1997). A significant proportion of the public have difficulty understanding numerical risk information (Weinstein, 1999). People often grossly overestimate risks, frequently exaggerating the risk when the hazard is great and exceptional, but the probability of exposure is low, and depreciating the risk when the hazard is small and familiar, but the probability is high, a classic example of this is deterring from flying due to a fear of a plane crash, preferring to use alternative means of travel (i.e., car) even though air travel is markedly safer than travelling by car (Bellaby, 2001). The presentation of the risk also influences comprehension of the risk. For example, Fischhoff et al. (1993) reported that availability biases have been found to impact on risk perception as people often report higher estimates of risk for factors that are more frequently visible in every day lives (i.e., through reports in the mass media, or through individual experience). Framing effects can also impact on decision making and risk perception through the presentation of the same piece of information in varying ways (Tversky & Kahneman, 1981; D. K. Wilson, Purdon, & Wallston, 1988). For example, information may be presented in a positive (e.g., 90% chance of survival) or negative (e.g., 10% chance of dying) way (Gigerenzer & Edwards, 2003), or as a gain (e.g., seeking treatment for infertility may give me a child) or loss (e.g., not seeking treatment for infertility may make me childless).

When developing a tool to assess risk it is imperative to explain to participants what is the risk being measured (for example, the risk of a fertility problem/not conceiving). Certain criteria to enhance understanding with regard to effective risk communication recommended by Berry (2004) were used in the present study. Firstly, it is important to avoid being ambiguous in the nature of the questions; text that has a

clear and comprehensible structure allows the participant to clearly obtain the rationale behind the task (Fischhoff et al., 1993). Secondly, many researchers have noted that graphical representations can be particularly effective for conveying information about risks (Lipkus & Hollands, 1999; Edwards, Elwyn & Mulley, 2002). Graphical images can give visual clues about how to rate risks, for example, scales (i.e., -10 to +10) allow for representation of increase and decrease risk from a precise starting point (such as 0) (Lipkus & Hollands, 1999). Alternatively, using symbol displays that use different types of icons (such as stick figures, faces, asterisks or dots) to represent frequencies (indicated by the number of icons in a specified group) have been found to aid people when understanding the risks of cancer (e.g., number of people with lung cancer in two groups: smokers and non-smokers; Berry, 2004). In addition research has shown that combining visual displays with numerical information can have a positive affect on comprehension of risk (Julian-Reynier, Welkenhuysen, Hagoel, Decrugenaere & Hopwood, 2003). Finally providing anchors and "adjunct aids" such as highlighting and summarising relevant information is another way to encourage better understanding (Fischhoff, et al., 1993) and divert participants to the most essential information. The risk assessment task used in the present study was designed taking into consideration these factors.

The Present Study

The main aims of the study were to first ascertain knowledge/awareness of the effect certain risk factors have on a woman's chance of achieving a pregnancy in a sample of 149 young men and women. To assess knowledge participants were asked to rate the impact that different factors (risks, misconceptions, healthy habits) would have on the chances of 100 women getting pregnant. A second aim was to determine whether participants could distinguish between factors that have an effect on

pregnancy rates (risk factors) and those that do not (healthy habits and misconceptions). In line with the current research presented it was hypothesised that participant's knowledge concerning the factors that affect fertility would be poor.

Materials and Methods

Design

A within-subjects design was employed to test participants knowledge of factors associated with female fertility. Dependent variables were percentage correct scores and gain/loss scores. Category (i.e., risk, healthy habit, myth) was treated as within subjects. This study was approved by the Ethics Committee of the School of Psychology, Cardiff University (for statement of approval see Appendix E).

Participants

The final sample consisted of 149 participants, 110 women and 39 men. On average the sample were 24.01 (SD = 7.81) years of age, with 61.7% educated to A-level standard (equivalent to the International Baccalaureate). The data was pooled from two waves of data collection. The first stage of collection (n = 83) were postgraduate (i.e., Master's and doctoral) university students and junior staff, the second undergraduate (i.e., Bachelor's) students (n = 66), all from Cardiff University. The first sample were older (M = 28.76 years, SD = 9.74) ($t(147) = 7.86$, $P<.001$) and educated to a higher standard (χ^2 95.49 df = 3, $P<.001$) compared to the undergraduate sample (M = 20.23 years, SD = 1.53).

Materials

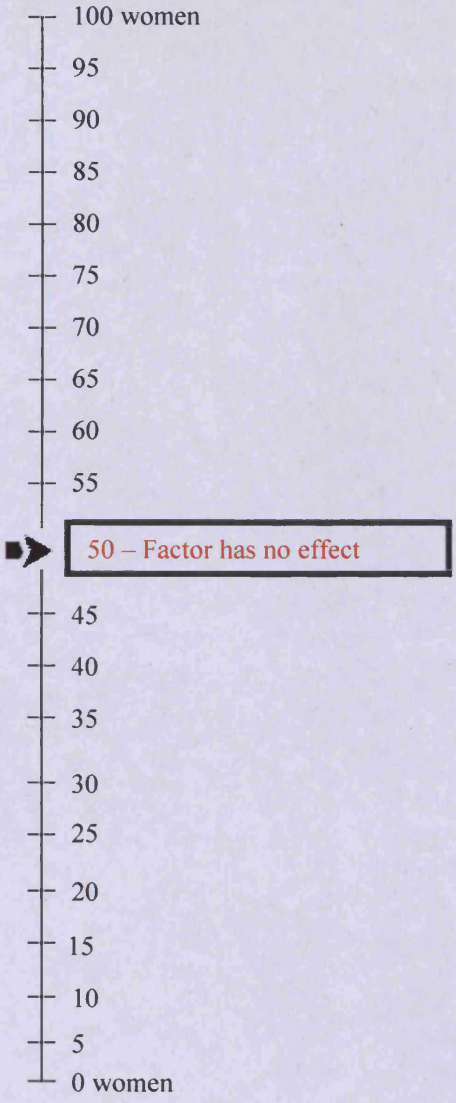
A background information form was developed for the study to obtain demographic information about the participants (3 items; gender, age, highest

educational qualification [coded 1: GCSE or equivalent College qualification, 2: A Level, 3: Degree, 4: Postgraduate qualification]).

The Factors Affecting Fertility Scale (FAFS) was designed for this study. For each question participants marked a number on the response scale (see Figure 4.1) that represented their perception of the effect a given factor (e.g., smoking) had on the chance of pregnancy of 100 women trying to get pregnant. The online survey was set up by iPsychExpts (Brand, 2005).

Participants were asked to rate factors belonging to three categories: risk factors (7 items, e.g., smoking), myths (7 items, e.g., living in the countryside) and healthy habits (7 items, e.g., being normal weight). Each factor was evaluated by a number of questions depending on the level of risk associated with that factor in the literature review, resulting in 30 questions being presented to participants. For example the risk factor smoking produced four questions, namely the effect of never smoking (healthy habit), smoking 1-9 cigarettes per day (considered a low risk factor), 10-19 cigarettes (considered a high risk factor) or over 20 cigarettes (considered a high risk factor) per day (See Table 4.1 for all 30 questions, page 93).

Figure 4.1. Example of the Factors Affecting Fertility Scale (FAFS).



Note. Scale presents the number of women from 0 – 100 who could get pregnant. Participants could slide the arrow up and down the scale to represent the number of women they perceived would get pregnant depending on the factor presented. Leaving the arrow on 50 meant the factor had no effect.

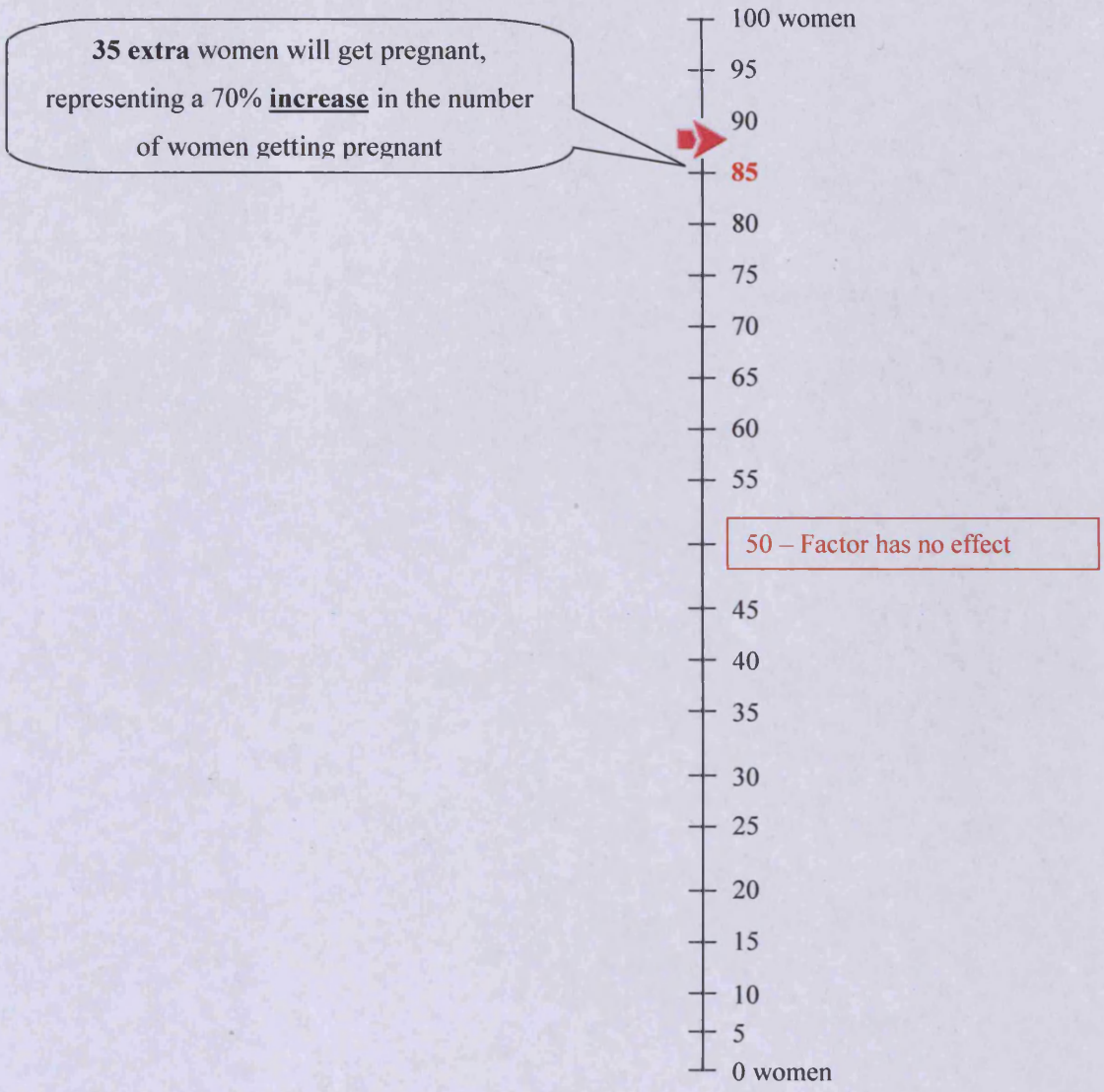
Table 4.1
Questions according to category.

High Risk Factors	Question
Age	Being aged between 35 and 39 years old
	Being aged between 40 and 44 years old
	Being aged between over 45 years old
Weight	Being overweight
Smoking	Smoking 10-19 cigarettes per day
	Smoking more than 20 cigarettes per day
Alcohol	Drinking more than 14 units of alcohol per week
Stress	Stress that a person finds unable/impossible to cope with
Chlamydia	Ever having Chlamydia (a Sexually Transmitted Disease, STD)
Marijuana	Smoking marijuana more than 4 times per week
Low Risk Factors	Question
Smoking	Smoking 1-9 cigarettes per day
Alcohol	Drinking less than 14 units of alcohol per week
Stress	Experiencing an event that one finds difficult to cope with
Marijuana	Smoking marijuana less than 4 times per week
Misconception	Question
Fruit and vegetable	Eating five portions of fruit and vegetables a day
Post coital behaviours	Not urinating after sex
	Lying down for 10 minutes after sex
	Placing a pillow under the women's hips during and after sex
Living area	Living in the countryside
	Living in the city
Adoption	Adopting a baby
Healthy Habits	Question
Age	Being aged 24 or younger
	Being aged between 25 and 34 years old
Weight	Being of normal weight
Smoking	Never smoking
Alcohol	Never drinking alcohol
Stress	Experiencing an event that one can cope with
Exercise	Less than 7 minutes of exercise per day
	7-59 minutes of exercise per day
Marijuana	Never smoking marijuana

The response scale ranged from 0 to 100 women (intervals of 5: See Figure 4.1 for scale, page 92). Participants were presented with 30 questions about 21 factors and asked to decide whether the given factor had an effect on the number of women in a group of 100 who would get pregnant in 3 months, and if so, the direction of the effect (i.e., an increase, decrease or no effect). The number 50 represented 'no effect' as population data predicts that 50 of 100 women would conceive after 3 months of unprotected intercourse[1]. The online response scale showed a vertical bar with 10 radio buttons (0-100). The number 50 was always highlighted with a written reminder that choosing it meant that the factor was perceived to have no effect. If the mouse was held over a number a pop-up caption appeared providing the participant with additional information. For example if the participant was to hover the mouse over the number 85, a caption would appear on the computer screen, stating '35 extra women will get pregnant, representing a 70% increase in the number of women getting pregnant' (see Figure 4.2 for example) whereas the pop-up for the score of 15 stated "35 fewer women will get pregnant, representing a 70% decrease in the number of women getting pregnant". The pop up box for each number contained the same amount of information.

[1] It was calculated that if 100 women were trying to get pregnant, on average after 3 months of unprotected sexual intercourse, it would be expected that half of these 100 women would have achieved a pregnancy (calculation was made from time to pregnancy data; te Velde et al., 2000).

Figure 4.2. Example of a caption produced by hovering over a number.



Two scores were derived from the FAFS. A percentage correct score was derived for each category (risk, myth and healthy habit) by summing the number of correct responses to the relevant items. For the correct response score, correct identification of the effect of the factor (i.e. correct identification that smoking decreases the number of women getting pregnant) was assigned a 1. An incorrect response (i.e., incorrectly responding that living in the countryside increases the number of pregnant women) was assigned a 0. The maximum correct score for each category was 7. The percentage correct score was obtained by dividing the total correct score (per category) by the maximum score (per category) (multiplied by 100).

The second score calculated was the pregnancy gain/loss score. A pregnancy gain/loss score was calculated to express the degree to which people believed a factor increased (positive score, maximum 50) or decreased (negative score, maximum 50) the number of women who would get pregnant. It was derived for each item by calculating an average deviation score from 50 (no effect).

Procedure

For the first wave of data collection participants were recruited through the university-wide electronic notice board system. Potential participants received a written announcement on the electronic notice board when they signed into their university account inviting them to participate in an online survey about fertility. In addition an email providing the same information was sent to all postgraduate students enrolled at the School of Psychology, Cardiff University. Those interested followed a link to the FAFS online survey website and were instructed on how to complete the survey (see Appendix F for instructions). In the second wave of data collection undergraduate participants were recruited through the electronic participant

panel that advertises research studies to psychology students. Data for the second wave was collected by the author and Laura Brighton. All participants in the second wave of data collection received course credit for their time.

For all participants questions were randomly presented and completion of all the questions took around 5 - 10 minutes. Once they completed the final question they were given a more detailed explanation of the study and the option to submit their answers if they wished (see Appendix F for additional information provided).

Data analysis

Preliminary data screening produced one participant that was excluded from the analyses due to incomplete data (>50% of data missing). An analysis of variance (ANOVA) was conducted with Category (Risk, Healthy Habit, Myth) as the within-subject factor and percentage correct score as the dependent measure. A significant Category effect was followed up with pairwise comparisons between categories using paired t-tests (using the Bonferroni correction, $P < .017$ for alpha inflation). To assess whether average scores were significantly different from no effect (50) one sample t-tests were conducted for the mean pregnancy gain/loss score per category (i.e., risk, myths, healthy habits). Pearson r correlation, t-tests and ANOVA were used to examine relationships between knowledge and demographic variables. A probability value of $P<0.05$ was regarded as statistically significant. Analyses were performed with the software Statistical Package for the Social Sciences.

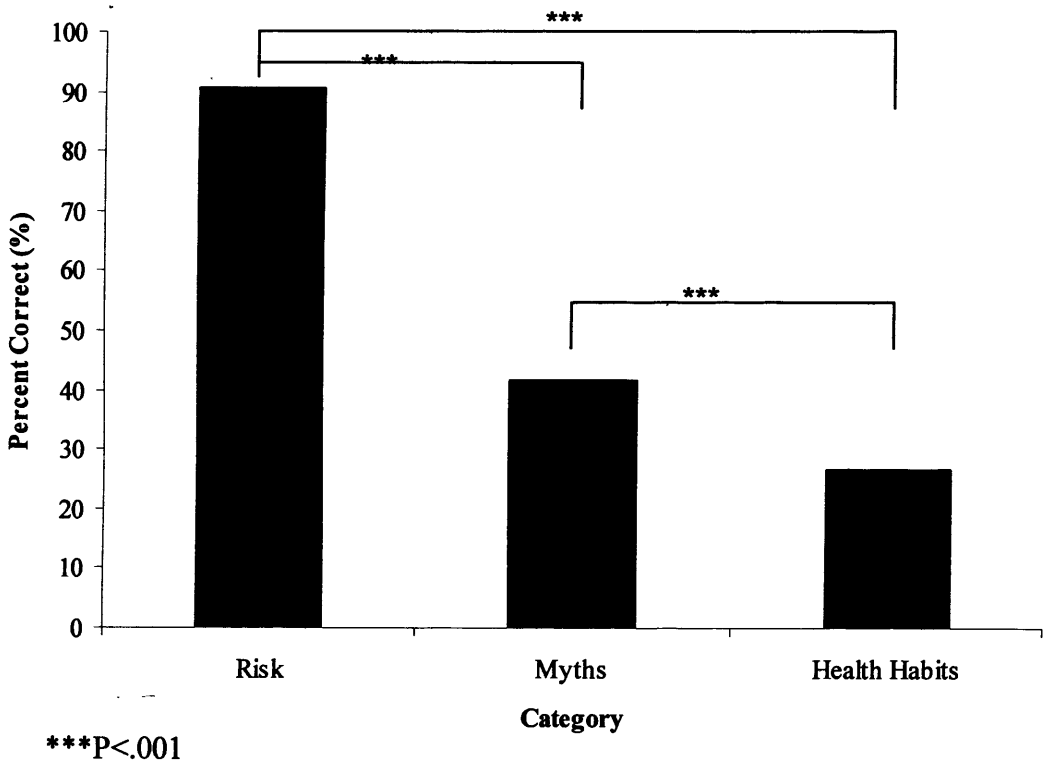
Results

Knowledge regarding factors associated with infertility

Figure 4.3 presents average percentage correct scores per category. An ANOVA showed an overall significant effect ($F(2,296) = 482.93, p<.001$) of

Category. Follow up tests revealed that participants had significantly higher percentage correct scores for risks compared to percent correct scores for myths ($t(148) = 22.43$, $P<.001$) and percentage correct scores for healthy habits ($t(148) = 30.70$, $P<.001$), with an average correct score of 90.70% compared to 41.53% and 26.46% (respectively). In addition participants had significantly higher percentage correct scores for myths compared to the percentage correct scores for healthy habits ($t(148)= 6.85$, $P<.001$). Knowledge level was not associated with age ($r = -.006$, $P = .942$) or gender ($t(147) = .925$, $P =.36$). A trend was found for education and knowledge ($F(3,145) = 2.59$, $P =.06$), with follow-up tests showing a trend for Degree students having higher knowledge scores compared to A-Level students ($P =.088$).

Figure 4.3. Average percent correct score per category ($n = 149$).



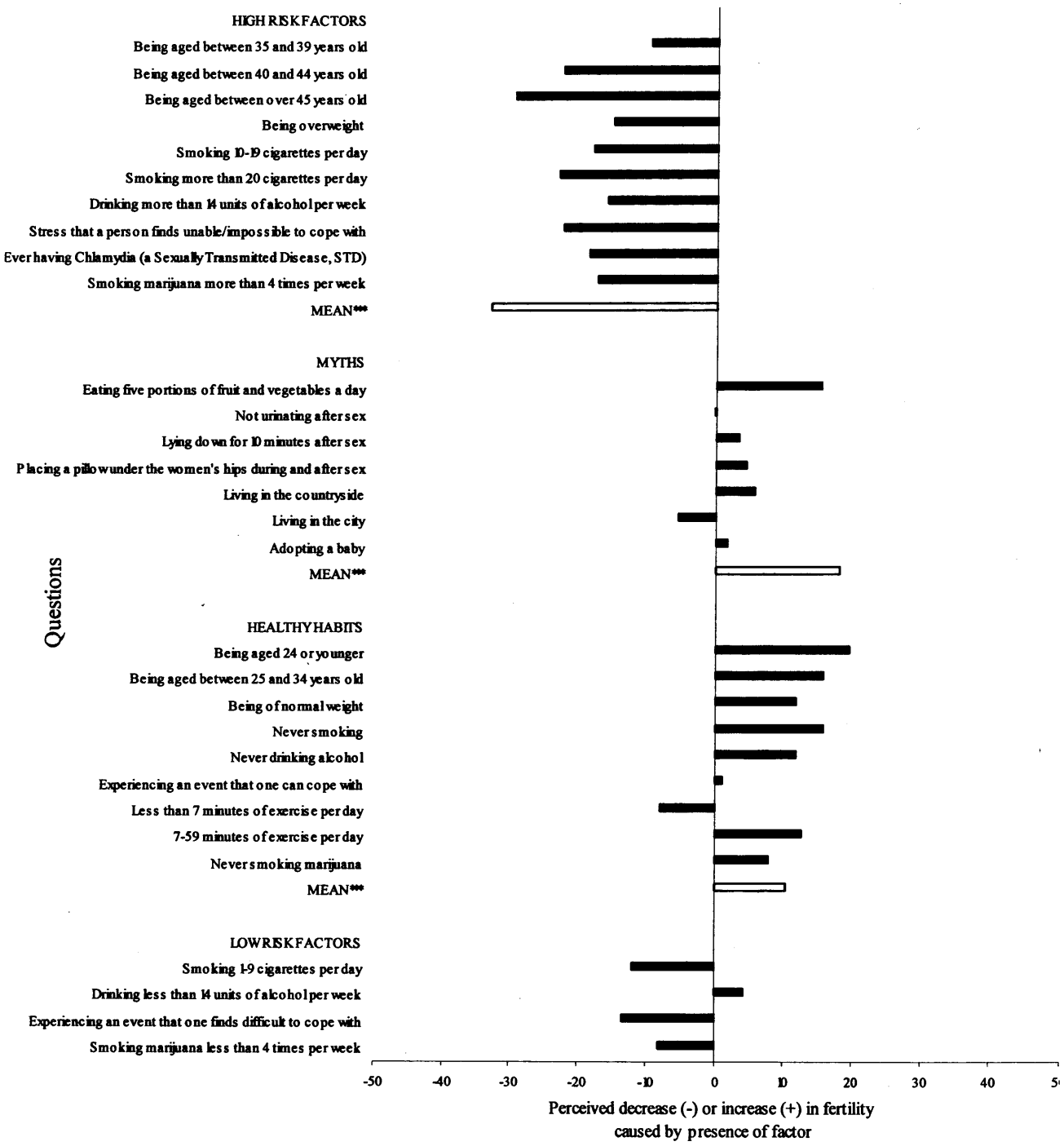
***P<.001

Figure 4.4 shows the pregnancy gain/loss score for each question in each category. Participants correctly identified all the high risk factors as decreasing the chances of getting pregnant as shown by negative deviations (i.e., loss). Being over 45 years of age had the highest loss score of all the risk factors on the number of women getting pregnant, whereas being aged 35-39 the smallest score.

Participants believed that myths and healthy habits were associated with the number of women who would get pregnant as evidenced by average positive gain/loss scores. With the exception of two factors (living in the city and postcoital urination) participants rated myths as increasing the chance of getting pregnant (see Figure 4.4). Eating five portions of fruit and vegetables had the largest gain score (15.50); meaning that just over 15 extra women would achieve pregnancy due to eating the recommended number of fruit and vegetables a day. Participants also believed that living in the city decreased the number of women getting pregnant by 5.40, while living in the countryside actually increased chances by 5.77 women.

Other than doing less than 7 minutes of exercise per day (average decrease in the number of women pregnant by 7.82), all the healthy habits were rated as having a positive influence on the pregnancy rate (see Figure 4.4). Being under the age of 24 was associated with a gain score of 19.56, with being able to cope with stressful events having the smallest gain (1.24).

Figure 4.4. Pregnancy gain/loss scores per item (black bars) and per category (white bar).



***P<.001

Figure 4.4 also includes the four low risk factors. These follow a similar pattern to the high risk factors, in that participants are rating the majority of these behaviours as having a negative effect on the number of women getting pregnant. With the exception of drinking under 14 units of alcohol per week that showed an increase (4.29) in pregnancy rates, all the factors suggest participants were rating healthy habits as increasing the number of women getting pregnant and the risk factors (high and low) as decreasing the number of women conceiving.

Finally, an average pregnancy gain/loss score was computed for each category (risk, myths and healthy habits) and compared to no effect (50). Averaged pregnancy gain/loss scores were significantly different from no effect (50) for the risk category ($t(148) = 34.61$, $P = 0.001$), myths category ($t(148) = 14.64$, $P = 0.001$) and healthy habits category ($t(148) = 21.64$, $P = 0.001$). Participants perceived a 33% reduction in the number of pregnant women in the risk category, an 18% increase in the myths category and a 10% increase in the number of pregnant women in the healthy habits category.

Discussion

Previous research has suggested that knowledge regarding fertility is very limited (Dyer et al., 2002; Kuang, Mahutte, Heyman, & Ouhilal, 2006; Lampic et al., 2006). This study aimed to establish level of knowledge concerning factors that affect female fertility. Contrary to previous research the results demonstrated that participants were knowledgeable about the risk factors for female infertility but were not as knowledgeable at recognising factors that had no effect on fertility (myths and

healthy habits), and believed that these factors actually increased a woman's fertility potential.

Taking into account only the correct identification of the risk factors one would conclude from these results that in this young, educated sample, knowledge regarding the potential risks associated with female infertility was high. All the risk factors were correctly identified as decreasing the number of women who would get pregnant. Although such results may reflect genuine knowledge given the lack of fertility information in the public domain (Fuentes & Devoto, 1994; Adashi et al., 2000; Dyer, et al., 2002; Kuang et al., 2006; Lampic et al., 2006;) it is more likely that participants were using their prior knowledge about negative lifestyle factors and their effect in other health conditions to make an assumption about the effect on fertility. All the risk factors used (e.g., smoking, obesity) have been associated with serious health conditions that have received extensive media coverage (e.g., lung cancer, heart disease; Newcomb & Carbone, 1992; Hecht, 1999; Edwards, 2004). Many studies have shown that people are aware of the impact of such risk factors on health (Sutton, 1998; Siahpush, McNeill, Hammond, & Fong, 2006) and research also shows that people apply scientific knowledge acquired from different sources (e.g., friends, acquaintances, and media) to novel domains (Collins & Evans, 2007). Whilst generalisation seems to be a good way to manage a large quantity of incoming health information it could occasionally lead to over-generalisation. For example, in the current study participants rated drinking small quantities of alcohol as beneficial to fertility possibly because of the perceived benefits of red wine as part of a healthy lifestyle (Gronbaek et al., 1999; Poikolainen & Vartiainen, 1999; Wollin & Jones, 2001;).

The results also show that people may perceive certain factors to be riskier than they actually are, and a number of low risk factors were perceived as reducing fertility to the same degree as high risk factors. For example being overweight is a major risk factor for female infertility (Hassan & Killick, 2004; Gesink Law, Maclehose, & Longnecker, 2007) but was rated as having a lesser effect than alcohol consumption and smoking (both tobacco and marijuana). This finding could be an artefact of the FAFS paradigm because gains/losses could only be made in intervals of 5, but even with this consideration gains and losses seemed exaggerated. Therefore the results would seem to suggest that whilst young people have broad knowledge of risk factors they lack specific knowledge of how much exposure is too much exposure in relation to fertility effects. There is much debate in the health literature about whether one ought to implement zero tolerance policies or educate people to know critical thresholds for negative effects. For example, whether pregnant women should be told not to drink at all or whether they should be told not to drink more than one small glass of wine per day (NICE, 2003). It could be important to relay threshold information to the public to reduce the possibility that without such specificity people would consider themselves outside the risky zone of behaviour. Although the current results suggest that people do not know critical threshold levels when it comes to fertility, more research is needed to find out whether knowing such thresholds would indeed change negative behaviours.

One limitation of the present study is that young people were not asked whether they engaged in the risk behaviours or how they felt their lifestyle was affecting their own fertility. Although people may be able to identify risk factors this does not mean they apply this risk to themselves. Smokers present an excellent example of this as they often have a misguided invulnerability concerning their

personal tobacco related health risks (Hay et al., 2005). There is evidence of similar beliefs for fertility, especially in relation to age. In the present study age was associated with the largest perceived pregnancy loss score (29.43%) with correct identification that fertility declines from 35 years of age. These results are consistent with numerous other studies that show people are aware of the relationship between age and declining fertility. Despite this, there is a steady increase in the number of women over the age of 35 having children in Western countries (Botting & Dunnell, 2003). The current research could therefore be extended by investigating differences between general versus personal risk as such work may show that people do not always apply risk to themselves in decision-making about everyday health habits (e.g., whether to smoke or not, at what age to have a child).

The Health Belief Model also proposes that a prerequisite of taking action (i.e., starting to try for a baby at an age before fertility declines) is if a person regards themselves as susceptible to negative aspects and realises the potential seriousness of not carrying out the behaviour (e.g., possibility of never having children). In addition having accurate knowledge may only be the first step in the process of behaviour change. It would be important to establish how people go from personal risk to actual behaviour change (i.e., reducing negative lifestyle habits) and what factors are important to this transition (i.e., perceived benefits versus barriers to change). Previous research has highlighted that the extent to which the person wants, desires, or wills to change (W. R. Miller & Rollnick, 2002) is imperative to successful behaviour change. The motivation to change (e.g., adapting one's lifestyle) could be particularly high in the context of fertility as having a child is a highly valued life goal for the majority of young people (Lampic et al., 2006).

In contrast to good risk knowledge, false beliefs were abundant. Participants erroneously believed they could increase fertility by, for example, moving to the countryside, using specific coital techniques, eating fruit and vegetables or adopting a child. All the myths chosen were the most frequently cited misconceptions (regarding factors affecting fertility) found on reputable infertility associated websites (e.g., RESOLVE.com, the national infertility association). In addition to these myths, participants also erroneously believed that one could be more fertile by being healthy (e.g., never drinking alcohol), which is an incorrect assumption to make as healthy lifestyles are only good because they reduce the exposure to risk and its effects rather than because they are in and of themselves health promoting. Healthy people have baseline fertility and not superior fertility.

Together these results would suggest that people could, if faced with a fertility problem, engage in ineffective behaviours that could delay seeking effective interventions. Indeed, people who keep a healthy lifestyle often express astonishment that they should be infertile given that they were the healthiest of their family and friends (Blenner, 1990). Further, White et al. (2006) found that possessing a perception of good overall health was the main barrier for women perceiving that a fertility problem existed. Feeling healthy has also been cited as a reason for delay in a number of other illnesses (e.g., heart disease; White & Johnson, 2000; cancer; Smith et al., 2005).

Methodological Implications and Limitations

The Factors Affecting Fertility Scale (FAFS) proved a useful tool to obtain data on people's beliefs about the factors presented. Only one participant had to be excluded due to incomplete data and no negative comments were given at the end of

the study by participants regarding the use and information provided by the scale. One problem with most attempts to learn whether people know what causes an illness is that the correct answer is often implied within the questions (Weinstein, 1999). Thus asking a person whether smoking is a risk factor for infertility reminds them of the health effects that are of concern and perhaps suggests it must have some effect. People might therefore assume that any factor questioned in the FAFS must have some effect, including the myths and healthy behaviours. To counteract this methodological artefact the instructions and scale were very specific in reminding participants that the marker could be left at 50 meaning the factor had no effect and the label attached to the number 50 stated that 50 meant 'no effect' (which always remained on the scale). The variability in responses (min 0 and max 100) showed that individuals were using all response options (the number 50 was chosen on average 22.41% of the time). Despite this the FAFS was able to detect subtle but important grades of knowledge, for example broad versus specific risk knowledge and could be used to better inform health campaigns.

The results of this study could be extended in a number of ways. In the current study the sample was well educated, with the majority achieving at least A-level education. Studies looking at a wide range of health areas (cancer, diabetes, HIV) have found that education levels have negative relationships between literacy skills and health outcomes (DeWalt, Berkman, Sheridan, Lohr, & Pignone, 2004) and the initiation and uptake of health care campaigns (e.g. quitting smoking; Sander, 1995). Although public health campaigns do not discriminate and target all people exposed to the advertising including people with less education, it would be important to replicate the findings in other samples with varied educational backgrounds, different cultures and so on. Similarly, more in-depth analysis of gender effects could be

carried out. Previous research has highlighted that women are more likely to express higher concern about health risks (Boholm, 1998) and that men often have a poor knowledge of matters related to health (Banks, 2001). In this sample no differences were found and this could be due to people not discriminating against gender, i.e. smoking is bad for anyone not just women. However, as the FAFS only included factors affecting female fertility it is not known to what extent people would show similar knowledge and false beliefs in regards to male fertility. It would be important to establish people's knowledge surrounding male fertility and whether gender differences occur in the way people rate the influence of a factor on fertility.

Clinical Implications and Future Directions

In conclusion, participants were aware of the risk factors that impacted negatively on a woman's fertility, however false beliefs about beneficial effects of benign factors were also abundant. Awareness about the genuine factors associated with female fertility (and infertility) is needed in order to resolve any erroneous beliefs people may have regarding fertility potential. In addition, once people are aware of what the risk factors are and can assess their own risk it would be important to establish clear guidelines of how to use the knowledge acquired (e.g., when should one seek advice, what can one modify) in order to minimise the chances of ineffective action (and perhaps delay) if a fertility problem is suspected (e.g., amenorrhea, no conception after 12 months of unprotected intercourse). In order to achieve the goal of raising personal awareness it is important to first ascertain what are the most important risk factors associated with female infertility, how people can assess their own risk and what are the effective actions people should take in order to maximise their chances of successfully conceiving. Therefore the next Chapter will focus on establishing the main risk factors for female infertility.

Chapter 5
Risk in female fertility

Introduction

The research to date has highlighted that 9% of couples will experience difficulties when trying to have a child. Given the importance of parenthood to the vast majority it is important to help people optimise their chances of eventual pregnancy. However, people may not be behaving in an optimal way to safeguard fertility potential; Chapter 4 demonstrated that young people have a good knowledge regarding the risk factors for female infertility, but possessed a number of misconceptions. In addition Chapter's 2 and 3 highlighted that, when faced with difficulties in conceiving, a significant number of couples are not seeking the help they require. Such delay in seeking help could further decrease chances of pregnancy and increase the cost of providing medical help if it was eventually sought due to greater disease progression and reduced fertility due to increasing age.

The research conducted in the previous chapters has led to the conclusion that people need accurate personal risk information in order to optimise their chances of future successes when trying to conceive. In order to achieve this goal an increase in awareness surrounding the factors that impact on personal fertility is needed, targeting two populations; those who are thinking of having children in the future and those currently trying to conceive. Women who wish to conceive in the future need to be educated about what personal factors impact on their fertility (e.g., their age), factors that should be minimised (e.g., their weight, smoking habits) to avoid reducing chances of eventually conceiving and the factors that will warrant medical attention when they eventually do decide to conceive (e.g., the irregularity of their cycle).

Making women aware of these personal factors is key to helping women realise that their actions now can impact on their future parenting goals. For those women who are currently trying to conceive it would be imperative for them to have practical information about factors that they themselves can take control of to improve fertility (e.g., reducing alcohol consumption) as well as guidance about when to seek medical advice (e.g., if they do not have a period). This chapter will focus on the early stages of the development of a tool that eventually aims to provide this information and guidance through the assessment of personal fertility status.

What is Health Promotion?

The awareness of signs and symptoms of disease is the critical motivating force for action and change according to health models. For example, the health belief model postulates that the likelihood of action is affected by perceived susceptibility and seriousness of a disease. Therefore if people are not aware of symptoms or signs of disease (i.e., do not perceive they are at risk) they may not engage in the action needed. Further, according to Prochaska's stages of change model, action (e.g., seeking medical advice) cannot occur without a person realising a problem exists (e.g., lack of fertility). It is only once this realisation occurs that one can weigh up the pros or cons of the problem and any potential solutions to resolve the issue (Prochaska, DiClemente, & Norcross, 1992). Making people aware of the significance of signs and symptoms of different illnesses (e.g., lump in breast for breast cancer) is therefore an integral part of most efforts to improve individual health, whether that is achieved via primary prevention, health promotion or health monitoring.

Primary prevention specifies practices for the avoidance of disease, and is often used as the umbrella term for a number of practices relating to effective health

promotion and monitoring (Last, 1995). Health promotion refers to the process of enabling people to increase control over their health thereby improving it. It is directed toward establishing the cause(s) of ill health (i.e., smoking is a risk factor for cancer), then finding the most efficient means of preventing such causes, for example, through warning people about the risk of it via the media or other public health campaigns (e.g., publication of written warnings such as 'smoking causes cancer' on all cigarette packaging sold in the UK) (WHO, 1986). Through effective health promotion, people can learn to monitor their health (e.g., regularly check one's breasts for any changes) which may, in turn, increase awareness about and significance of potential signs and symptoms of disease for which action may be needed. For example, the promotion of self examination of one's breasts has been widely publicised as a simple, low-cost, non-invasive and non-hazardous means of detecting breast cancer (Clarke & Savage, 1999). Breast self examination (BSE) has been shown to be effective in detecting breast cancer at an earlier stage (Hill, White, Jolley, & Mapperson, 1988). Making people aware of signs and symptoms and their significance can be beneficial but it can also have disadvantages as will be seen in next section.

Benefits and Drawbacks of Health Promotion and Monitoring

Benefits

Educating people about true risks and dispelling myths.

Campaigns promoting signs and symptom awareness are beneficial because they provide the public with accurate information based on scientific research establishing an association between a known risk (e.g., unprotected sexual intercourse) and the subsequent increased risk of ill health (e.g., sexually transmitted disease; STD). For example, the 2006 UK campaign to encourage young adults to

always carry and use condoms when having sexual intercourse was based on research demonstrating that condoms provide protection against sexually transmitted diseases (W. Jr. Cates & Stone 1992). As well as providing accurate information regarding known risk factors, campaigns can also dispel myths and correct inaccuracies. For example, in New Zealand a 6 – week public campaign regarding herpes raised awareness about the increasing prevalence of the disease, the need for people to get themselves tested and treated (if necessary) and in addition the campaign also emphasised that herpes was common, manageable and treatable and not a result of being dirty or bad (New Zealand Herpes Foundation, 2007; "Herpes – Myth vs. Fact": http://www.herpes.org.nz/patient/myths.htm).

Dispelling myths and correcting inaccurate knowledge is vital because evidence suggests these are common and may potentially inhibit proactive health monitoring. For example Hawkins, Berkowitz, and Peipins (2007) found that while the public were familiar with commonly advocated cancer prevention strategies people also frequently ascribed the onset of cancer to factors that had no scientific support (e.g., religious practices, drinking adequate amounts of water). In Chapter 4, young people were shown to possess a number of erroneous beliefs about factors impacting on female fertility. It would be important to ascertain whether erroneous beliefs impact on decision making when faced with health issues. The beliefs held by many teenagers regarding birth control use and risk of pregnancy is a prime example of the negative impact of erroneous beliefs. For example, beliefs that girls cannot get pregnant at first intercourse (Senderowitz, 1999) or that teenagers are immune to pregnancy (Kaiser Family Foundation Survey, 1996). Ultimately, a lack of accurate knowledge regarding risk factors and ways of promoting good health habits is highly likely to reduce the chances that individuals will be able to take steps to improve their

day-to-day health (Hawkins et al., 2007) and timely decision making when faced with ill health issues.

Reduce fear and unnecessary delay through early detection.

An important benefit of making people aware of signs and symptoms is that it can reduce delay in seeking medical advice. A systematic review of the literature on reactions to discovering a symptom of breast cancer demonstrated that while the majority of women promptly sought medical advice 20 – 30% delayed seeking any medical help for three months or more (Richards, Smith, Ramirez, Fentiman, & Rubens, 1999; Richards, Westcombe et al., 1999). Delay of this duration decreases potential for breast cancer survival (Facione, 1993; Richards et al., 1999). In Chapter 2 it was established that just under half of couples faced with a fertility problem ever seek any medical advice/treatment and if they do, 20% or so delay for more than 2 years as found in Chapter 3. Research on the reasons for delay indicates that a lack of knowledge/awareness of the signs and symptoms of disease (Oliveria et al., 1999; Grunfeld et al., 2002; Facione & Facione, 2006) and fear of what may happen (Facione, 1993; Carney et al., 2002; Bish et al., 2005; Smith et al., 2005) are important contributing factors; nobody likes to hear bad news and the possibility of a threatening diagnosis may inhibit some people from seeking advice or medical help in a timely way. These issues can be readily tackled in public awareness campaigns by increasing knowledge about the advantages of early detection (e.g., improved prognosis: Hillis, Joesoef, Marchbanks, Wasserheit, Cates, & Westrom, 1993) and by reducing the threat that seeking medical advice/treatment may pose for some individuals (e.g., better understanding of what happens during a biopsy or scan: Smith et al., 2005).

Reducing delay through awareness of signs and symptoms may also impact on health care costs. For example, the Mary Woodward Lasker Charitable Trust found that the decline in deaths in the US between 1972 and 1992 from cardiovascular disease and stroke was worth more than 1.5 trillion dollars per year to the US economy (Ratzan, 2008). With regards to infertility treatment, if couples entered the health care system earlier for suspected fertility difficulties then their chance of success would be greater due to less disease progression and earlier age. In the UK, the average age for first births is now 27.1 years of age (Office of National Statistics, 2000) so that a 2-3 year delay will mean entering treatment at an age when fertility and treatment success are beginning to decline. A delay in seeking medical help for fertility problems results in an increase in age and according to Collins (2002) each year of infertility reduces the likelihood of IVF conception by 2%, impacting on the costs to health care systems providing subsidised treatment.

Reducing delay also increases the chances of earlier detection of a disease. Early detection of a problem is often the goal in health promotion campaigns because early detection generally improves prognosis. For example in cancer campaigns the aim is to engage the public into looking out for early signs and symptoms of the disease (i.e., the detection of a new lump in the breast or testicle). Fries, Koop, Sokolov, Beadle, and Wright (1998) suggest that the best way to reduce costs and improve health at the same time, are not just to control the services provided but also reduce the need and demand for care. Early detection of a problem may reduce the need and demand for medical care. For example early detection (and treatment) of a sexually transmitted disease may reduce the likelihood of further infections, such as PID, as a result of the initial disease, that may lead to an increased risk of infertility that would require further, more expensive treatment than if the initial infection had

been detected and treated (Scholes, Stergachis, Heidrich, Andrilla, Holmes, & Stamm, 1996). Similarly, identifying and treating obesity-linked infertility may reduce the need for costly infertility treatment. A. M. Clark, Thornley, Tomlinson, Galletley, and Norman (1998) reported that prior to a weight loss programme 67 women had treatment costing just over ½ million American dollars resulting in two live births. However, after the programme the same women had 18 babies spontaneously for the minimal costs of the weight-loss program. A. M. Clark et al., (1998) concluded that weight loss should always be considered first for women who are infertile and overweight.

Delay may not just be a factor to tackle with the individual who discovers a potential symptom, but one to also address with the medical provider (e.g., general practitioner). Studies have found that a barrier for couples seeking treatment for persistent failed attempts when trying to conceive is due to delay caused by incorrect diagnosis and/or delayed referral from general practitioners. Gunnell and Ewings (1994) found that many infertile couples were not referred for specialist medical advice and therefore did not access the expertise they needed. They concluded that this was primarily due to a lack of concrete referral guidelines for general practitioners to use when couples presented with difficulties conceiving. NICE (2004) recently developed guidelines but degree of adherence to these strategies is not fully known. One report by the Audit Commission highlighted that few respondents to their survey (recruited through all primary care trusts) were fully aware of the guidelines (especially those relating to cost implementations: Audit Commission, 2005). Therefore awareness campaigns may also contribute to better health via effects on providers in the medical setting (e.g., general practitioners).

Generating motivation to change.

Increasing personal awareness of risk may be beneficial because it provides greater motivation to act then does more general risk information. Even when general awareness and knowledge about risk factors for certain diseases is good a lack of awareness about ones own risk has been cited as a barrier to uptake of medical care in health care settings, such as cancer (Sabates & Feinstein, 2004). It is well documented that people do not apply the same risk to themselves as they do to others and people inherently believe that negative events are less likely to happen to them than to others, (Weinstein, 1980). In addition people do not make the same estimate when they rate the risk to themselves and/or their family, compared to people in general (Sjöberg, 2000). Smokers present an excellent example of this as even though all the available studies indicate that the majority of people realise that smoking is harmful and believe that the risk of diseases like emphysema and lung cancer is higher for smokers than non-smokers, a large percentage of people still smoke (Hay et al., 2005). Personal risk calculators can be useful in providing individualised information about one's own risk. For example the introduction of the cardiovascular risk calculator allows a person to enter in their personal information (e.g., smoking status, cholesterol) and then calculate a score that is their risk of cardiovascular problems (P. W. F. Wilson, D'Agostino, Levy, Belanger, Silbershatz, & Kannel, 1998). Such tools may also allow an individual to see what effect a reduction in negative lifestyle habits (e.g., smoking) would have on their chances of a disease (e.g., reduction in risk of heart attack), highlighting the positive impact health monitoring can have on the chances of developing a disease. This is of great importance with regards to the factors associated with female fertility difficulties as the prevalence of some negative lifestyle factors are on the increase in Western society. Negative lifestyle factors such as obesity, illicit

drug and alcohol use (especially in young people), and reproductive factors such as sexually transmitted diseases, have all increased markedly over the past decade; for example, there has been a 60% increase in the number of STDs since 1997 in the United Kingdom (Health Protection Agency, 2007) and the WHO estimate that 1.6 billion adults were overweight in 2005, with approximately 2.3 billion adults' projected to be overweight by 2015 (WHO, 2006). Further still, there has also been a steady increase in the age at first pregnancy in Western societies. This increase is believed to be a direct result of a change in the social status of women in western societies, whereby an increasing number of women are delaying childbearing to an age where their reproductive abilities have substantially declined in order to fulfil education and career desires (Weston & Vollenhoven, 2002, Ryan, Maassen, Dokras, Syrop, & VanVoorhis, 2005). In the UK, the proportion of babies with mothers aged 35 years or more increased markedly from 6.5% in 1976 to 22.5% in 2000 (Bakeo, 2004) and in the US this rate has more than doubled since 1978 (Hamilton et al., 2004). Increasing awareness of the impact these factors may have on a woman's chances of pregnancy may aid motivation to change or reduce behaviours that may impact on their future life goals.

Drawbacks

Provoking unnecessary worry and fear.

While educating individuals regarding the factors associated with certain diseases may reduce fear in a number of cases it may also have the adverse affect in actually provoking fear unnecessarily. For example, the media often covers stories on the link between mobile phone use and brain tumours leading to suggestions of how long people should spend using their phone or how phones should be held against the head when making phone calls (e.g., Telegraph, January 26, 2007) despite a lack of

concrete research to suggest whether a relationship actually exists (Hepworth, Schoemaker, Muir, Swerdlow, van Tongeren, & McKinney, 2006).

Communicating risk information as a precautionary measure may not always be the best for the public as a whole; often providing precautionary advice is interpreted as causing concern rather than providing reassurance (Barnett, Timotijevic, Shepherd, & Senior, 2007). For example, campaigns that are 'hard hitting' such as a cancer poster showing three young girls sitting together with tags above their heads depicting their future; 'teacher', 'lawyer', 'cancer' (Kent, 2000), attempt to highlight the lifetime statistic of an individual's chance of developing cancer (one in three: Quinn, Babb, Kirby, & Brock, 2000). However, according to Kent (2000) such campaigns induce fear rather than the intended goal of increasing personal knowledge regarding one's individual risk. Further, Kent (2000) argues that campaigns and media involvement can often mislead the public, for example breast cancer campaigns have been criticised for focusing too much on young women when in reality the majority of cases are in older women (Office of National Statistics, 2004b).

Modest benefits of health monitoring.

Case study evidence, meta-analysis, and systematic literature reviews have each concluded that public health communication initiatives are, on the whole, effective in changing behaviour, but usually only modestly so (Maibach, Abroms, & Marosits, 2007). Noar (2006) believes that evidence is beginning to converge that targeted, well-executed mass media health campaigns that are capable of reaching a wide audience of people can have small-to-moderate effects on health knowledge, beliefs and attitudes, and behaviours. However, while campaigns may have initial

impact in preventing risky behaviours the long-term impact on behaviour change and cost of this may be questionable. The UK government planned to invest 50 million pounds over 3 years to increase public awareness regarding the link between STDs and unprotected sexual intercourse (House of Commons Health Committee, 2005) but while the campaign is still running so concrete conclusions on its success cannot be determined, a recent report from the Health Protection Agency (2007) revealed that STDs are still on the rise.

Raising awareness without support to implement change.

Another problem inherent in the battle to promote health is changing existing behaviours. Health monitoring increases awareness but does not help to overcome hurdles of getting people to reduce or cut-out unhealthy habits that people enjoy and/or are prevalent in society (e.g., smoking, drinking alcohol). Research has shown that campaigns that promote the adoption of a behaviour that is new (e.g., encourage parents to place the baby to sleep on its back to reduce the risk of Sudden Infant Death Syndrome; Maibach et al., 2007) have a greater success rate than campaigns aiming to cease an unhealthy behaviour people are already doing, or prevent commencement of a risky behaviour (e.g., tobacco use; Snyder, 2007). A. M. Clark et al. (1998) showed that only 18 of 30 (60%) women took up the offer of a weight-reduction program that could reduce or eliminate the need for invasive fertility treatment with a further 28% of women dropping out before the end of the six-month bi-weekly program, despite the program being very good at improving pregnancy rates (i.e., 84% pregnancy rates).

The Present Studies

The literature review on the benefits and costs to making people aware of signs and symptoms of disease generally supports that doing so helps people in decision-making about their health. To this authors knowledge there has only been one initiative (i.e., mass media campaign) to help people take better care of their fertility and it was a general campaign. In 2001 the American Society for Reproductive Medicine (ASRM) ran an advertising campaign to promote the message of protecting one's fertility through a number of posters highlighting key factors associated with infertility, such as age, smoking, weight and practising safe sex (See Appendix G for posters). These posters were displayed in a variety of settings (e.g., tube stations, college health centres, community health centres, and YWCA gyms) across America. However, the ASRM never assessed the impact of the campaign but evidence reviewed would suggest that effects might have been modest (Rebar 2008, personal communication). The results from Chapter 4 indicated that people were generally already aware that these factors influenced fertility. Furthermore, past research shows that a focus on personal risk is likely to be more effective in promoting change than awareness of general risk (Fischhoff et al., 1993; Elton et al., 1994; NHS centre for reviews and dissemination, 1998; Sjöberg, 2000; Strychar et al., 1998; McClure, 2002; Greening, Chandler, Stoppelbein, & Robison, 2005). In light of the review and lack of initiatives concerned with fertility the ultimate goal of the present research programme is to produce a risk assessment tool that will raise public awareness about risk of reduced fertility by enabling women to assess their own fertility status. Such tools are now increasingly used by the National Health Service (NHS) to help people make healthier choices. The NHS 'Choices' (http://www.nhs.uk/tools/Pages/Toolslibrary.aspx) website currently has more than 30

health check tools from body mass index calculators to mole self-assessment tools. The aim of the two studies presented in this chapter was to carry out foundational research for a fertility risk assessment tool by (1) identifying the risk factors for reduced fertility (Study 5.1) by conducting a comprehensive literature review and (2) assessing whether such factors could differentiate between pregnant and non-pregnant women (Study 5.2).

Study 5.1
Literature review of potential risk factors for reduced female fertility

Introduction

In order to develop a tool that allows the assessment of personal fertility status, one needs to define risk, identify the factors associated with female infertility, and establish the outcomes for which the risk is relevant (e.g., effect on fertility; longer time to pregnancy).

Defining Risk and a Risk Factor

According to the WHO (2002) preventing diseases from occurring in the first place requires systematic assessment and reduction of their causes. There are a number of factors, known as health determinants, that are linked to the development of an illness and that impact on a person's health status (i.e., genetic, environmental, social, economic & lifestyle; Calman, 1998). Health determinants for specific diseases (e.g., lung cancer) have been rigorously studied in order to identify the risk factors associated with the onset, progression and underlying causes of a disease. Once such determinants have been recognised a number of preventative measures can be put in place in an attempt to reduce the development and/or prevention of such diseases (i.e., governmental regulations, public health campaigns). Risk is often defined as a

probability of an adverse outcome occurring (i.e., heart attack), and a risk factor (i.e., smoking) is a factor that raises this probability (WHO, 2002). To prevent the onset of a disease, such as heart disease, one must establish the risk factors that are known to increase the risk of onset of the disease. Establishing the presence of known risk factors for a disease is a method often used in order to ascertain a person's individual risk for such a disease. For example, the Gail Model uses a number of risk factors to estimate the chance that a woman will develop breast cancer over a particular interval of time (Gail et al., 1989; Decarli, Calza, Masala, Specchia, Palli, & Gail, 2006).

A main principle of identifying risk factors has been to highlight the need for prevention (e.g., promoting the use of sun cream to reduce the risk of skin cancer) and early detection (e.g., noticing changes or new lumps in the breast or testicle) of potentially fatal diseases. Research from the Framingham Heart Study has shown that personal blood pressure, total cholesterol, and low-density lipoprotein (LDL) cholesterol can effectively predict individual risk of coronary heart disease in middle-aged white men and women (P. W. F. Wilson et al., 1998). Self-detection of risk factors enables people to assess their own risk for a disease by ascertaining the presence or absence of various risks or indicators.

As well as establishing that certain factors appear to be risks for the onset of a disease, for example, more smokers develop chronic obstructive pulmonary disease [COPD] than non-smokers, it is also important to ascertain how much of a risk the factor poses, for example, male smokers are 11.7 times more likely to develop COPD than male non-smokers (National Cancer Institute, 1997). Such information is often provided as a relative risk ratio or as an odds ratio. To explain the difference between odds ratios and relative risks one needs to start with odds. An odds is the probability

of an event (i.e., pregnancy) occurring in one group (e.g., number of pregnancies/sample size).

For example if you had two groups of 100 women and in one group 30 women fell pregnant the odds of pregnancy in this group would be 30%, if in the other group of 100 women 15 fell pregnant the odds of pregnancy in this group would be 15%. If you wanted to compare these groups you could compute a relative risk (RR). A relative risk compares the number of pregnant women in one group (i.e., 30) to the number of pregnant women in the other group (i.e., 15) by dividing the two (i.e., 30/15), therefore the relative risk of pregnancy is two times higher in group one (30 pregnant women) compared to group two (15 women). An odds ratios (OR) also provides an estimate for risk by comparing the event occurring in one group compared to the event occurring in another group but adjusts for the frequency of the event in each of the groups (i.e., (pregnant women in group one/sample size of group one)/(pregnant women in group two/sample size of group two)) therefore the odds ratio for the two groups would be 2.43 ((30/70)/(15/85)), representing a 2.43 higher odds of pregnancy in group one compared to group two. Whilst odds ratios and relative risks are slightly different in their meaning they are often used interchangeable as the two numbers are often similar, as can be seen in the example, RR was 2 and OR was 2.43. Odds ratios and relative risks will however diverge when the frequency of the event becomes more frequent (i.e., more than 10%) or the effect size is large (Davies, Crombie, & Tavakoli, 1998; Scott, 2008). Odds ratios and relative risks are interpreted using confidence intervals (CI). A CI is a statistically defined range of population values with which a sample statistic is likely to represent at a given level of confidence (most often, 95%: Heiman, 1999; Sin & Reid, 1999). When used to interpret odds ratios if the confidence interval includes unity, that is, it

overlaps 1.0 the increased risk is not statistically significant, and could have been due to chance (Fathalla & Fathalla, 2004).

In regard to infertility there are a number of different categories of risks and indicators that could help establish a woman's fertility status, for example those connected to lifestyle factors, reproductive disease or other diseases that impact on fertility (e.g., cancer and its treatment). The effect a risk factor may have on fertility can be measured in a number of ways. For example, a risk factor may be associated with a longer time or delay in achieving a pregnancy (measured in months and/or years) or an increased risk of a type of infertility (e.g., ovulatory infertility) that may reduce success of conception attempts. Alternatively a factor may have an impact on fertility once conception has occurred, for example by increasing the risk of miscarriage or perinatal morbidity or mortality. A factor may have a short-term effect on fertility, for example, ceasing once the risk factor has been eliminated (i.e. cessation of smoking) or a long-term irreversible effect on fertility, for example blocked tubes as a consequence of an untreated sexually transmitted disease.

Assessment of study quality.

In this study a review of risk factors associated with female infertility was carried out. When conducting a literature review it is important to consider the quality of the designs employed by each study reviewed, in particular strengths or limitations that may lead to systematic errors or bias (Ryan, Hill, Broclain, Horey, Oliver, & Prictor, 2007). The quality of the design can be assessed on a number of levels. Randomised Control Trials (RCTs) aim to reduce any biases that could lead to any invalid conclusions and are often thought of as the most robust and effective research designs (Barlow, 2003). However, RCTs are not always practical to implement (e.g.,

not having a 'no treatment' group) and in some fields of research non-randomised controlled trials or quasi-experimental designs (e.g., prospective studies with a control group) provide the best evidence (Petticrew & Roberts, 2006). Within non-randomised controlled designs there are some methods deemed of 'better quality' than others, for example prospective studies (i.e., cohort studies) are considered of superior quality to retrospective designs (i.e., cross-sectional studies) as participants are followed over a period of time to observe the development of the outcome in question (Petrie & Sabin, 2000) and can be designed to reduce the impact of certain biases that may influence the outcome, that are not as easily controlled in retrospective studies (e.g., recall bias). However, prospective studies are more costly and time consuming to develop and are not always as practical to set-up and implement compared to retrospective designs (Petrie & Sabin, 2000).

According to Khan, Riet, Popay, Nixon, and Kleijnen (2001) there are a number of types of bias that should be taken into account when reviewing studies, such as selection bias (i.e., were the groups comparable; representative), performance bias (i.e., were there any differences in the care provided apart from the intervention being evaluated?), attrition bias (i.e., were there any differences between groups due to drop out within groups?), and measurement bias (i.e., were there any differences between comparison groups in how outcomes were ascertained?). In addition the use of different outcome measures may impact on the ability to generalise effects across studies. For example, time to pregnancy (TTP) is a widely used means of measuring differences among populations of women trying to conceive. However, women reporting TTP based on an early pregnancy test (i.e., hormonal pregnancies detected by human chorionic gonadotropin, hCG) may lead to an overestimation of eventual live birth rates compared to women reporting TTP based on a clinical pregnancy test

(detected by a fetal heart beat; Zegers-Hochschild, Nygren, Adamson, de Mouzon, Lancaster, Mansour, & Sullivan, 2006) as the former pregnancy has a much higher risk of miscarriage compared to the later definition of pregnancy (Wang, Chen, Wang, Chen, Guang, & French, 2003).

Expert consultation and consensus.

The principles of evidence-based medicine (EBM) offer a framework to guide the search for and appraisal of clinically relevant information and these would support the use of empirically determined risk factors to guide clinical judgement about whether a fertility problem exists and if it does what its causes might be (e.g., Straus & Sackett, 1998). EBM underpins practice guidelines such as the NICE series. However where evidence is lacking more emphasis may be placed on expert opinion. In the present study the set of empirically selected risk factors were presented to fertility experts to ascertain consensus about their relevance in predicting potential fertility status, using a similar method to that of the Delphi technique. The Delphi technique is used to aid decision-making and to obtain the most reliable consensus of opinion from a group of experts (Dalkey & Helmer, 1963, p. 458 in Rowe & Wright, 1999). Using such a procedure allows access to the collective knowledge from a variety of experts, with potentially differing opinions (Rowe & Wright, 1999). For the present study not all the main principals of conducting a Delphi technique (e.g., expert anonymity, re-iteration, controlled feedback: Okoli & Pawlowski, 2004) could be adhered to due to time constraints of the experts, therefore only one meeting was held to discuss the results of the literature review of the empirical evidence.

The Present Study

The aim of the present study was to determine which risk factors would be essential indicators of female fertility potential that could be used to develop a tool to assess personal fertility status. A comprehensive literature review was conducted to establish all factors that have been previously associated with female fertility difficulties. All risk factors identified in the literature were examined using odds ratios extracted and then presented to the panel of fertility and reproductive experts for a consensus on which factors were the most important. All experts were asked to discuss and justify reasons for and against each risk factor until all were happy with the final selection. The 14 risk factors identified in the literature review and selected through the expert consultation will be discussed in the results section.

Materials and Methods

Procedure for Extraction of Risk Factors

Literature review.

A number of PubMed searches were conducted to establish factors associated with female infertility. Firstly, the term Female Infertility [MeSH] was searched resulting in 19,026 records and 2,335 reviews, which was narrowed by including the term Risk Factors [MeSH]. The 600 records and 157 reviews were then scanned for relevance, full reports were obtained as necessary and other citations were identified in the reference lists of the relevant citations. All records and reviews were excluded if the outcome reported was assessing a risk factors impact on treatment outcome (e.g., smoking during a cycle of IVF associated with a reduced chance of treatment success). Studies were classified according to the outcomes and whether a definition of the outcome had been provided. The outcomes were: (1) 'risk of infertility' referred to no conception after 12 months and/or a medical diagnosis (e.g., tubal

factor infertility); (2) 'time to pregnancy' referred to the number of months needed to achieve pregnancy; (3) 'reduced conception rate' referred to a reduced chance of clinical pregnancy; (4) 'menstrual irregularities' referred to either short (< 21 days) or long (> 35 days) menstrual cycles and/or sporadic or unpredictable periods; (5) 'specific diagnosis' referred to medical diagnosis of a reproductive disorders (e.g., pelvic inflammatory disease, endometriosis).

All risk factors identified were then individually searched for using PubMed with the term (e.g., Female Age) and Female Infertility (i.e., 'Female age AND Female Infertility'); see Appendix H for a full search history. In addition a number of other reproductive health references/guidelines were searched to ascertain any additional factors not detected in the original review (i.e. National Institute for Health and Clinical Excellence [NICE], WHO).

Expert consultation and consensus building.

Twenty-five medical reproductive experts and patient advocacy group leaders were contacted through the Assisted Conception Taskforce (ACT) which provides information for people with fertility problems (see Appendix I for a full list of reviewers). At the annual meeting of the taskforce (December, 2006), experts were provided with the list of the factors identified in the review and asked to discuss the importance of each risk factor with the goal of producing a list of critical factors that would be associated with a woman's fertility status. During the meeting panellists were asked to provide explanations for their chosen risk factors, and to respond to the reasons and justifications for risk factors identified by other experts. Each chosen risk factor was discussed within the group until all contributors were happy with a final

list of risk factors (all information was documented by Dr Jacky Boivin who attended the meeting).

Assessment of Study Quality

The NICE Hierarchy of Evidence (NICE, 2004) and the Cochrane Study Quality Guide (Ryan et al., 2007) were used to assess the quality of the studies extracted. These guidelines emphasise the importance of assessing the quality of studies through the review of a number of elements that may lead to the misinterpretation of the research findings, such as the methodological design utilised (e.g., Randomised Control Trials [RCT]; observational studies), any study bias or potential confounding factors (e.g., attrition), and outcome measures used (e.g., live birth, clinical pregnancy). In the present review each study was categorised according to the following elements:

Design.

Studies that assessed the risk factor prior to the occurrence of the outcome were categorised as prospective whereas studies that assessed risk after the occurrence of the outcome were categorised as retrospective.

Pregnancy confirmation.

If the pregnancy had been confirmed with an ultrasound scan (clinical pregnancy, at least 12 weeks gestation) or delivery then the study was categorised as confirmed if the outcome was based solely on a positive pregnancy test then the study was categorised as unconfirmed pregnancy (only studies using pregnancy as an outcome were categorised on this measure).

Analytic approach.

Studies were also categorised according to components of the analysis, namely whether power calculations had been computed and whether analyses controlled for confounding factors (e.g., smoking, body mass index, age).

Results

Assessment of Study Quality

In total 58 studies were reviewed (46 original articles and one review paper), of which 45 (76%) were retrospective in design and 13 (22%) prospective. Twenty-four studies reported risk of infertility, 23 studies reported time to pregnancy (TTP), seven studies reported reduced conception rate, two studies reported menstrual irregularities and two studies reported specific diagnosis.

Of the studies (n = 29) sampling women either currently pregnant or those who had had a pregnancy in the past, 21 studies (72.41%) reported the pregnancy was clinically recognised or had resulted in a live birth. Finally, 50 studies (86.21%) reported controlling for confounding variables (47 [94%] studies provided information on the factors controlled), 45 studies (77.59%) provided information on potential biases due to the study design and three studies (5.17%) reported performing power calculations prior to conducting the studies (Juhl, Olsen, Nybo Anderson, & Grønbæk, 2003; Urbach, Marrett, Kung, & cohen, 2001; Maheshwari, Hamilton, & Bhattacharya, 2008). (See Table 5.1.1, 5.1.2 & 5.1.3 for breakdown per risk factor and Appendix J, Table A2 for further information on quality assessment of each study)

In total 31 risk factors were identified from the literature review categorised into the following four areas; demographic (3 factors), reproductive (6 factors), lifestyle (11 factors) and medical factors (11 factors).

Expert Consultation and Consensus

From the original list of 31 factors, 14 were chosen by the experts as the most vital factors for assessing fertility potential. Appendix K shows the 17 factors made redundant after the expert meeting. There were four main reasons why factors were not included in the final list. First, factors that were not deemed independent were excluded. For example, excessive exercise is only important if it is associated with a negative effect on menstruation (e.g., anovulation); otherwise it is not predictive of reduced fertility. It was therefore decided that having questions about a woman's menstrual cycle would be more informative to determine a female's fertility status then questions about causes that may or may not produce cycle effects in individual cases. Five factors were excluded for this reason: exercise, underweight (BMI <19), ethnicity, polycystic ovarian syndrome (PCOS), and epilepsy.

Second, some factors were eliminated because the evidence was weak or too inconsistent about the effects of the given factor on fertility. The review showed a substantial number of studies exploring the association between alcohol consumption and fertility, producing both positive and negative impacts, often measured by longer or shorter TTP. In the end the experts decided that the evidence supporting a link between moderate to large amounts of alcohol consumption and reduced female fertility was sufficient and this factor was included in the final list. However the effects of four other factors were deemed too inconclusive and were excluded: asthma medication; occupational and environmental factors; contraception use; prescribed drug use. Factors identified in the review as having an inconsistent evidence-base were rigorously discussed until all experts were content with inclusions and exclusions.

Third, while miscarriage and perinatal problems encompass female fertility they are problems occurring after conception. When conducting the review and the expert consultation the emphasis was placed on factors associated with fertility problems impacting on conception (i.e., inability to conceive, longer time trying to conceive). Three factors (heart disease; coeliac; thrombophillia) were excluded because their primary effect on female fertility was associated with an increased risk of miscarriage, ectopic pregnancy, genetic abnormalities and/or perinatal risks (Molteni, Bardella, & Bianchi, 1990; Sher & Mayberry, 1994; Buchholz & Thaler, 2003).

Finally, all the non-reproductive medical diseases not already excluded were removed ($n = 5$) and there were two reasons for this decision. First, when conducting the review it was established that the incidence of a number of these medical conditions was very low in the general population and it was decided that it would be impractical to have an exhaustive list of questions about relatively rare diseases for a tool with the aims proposed. Second, it was thought that in such cases the individual concerned would already be aware of the detrimental impact of the disease and/or its treatment on her fertility status through information provided in specialist clinics and/or through consenting to procedures for treatment and as such would not benefit additionally from an awareness tool as proposed. On the basis of these two issues it was decided that the following non-reproductive medical diseases would be excluded: sickle cell anaemia; lupus erythematosus (SLE); cancer; diabetes; kidney disease and transplantation.

Risk Factors

The following section details the 14 risk factors identified in the literature review and retained after the expert consultation. The factors have been divided into three categories; demographic factors (1), reproductive factors (5), and lifestyle factors (8). Each of the following sections will identify what the risk factor was and the outcome it had on fertility potential. A number of the studies computed odds ratios or relative risks to highlight the impact the factor had on female fertility. Table 5.1.1, 5.1.2 and 5.1.3 present the odds ratio or relative risks for each risk factor identified in the literature review and the outcome measure (i.e., longer time trying to conceive) according to category.

Demographic Factors

Age.

When females are born they already have the entire stock of follicles needed for reproduction, as they get older the number of follicles decline to the point that by the time the menopause is reached (mean age of 51 years), not enough remain to sustain the process necessary for menstruation, and thus reproduction (Faddy, Gosden, Gougen et al., 1992). Research has shown that even from the age of 20 a woman's fertility is unavoidably declining, with a steep drop after the age of 35 (Menken, Trussell & Larsen, 1986; Dunson, Colombo & Baird, 2004). Thus increasing age is associated with a number of fertility problems, relating to both the decline of the quantity and quality of the oocytes (Velde & Pearson, 2002) and the uterus (Stein & Susser, 2000). In Table 5.1.1 a total of one prospective and six retrospective studies demonstrated that increasing age was significantly associated with female infertility. Two studies established an increased TTP with advancing age with Axmon et al. (2006) reporting a 3% longer TTP when women were compared to women one year

younger. However Hassan & Killick (2003) found a significant effect of age only in relation to the chance of a TTP greater than 24 months. Specifically women aged 30 to 35 years had nearly a 5 fold increase TTP and women over the age of 35 years a 7 fold longer TTP compared to women aged 25 years or less. Kaplan et al. (2005) found that older women were more likely to encounter a failure when trying to conceive compared to younger women: women $\geq$ 36 years were 3.52 times less likely to have conceived within 3 months. Dunson, Baird, and Columbo (2004) also found that older women were less likely to have conceived within 12 months using a prospective study design whereby women were asked to collect and record daily fertility and menstrual characteristics (e.g., basal body temperature) over several menstrual cycles. In La Rochebrochard and Thonneau (2003) study they interviewed 6,188 women, finding that women aged 35 to 39 years were significantly more likely to experience a delay in conception compared to women 26 years and younger. Finally two studies (Urbach et al., 2001; Maheshwari et al., 2008) sampling over 7,000 women found that progressing age was a significant risk factor for tubal infertility in women over the age of 30 (OR range 1.70 – 33.00) and for unexplained infertility in women aged 30 to 34 (OR 1.50) and 35 to 39 years (OR 1.80) compared to women under the age of 30.

Table 5.1.1
Effect of demographic factors on female fertility (see page 135 for notes).

Risk Factor, Study Design	Outcome Measure	Odds ratio CI)	N (Age), Sample, Country and Year	Sources of Bias	Control of Confounding Factors	Authors
AGE						
Prospective studies						
19 - 26 years old (R)[a]	Risk of	1.00[d]	782 women (18 - 40),	No information	No information available	Dunson et al.
27 - 34 years old	Infertility	1.80[e]	randomly selected, daily	available		(2004)
35 - 39 years old		2.53	fertility & menstrual characteristics recorded, Europe 1992 - 1996			
Retrospective studies						
Compared to 1 year younger	Increased TTP[c]	0.95[b] (0.93, 0.96)	1,578 women (23 - 39), randomly selected from general population, questionnaire, Sweden, 2000	Selection	Yes (menstrual cycle, age at conception, use of oral conception, nulliparity)	Axmon et al. (2006)
25 years old or less (R)	Increased TTP	1.00	1,976 pregnant women (25 - 44), antenatal units, questionnaire, United Kingdom 2000 - 2001	No information available	Yes (coital frequency, weight, smoking, partner's age, alcohol, caffeine, age at menarche)	Hassan & Killick (2003)
25 - 30 years old	> 12 months	1.10 (0.60, 2.00)[f]				
30 - 35 years old		0.90 (0.40, 1.80)[f]				
> 35 years old		2.20 (0.80, 5.80)[f]				
25 years old or less (R)	Increased TTP	1.00				
25 - 30 years old	> 24 months	1.60 (0.60, 4.60)[f]				
30 - 35 years old		4.80 (1.50, 16.00)[f]				
> 35 years old		7.70 (1.50, 38.90)[f]				
≤ 30 years old (R)	Increased TTP	1.00[d]	798 pregnant women (20 - 40), antenatal unit, questionnaire, Israel 2003	No information available	No information available	Kaplan et al. (2005)
≥ 36 years old		3.52**				

Table 5.1.1
Effect of demographic factors on female fertility (continued).

Risk Factor, Study Design	Outcome Measure	Odds ratio CI)	N (Age), Sample, Country and Year	Sources of Bias	Control of Confounding Factors	Authors
AGE						
Retrospective studies (continued)						
< 30 years old (R)	Risk of	1.00	3,287 women (25 - 44),	Selection &	Yes (country of origin,	La
30 - 34 years old	Infertility	1.16 (0.96, 1.41)	randomly selected from	recall	number of previous	Rochebrochard
35 -39 years old		1.79 (1.30, 2.46)	census registers, interview,		pregnancies, smoking,	& Thonneau
			Europe 1991 - 1993		coital frequency, history	(2003)
					of miscarriage, history of	
					induced abortion)	
< 30 years old (R)	Risk of tubal	1.00	7,172 infertile women (20 -	Change in	Yes (partner's age,	Maheshwari et
30 - 34 years old	infertility	1.70 (1.40, 1.90)	50), medical records based	diagnostic	diagnosis of male factor,	al. (2008)
35 - 39 years old		2.20 (1.70, 2.70)	on first clinic visit, United	methods over	duration of infertility)	
≥ 40 years old		2.20 (1.60, 3.00)	Kingdom 1993-2006	time		
< 30 years old (R)	Risk of	1.00				
30 - 34 years old	unexplained	1.50 (1.30, 1.80)				
35 - 39 years old	infertility	1.80 (1.40, 2.20)				
≥ 40 years old		1.20 (0.90, 1.60)				
20 - 24 years old (R)	Risk of	1.00	121 primary infertile cases	Selection, recall,	Yes (socioeconomic	Urbach et al.
25 - 29 years old	primary tubal	5.10 (0.60, 44.70)	& 490 clinically pregnant	cases not aged	status, smoking, PID,	(2001)
30 - 34 years old	infertility	12.20 (1.50, 100.80)	controls (20 - 44),	matched	endometriosis, oral &	
35 - 39 years old		13.30 (1.60, 111.70)	questionnaires, Canada		intrauterine contraceptive	
40 - 44 years old		33.00 (3.60, 301.80)	1998		use, appendectomy)	

[a] R refers to reference group. [b]Based on fecundibility ratio (FR), i.e., the monthly conception rate among exposed compared with that among the unexposed (1/0.94 = 1.03) 0.94 indicates 3% longer TTP compared with women one year younger. [c]TTP refers to Time Trying to Pregnancy. [d]Odds ratios calculated from data available in publication see Appendix L for full calculations. Calculations for odds ratios were from Bland and Altman (2000). No confidence Intervals available. [e]No significance levels provided. [f]Relative risk ratio. *P<0.05, **P<0.01, ***P<0.001.

Reproductive Factors

Endometriosis.

Endometriosis is defined as the presence of endometrial glands and stroma outside the uterine/endometrial cavity and musculature commonly characterised by general pelvic pain, dysmenorrhea (pain presenting around the time of menstruation), dyspareunia (pain during sexual intercourse), abnormal uterine bleeding and infertility (Olive & Schwartz, 1993; Schenken, 1999). According to Khadem and Mazlouman (2004) the most established cause of the disorder is the retrograde flow of menstrual flow through the fallopian tubes and deposition of viable endometrial tissue, with subsequent implantation on the peritoneal surface. The disease is almost exclusively found in women of reproductive age (Olive & Schwartz, 1993), with a prevalence rate estimated at 3-15% (Jones, 1997; Keye, 2006), although this rate can vary depending on the technique used for diagnosis (Olive & Schwartz, 1993). As Table 5.1.2 (page 142) shows four retrospective studies reported a negative impact on female fertility potential in women suffering from endometriosis. In the Akande et al. (2004) study they split endometriosis sufferers into two groups; women presenting with primary or secondary infertility and by age and found that younger women with endometriosis were significantly more likely to have a reduced chance of a natural pregnancy in the primary and secondary infertility groups compared to women with a diagnosis of secondary unexplained infertility. Three case-controlled studies established an association between endometriosis and infertility. Khadem and Mazlouman (2004) demonstrated that women with endometriosis were nearly 5 times more likely to have infertility compared to women without endometriosis. Lalos (1988) also reported increased risk of infertility in women diagnosed with moderate endometriosis compared to women without endometriosis (OR 3.91). In addition both Lalos (1988)

and Urbach et al. (2001) found that women suffering from endometriosis were at an increased risk of tubal infertility (OR 3.50), including women who had ever had the condition (OR 6.00; Urbach et al., 2001).

Menstrual Cycle.

Menstruation centres on the development of the egg and ovulation (Gersh & Gersh, 1981). The menstrual cycle averages the length of a lunar month (29.5 days), however it is estimated that only 10-15% of cycles are exactly 29.5 days (Jones, 1997). It is estimated that between 91-97 % of women with a regular cycle will have evidence of ovulation (Taylor & Collins, 1992). Cycle length can vary greatly within and between women and there are a number of problems related to menstrual cyclicity that are associated with infertility. Two studies used prospective designs to assess the impact of menstrual cycle irregularities on conception. Specifically, Small et al. (2006) found that shorter bleed length (≤ 4 days) and shorter cycle lengths (i.e., 26 to 29 days) were associated with a reduced chance of clinical pregnancy compared to 5-day bleeds or cycles of 30 to 31 days, respectively. Conversely longer cycles (i.e., ≥ 32 days) were also found to have reduced chance of clinical pregnancy (OR 0.63) although the confidence intervals (CI) included unity. Kolstad et al. (1999) also found that longer cycles (i.e., ≥ 40 days) were associated with reduced conception rate (OR 1.54).

Two retrospective studies (Axmon, Rylander, Albin, & Hagmar, 2006; Rowland et al., 2002) also reported longer menstrual cycle length significantly associated with an increased TTP and risk of infertility. Rowland et al. (2002) also found that irregular cycles (OR 2.80) and inter-menstrual bleeding (OR 1.70) were also significantly related to an increased risk of infertility.

Chronic Menstrual Pain.

It is estimated that between 30 – 90% of women will experience a certain amount of discomfort during menstruation and that for roughly 7 – 15% this menstrual pain will be so severe it will impinge on normal day to day functioning (Svanberg & Ulmsten, 1981; Pullon, Reinken, & Sparrow, 1988; C. A. Wilson & Keye, 1989; Ng, Tan & Wansaicheong, 1992; Jamieson & Steege, 1996; Zondervan et al., 1998). Dysmenorrhea is the medical term to define chronic menstrual pain, caused by severe contractions of the uterine smooth muscle (Jones, 1997) and as Table 5.1.2 (pages 143-145) shows it is associated with an increased risk of infertility (OR 3.71), as is chronic pelvic pain (OR 12.57), and dyspareunia (medical term to define pain in the lower pelvic region experienced during sexually intercourse; OR 4.41).

Pelvic Surgery.

Women who undergo surgery in their pelvic region are at risk of adhesions or infections as a result of such operations (van Goor, 2007). According to Lalos (1988) such tubal occlusion and/or adhesions in the pelvic region are a major cause of infertility and in Table 5.1.2 (page 143) two case-controlled studies reported significant associations. Thonneau et al. (1992) found that women with a history of pelvic surgery were 1.80 times more at risk of primary and secondary infertility. Lalos (1988) found that previous abdominal surgery was the most frequent risk factor for tubal infertility (OR 4.32).

Sexually Transmitted Infections (STI)/Diseases (STD).

Research on the effect of STDs on fertility strongly indicates that such diseases are the primary aetiology of tubal infertility, acting through the intermediary of pelvic inflammatory disease (R. T. Cates, Rolfs, & Aral, 1990). Six retrospective

studies were reviewed. Thonneau et al. (1992) found that women who have ever had a STD were 10 times more at risk of secondary infertility compared to women who had never had an incidence of an STI (see Table 5.1.2, pages 145-147).

Chlamydia infections occur twice as frequently as other STI's such as gonorrhoea in most population studies (R. T. Cates et al., 1990). Chlamydia is suggested to cause more severe sub-clinical inflammation and subsequent tubal damage compared to other STD's (Sciarra, 1997). Hills et al. (1997) reported that women who contracted the infection more than once had a significantly increased risk of pelvic inflammatory disease (PID) compared to women infected once. Wiesenfeld et al. (2002) also reported a significant association between positive chlamydia infection and sub-clinical PID. Chlamydia was also associated with an increased risk of infertility in two case-controlled studies. Women who had suffered from chlamydia were 11.45 times at risk of infertility (Malik, Jain, Hakim, Shukia, & Rizvi, 2006) and 3.20 times at risk of tubal infertility (Swasdio et al., 1996) compared to women who had never tested positive for chlamydia.

Gonorrhoea (often referred to as gonococcal infection, Jones, 1997) is less prevalent compared to chlamydia infection. Gonorrhoea is often asymptomatic; with at least 50% of women having no symptoms at all (Eschenbach, 1999). Two studies reported a significant increased risk of tubal infertility following this infection, with Swasdio et al. (1996) reporting that women had a 32.40 fold increase of tubal factor infertility and Lalos (1988) a 7 fold increase compared to women who had never had the disease (see Table 5.1.2, pages 145-147). Past gonorrhoea infection was also associated with a 2.40 times increased risk of sub-clinical PID.

Pelvic Inflammatory Disease (PID).

Pelvic Inflammatory Disease (PID) also known as acute salpingitis (Rhoton-Vlasak, 2000) refers to infection of the uterus, fallopian tubes and adjacent pelvic structures unrelated to prior surgery or pregnancy (McCormack, 1994). The exact incidence of PID is unknown because the disease cannot be diagnosed reliably from clinical symptoms and signs (Ross, 2008); however of those diagnosed it is thought to affect around 1.5 million women in the United States (Crossman, 2006). Symptoms of PID include lower abdominal pain, abnormal vaginal discharge, abnormal uterine bleeding, dysuria (painful or problematic urination), dyspareunia, nausea, vomiting and fever (Rhoton-Vlasak, 2000). If the disease is left untreated, it can ascend to the upper genital tract (Land & Evers, 2002), causing tubal obstruction, pelvic adhesions and/or endometriosis (Sciarra, 1997). Research suggests that PID is predominately caused by chlamydia, gonorrhoea and anaerobes infections with 20-50% of cases in the U.S. occurring in association with chlamydia and 20-80% in association with gonorrhoea (Rhoton-Vlasak, 2000).

In Table 5.1.2 (pages 147-148) all four studies reviewed found a significant association between PID and infertility. One prospective study (Weström, 1993) found that the incidence of PID significantly increased the risk of infertility compared to women with no history of the infection (OR 7.00) and that the risk of infertility significantly increased as the number of episodes of PID increased (OR two episodes = 16.20, three or more episodes = 28.30). In addition for those women who had the infection a significant association was found with the severity of the disease and subsequent risk of infertility (OR moderate = 1.80, severe = 5.60).

Urbach et al. (2001) found that women suffering from PID were six times more at risk of tubal infertility and Lalos (1988) reported women with PID had a four fold increase risk of tubal infertility compared to women not suffering from PID. Finally Thonneau et al. (1992) reported a significant increased risk of primary and secondary infertility in women who had a past episode of salpingitis.

Table 5.1.2
Effect of reproductive factors on female fertility (see page 148 for notes).

Risk Factor, Study Design	Outcome Measure	Odds ratio (CI)	N, Sample, Country and Year	Sources of Bias	Control of Confounding Factors	Authors
ENDOMETRIOSIS Retrospective studies						
Unexplained infertility (R)[a] Mild Endometriosis (at median age 31 years) Primary infertility Secondary infertility Mild Endometriosis (at maximum age 39 years) Primary infertility Secondary infertility	Reduced conception rate	1.00 0.26 (0.11, 0.62)[bf] 0.21 (0.10, 0.43)[bf] 0.68 (0.16, 2.88)[bf] 0.53 (0.13, 2.20)[bf]	117 unexplained infertile women & 75 women with laparoscopic diagnosed endometriosis (< 40), questionnaire & 3 year follow-up United Kingdom 1985 - 1995	Selection, drop out	Yes (age, duration of infertility, type of infertility, smoking)	Akande et al.(2004)
Yes (versus no)	Risk of infertility	4.67**[c]	100 infertile women & 120 fertile age-matched controls (25 - 40), laparoscopy performed & medical records, Iran	Selection	No information available	Khadem & Mazlouman (2004)
Yes moderate endometriosis (versus no)	Risk of Infertility	3.91**[c]	120 infertile cases & 126 pregnant controls with no history of infertility (18 - 43), questionnaire & medical records, Sweden 1978 - 1982	Small sample size	No information available	Lalos (1988)
Yes (versus no)	Risk of tubal infertility	3.59[c]				
Ever (versus never)	Risk of tubal infertility	6.00 (2.80, 12,80)	121 primary infertile cases & 490 clinically pregnant controls (20 - 44), questionnaires, Canada 1998	Selection, recall, cases not aged matched	Yes (socioeconomic status, age, smoking, PID, oral & intrauterine contraceptive use, appendectomy)	Urbach et al. (2001)

Table 5.1.2
Effect of reproductive factors on female fertility (continued, see page 148 for notes).

Risk Factor, Study Design	Outcome Measure	Odds ratio (CI)	N, Sample, Country and Year	Sources of Bias	Control of Confounding Factors	Authors
PELVIC SURGERY						
Retrospective studies						
Yes (versus no)	Risk of primary infertility	1.80 (1.20, 1.90)	301 infertile cases & 380 controls who had just given birth, interview, France 1988 - 1989	Recruitment	Yes (age)	Thonneau et al.(1992)
Yes (versus no)	Risk of secondary infertility	1.80 (1.10, 3.00)				
Yes (versus no)	Risk of tubal infertility	4.32***[c]	120 infertile cases & 126 pregnant controls with no history of infertility (18 - 43), questionnaire & medical records, Sweden 1978 - 1982	Small sample size	No information available	Lalos (1988)
MENSTRUAL CYCLE IRREGULARITIES						
Prospective studies						
Cycle length						
≤ 28 - 29 days (R)	Reduced conception rate	1.00	295 trade union women (20 - 35), daily urine samples for 5 menstrual cycles or until conception, Denmark 1992 - 1995	Selection	Yes (age, history of STD & salpingitis, appendectomy, history of andrologic disease, contraceptive use, BMI, study centre, coital frequency)	Kolstad et al.(1999)
≥ 40 days		1.54[c]				

Table 5.1.2
Effect of reproductive factors on female fertility (continued, see page 148 for notes).

Risk Factor, Study Design	Outcome Measure	Odds ratio (CI)	N, Sample, Country and Year	Sources of Bias	Control of Confounding Factors	Authors
MENSTRUAL CYCLE IRREGULARITIES *(continued)*						
Prospective studies *(continued)*						
Bleed length	Reduced		470 women employed by government (< 40), interviews & urine collection 2 days per cycle for 1 year or until a clinical pregnancy, United States 1990 - 1994	Sample size	Yes (coital frequency, number of cycles women at risk of pregnancy, age, BMI, race, caffeine, alcohol, smoking)	Small et al.(2006)
< 4 days	conception rate	0.50 (0.29, 0.87)[e]				
4 days		0.57 (0.36, 0.90)[e]				
5 days (R)		1.00				
6 days		0.90 (0.56, 1.44)[e]				
≥ 7 days		0.70 (0.40, 1.24)[e]				
Cycle length	Reduced					
< 26 days	conception rate	0.60 (0.34, 1.06)[e]				
26 - 27 days		0.56 (0.32, 0.99)[e]				
28 - 29 days		0.52 (0.31, 0.88)[e]				
30 - 31 days (R)		1.00				
≥ 32 days		0.63 (0.38, 1.03)[e]				
Retrospective studies						
1 day increase in menstrual cycle length						
Yes (versus no)	Increased TTP[d]	0.96 (0.94, 0.98)[e]	1,578 women (23 - 39), randomly selected from general population, questionnaire, recall menstrual cycle length every 3 months of trying to conceive, Sweden, 2000	Selection	Yes (menstrual cycle, age at conception, use of oral conception, nulliparity)	Axmon et al.(2006)
Long cycle						
Yes (versus no)	Risk of infertility	2.40 (1.60, 3.50)	3,941 women (21 - 40), questionnaire, United States 1994 - 1996	Selection	Yes (age)	Rowland et al. (2002)
Irregular cycle						
Yes (versus no)	Risk of infertility	2.80 (2.00, 3.90)				
Inter-menstrual bleeding						
Yes (versus no)	Risk of infertility	1.70 (1.30, 2.10)				

Table 5.1.2
Effect of reproductive factors on female fertility (continued, see page 148 for notes).

Risk Factor, Study Design	Outcome Measure	Odds ratio (CI)	N, Sample, Country and Year	Sources of Bias	Control of Confounding Factors	Authors
MENSTRUAL CYCLE IRREGULARITIES *(continued)*						
Prospective studies *(continued)*						
Menstrual Pain			100 infertile women & 120 fertile age-matched controls (19 - 39), laparoscopy performed & medical records, Iran	Selection	No information available	Khadem & Mazlouman (2004)
Dysmenorrhea (pain during menstruation)	Risk of infertility					
Yes (versus no)		3.71*[c]				
Chronic pelvic pain	Risk of infertility					
Yes (versus no)		12.57*[c]				
Dyspareunia (pain during sexual intercourse)	Risk of infertility					
Yes (versus no)		4.41*[c]				
Yes (versus no)	Risk of secondary infertility	10.00 (3.00, 36.30)	301 infertile cases & 380 controls who had just given birth, interview, France 1988 - 1989	Recruitment	Yes (age)	Thonneau et al.(1992)
SEXUALLY TRANSMITTED INFECTIONS (STIs)						
Retrospective studies						
Chlamydia Trachomatis						
No. of chlamydial infections						
1 (R)	Risk of PID	1.00	11,000 women known to have had chlamydia trachomatis (10 - 44), medical records of registered hospitalisation for PID, United States 1985 - 1992	Under-representation of all chlamydia cases	Yes, but for a number of lifestyle factors no information ascertained	Hillis et al. (1997)
2		4.00 (1.30, 9.90)[f]				
≥ 3		6.40 (2.20, 18.40)[f]				
Yes (versus no)	Risk of subclinical PID	3.40 (1.80, 6.30)	556 women (15- 30) with lower genital tract infections or determined at risk of such infections, sexual & reproductive health clinics, endometrial sampling for histologic analysis, United States 1998 - 2000	No information available	Yes (menstrual cycle, previous pregnancy, race, positive for chlamydia, gonorrhoea	Wiesenfeld et al.(2002)

Table 5.1.2
Effect of reproductive factors on female fertility (continued, see page 148 for notes).

Risk Factor, Study Design	Outcome Measure	Odds ratio (CI)	N, Sample, Country and Year	Sources of Bias	Control of Confounding Factors	Authors
SEXUALLY TRANSMITTED INFECTIONS (STIs) *(continued)*						
Chlamydia Trachomatis *(continued)*						
Yes (versus no)	Risk of infertility	11.45**	110 primary & secondary infertile cases & 30 healthy term pregnant controls (18 - 40), hysterosalpingography performed on all patients, India 2003 - 2004	No information available	No information available	Malik et al. (2006)
Yes (versus no)	Risk of tubal infertility	3.20 (1.20, 8.50)	55 primary infertile confirmed tubal damage cases & 59 postpartum controls, past infections assessed measuring serum IgG antibodies, Thailand 1990 - 1992	No information available	Yes	Swasdio et al.(1996)
Neisseria Gonorrhoea						
Yes (versus no)	Risk of subclinical PID	2.40 (1.10, 5.10)	556 women (15- 30) with lower genital tract infections or determined at risk of such infections, sexual & reproductive health clinics, endometrial sampling for histologic analysis, United States 1998 - 2000	No information available	Yes (phase of menstrual cycle, previous pregnancy, race, positive for chlamydia, neisseria gonorrhoea, bacterial vaginosis or T vaginalis	Wiesenfeld et al.(2002)
Yes (versus no)	Risk of tubal infertility	7.32***[c]	120 infertile cases & 126 pregnant controls with no history of infertility (18 - 43), questionnaire & medical records, Sweden 1978 - 1982	Small sample size	No information available	Lalos (1988)

Table 5.1.2
Effect of reproductive factors on female fertility (continued, see page 148 for notes).

Risk Factor, Study Design	Outcome Measure	Odds ratio (CI)	N, Sample, Country and Year	Sources of Bias	Control of Confounding Factors	Authors
SEXUALLY TRANSMITTED INFECTIONS (STIs) *(continued)*						
Neisseria Gonorrhoea *(continued)*						
Yes (versus no)	Risk of tubal infertility	32.40 (4.30, 242.20)	55 primary infertile confirmed tubal damage cases & 59 postpartum controls, past infections assessed measuring serum IgG antibodies, Thailand 1990 - 1992	No information available	Yes	Swasdio et al.(1996)
PELVIC INFLAMMATORY DISEASE (PID)						
Prospective studies						
None (R)	Risk of infertility	1.00	1,966 women all diagnosed with acute salpingitis (15 - 34), laparoscopy & follow-up interviews, Sweden 1960 - 1989	No information available	Yes	Westrom (1993)
1 episode of PID		7.00*[g]				
2 episodes of PID		16.20*[g]				
≥3 episodes of PID		28.30*[g]				
Mild (R)		1.00				
Moderate		1.80*[g]				
Severe		5.60*[g]				
Retrospective studies						
Yes (versus no)	Risk of tubal infertility	4.27***c	120 infertile cases & 126 pregnant controls with no history of infertility (18 - 43), questionnaire & medical records, Sweden 1978 - 1982	Small sample size	No information available	Lalos (1988)
Past Salpingitis						
Yes (versus no)	Risk of primary infertility	21.20 (4.90, 129.00)	301 infertile cases & 380 controls who had just given birth, interview, France 1988 - 1989	Recruitment	Yes (age)	Thonneau et al.(1992)
Yes (versus no)	Risk of secondary infertility	12.20 (5.10, 30.30)				

Table 5.1.2
Effect of reproductive factors on female fertility (continued).

Risk Factor, Study Design	Outcome Measure	Odds ratio (CI)	N, Sample, Country and Year	Sources of Bias	Control of Confounding Factors	Authors
PELVIC INFLAMMATORY DISEASE (PID) *(continued)*						
Retrospective studies *(continued)*						
Ever (versus never)	Risk of tubal infertility	6.00 (2.80, 12.80)	121 primary infertile cases & 490 clinically pregnant controls (20 - 44), questionnaires, Canada 1998	Selection, recall, cases not aged matched	Yes (socioeconomic status, age, smoking, endometriosis, oral & intrauterine contraceptive use, appendectomy)	Urbach et al. (2001)

[a] R refers to reference group. [b]Odds ratios below 1 represent a reduction in fecundity/conception. [c]Odds ratios calculated from data available in publication see Appendix L for full calculations. Calculations for odds ratios were from Bland and Altman (2000). No confidence Intervals available. [d]TTP refers to Time Trying to Pregnancy. [f]Based on fecundability ratio (FR), i.e., the monthly conception rate among exposed compared with that among the unexposed (1/0.94 = 1.03) 0.94 indicates 3% longer TTP compared with women one year younger. [g]Relative risk ratio. * P< 0.05. ** P< 0.01. *** P< 0.001.

Lifestyle Factors

Alcohol consumption.

Eleven studies (four prospective and seven retrospective) investigated the association between alcohol consumption and female infertility. In Table 5.1.3 (pages 157 – 159) four retrospective studies found that consumption of alcohol had a significant negative effect on time trying to conceive (Hassan & Killick, 2004; Olsen, Bolumar, Boldsen, & Bisanti, 1997; Axmon et al., 2006; Juhl et al., 2003). However one large cohort study (Juhl et al., 2003) found that while consumption of more than seven spirits per week was associated with a longer TTP (OR 2.40), consumption of wine was actually associated with a shorter TTP (OR 0.71) and consumption of beer had no effect (OR 0.98). Two prospective studies (Hakim, Gray, & Zacur, 1998; Jensen et al., 1998) found that increased alcohol consumption reduced conception rates (OR range 0.34 – 0.61 [for these studies an OR below 1 indicated a reduction in conception rate]). In addition, higher consumption was associated with an increased risk of infertility in three studies (Grodstein, Goldman, & Cramer, 1994; Greenlee, Arbuckle, & Po-Huana, 2003; Tolstrup et al., 2003). In the Tolstrup et al. (2003) study however, the increased risk of infertility was only significant in women aged ≥ 30 years. Alcohol consumption was also associated with an increased risk of ovulatory infertility, endometriosis, tubal disease and cervical disease (Grodstein et al., 1994), however the confidence intervals for the latter two included unity.

Finally, in a prospective diary study of women providing a daily urine sample and a record of lifestyle habits Liu, Larson, and Wyshak (2004) found that women who drank one or more drinks per week were significantly more likely to have menstrual irregularities.

Caffeine Consumption.

In Table 5.1.3 (pages 159-162) eight studies (two prospective and six retrospective) reported the effect of caffeine consumption on female fertility. Four studies reported caffeine consumption and TTP irrespective of whether the woman was a smoker or not. All these studies reported a significant impact on consumption of caffeine and a longer TTP, with Hassan and Killick (2004) finding that women who drank seven or more cups of caffeine per day (≈ 700mg) were 1.70 times more likely to have an increased TTP compared to women who drank less than 7 cups per day. Hatch et al. (1993) found that caffeine consumption of more than 151 mg per day (≈ 1 – 2 cups of coffee) was also associated with a significantly longer TTP, especially in women who drank ≥301 mg per day (≈ 3 cups of coffee). Bolũmar, Olsen, Rebagliato, and Bisanti (1997) reported women who drank ≥301 mg per day (≈3 cups of coffee) were 1.45 times more likely to have an increased TTP of 9 or more months compared to women who drank 0 – 100 mg of caffeine per day (≈ 1 cup of coffee). In addition women who consumed more than 7000 mg per month (≈ 70 cups of coffee) were significantly less likely to have conceived within 13 months compared to women who drank less than 501 mg per month (Wilcox, Weinberg, & Baird, 1988). Three studies showed an association between smoking and caffeine consumption on waiting times to conception. One of these studies found an association only in women who smoked and drank ≥ 8 coffee/teas per day (Stanton & Gray, 1995). A similar finding by Jensen et al. (1998) showed that women who smoked and consumed 0 – 299 mg caffeine per day (≈ 2 cups of coffee) had a reduction in fertility. However another study found an association in women who did not smoke and drank ≥ 301 mg per day (≈3 cups of coffee) and in women who smoked but drank no caffeine or 1 – 150 mg per day (≈ 1 – 2 cups of coffee). Caffeine consumption was also associated with an increased risk of

infertility. Drinking more than 7 grams of caffeine per month (≈ 70 cups of coffee) was associated with a significant increased risk of tubal infertility and endometriosis related infertility.

Anabolic Steroids.

Anabolic steroids or anabolic-androgenic steroids (AAS) are a group of synthetic derivatives related to the male hormone testosterone (Hartgens & Kuipers, 2004), and are frequently used illegally as performance enhancing drugs. Anabolic steroids work by increasing the protein synthesis within cells resulting in the build-up of cellular tissue in the muscles (Kuhn, 2002) thereby improving muscle strength. Research on the prevalence of its use in society is limited (Talih, Fattal, & Malone, 2007), however, its use is increasing among women (Kutscher, Lund, & Perry, 2002). There has however been very limited research on investigating the impact of anabolic steroid use on female reproduction (De Crée, 1998; Hartgens & Kuipers, 2004). The literature search produced six studies reporting the effect of anabolic steroids on human female reproduction, with none reporting odds ratios. Orchard, Fricker, White, Burke, and Healey (2006) found that women who reported use of the drug were at a higher risk of infertility. In addition menstrual irregularities have been reported in women using the substance (Hartgens & Kuipers, 2004). Korkia and Stimson (1997) reported that out of the 13 women interviewed on the effects of anabolic steroid use eight (62%) reported menstrual irregularities. Misuse has also been found to have irreversible effects on menstruation (Strauss, Liggett & Lanese, 1985; Elliot & Goldber, 2000; Kutscher et al. 2002). However, Strauss and Yesalis (1991) reported that menstrual cessation or irregularity does return after termination of use of the drug, but that the menopause may be reached sooner in women with long history of drug misuse. Finally, Bolch and Warren (1973) found that menstrual irregularities

(e.g., inhibited ovulation, shortened the luteal phase and induced premature menstruation and amenorrhoea) only occurred when women used certain types of anabolic steroid.

Class A drugs.

Illegal drugs are categorised by the British Home Office into three classes; A, B and C (The Misuse of Drugs Act 1971). Class A drugs are deemed the most harmful of all drugs due to the addictive nature of them and the consequences of developing a dependency on the life of the user and those around them (Home Office, 2007) and include ecstasy, heroin, cocaine, LSD, psilocybin mushrooms, and when prepared for by injection, amphetamines (The Misuse of Drugs Act 1971). As Table 5.1.3 (page 162) shows Hassan & Killick (2004) found that women who had ever taken a Class A drug had an increased TTP (CI included unity). However, the outcome of these drugs on infertility is not fully understood with only a few studies testing the effects, and this mainly for cocaine. Cocaine is a stimulant that is strictly regulated by law due to its toxicity and addictive potential (Rizk, Atterbury, & Groome, 1996). In Table 5.1.3 (page 162) women who reported ever taking cocaine had a higher risk of primary tubal infertility (OR – 11.10), however, another study found conversely that women had a shorter TTP (OR – 1.20) compared to women who had never taken the drug.

LSD is an illegal drug that induces hallucinogenic effects in its users. Mueller, Daling, Weiss, and Moore (1990) reported that women who had ever taken LSD were 2.20 times more at risk of primary tubal infertility (OR – 2.20) however this was not significant (CI 0.60 – 7.90; see Table 5.1.3, page 162).

Smoking marijuana.

Marijuana is one of the most commonly used illegal drugs (Roe & Man, 2006). The majority of research focusing on the effects of marijuana on fertility has been carried out on non-human animals; such research suggests that these substances (marijuana, tetrahydrocanabinnol and cannabinoids) can have powerful effects on the reproductive health of females (B. Park, McPartland, & Glass, 2004). In regard to human (female) studies, Table 5.1.3 (page 163) shows that women who reported smoking marijuana within 12 months prior to trying to conceive were 2.10 times more likely to present with ovulatory infertility compared to those who had never used the drug. However one study did report a shorter TTP in women who regularly and irregularly smoked marijuana, however these OR's including unity.

Smoking tobacco.

As Table 5.1.3 (pages 165-167) shows several observations suggest that cigarette smoking (actively and passively) is associated with a detrimental effect on female fertility. One prospective study that was conducted (Liu et al., 2004) reported longer and shorter menstrual cycles in women who smoked (actively and passively) compared to women who did not smoke (actively and passively); all the CI's however, included unity.

Three retrospective studies (Hull, North, Taylor, Farrow, & Ford, 2000; Hassan & Killick, 2004; Axmon et al., 2006) reported an association between time to pregnancy (TTP) and smoking habits, although in the Axmon et al. (2006) the OR was not significant. In Hassan & Killick's (2004) study women who smoked lightly ($\leq$15 cigarettes per day) and heavily (>15 cigarettes per day) had a significantly increased TTP of more than 12 months compared to women who were non-smokers.

Similarly, Hull et al. (2000) reported increased TTP of more than 6 and 12 months, but, when looking at the six month analysis of TTP the only significant findings were in women smoking 20 or more cigarettes a day (OR 1.59), those smoking passively only (OR 1.17) or those smoking actively and passively (OR 1.51) when compared to women who never smoked. In the 12 month analysis of TTP women who smoked 1 – 4 cigarettes a day (OR 1.67), 15 – 19 cigarettes a day (OR 1.99), ≥ 20 cigarettes a day (OR 1.58), women who actively smoke (OR 1.54) and women who actively and passively smoke (OR 1.57) all had a significant TTP of more than 12 months when compared to women who never smoked. Smoking was also associated with an increased risk of infertility in women who were passively exposed for 1 – 5 hours a week (OR 1.80) and ≥ 7 hours a week (OR 1.80) but not significant in the women who were exposed 6 – 12 hours a week (OR 1.50 CI 0.80, 2.50). Finally a review by Augood, Duckitt, and Templeton (1998) found that of 12 primary studies (11 retrospective and one prospective) all indicated a detrimental effect of smoking on reproduction (average OR 1.60).

Stress.

The literature to date on the effect of psychological stress on fertility is somewhat inconsistent, but there does appear to be converging opinion that increasing levels of stress are associated with reduced fertility (Homan, Davies, & Norman, 2007; Boivin & Schmidt, 2005). In Table 5.1.3 (pages 163-165) five studies were reviewed, of which three were prospective in design and two retrospective. Women who reported perceived work stress had an increased TTP of more than 12 months compared to women reporting no work stress (OR = 0.78). Women reporting higher distress scores in relation to three factors assessing the quality of experiences related to the project of having a child (i.e., maternal, child and marriage factors) were at

more risk of infertility compared to women who scored lower on the individual factors (Stoleru, Teglas, Fermanian, & Spria, 1993). Psychological stress may reduce female reproductive performance in a number of ways. The biological interaction between stress and reproduction is the result of the stress hormones and the hypothalamic-pituitary adrenal axis interacting with the hormones that are responsible for normal ovulatory cycles (Schenker, Meirow, & Schenker, 1992), thus potentially affecting the menstrual cycle. A number of studies in the literature review found a significant relationship between stress and menstrual irregularities. In Hjollund et al. (1999) women trying to conceive completed the General Health Questionnaire (GHQ) each month (Day 21) and results showed that women who had a menstrual cycle length of $\geq$ 35 days and poor GHQ scores were 8.40 times less likely to conceive in the next menstrual cycle. Fenster et al. (1999) also reported menstrual irregularities in women experiencing extreme stress in the work place, finding that women were 2.24 times more likely to experience short cycles (<24 days) compared to women experiencing no stress. Finally, Gordley, Lemasters, Simpson, and Yiin (2000) found women reporting life events were significantly more likely to have a number of menstrual irregularities (dysmenorrhea OR 2.20; hypermenorrhea OR 2.99; and abnormal cycle lengths OR 3.42) than women who did not report life events.

Weight.

Weight is most commonly assessed according to Body Mass Index (BMI). The BMI is calculated as the weight in kilograms divided by the square of the height in metres (kg/m^2) (World Health Organisation; WHO, 2000). According to the WHO a BMI < 18.5 is considered underweight, 18.5 to 24.99 a normal range, >25.00 overweight and obese (WHO, 2000).

As Table 5.1.3 (pages 167-169) shows a high BMI was associated with a number of fertility problems. Four retrospective studies reported a longer time to conception in women with a high BMI. Specifically Bolũmar, Rebagliato, Saez-Lloret, and Bisanti (2000) found women with a BMI of ≥ 30 had nearly a 12 fold increase in their TTP compared to women with a BMI range within 20 – 24.99. Gesink-Law et al. (2007), Hassan and Killick (2004) and Ramlau-Hansen, Thulstrup, Nohr, Bonde, Sorensen, and Olsen (2007) all reported that women with a BMI of 25 or more had a significantly longer TTP compared to women with BMI in the range of 18.5 – 24.99. Kaplan et al. (2005) found that women with a BMI > 25 were 1.34 times more likely to not have conceived within 3 months, and 2.42 times more likely to not have conceived within 6 months compared to women with a BMI <25. Higher BMI in women was also associated with a significant increased risk of infertility (Greenlee et al., 2003; Rich-Edwards et al., 1994) and in particular ovulatory infertility (Green et al., 1988; Grodstein et al., 1994).

Table 5.1.3
Effect of lifestyle factors on female fertility (see page 169 for notes).

Risk Factor, Study Design	Outcome Measure	Odds ratio (CI)	N (Age), Sample, Country and Year	Sources of Bias	Control of Confounding Factors	Authors
ALCOHOL CONSUMPTION						
Prospective studies						
< 30 years old			7,760 women (20 - 29), randomly selected from general population, interview, Denmark 1991 - 1993	Recruitment	No control for variables developing over time (e.g., endometriosis)	Tolstrup et al. (2003)
< 1 alcoholic drink per week (R)[b]	Risk of infertility	1.00				
1 - 6 per week		0.87 (0.60, 1.27)				
≥ 7 per week		0.79 (0.51, 1.22)				
≥ 30 years old						
< 1 alcoholic drink per week (R)	Risk of infertility	1.00				
1 - 6 per week		1.95 (1.04, 3.66)				
≥ 7 per week		2.26 (1.19, 4.32)				
1 - 12 g/wk (versus none)	Reduced conception rate	0.43 (0.25, 0.76)[a]	124 women (23 - 41), daily urine samples & reports of lifestyle habits, United States 1989 - 1991	Recall & sample size	Yes (age, race, education, pregnancy & fertility history, coital frequency, smoking)	Hakim et al. (1998)
13 - 90 g/wk (versus none)		0.40 (0.21, 0.77)[a]				
≥ 91 g/wk (versus none)		0.65 (0.20, 2.15)[a]				
1 - 5 drinks per week (versus none)	Reduced conception rate	0.61 (0.40, 0.93)[a]	423 women (20 - 35), monthly questionnaires for 6 menstrual cycles or until clinical pregnancy, Denmark 1992 - 1995	Recruitment & Selection	Yes (age, smoking, diseases in the reproductive system, menstrual cycle, oral contraceptives, BMI)	Jensen et al. (1998)
6 - 10 drinks per week (versus none)		0.55 (0.36, 0.85)[a]				
11 - 15 drinks per week (versus none)		0.34 (0.22, 0.52)[a]				
> 15 drinks per week (versus none)		0.34 (0.11, 1.07)[a]				
6 - 10 drinks per week (versus none)		0.55 (0.36, 0.85)[a]				
≥ 1 drinks per week (versus none)	Short follicular phase	1.19 (0.70, 2.03)	338 women (20 - 44), daily urine samples & reports of lifestyle habits, United States 1989 - 1991	Selection	Yes (age, ethnicity, BMI, smoking, physical activity)	Liu et al. (2004)
Retrospective studies						
Yes (versus no)	Increased TTP[c] > 12 months	0.83 (0.72, 0.95)[d]	1,578 women (23 - 39), randomly selected from general population, questionnaire, Sweden, 2000	Selection	Yes (menstrual cycle, age at conception, use of oral conception, nulliparity)	Axmon et al. (2006)

Table 5.1.3
Effect of lifestyle factors on female fertility (continued, see page 169 for notes).

Risk Factor, Study Design	Outcome Measure	Odds ratio (CI)	N (Age), Sample, Country and Year	Sources of Bias	Control of Confounding Factors	Authors
ALCOHOL CONSUMPTION *(continued)*						
Retrospective studies *(continued)*						
Yes (versus no)	Increased TTP[c] > 12 months	0.83 (0.72, 0.95)[d]	1,578 women (23 - 39), randomly selected from general population, questionnaire, Sweden, 2000	Selection	Yes (menstrual cycle, age at conception, use of oral conception, nulliparity)	Axmon et al. (2006)
Mild ≤ 20 units per week (verses none)	Increased TTP	0.80 (0.60, 1.00)[i]	1,976 pregnant women (25 - 44) antenatal units, questionnaire, United Kingdom 2000 - 2001	Sample size within groups	Yes (coital frequency, weight, smoking, partner's age, alcohol, caffeine, age at menarche)	Hassan & Killick (2004)
Spirits > 7 per week (verses none)	Increased TTP > 12 months	2.40 (1.00, 5.75)	29,844 pregnant women at least 12 weeks gestation (14 - 44), national birth cohort, interview, Denmark 1997 - 2000	Sample size within groups	Yes (age, parity, smoking, BMI, PID, occupational status)	Juhl et al. (2003)
Wine > 7 per week (verses none) Beer > 7 per week (verses none)	Shorter TTP	0.71 (0.58, 0.88) 0.98 (0.67, 1.43)				
1 - 7 drinks per week (verses none) 8 - 14 drinks per week (verses none) ≥ 15 drinks per week (verses none)	Increased TTP > 9.5 months	1.20 (1.00, 1.50) 1.70 (1.10, 2.70) 1.70 (0.80, 3.50)	2,587 pregnant women at least 20 weeks gestation & those just given birth (25 - 44), interview, Europe, 1992	Selection & Recall	Yes (education, occupation, age, parity, alcohol, caffeine, oral contraceptives within 12 months before starting to try, coital frequency)	Olsen et al. (1997)
Low consumption Moderate consumption (R) High consumption	Risk of infertility	0.65 (0.46, 0.92)[i] 1.00 1.58 (1.07, 2.34)[i]	7,393 (18 - 28) randomly selected women from general population, questionnaire, Sweden, 1969	No information available	No, did not ascertain information on lifestyle factors other than alcohol	Eggert et al. (2004)

Table 5.1.3
Effect of lifestyle factors on female fertility (continued, see page 169 for notes).

Risk Factor, Study Design	Outcome Measure	Odds ratio (CI)	N (Age), Sample, Country and Year	Sources of Bias	Control of Confounding Factors	Authors
ALCOHOL CONSUMPTION *(continued)*						
Retrospective studies *(continued)*						
1 - 2 per week (verses none)	Risk of infertility	1.80 (1.20, 2.80)	322 primary infertile cases & 322 age-matched pregnant (during 1st trimester) controls (18 - 35), interview, Canada 1997 - 2001	No information available	Yes (education, income, smoking, alcohol, time spent reviewing exposure lists, BMI, partner's age, age at menarche, number of sexual partners)	Greenlee et al. (2003)
3 - 6 per week (verses none)		2.00 (1.20, 3.50)				
≥ 7 per week (verses none)		6.70 (1.50, 30.30)				
≤ 100 g/week (verses none)	Risk of ovulatory infertility[f]	1.30 (1.00, 1.70)	1,050 infertile women & 3,833 women admitted for delivery of pregnancy, interview, United States & Canada 1981 - 1983	Interviewer bias	Yes (fertility centre, age, number of sexual partners, smoking, caffeine, exercise, BMI, intrauterine device)	Grodstein et al. (1994)
≥ 100 g/week (verses none)		1.60 (1.10, 2.40)				
≤ 100 g/week (verses none)	Risk of tubal disease	1.00 (0.70, 1.40)				
≥ 100 g/week (verses none)		1.20 (0.70, 1.90)				
≤ 100 g/week (verses none)	Risk of cervical factor	1.70 (0.80, 2.10)				
≥ 100 g/week (verses none)		1.80 (0.80, 3.30)				
≤ 100 g/week (verses none)	Risk of endometriosis[g]	1.60 (1.20, 2.50)				
≥ 100 g/week (verses none)		1.50 (1.00, 3.20)				
CAFFEINE CONSUMPTION						
Prospective studies						
Non-smokers	Reduced conception rate		423 women (20 - 35), monthly questionnaires for 6 menstrual cycles or until clinical pregnancy, Denmark 1992 - 1995	Recruitment & Selection	Yes (age, smoking, diseases in the reproductive system, menstrual cycle, oral contraceptives, BMI)	Jensen et al. (1998)
0 - 299 mg per day (R)		1.00				
300 - 699 mg per day		0.88 (0.60, 1.31)[a]				
≥ 700 per day		0.63 (0.25, 1.60)[a]				
Smokers						
0 - 299 mg per day		0.55 (0.32, 0.98)[a]				
300 - 699 mg per day		0.68 (0.42, 1.11)[a]				
≥ 700 per day		0.77 (0.35, 1.72)[a]				

Table 5.1.3
Effect of lifestyle factors on female fertility (continued, see page 169 for notes).

Risk Factor, Study Design	Outcome Measure	Odds ratio (CI)	N (Age), Sample, Country and Year	Sources of Bias	Control of Confounding Factors	Authors
CAFFEINE CONSUMPTION *(Continued)*						
Prospective studies *(Continued)*						
< 501 mg per month (R)	Risk of	1.00	221 women, daily menstrual	No	Yes, but did not measure all	Wilcox et al.
> 7000 mg per month	infertility	4.70**	characteristics recorded & interviews at 0, 3, 6, 12 & 24 months or until clinical pregnancy, United States	information available	lifestyle factors	(1988)
Retrospective studies						
0 - 100 mg per day (R)	Increased TTP	1.00	3,187 women (25 - 44) randomly	Selection	Yes (oral contraceptives	Bolũmar et al. (1997)
101 - 300 mg per day	≥ 9.5 months	1.02 (0.77, 1.36)	selected from general population,		within 12 months prior to starting time,	
301 - 500 mg per day		1.01 (0.74, 1.37)	interview, Europe 1991 - 1993		education, occupation,	
≥ 501 mg per day		1.45 (1.03, 2.04)			alcohol, smoking, coital frequency, PID, parity, age)	
Mild < 7 cups per day (R)	Increased	1.00	1,976 pregnant women (25 - 44)	Sample size	Yes (coital frequency,	Hassan &
Heavy > 7 cups per day	TTP	1.70 (1.10, 2.70)[i]	antenatal units, questionnaire, United Kingdom 2000 - 2001	within groups	weight, smoking, partner's age, alcohol, caffeine, age at menarche)	Killick (2004)
1 - 150 mg per day (verses none)	Increased	1.39 (0.90, 2.13)	1,909 pregnant women antenatal	Misclassification	Yes (last contraceptive	Hatch &
151 - 300 per day (verses none)	TTP	1.88 (1.13, 3.11)	unit, interview, United States		used, parity, smoking)	Bracken
≥ 301 per day (verses none)		2.24 (1.06, 4.73)	1980 - 1982			(1993)

Table 5.1.3
Effect of lifestyle factors on female fertility (continued, see page 169 for notes).

Risk Factor, Study Design	Outcome Measure	Odds ratio (CI)	N (Age), Sample, Country and Year	Sources of Bias	Control of Confounding Factors	Authors
CAFFEINE CONSUMPTION *(continued)*						
Retrospective studies *(continued)*						
Non-smokers			10,886 pregnant women at 36th week of gestation, questionnaire, Denmark 1984 - 1987	Recall	Yes	Olsen (1991)
0 - 3 cups coffee/tea per day (R)	Increased TTP > 12 months	1.00				
4 - 7 cups coffee/tea per day		1.05 (0.87, 1.27)				
≥ 8 coffee/tea per day		0.98 (0.70, 1.37)				
Smokers						
0 - 3 cups coffee/tea per day (R)		1.00				
4 - 7 cups coffee/tea per day		1.03 (0.90, 1.41)				
≥ 8 coffee/tea per day		1.35 (1.02, 1.48)				
1 - 150 mg per day (verses none)	Increased TTP > 12 months	0.91 (0.64, 1.29)	2,501 pregnant women employed at semioconductor plants, interview, United States, 1989 - 1990	Selection	Yes (age at conception, parity, smoking, last method of contraception, known history of infertility, race)	Stanton & Gray (1995)
151 - 300 per day (verses none)		0.92 (0.59, 1.42)				
≥ 301 per day (verses none)		1.44 (0.85, 2.44)				
Non-smokers						
1 - 150 mg per day (verses none)		0.92 (0.61, 1.37)				
151 - 300 per day (verses none)		1.20 (0.70, 2.02)				
≥ 301 per day (verses none)		2.65 (1.38, 5.07)				
Smokers						
None (R)		2.99 (1.52, 5.89)				
1 - 150 mg per day		2.99 (1.40, 3.75)				
151 - 300 per day		1.52 (0.84, 2.74)				
≥ 301 per day		1.75 (0.89, 3.62)				

Table 5.1.3
Effect of lifestyle factors on female fertility (continued, see page 169 for notes).

Risk Factor, Study Design	Outcome Measure	Odds ratio (CI)	N (Age), Sample, Country and Year	Sources of Bias	Control of Confounding Factors	Authors
CAFFEINE CONSUMPTION *(continued)*						
Retrospective studies *(continued)*						
> 7 grams per month (verses none)	Risk of tubal infertility	1.50 (1.10, 2.00)[i]	1,050 infertile women & 3,833 women admitted for delivery of pregnancy, interview, United States & Canada 1981 - 1983	Interviewer bias	Yes (fertility center, age, number of sexual partners, smoking, caffeine, exercise, BMI, intrauterine device)	Grodstein et al. (1994)
> 7 grams per month (verses none)	Risk of endometriosis-related infertility	1.60 (1.20, 2.90)[i]				
RECREATIONAL DRUG USE						
Class A drugs						
Retrospective studies						
Previous/current (verses never)	Incresaed TTP	1.60 (0.30, 7.80)[i]	1,976 pregnant women (25 - 44) antenatal units, questionnaire, United Kingdom 2000 - 2001	Sample size within groups	Yes (coital frequency, weight, smoking, partner's age, alcohol, caffeine, age at menache)	Hassan & Killick (2004)
Ever use cocaine (verses never)	Shorter TTP	1.20 (1.10, 1.40)	1,818 infertile cases & 2,817 controls given birth same year, interview, United States & Canada 1981 - 1983	Limited information	Yes (age, BMI, education, age at menarche, number of previous pregnancies, coital frequency, number of previous miscarriages, alcohol, smoking)	Joesoef et al. (1993)
Ever use cocaine (verses never)	Risk of primary tubal infertility	11.10 (1.70, 70.80)[i]	84 infertile cases & demographic & socioeconomic-matched controls given birth same year (20 - 39), interview, United States 1979 - 1981	Response & Recall	Yes (Smoking, number of sexual partners, intrauterine contraceptive device use)	Mueller et al. (1990)
Ever use LSD (verses never)		2.20 (0.60, 7.90)[i]				

Table 5.1.3
Effect of lifestyle factors on female fertility (continued, see page 169 for notes).

Risk Factor, Study Design	Outcome Measure	Odds ratio (CI)	N (Age), Sample, Country and Year	Sources of Bias	Control of Confounding Factors	Authors
RECREATIONAL DRUG USE *(continued)*						
Smoking marijuana						
Retrospective studies						
Irregular (verses never)	Shorter TTP	1.10 (0.90, 1.20)	1,818 infertile cases & 2,817 controls given birth same year, interview, United States & Canada 1981 - 1983	Limited information	Yes (age, BMI, education, age at menarche, number of previous pregnancies, coital frequency, number of previous miscarriages)	Joesoef et al. (1993)
Regular (verses never)		1.10 (1.00, 1.20)				
Ever (verses never)	Risk of ovulatory infertility	1.70 (1.00, 3.00)[i]	84 infertile cases & demographic & socioeconomic-matched controls given birth same year (20 - 39), interview, United States 1979 - 1981	Response & Recall	Yes (Smoking, number of sexual partners, intrauterine contraceptive device use)	Mueller et al. (1990)
Used > 1 year before reference date (verses never)		1.40 (0.70, 2.60)[i]				
Used within 1 year of reference date (verses never)		2.10 (1.10, 4.00)[i]				
Ever (verses never)	Risk of primary tubal infertility	1.30 (0.50, 3.30)[i]				
STRESS						
Prospective studies						
Menstrual cycle length < 35 days	Reduced conception rate		393 women (20 - 35) monthly questionnaires for 6 menstrual cycles or until clinical pregnancy, Denmark 1992 - 1995	Planning[h]	Yes (cycle number, trade union, education, age, BMI, contraceptive method 12 months prior to time starting, self-reported male or female reproduction-related disease, partner's sperm count, smoking, caffeine, alcohol	Hjollund et al. (1999)
Same score (R)		1.00				
Lower score		1.10 (0.60, 1.90)				
Higher score		1.50 (0.90, 2.40)				
Menstrual cycle length ≥ 35 days						
Same score (R)		1.00				
Lower score		8.40 (1.60, 45.30)				
Higher score		1.70 (0.30, 8.90)				

Table 5.1.3
Effect of lifestyle factors on female fertility (continued, see page 169 for notes).

Risk Factor, Study Design	Outcome Measure	Odds ratio (CI)	N (Age), Sample, Country and Year	Sources of Bias	Control of Confounding Factors	Authors
STRESS *(continued)*						
Prospective studies *(continued)*						
Factor I: Need for parenthood & marital relationship	Risk of infertility		63 women (20 - 35) trying to conceive, questionnaire at 1 & 12.8 months, France	Selection	Yes (age, medical history, time of marriage, time interval between contraception cessation & first psychological assessment)	Stoleru et al. (1993)
Low Scores (R)		1.00				
High Scores		16.50[t]				
Factor II: Negative thoughts & concerns for child						
Low Scores (R)		1.00				
High Scores		3.84				
Factor III: Quality of expectations related to mother, child & marriage						
Low Scores (R)		1.00				
High Scores		45.60*				
Stressful work			403 women (18 - 39) daily menstrual characteristics, urine samples & interviews, United States 1990 - 1991	Selection	Yes (age, race, smoking, alcohol, caffeine, life events, noise level at work, frequency of overexertion at work)	Fenster et al. (1999)
Yes (verses no)	Short menstrual cycle < 24 days	2.24 (1.09, 4.59)				
Yes (verses no)	Risk of anovulation ≥ 36 days	1.34 (0.35, 4.28)				
Perceived work stress	Increased TTP >		1,578 women (23 - 39), randomly	Selection	Yes (menstrual cycle, age	Axmon et al.
Yes (verses no)	12 months	0.78 (0.67, 0.91)[d]	selected from general population, questionnaire, Sweden, 2000		at conception, use of oral conception, nulliparity)	(2006)

Table 5.1.3
Effect of lifestyle factors on female fertility (continued, see page 169 for notes).

Risk Factor, Study Design	Outcome Measure	Odds ratio (CI)	N (Age), Sample, Country and Year	Sources of Bias	Control of Confounding Factors	Authors
STRESS *(continued)*						
Retrospective studies *(continued)*						
Life event	Menstrual irregularities		170 women employed by the US Air Force (18 - 41), questionnaire about menstrual patterns in preceding 3 months , United States	Selection, measurement error	No information available	Gordley et al. (2000)
Yes (verses no)	Dysmenorrhea	2.20 (1.08, 4.50)				
Yes (verses no)	Hypermenorrhea	2.99 (1.20, 7.42)				
Yes (verses no)	Abnormal cycle length	3.42 (1.12, 10.50)				
SMOKING TOBACCO						
Prospective studies						
Smokers (verses non-smoker)	Short menstrual cycle < 25 days	1.05 (0.54, 2.07)	338 women (20 - 44), daily urine samples & reports of lifestyle habits, United States 1989 - 1991	Selection	Yes (age, ethnicity, BMI, smoking, physical activity)	Liu et al. (2004)
	Long menstrual cycle > 35 days	1.52 (0.64, 3.66)				
Passively exposed (verses never)	Short menstrual cycle < 25 days	1.13 (0.59, 2.18)				
	Long menstrual cycle > 35 days	1.79 (0.90, 3.54)				
Retrospective studies						
Median number per day = 10 (verses none)	Increased TTP > 12 months	0.93 (0.79, 1.08)[d]	1,578 women (23 - 39), randomly selected from general population, questionnaire, Sweden, 2000	Selection	Yes (menstrual cycle, age at conception, use of oral conception, nulliparity)	Axmon et al. (2006)

Table 5.1.3
Effect of lifestyle factors on female fertility (continued, see page 169 for notes).

Risk Factor, Study Design	Outcome Measure	Odds ratio (CI)	N (Age), Sample, Country and Year	Sources of Bias	Control of Confounding Factors	Authors
SMOKING TOBACCO *(continued)*						
Prospective studies *(continued)*						
Light ≤ 15 per day (verses none)	Increased TTP > 12 months	1.50 (1.10, 2.20)[i]	1,976 pregnant women (25 - 44) antenatal units, questionnaire, United Kingdom 2000 - 2001	Sample size within groups	Yes (coital frequency, weight, smoking, partner's age, alcohol, caffeine, age at menarche)	Hassan & Killick (2004)
Heavy > 15 per day (verses none)		3.60 (1.90, 7.10)[i]				
1 - 4 per day (verses none)	Increased TTP > 6 months	1.22 (0.92, 1.62)	8,515 pregnant women at least 18 weeks gestation, questionnaire, United Kingdom 1991 - 1992	Recall, selection	Yes (age, alcohol, caffeine, recreational drugs, industrial pollutants, heat, education, occupation)	Hull et al. (2000)
5 - 9 per day (verses none)		1.24 (0.93, 11.64)				
10 - 14 per day (verses none)		0.93 (0.71, 1.22)				
15 - 19 per day (verses none)		1.47 (0.71, 1.22)				
≥ 20 per day (verses none)		1.59 (1.28, 1.99)				
Passive only (verses never)		1.17 (1.02, 1.37)				
Active only (verses never)		1.23 (0.98, 1.49)				
Active & passive (verses never)		1.51 (1.27, 1.78)				
1 - 4 per day (verses none)	Increased TTP > 12 months	1.67 (1.18, 2.38)				
5 - 9 per day (verses none)		1.29 (0.88, 1.90)				
10 - 14 per day (verses none)		0.95 (0.63, 1.36)				
15 - 19 per day (verses none)		1.99 (1.48, 2.69)				
≥ 20 per day (verses none)		1.58 (1.18, 2.12)				
Passive only (verses never)		1.14 (0.92, 1.42)				
Active only (verses never)		1.54 (1.19, 2.01)				
Active & passive (verses never)		1.57 (1.26, 1.96)				

Table 5.1.3
Effect of lifestyle factors on female fertility (continued, see page 169 for notes).

Risk Factor, Study Design	Outcome Measure	Odds ratio (CI)	N (Age), Sample, Country and Year	Sources of Bias	Control of Confounding Factors	Authors
SMOKING TOBACCO *(continued)*						
Prospective studies *(continued)*						
Former (verses never)	Risk of infertility	1.40 (0.90, 2.10)	322 primary infertile cases & 322 age-matched pregnant (during 1st trimester) controls (18 - 35), interview, Canada 1997 - 2001	No information available	Yes (education, income, smoking, alcohol, time spent reviewing exposure lists, BMI, partner's age, age at menarche, number of sexual partners)	Greenlee et al. (2003)
Current (verses never)		1.60 (0.90, 2.90)				
Passive smoke exposure						
1 - 5 hours per week (versus none)	Risk of infertility	1.80 (1.20, 2.50)				
6 - 12 hours per week (versus none)		1.50 (0.80, 2.50)				
≥ 7 hours per week (versus none)		1.80 (1.10, 2.90)				
Ever (verses never)	Risk of primary tubal infertility	2.00 (1.20, 3.20)	121 primary infertile cases & 490 clinically pregnant controls (20 - 44), questionnaires, Canada 1998	Selection, recall, cases not aged matched	Yes (socioeconomic status, age, PID, endometriosis, oral & intrauterine contraceptive use, appendectomy)	Urbach et al. (2001)
Review - meta analysis						
Smoker (versus non-smoker)	Risk of infertility	1.60 (1.34, 1.91)	Meta analysis of 12 cohort and case-control studies in the general population 1985 - 1997. 11 retrospective & 1 prospective	Publication, self-report, recall, misclassification, selection	Yes, in all studies reviewed	Augood et al. (1998)
WEIGHT						
Retrospective studies						
20 - 24.9 kg/m^2 (R) (smoker)	Increased TTP	1.00	2,587 pregnant women at least 20 weeks gestation (25-44), prenatal care unit, questionnaire or interview, Europe 1992	No information available	Yes (age, education, occupation, menstrual cycle, coital frequency, oral contraceptives, number of miscarriages, previous pregnancies, caffeine, alcohol, smoking)	Bolũmar et al. (2000)
25 -29.9 kg/m^2 (smoker)		0.80 (0.35, 1.81)				
≥ 30 kg/m^2 (smoker)		11.54 (3.68, 36.15)				

Table 5.1.3
Effect of lifestyle factors on female fertility (continued, see page 169 for notes).

Risk Factor, Study Design	Outcome Measure	Odds ratio (CI)	N (Age), Sample, Country and Year	Sources of Bias	Control of Confounding Factors	Authors
WEIGHT *(continued)* Retrospective studies *(continued)*						
20 - 24.9 kg/m^2 (R) (smoker) 25 -29.9 kg/m^2 (smoker) ≥ 30 kg/m^2 (smoker)	Increased TTP	1.00 0.80 (0.35, 1.81) 11.54 (3.68, 36.15)	2,587 pregnant women at least 20 weeks gestation (25-44), prenatal care unit, questionnaire or interview, Europe 1992	No information available	Yes (age, education, occupation, menstrual cycle, coital frequency, oral contraceptives, number of miscarriages, previous pregnancies, caffeine, alcohol, smoking)	Bolũmar et al. (2000)
18.5 - 24.9 kg/m^2 (R) 25.0 - 29.9 kg/m^2 ≥ 30.0 kg/m^2	Increased TTP	1.00 0.84 (0.77, 0.92)[a] 0.72 (0.63, 0.83)[a]	7,327 pregnant women median gestation 16 weeks, interview, United States 1959 - 1965	No information available	Yes (smoking, race, education, occupation, study centre)	Gesink Law et al. (2007)
19 - 24 kg/m^2 (R) 25 - 39 kg/m^2 > 39 kg/m^2	Increased TTP > 12 months	1.00 2.20 (1.60, 3.20)[i] 6.90 (2.90, 16.80)[i]	1,976 pregnant women (25 - 44) antenatal units, questionnaire, United Kingdom 2000 - 2001	Sample size within groups	Yes (coital frequency, weight, smoking, partner's age, alcohol, caffeine, age at menarche)	Hassan & Killick (2004)
< 25 kg/m^2 (R) > 25 kg/m^2	Increased TTP ≤ 3 months	1.00 1.34[e]	798 pregnant women (20 - 40), interview & questionnaire, Israel 2003	No information available	No information available	Kaplan et al. (2005)
< 25 kg/m^2 (R) > 25 kg/m^2	Increased TTP ≥ 6 months	1.00 2.42[e]				

Table 5.1.3
Effect of lifestyle factors on female fertility (continued).

Risk Factor, Study Design	Outcome Measure	Odds ratio (CI)	N (Age), Sample, Country and Year	Sources of Bias	Control of Confounding Factors	Authors
WEIGHT *(continued)*						
Retrospective studies *(continued)*						
18.50 - 24.99 kg/m^2 (R) 25.00 - 29.99 kg/m^2 ≥ 30 kg/m^2	Increased TTP > 12 months	1.00 1.27 (1.18, 1.36) 1.78 (1.63, 1.95)	47,835 pregnant women at least 16 weeks gestation (15-44), two telephone interviews during & after pregnancy, Denmark 1996 - 2002	No information available	Yes (age, partner's age, number of previous pregnancies, socioeconomic status)	Ramlau-Hansen et al. (2007)
<120% ideal weight >120% ideal weight	Risk of ovulatory infertility	1.00 2.10 (1.00, 4.30)[i]	380 infertile cases & 1,520 demographic & socioeconomic-matched controls given birth same year (20 - 39), interview, United States 1979 - 1981	Misclassification, recall	Yes (race, age, census tract, reference year)	Green et al. (1988)
18.5 - 24.9 kg/m^2 (R) 25.0 - 29.9 kg/m^2 ≥ 30.0 kg/m^2	Risk of infertility	1.00 1.10 (0.70, 1.70) 1.30 (0.90, 2.00)	322 primary infertile cases & 322 age-matched pregnant (during 1st trimester) controls (18 - 35), interview, Canada 1997 - 2001	No information available	Yes (education, income, smoking, alcohol, time spent reviewing exposure lists, BMI, partner's age, age at menarche, number of sexual partners)	Greenlee et al. (2003)
20 - 21.9 kg/m^2 (R) 22 - 23.9 kg/m2 24 - 25.9 kg/m2 26 - 27.9 kg/m2 28 - 29.9 kg/m2 30 - 31.9 kg/m2 ≥ 32 kgm^2	Risk of infertility	1.00 1.10 (1.00, 1.20)[i] 1.30 (1.20, 1.60)[i] 1.70 (1.40, 2.10)[i] 2.40 (1.80. 3.10)[i] 2.70 (1.90, 3.80)[i] 2.70 (2.0, 3.70)[i]	2,527 infertile women & 46,718 women whose first pregnancy lasted > 6 months with no history of infertility (25 - 42), questionnaires, United States 1989 - 1995	Selection, recall	Yes (age at menarche, age at reference event, year of birth, ethnicity, coital frequancy, smoking, alcohol, diabetes meilitus, oral contracpetives)	Rich-Edwards et al. (1994)

[a] Odds ratios below 1 represent a reduction in fecundity/conception. [b] R refers to reference group. [c] TTP refers to Time Trying to Pregnancy. [d] Based on fecundability ratio (FR), i.e., the monthly conception rate among exposed compared with that among the unexposed (1/0.94 = 1.03) 0.94 indicates 3% longer TTP compared with women one year younger. [e] Odds ratios calculated from data available in publication see Appendix L for full calculations. Calculations for odds ratios were from Bland and Altman (2000). No confidence Intervals available. [f] Excluding women with additional diagnosis of endometriosis. [g] Excluding women with additional diagnosis of ovulatory infertility. [h] Planning bias refers to under-representation of highly fertile women in the sample. [i] Relative risk ratio. * P< 0.05. ** P< 0.01. *** P< 0.001. [t] P< 0.10.

Evaluation and Synthesis of the Risk Factors

In order to compare risks across the studies and types of risks, the odds or relative ratio (hereafter referred to as ratio) in the highest category for each risk factor per study (i.e., oldest age, largest unit of alcohol) was examined in a set of secondary analyses[2]. No significant difference was found between the average relative risk (overall $M = 4.90$, $SD = 6.78$) and the average odds ratio (overall $M = 4.92$, $SD = 7.87$) and these were treated as comparable in the following secondary analysis.

Table 5.1.4 shows the average ratios for each risk factor. As can be seen pelvic inflammatory disease had the largest average ratios ($M = 14.94$, $SD = 11.71$) and marijuana the smallest ratios ($M = 1.70$, $SD = 0.57$). Risk factors were grouped according to whether they were lifestyle ($n = 29$ studies, sampling 189,214 women), reproductive ($n = 13$ studies, sampling 20,378 women) or demographic ($n = 7$ studies, sampling 19,105 women) risk factors. An analysis of variance (ANOVA) comparing the average ratio per risk category (i.e., demographic, lifestyle, reproductive) was not significant ($P = 0.16$). The average ratio was 5.94 ($SD = 10.96$) for the demographic factor, 3.63 ($SD = 6.67$) for the lifestyle factors, and 7.05 ($SD = 8.03$) for the reproductive factors.

Average ratios were compared against the main quality indicator; study design. A t-test showed that the difference between the average ratio for retrospective studies ($M = 4.43$, $SD = 6.07$) was not significantly different from the average ratio for prospective studies ($M = 7.05$, $SD = 12.21$) ($t(83)=1.26$, $P = 0.21$). However,

[2] All fecundability ratios were reversed according to Axmon et al. (2006) so they would be in the same direction as the odds ratios or relative risks. Any odds or relative risks that were in the opposite direction (i.e., below 1 indicated an increased risk of infertility) compared to the rest of the numbers (i.e., above 1 indicated an increased risk of infertility) and could not be reversed were not included in the calculation of the means (n = 5).

when within risk category (i.e., demographic, lifestyle, reproductive) there was a significant difference for the lifestyle prospective ($M = 7.04$, $SD = 12.87$) and retrospective average ($M = 2.61$, $SD = 2.45$) (t(48)=2.05, P=0.04) ratios. The difference between the reproductive prospective ($M = 8.22$, $SD = 13.39$) and retrospective average ratio ($M = 6.84$, $SD = 7.18$) (t(25)= 0.31 $P = 0.76$) was not significant. A statistical test could not be performed for the demographic category as there was only one prospective study (prospective OR 2.53, retrospective $M = 6.42$, $SD = 11.75$).

Table 5.1.4
Average odds ratios for each risk factor and according to category.

Factors	Average odds ratio	SD
Demographic	5.94	10.96
Age	5.94	10.96
Lifestyle	3.63	6.67
Alcohol	2.07	1.51
Caffeine	1.88	1.11
Class A drugs	6.35	6.72
Marijuana	1.70	0.57
Smoking	1.79	0.86
Stress	8.09	13.94
Weight	3.98	3.51
Reproductive	7.05	8.03
Endometriosis	4.86	1.06
Menstrual irregularities	3.32	3.43
Pelvic surgery	3.06	1.78
Sexually transmitted disease	9.57	9.78
Pelvic inflammatory disease	14.94	11.71

Note. Menstrual irregularities include pelvic pain. No odds ratios were found for anabolic steroid use.

Discussion

The results from the present study demonstrate that there are identifiable determinants of reduced fertility potential in women and many of these are risks that women could avoid. The literature review and expert consultation produced 14 risk factors associated with a detrimental effect on female fertility in three categories:

demographic (one factor); reproductive (five factors) and lifestyle habits (eight factors). Pelvic inflammatory disease, sexually transmitted diseases, misuse of illegal drugs, stress and age had the largest averaged odds ratios, suggesting that these factors could be the most important determinants to target in public health campaigns about fertility in women.

The ultimate goal of the present research programme is to produce a risk assessment tool that will raise public awareness about risks of reduced fertility by enabling women to assess their own fertility status. The results of this study clearly showed that such a tool was possible. The literature review and expert consultation produced 14 risk factors. These factors were identified from research that spanned 35 years of investigation, much of which was of relatively good quality using NICE and Cochrane criterion. Specifically, nearly a quarter of the studies used prospective designs, with the majority of all studies controlling for confounding variables and identifying potential biases associated with the methodologies used, sampling over 200,000 women. Further, the majority of studies focused on pregnancy reported that the pregnancy was clinically recognised (at least 12 weeks gestation) or had resulted in a live birth indicating that risks were associated with genuine markers of fertility. To confirm relevance of these empirical factors to clinical practice the 14 factors were the subject of in-depth discussion among 25 medical experts and patient leaders in reproductive health. These experts discussed and established which of the risk factors were critical, which were common and which, in their clinical judgement, were not important or associated with female infertility. The experts based their decision making on their prior clinical experience and the odds ratios extracted from the literature review. Odds ratios across factors showed that the presence of these factors

were associated with an averaged 4.92 (SD = 7.64)[3] times higher risk of reduced fertility, clearly demonstrating that these are genuine risks for reduced fertility. Other reviews of risk factors exist but these are mainly focused on a single or at most five risk factors (Augood et al., 1998; Greenlee et al., 2003; Hassan & Killick, 2004; Khadem & Mazlouman, 2004; Axmon et al., 2006). To this authors knowledge this is the first comprehensive review of all risk factors for reduced fertility.

The goal of raising public awareness about fertility issues is to motivate people to take care of their fertility whether they are trying to conceive now or expect to do so sometime in the future. All the lifestyle factors identified in the current review are modifiable by individuals (e.g., cessation of smoking habits). In addition awareness of the detrimental effects of reproductive factors such as STDs or PID may lead to greater use of condoms or early diagnosis and treatment which is the most cost-effective means of preventing their long term consequences on female fertility (R. T. Cates, Rolfs, & Aral, 1990; Ray, 2006). Indeed the UK National Health Service (NHS) is increasingly focusing on such awareness to help people make healthier choices in their day to day life (e.g., what to eat, whether to exercise) (Department of Health, 2006). Finally, even if a factor cannot be changed (e.g., age, menstrual irregularity) awareness of its association with fertility may impact on reproductive decision-making, for example a reduction in time taken before seeking expert medical advice. Interestingly, in the present study there was no difference in the odds according to risk category (lifestyle, reproductive, demographic) suggesting that targeting any variable would produce equal benefits to fertility.

---

[3] Averaged odds ratios does not include the odds that were in the opposite direction (i.e., below 1 associated with reduced female fertility as opposed to above 1 in the majority of the studies reviewed), these ranged from 0.21 – 0.93.

Raising awareness about the impact the 14 risk factors may have on female fertility is all the more relevant when one looks at the increasing prevalence of a number of these factors in Western society. Negative lifestyle factors such as obesity, illicit drug and alcohol use (especially in young people), and reproductive factors such as sexually transmitted diseases, have all increased markedly over the past decade. While it cannot be guaranteed that individuals would act to modify risk factors there is evidence that using the presence/absence of risk factors (as identified here) to help people derive their own health status vis-à-vis a given condition can change behaviour. For example, Alm-Roiier, Fridlund, Stagmo, and Erhardt (2006) found that self-reported lifestyle change was significantly correlated with a participant's knowledge about their personal risk for future coronary heart disease and the risk factors associated with the disease. Further research needs to establish whether the 14 factors, taken together, adequately discriminate between pregnant and non-pregnant women and/or allow some prediction of time to pregnancy and thus whether they would be useful for women to aid decision making regarding having children in the present day or future.

Methodological Implications and Limitations

The strengths of this study were its comprehensive search and critical evaluation of all studies reporting an association between a risk factor and female fertility potential as well as in-depth discussion of the value of each indicator with fertility experts. Whilst most of the studies used were good quality and one can be confident that claims for the effects on fertility are valid, cross study comparisons were difficult to make because of variations in methodology, therefore some aspects of the present methodology warrants further discussion. First, the inclusion and exclusion of risk factors relied heavily on the opinions of the experts and these were

not selected randomly, since they were experts attending the annual meeting of a fertility taskforce. There is no reason to suspect that the experts would have promoted one factor over another but their clinical intuition may not necessarily have been empirically based. For example the inclusion of Class A drugs and anabolic steroids was weighted more on the basis of their clinical impression since the literature review produced few studies on this topic. However, the experts were asked to discuss all risk factors (inclusions and exclusions) and to achieve a consensus therefore one can at least be confident that factors were not reflective of idiosyncratic judgements.

A second methodological issue is that the majority of studies (78%) reported potential biases. Two types of bias were frequently mentioned: selection bias and recall bias. Forty-six studies (76%) in the review were retrospective and relied on recall of past behaviours such as lifestyle habits. Recall of TTP and lifestyle habits may be less accurate compared to prospective designs. Of the retrospective studies in the current review 21 (47%) were based on accounts of a current pregnancy or women currently trying to conceive. According to Joffe et al. (2005) this type of sample maintains a good level of accuracy and is the most reliable approach, which is confirmed in studies that show that retrospective recall of TTP is reasonably accurate when compared to actual TTP (Zielhuis, Hulscher & Florack, 1992; Joffe, 1997; Hull et al., 2000; Joffe et al., 2005) even with recall up to 20 years (Joffe, Villard, Plowman, & Vessey, 1993). Further, some studies also show excellent recall of other events such as smoking during pregnancy (six to nine years after pregnancy) compared to medical records taken at the time of pregnancy (Rice et al., 2007). Nevertheless it would be important to cross-validate this work in prospective evaluation, especially to evaluate the relative importance of each category of risk (lifestyle, reproductive, demographic) to the outcomes of interest.

Selection bias was an issue in a number of the studies. In the cross-sectional studies, all infertile women were recruited from clinics and hospitals prior to the start of any treatment (usually after diagnostic tests). Using these women compared to pregnant women is a useful way to assess the discriminatory power of a risk indicator. However, as the results from chapter 2 and 3 demonstrated, not everyone seeks treatment when fertility difficulties occur therefore these studies may not represent all women facing difficulties conceiving, and may under or overestimate the degree of association between risk and outcome to an unknown degree. Furthermore, having been diagnosed with fertility problems may influence recall in a way that underestimates the risk-outcome association perhaps to avoid self-blame (e.g., recall less smoking, alcohol consumption). A further selection bias issue was due to the exclusion of women with unplanned pregnancy because one cannot establish TTP. However, those women who have an unplanned pregnancy may differ in their health-related behaviours compared to women planning to achieve a pregnancy (Augood et al., 1998). For example unplanned pregnancy is more common in younger compared to older mothers, meaning that selecting only planned pregnancy may truncate the age distribution and therefore its association to the outcome (Delgado-Rodriguez, Gómez-Olmedo, Bueno-Cavanillas, & Gálvez-Vargas, 1997).

Clinical Implications and Future Directions

Future research should be focused on the evaluation of existing risk factors for infertility and their ability to predict, uniquely or in combination, fertility potential if the ultimate goal is to use these in an applied way (i.e., as a fertility risk tool). It would be important to update the literature on each of the risk factors (e.g., prevalence) particularly those factors that have received comparatively little research attention but which experts felt were important based on clinical intuition. This update

would also need to identify critical thresholds demarcating dose at which a factor has an impact. For example, how many cigarettes or extra pounds make a difference to fertility? As noted previously, none of the studies in the current review investigated the impact of all the risk factors and only 19% investigated more than one risk factor simultaneously despite evidence of a significant association between longer time trying to conceive and increasing number of negative lifestyle habits (Hassan & Killick, 2004). Some factors may only be important because of their shared association with other risk factors and/or may only exert their influence when in the presence of another risk. Indeed in the present study shared associations were found between smoking and caffeine intake (Stanton & Gray, 1995). Another important consideration is to what extent the potency of risk factors are due to other uncontrolled factors. Tjønneland, Grønbæk, Stripp and Overvad (1999) found that women who drank in moderation were more likely to lead a healthier lifestyle in comparison to women who drank moderate to large amounts of alcohol. Finally, the studies used different outcomes to assess fertility. Some studies assessed the impact of risk factors on risk of infertility, others investigated TTP and still others risks associated with fertility problems (i.e., menstrual irregularities, PID). Measuring different outcomes can make the interpretation of the results across studies difficult and there should be a minimum amount of information on the effects of each risk on each outcome as the importance of the risk may vary according to outcome.

The results of the current study demonstrated that it was possible to identify a list of critical factors that could help people assess their fertility status. The next step in the research was to validate the risk factors by assessing whether such factors can discriminate between pregnant and non-pregnant women and length in time trying to conceive (i.e., more than or less than 12 months).

Study 5.2
Univariate and multivariate risk correlates of pregnancy and time to pregnancy

Introduction

Study 5.1 identified 14 risk factors associated with reduced female fertility and in the empirical reports each factor demonstrated significant association with at least one aspect of fertility potential (e.g., pregnancy, time to pregnancy). However, as risk factors are correlated (e.g., smoking and cannabis use; sexually transmitted infection (STI) and pelvic inflammatory disease (PID)) it is not known to what extent the significant association reported between risk and fertility indicator is due to the unique aspects of the risk factor (e.g., STI) or due to its shared variance with another risk factor (e.g., PID) that is itself more critical to fertility potential. Too few studies examining more than one risk factor exist to separate unique from shared contributions to fertility potential. Therefore the aims of the current study were to (1) replicate the association between the identified 14 risk factors and fertility potential by examining whether the identified risk factors could differentiate between pregnant and not yet pregnant women, and between fertile and infertile women (according to time to pregnancy) and (2) examine whether individual factors remained significant in their association to fertility potential when considered as a group by comparing the results of univariate and multivariate analyses.

Taking a multifactorial approach to assessing the impact of the risk factors is vital in the development of a risk tool to assess female fertility status for a number of reasons. First, it is important to ascertain whether all risk factors are important to all outcomes or just some outcomes, and if the latter, which risk influences which

outcome. While it has been previously established that all the identified factors were related to female fertility potential they were all assessed using different designs and outcome measures (e.g., longer time trying to conceive, menstrual irregularities, increased risk of PID), therefore one needs to confirm their importance when using one design assessing the same outcome. Second, one needs to establish whether the risk factor explains unique variance in the outcome when assessed together with other correlated risks. In the literature review in study 5.1 Tolstrup et al. (2003) reported that alcohol consumption was significantly associated with an increased risk of infertility but in reality the association was not significant in women less than 30 years of age, when age was taken into account in the statistical analyses. Establishing such relationships could give greater specificity on the critical factors to address to improve fertility but also would help from a methodological perspective about key questions to put in a self-administered fertility risk tool and the feedback women would get regarding their personal scores.

The best design to establish a relationship between an outcome of interest (e.g., chance of pregnancy) and an exposure variable (e.g., smoking tobacco) when participants cannot randomly be exposed to the risk is the prospective design. In these designs, participants can be followed over a period of time to determine whether an outcome occurs (e.g., pregnancy) and whether there are any factors (e.g., smoking tobacco) predictive of that outcome. To investigate the predictive validity of the 14 risk factors identified in the literature review (see study 5.1), women would report on the presence of all the risk factors, and then be followed from the time they decided to start trying to conceive until pregnancy. One could then establish which risk factors measured prior to the start of trying to conceive predicted pregnancy.

Examples of such designs include the prospective observational study (Petrie & Sabin, 2000). In prospective observational studies information is collected on a number of different variables (measured at time one, T1) to see who develops the outcome of interest (e.g., lung cancer, heart disease, mortality) at time two (T2). People who develop the outcome are then compared to those who did not on the T1 to identify variables that could have potentially caused the outcome (e.g., smoking, diet, alcohol consumption). The advantage of the observational design is that a large group of individuals, usually representative of the population, are assessed and monitored over a period of time, and that the measurement of risk factors precedes the occurrence of the outcome. The main limitation is that because the true causes of the diseases of interest are not known many different variables need to be measured at T1 in the hope of identifying the genuine causes. However, measuring multiple factors for different purposes (i.e., multiple outcomes) may reduce the likelihood that all the relevant information specific to one outcome has been collected and/or that there will be sufficient cases in risk groups to powerfully test the link between risk and outcome (Mann, 2003). In the current study a prospective observational design could not be conducted because none were in progress that collected data on all the risk factors of interest.

An alternative approach to this design would be the cohort prospective design with pre-selected samples based on a specific factor, for example smoking (smokers and non-smokers), who would then be followed over time to see the frequency of outcomes (e.g., lung cancer). The advantage here is that one has a sufficient number of cases in the risk groups to detect effects if these exist. However, employing such a design for the present thesis would have been too expensive and timely to set-up (e.g., finding and recruiting a cohort of women trying to conceive), and to follow-up over

time (Petrie & Sabin, 2000) and these practical issues made the prospective study impractical in the context of the present doctoral work.

In the present study a cross-sectional design was employed to examine associations between risk (e.g., smoking) and fertility indicators (pregnancy status, infertility status). Cross-sectional studies are conducted at a single point in time taking a 'snap shot' of the situation at that time and can be the most economically and convenient first step in investigating and establishing associations between risk factors and disease which can then lead to further prospective assessment of the causes of disease (Mann 2003; Beaglehole, Bonita, & Kjellström, 2006). Such a design is relatively inexpensive and quick to run (Petrie & Sabin, 2000), with no risk of loss of follow-up often seen in prospective designs. In such designs people report on risk and outcome at the same time (concurrent assessment) or people recall risk after the outcome has occurred (retrospective assessment). A major limitation of the cross-sectional design is that it cannot be used to infer causal associations. For example, finding an association between stress and infertility (measured as time trying to conceive), for instance that women who report higher levels of stress also report longer time trying to conceive, does not demonstrate whether infertility causes stress, or stress causes infertility, but merely that a relationship exists between the two variables.

Another disadvantage of a cross-sectional design is due to the recall of information prior to the outcome in question. This is an issue as recollection can be biased by the experience of the outcome (e.g., pregnancy) and/or the passage of time, subsequent life events and so on. This is of particular relevance to the present study as cross-sectional designs can limit the use of certain outcome measures and thus often

rely on recall. For example, when assessing associations between risk factors and pregnancy or fertility potential one cannot measure changes in hormonal levels to indicate an early pregnancy, or conduct tests to diagnose tubal factor infertility since these outcomes have already occurred. Previous cross-sectional studies assessing female fertility potential have often relied on the time to pregnancy (TTP) when biological markers of fertility potential were not available. Using TTP women are asked to recall how long had they been having unprotected sexual intercourse while trying to conceive. In TTP studies pregnant women provide time to pregnancy whereas women still trying to conceive provide time trying to conceive. Consequently, a main issue with using TTP is how comparable is recall of pre-pregnancy behaviour to actual behaviour at the time. However, a number of studies have found that retrospective recall of TTP is reasonably accurate when compared to actual TTP (Zielhuis et al., 1992; Joffe et al., 1993; Joffe, 1997; Hull et al., 2000; Joffe et al., 2005). Moreover, recall of risk factors in infertile populations (e.g., smoking) has been shown to be fairly accurate. For example in a sample of women who had conceived with fertility treatment recall of smoking pre, during and post pregnancy, even up to nine years after pregnancy showed high concordance with actual medical records (Rice et al., 2007).

While cross-sectional designs cannot determine whether a factor is likely to have caused a disease, they can show associations between factors (Mann, 2003) and thus in the present study a cross-sectional study design was employed to test associations between a factor and fertility to replicate associations reported in study 5.1. This design was mainly used due to resource limitations but designs that could be used for future research are described in the Discussion.

The Present Study

The aim of the present study was to replicate the association between the 14 risk factors and female fertility by testing whether these factors could discriminate pregnant and not yet pregnant women, and time to pregnancy (more than versus less than 12 months trying to conceive) using a cross-sectional study design. Women participated in either an online or a clinic survey. All women completed the Fertility Risk Factor Survey that included questions ascertaining information on the 14 risk factors identified in study 5.1. Women were then categorised according to their fertility status. In light of past empirical and clinical data it was expected that risk factors would differentiate pregnant and not yet pregnant women, and women trying for more than or less than 12 months.

Materials and Methods

Design

A cross-sectional design involving a between-subjects comparison of different groups (i.e., pregnant/not pregnant) was employed. Dependent variables were Time Trying to get Pregnant (or time trying to conceive for those not pregnant) (TTP) and currently Pregnant/Not Pregnant. Independent variables were the presence or absence of the 14 risk factors. This study was approved by the Ethics Committee of Cardiff University (UREC) and by the South Wales Ethics Research Committee (for statements of approval see Appendix M).

Participants

During an eight-month period 1073 women completed the Fertility Risk Factors Survey. To achieve the study goals (i.e., assess presence of risk factors in pregnant women and women actively trying to conceive) it was decided to recruit only women who were of reproductive age (18 – 44), and of an age to consent to

participate in line with the School of Psychology, Cardiff University ethics guidelines (18 and above).

Table 5.2.1 shows the demographic characteristics of the sample. On average women were 29.57 (*SD* = 5.80) years of age, with the majority educated to university level and from the United Kingdom.

Table 5.2.1
Demographic characteristics of total sample (N = 1072).

	Total	%
Sample Size	1073	100
Country of Origin[a]		
United Kingdom	730	77.00
America	128	13.50
Canada	43	4.54
Australia	18	1.90
Other	29	3.06
Highest Educational level[b]		
University	386	48.37
Post secondary/college	285	35.71
Secondary	119	14.91
Primary	8	1.00
Age (SD)[c]	29.57 (5.80)	
Age range		
18 - 25	250	24.20
26 - 30	349	33.79
31 - 34	219	21.20
35 - 39	155	15.00
40 - 44	60	5.81
Recruitment Source		
Online (n = 603)		
Askbaby	172	16.03
Myspace	115	10.72
Facebook	158	14.73
Verity	26	2.42
University	132	12.30
Clinic (n = 470)		
Antenatal	326	30.38
Fertility	103	9.60
Abortion	41	3.82

[a]Due to missing data $N = 948$. [b]Due to missing data $N = 816$. [c]Due to missing data $N = 1033$.

The sample was pooled from two waves of data collection. The first wave of data was collected on women (n = 603) recruited using an online version of the survey (via four websites and the Cardiff University electronic notice board). As the survey was online it was not possible to estimate participation rates for this wave of data collection. The second sample (n = 470) consisted of women recruited via three medical clinics (fertility, antenatal and abortion). A total of 1,450 questionnaires were distributed to these clinics by the researcher, making the participation rate 32.41% (*n* = 470).

Participant's level of education ($\chi^2(18, 798) = 51.00$, $P = 0.001$) and age ($F(7, 1025) = 22.52$, $P = 0.001$) differed significantly according to recruitment source with the fertility sample being the oldest (mean age = 34.07, *SD* = 4.97) and the abortion sample the youngest (mean age = 25.10, *SD* = 5.30). The abortion sample had fewer women educated to University level (*n* = 9, 25%) and the infertility website (Verity) sample the highest (*n* = 16, 61.53%). There was no significant difference between groups on country of origin, with the majority of the women in each sample coming from the United Kingdom.

Study groups.

To ensure the sample was representative in terms of risk the prevalence of risk factors in the sample was compared to population values. The analysis on the prevalence of risk factors was carried out on the total sample of women (*N* = 1073). The remaining analyses required women to be grouped according to pregnancy status or infertility status but within the total sample 339 women stated that they were not currently trying to conceive or currently pregnant and these women were excluded

from further analysis since they could not be grouped (i.e., not pregnant because they were not trying).

The remaining participants were grouped according to two indicators of fertility: pregnancy status (n = 734) and infertility status (n = 399). For the pregnancy status variable, women who were currently pregnant were assigned to 'pregnant' (n = 532), regardless of whether the pregnancy was planned or not, the number of weeks pregnant (weeks pregnant range = 3 – 40 with 78.82% 12 weeks or more) or how long it had taken them to achieve the pregnancy. All other women were assigned 'not pregnant' (n = 202). For the infertility status variable, women who had been trying to get pregnant for less than 12 months were assigned [presumed] 'fertile'. Women were assigned 'infertile' if they had been trying (or tried) to get pregnant for more than 12 months (or 6 months if the woman was > 35 years: NICE, 2004) regardless of whether she was currently pregnant or not. In analyses on infertility status women who had become pregnant unexpectedly (n = 335) were excluded because the period of exposure to unprotected sexual intercourse could not be ascertained.

Materials

The Fertility Risk Factors Survey (FRFS, see Appendices N and O) was developed for this study and contained 21 questions. Participants were presented with the FRFS containing the 14 risk factors identified in study 5.1 resulting in 19 risk factors. The five additional risk factors were made up of two risk factors. Specifically, the risk factor menstrual irregularities was separated into four questions ascertaining information on whether the participants had a period and whether the cycle was short, long or irregular. An item on unprotected sexual intercourse was included to assess risk of sexually transmitted infection (W. Jr. Cates & Stone 1992). The 19 risk factors

were grouped into three categories: demographic (age), reproductive (8 questions), and lifestyle (10 questions). Reproductive factors were defined as risk factors associated with the female reproductive system, for example menstrual cycles. Lifestyle factors were defined as risk factors associated with general unhealthy behaviours, for example smoking, drinking alcohol, having unprotected sexual intercourse.

All 19 questions were derived from the specific risks identified in the literature (e.g., "I am a smoker who regularly smokes 10 or more cigarettes a day") and the response scale for all risk factors was either 'yes' for the presence of the factor (coded 1) or 'no' for the absence of the factor (coded 0). Therefore higher scores mean more of the risk.

Six questions were added to establish the exact amount of exposure (i.e., "How many cigarettes do you smoke per day?"). These exact questions inquired about weight (and height), smoking (tobacco and marijuana), alcohol, caffeine (coffee, tea and caffeinated soft drinks) and Class A drug use (see FRFS, Appendices N and O). A total caffeine score (coffee = 1 unit of caffeine, tea/soft drink = 0.5 unit of caffeine: Ministry of Agriculture, Fisheries and Food [MAFF], 1998) and a total marijuana use score (one joint = 0.5 grams: McGlothlin, 1972, 1975) was calculated for these variables. Body mass index was calculated from self-reported weight and height scores using the formula kilograms/metres^2 (WHO, 2000).

Three questions concerned educational status, intentions to conceive, parity and contraceptive use. Education status was coded '1' primary, '2' secondary, '3' post secondary/college and '4' university. Intentions to conceive were ascertained via two questions. Women were asked length of time trying to conceive (months and years)

and contraceptive use (e.g., always using contraception, not using contraception and trying to get pregnant, not using contraception but not particularly intending or trying to get pregnant)[4].

Finally, three questions referring to risk factors associated with male infertility were included in the survey (mumps after puberty, undescended testicles and use of anabolic steroids). These three items were not included in the data analysis as they concerned another project.

The online version of the survey (see Appendix N) was developed using SurveyTracker (Survey Tracker for Windows, Training Technologies Inc, Cincinnati, Ohio, 2007).

All FRFS questions were developed with the help of reproductive and medical specialists from the expert consultation group in order to ensure wording was appropriate to the risk (e.g., I have versus I have had endometriosis). The webmaster at askbaby.com and the medical staff at each clinic (fertility, antenatal, and abortion) were similarly consulted for wording and suitability among participants from their site or clinic. For example, care was taken that the wording for pregnancy items were suitable to women in both the abortion and the antennal clinic and, where necessary, wording was adapted to avoid any potential upset. The tense used in the FRFS was adapted according to the recruitment method and target sample. For the pregnant

---

[4] For the online version of the FRFS women were asked an additional feeder question regarding their intentions to conceive ('are you currently trying to get pregnant, coded 0 'no', 1 'yes') prior to receiving questions on contraceptive use.

women all questions were presented in the past tense asking them to recall their lifestyle habits and reproductive history prior to their current pregnancy. For the women who were not pregnant but trying to conceive all questions were presented in the present tense to ascertain their current lifestyle habits and reproductive history.

Population values were used to compare the sample frequency of demographic variables (i.e., education) and risk factors. Population values were extracted from a number of sources (e.g., United Kingdom office of national statistics, WHO) and where available from large population surveys (e.g., General Household Survey, British Crime Survey). Precise sources are given in data Table 5.2.2 (page 194).

Procedure

Websites and university notice board.

Websites and groups on social networking sites (Myspace.com) aimed at women just 'starting out' in the process of trying to get pregnant and those aimed at women already pregnant were contacted via email to ask whether they would post the FRFS on their site (for survey see Appendix N). Two websites (Askbaby.com and groups on Mypsace.com) posted the link on their sites. In addition Verity.org.co.uk also posted a link indirectly through a group on Myspace.com. For Facebook.com the study was promoted through their advertisement scheme, whereby adverts pop-up by the side of individual users homepage. Adverts can be tailored depending on the aim, and desired sample characteristics (i.e., age, gender) can be pre-set so the advert is presented only to people who meet a selected criterion (i.e., age restricted to target sample: 18 – 44). Participants recruited via the university-wide electronic notice board system received a written announcement on the electronic notice board when they

signed into their university account inviting them to participate in an online survey about fertility health issues.

A sentence about the survey ("Survey about fertility health issues") and an option button was placed on each site. Clicking on the option button took the participants to a consent form and description of the content of the survey. To continue to complete the survey they were asked to give their consent by following the instructions, otherwise they could close the page and leave the survey. Questions were presented in specific sections outlined above and once a participant clicked to move to the next page they were unable to go back and change answers. The survey took around 5 – 10 minutes to complete. Throughout the survey participants had the option to click out and close the survey with no data being submitted. Once they came to the final page they were given a more detailed explanation of the study and the option to submit their data if they wished. For the online version of the survey a number of questions such as age, pregnant/not pregnant, trying/not trying were fixed, that is, participants could not continue to the next page until such questions were answered. If participants closed the survey window at any point or did not click submit on the debriefing page no information was submitted.

Clinic recruitment.

All participants in the clinics samples were provided with a pack including an invitation letter, an instruction form, the FRFS, a debriefing form (see Appendix O) and a pre-paid pre-addressed envelope. The survey took around 5 – 10 minutes to complete. For all clinics, consent to participate was provided by returning the completed anonymous survey in the marked collection box in the waiting room or via post using the pre-paid self addressed envelope provided. If women did not wish to

take part in the survey they were informed that they could leave unfilled surveys in the collection box at the clinic. The distribution of survey packs differed according to the specific clinic.

Women (aged 18 and above) presenting at the antenatal clinic for their 12 week pregnancy scan were presented with the information pack by the nurse and asked if they were willing to participate in a survey about fertility health issues. Women completed the survey while they waited for their scan or posted it using the pre-paid envelope at a later date.

Two recruitment methods were employed in the fertility unit. First, all new patients (aged 18 and above) were sent a survey pack at the same time as their booking letter, asking them to participate in the study. If they wished to take part they could fill out the survey and bring it with them to their first appointment. Second, as patients came into clinic and registered for their appointment survey packs were handed out by the secretary. Potential participants were informed that if they wished to fill out the survey they could do so in the waiting room or return it in the post using the pre-paid self addressed envelope.

All women being admitted to the abortion clinic were taken to a private room while waiting for the medication to take affect. As per routine procedures for research a nurse would inform the potential participant (aged 18 and above) that a survey was on the participant's bedside locker if they wished to fill it out while they waited. Completed surveys could be placed in sealed collection boxes or posted in the pre-paid envelope provided. If the patient did not wish to take part in the study they were asked to place the incomplete survey into the pre-paid envelope, sealed, on their bedside locker. At the end of each day/once the room was vacated a nurse would

collect all envelopes and place them in the box by the nurses' station. At the end of each week all packs were sent back to the university.

A summary of the main research findings was provided to the websites and clinics at the end of data collection.

Data Analysis

Preliminary data screening produced two participants for exclusion due to extreme outliers for the variable years/months trying to conceive (37.83 and 37.5 years trying to conceive: more than 3 SD ± Mean) (final sample $N = 1073$). Data screening produced a further 28 scores that were outliers (more than 3 SD ± Mean) on a number of the lifestyle factors (e.g., number of alcohol units). These scores were adjusted by assigning the outlying case a score that is one unit greater than the next most extreme score in the variable distribution according to Tabachnick & Fidell's (2001) recommendations. A minimum of 1008 participants was required to detect low frequency events (e.g. drug use, calculated using G-Power computer program; Faul & Erdfelder, 1992).

Preliminary analysis examined differences according to recruitment source. Prevalence of the risk factors was compared to population values. Logistic regressions were conducted on individual risk factors (univariate) and combined risk (multivariate) to determine associations with outcome measures. The dependent measure in these analyses was pregnancy status (pregnant (coded 1) versus not pregnant (coded 0)) or infertility status (trying for >12 months (coded 1) or trying ≤ 12 months (coded 0)). In multivariate logistic regressions all the risk factors were entered in the same step. The odds ratio (± 95% confidence interval [CI]) is presented. Secondary analysis compared participants according to fertility category using

ANOVA and Chi-square. Significant effects were followed up with Tukey (continuous variables) or Chi-square (categorical variables). A probability value of $p<0.05$ was regarded as statistically significant. All analyses were performed with the software Statistical Package for the Social Sciences (SPSS).

Results

Prevalence of Risk Factors Compared to Population Values

As can be seen in Table 5.2.2 total sample frequencies ($N = 1073$) were similar to the population values (i.e., about 5% or smaller difference between the sample score and the population value) with a few exceptions. First, the number of women educated to university level in the sample was higher than in the general population. Second, the frequency of period pains, unprotected sexual intercourse and being overweight were higher in the population than the sample. Finally the sample reported more alcohol consumption per week (any amount) compared to the population but reported less excessive alcohol consumption (e.g., more than 14 units a week). For these factors the average difference score was 12.50%. If we exclude the women who were not actively trying to conceive or currently pregnant the results are similar except that the smaller sample report less unprotected sex with multiple partners, less stress and less Class A drug use (ever) and more of these women are overweight (see difference score 2 in Table 5.2.2).

Table 5.2.2
Frequency of risk factors compared to population values.

Factors	Sample (%)	Population (%)	Difference score[1]	Difference score[2]
Demographic				
Education (University level)	48.37	31.20[a]	17.17	16.76
Reproductive				
Period pains	32.92	46.83[b]	-13.91	-16.98
Endometriosis	5.48	6.00 - 10.00[c]	0.52 - 4.52	1.38 - 5.38
Pelvic Inflammatory Disease (PID)	2.19	2.00[d]	0.19	0.08
Menstrual cycle less than 21 days	8.54	3.20[e]	5.34	5.46
Menstrual cycle more than 35 days	13.19	8.05[f]	5.14	7.09
Menstrual cycle irregular	34.03	30.00[f]	4.03	3.24
Period	5.84	3.10[f]	2.74	2.82
Pelvic surgery	11.89[g]			10.00[s]
Sexually Transmitted Disease (STD)	11.57	12.60[h]	-1.03	-1.43
Lifestyle				
Overweight	23.40	33.00[i]	-9.60	-5.07
Unprotected sexual intercourse with multiple partners	23.96	32.00[jr]	-8.04	-14.39
Stress	16.12	11.00[k]	5.12	2.6
Class A drug ever used	13.43	10.00[l]	3.43	-0.02
Last 12 months	3.96	2.10[l]	1.86	1.62
Anabolic Steroid	0.85	0.60[mr]	0.25	0.09
Alcohol	69.25[*]	56.50[n]	12.75	12.12
≥ 14 units a week	10.00	23.50[o]	-13.50	-14.80
Smoke	23.58[*]	26.67[p]	-3.09	-4.48
Caffeine	91.59[*]	97.10[qr]	-5.51	-6.34
Marijuana	4.56[*]	9.70[mr]	-5.14	-5.82

Note. [*]Number based on participants reporting of any consumption of the variable. [1]Difference score for total sample minus population values. [2]Excluding women not actively trying to conceive (n=734). [a]Office of National Statistics (2008). The level of highest qualification held by adults in England. [b]Zondervan et al. (1998) review of United Kingdom community and hospital based studies. Percentage based on an average of all studies reported (Table 1, page 95). [c]Giudice & Kao (2004). Review paper. [d]Percentage obtained from NHS Choices website (one in 50 women per year develop the disease). [e]World Health Organisation study in family planning programs (1983). [f]Harlow & Ephross (1995). Percentage based on an average of studies reviewed. [g]No data could be obtained for comparison. [h]Fenton et al. (2001). Survey of 11,161 men and women in Britain. Percentage recorded refers to women only. [i]Health Survey for England, Department of Health, Social Trends 33 Figure 7.20. [j]Fontes & Roach (2007). Web-based survey of 10,138 men and women from the United Kingdom. Percentage based on those reporting having had up to five sexual partners. [k]National Statistics Online. Survey of Psychiatric Morbidity among Adults in Great Britain, 2006. [l]Roe & Man (2006). Drug Misuse & Declared: Findings from the 2005/06 British Crime Survey (Table4.6, page 24). [m]Roe & Man (2006). Drug Misuse & Declared: Findings from the 2005/06 British Crime Survey (TableA2.1, page 45). [n]Goddard (2006). General Household Survey 2006: smoking and drinking among adults, 2006. Number based on an average of women aged 16 - 44 (Table 2.3, page 63). [o]Goddard (2006). General Household Survey 2006: smoking and drinking among adults, 2006. Number based on an average of women aged 16 - 44 (Table 2.2, page 62). [p]Goddard (2006). General Household Survey 2006: smoking and drinking among adults, 2006. Number based on an average of women aged 20 - 49 (Table 1.1, page 15). [q]Heatherley et al. (2006). The Dietary Caffeine and Health Study. [r]Percentage includes men. [s]Percentage of women who report pelvic surgery excluding the women not actively trying to conceive.

Univariate and Multivariate Association Between Risk Factor and Fertility Outcomes

Table 5.2.3 and 5.2.4 presents the odds ratios between the risk factors and (a) pregnancy status (Table 5.2.3) and (b) infertility status (Table 5.2.4) for the univariate and multivariate logistic regressions.

a) Pregnancy status (n = 734).

For pregnancy status analyses, an odds ratio below 1 was associated with a decrease in the chances of pregnancy and an odds ratio above 1 is associated with an increased chance of pregnancy. The risk factors significantly associated with a decreased chance of pregnancy in the univariate analysis were age, endometriosis, pelvic inflammatory disease, reporting a long menstrual cycle (>35 days), reporting an irregular menstrual cycle, not having a period, previous pelvic surgery, being overweight, and having unprotected sexual intercourse. A trend was found for reporting period pains and reduced chance of pregnancy. In addition the odds were in the predicted direction for reporting a prior sexually transmitted disease, use of class a drug[5], and stress. Risk factors significantly associated with an increased chance of pregnancy were short menstrual cycles (< 21 days), consuming more than 14 units of alcohol per week, smoking more than 10 cigarettes a day and misusing marijuana.

For the multivariate analysis the model was significant (χ^2=119.94, df=18, P=0.001). As found in the univariate analysis age, endometriosis, menstrual irregularities, no period, pelvic surgery, being overweight and reporting unprotected sexual intercourse with multiple partners remained significantly associated with a reduction in likelihood of pregnancy. The odds ratios for pelvic inflammatory disease

[5] The variable 'Class A drug use ever' was used in the analysis (univariate and multivariate) as the frequency of Class A drug use in the past 12 months was too few.

and long menstrual cycles (>35 days) were in the same direction to that of the univariate analysis but were no longer significant. Previous sexually transmitted diseases remained non-significant but still in the same direction as would be predicted. Two variables (period pains and Class A drug use) changed predicted direction but neither was significant.

For the variables that were significantly associated with an increased likelihood of pregnancy in the univariate analysis only alcohol remained significant in the multivariate analysis. Short menstrual cycles (<21 days), smoking tobacco and marijuana all remained in the same direction (increased pregnancy) but smoking tobacco was no longer significant and marijuana was a trend. Finally, the odds ratio for caffeine consumption changed direction, suggesting drinking more than seven units of caffeine a day was associated with decreased likelihood of pregnancy; however, the confidence intervals included unity.

Table 5.2.3

Frequencies and odds ratios between risk factors and pregnancy status in univariate and multivariate analysis (n = 734).

Factors	Pregnant n = 532	Not pregnant n = 202	Univariate analysis Pregnancy Status[a]	CI[b]	Multivariate analysis Pregnancy Status[a]	CI[b]
Time to pregnancy (SD)[c]	9.16 (18.47)[d]	48.14 (40.61)				
Demographic						
Age (SD)	29.16 (5.86)	30.81 (5.37)	0.95**	1.02, 1.10	0.94**	0.90, 0.98
Reproductive, n (%)						
Period pains	147 (27.95)	70 (34.83)	0.73[t]	0.51, 1.03	1.07	0.62, 1.86
Endometriosis	12 (2.31)	21 (10.77)	0.20***	0.09, 0.41	0.27**	0.09, 0.86
Pelvic Inflammatory Disease (PID)	6 (1.15)	9 (4.50)	0.25**	0.09, 0.70	0.91	0.17, 5.01
Menstrual cycle less than 21 days	55 (10.68)	7 (3.48)	3.31**	1.48, 7.41	2.61	0.74, 9.18
Menstrual cycle more than 35 days	66 (13.07)	40 (20.51)	0.58*	0.38, 0.90	0.81	0.41, 1.60
Menstrual cycle irregular	156 (29.89)	84 (42.00)	0.59**	0.42, 0.82	0.42**	0.23, 0.74
Period	23 (4.47)	19 (9.70)	0.43**	0.23, 0.81	0.26**	0.10, 0.65
Pelvic surgery	30 (5.75)	42 (21.21)	0.23***	0.14, 0.37	0.24***	0.11, 0.54
Sexually Transmitted Disease (STD)	54 (10.27)	27 (13.57)	0.73	0.44, 1.19	0.86	0.38, 1.95
Lifestyle, n (%)						
Overweight	89 (17.45)	67 (34.72)	0.40***	0.27, 0.58	0.40***	0.24, 0.68
Unprotected sexual intercourse with multiple partners	66 (12.67)	61 (30.50)	0.33***	0.22, 0.49	0.20***	0.10, 0.38
Stress	63 (12.40)	33 (16.67)	0.71	0.45, 1.12	0.84	0.40, 1.76
Class A drug ever	63 (12.40)	33 (16.67)	0.74	0.43, 1.27	1.00	0.40, 2.47
Alcohol	55 (10.48)	9 (4.52)	2.47*	1.20, 5.10	3.68*	1.22, 11.12
Smoke	92 (17.66)	18 (9.09)	2.15**	1.26, 3.66	1.22	0.55, 2.68
Caffeine	39 (7.44)	13 (6.47)	1.16	0.61, 2.23	0.95	0.34, 2.68
Marijuana	24 (4.68)	2 (1.01)	4.81*	1.13, 20.55	5.52[t]	0.77, 39.31
Anabolic steroid[e]	4 (0.76)	1 (0.50)				
					P = 0.001[f]	

[a]DV = 0 (Not Pregnant), 1 (Pregnant). [b]CI = Confidence Intervals. [c]For not pregnant time to pregnancy = months trying to conceive. [d]Time to pregnancy only available for 197 pregnant women. [e]Anabolic Steroid was excluded from univariate and multivariate analysis due to low frequency. [f]Overall multivariate model significance level. [t]P< 0.10. *P< 0.05. **P<0.01. ***P<0.001.

b) Infertility status (n = 399).

In the univariate and multivariate analysis for infertility status an odds ratio below 1 indicated fertile (i.e., trying for < 12 months) and an odds ratio above 1 indicated infertile (i.e., trying for > 12 months or > 6 months if woman age > 35 years). Being older, experiencing painful periods, endometriosis, irregular menstrual cycles, previous pelvic surgery, being overweight, having unprotected sexual intercourse and experiencing stress one cannot cope with were all significantly associated with increased odds of trying for more than 12 months. The odds ratios for pelvic inflammatory disease, sexually transmitted disease, Class A drug use, alcohol and caffeine consumption were all in the predicted direction but were not significant.

Reporting short menstrual cycles was significantly associated with shorter time trying to conceive. Further, reporting long menstrual cycles (>35 days), no period, smoking tobacco and marijuana misuse were all in the opposite direction to predicted (that is increased risk of longer time trying) but were not significant.

For the multivariate analysis the model was significant (χ^2=68.93, df=18, P=0.001). In the multivariate analysis being older, suffering from period pain, having irregular menstrual cycles, having unprotected sexual intercourse and experiencing high levels of stress were all significantly associated with an increased time trying to conceive. Further a trend was found for endometriosis and increased time trying to conceive. Being overweight and reporting previous pelvic surgery were in the same direction as the univariate analysis but were no longer significant. Similarly, sexually transmitted disease and caffeine consumption remained in the same direction as predicted. The odds ratio for reporting no period changed to the direction from that reported in the univariate analysis and became significant in the multivariate analysis.

Contrary to the univariate analysis and prior predictions the odds ratios for pelvic inflammatory disease and alcohol consumption reversed direction, although all the confidence intervals included unity, indicating a lack of significance. The odds ratio for Class A drugs changed to 1.00, showing no effect.

Finally, while the odds ratio for short menstrual cycles (<21 days) remained in the opposite direction to predicted it was no longer significant in the multivariate analysis. Further, long menstrual cycles (>35 days), smoking and marijuana misuse all remained in the opposite direction to predicted, although none were significant.

Table 5.2.4

Frequencies and odds ratios between risk factors and fertility status in univariate and multivariate analysis (n = 399).

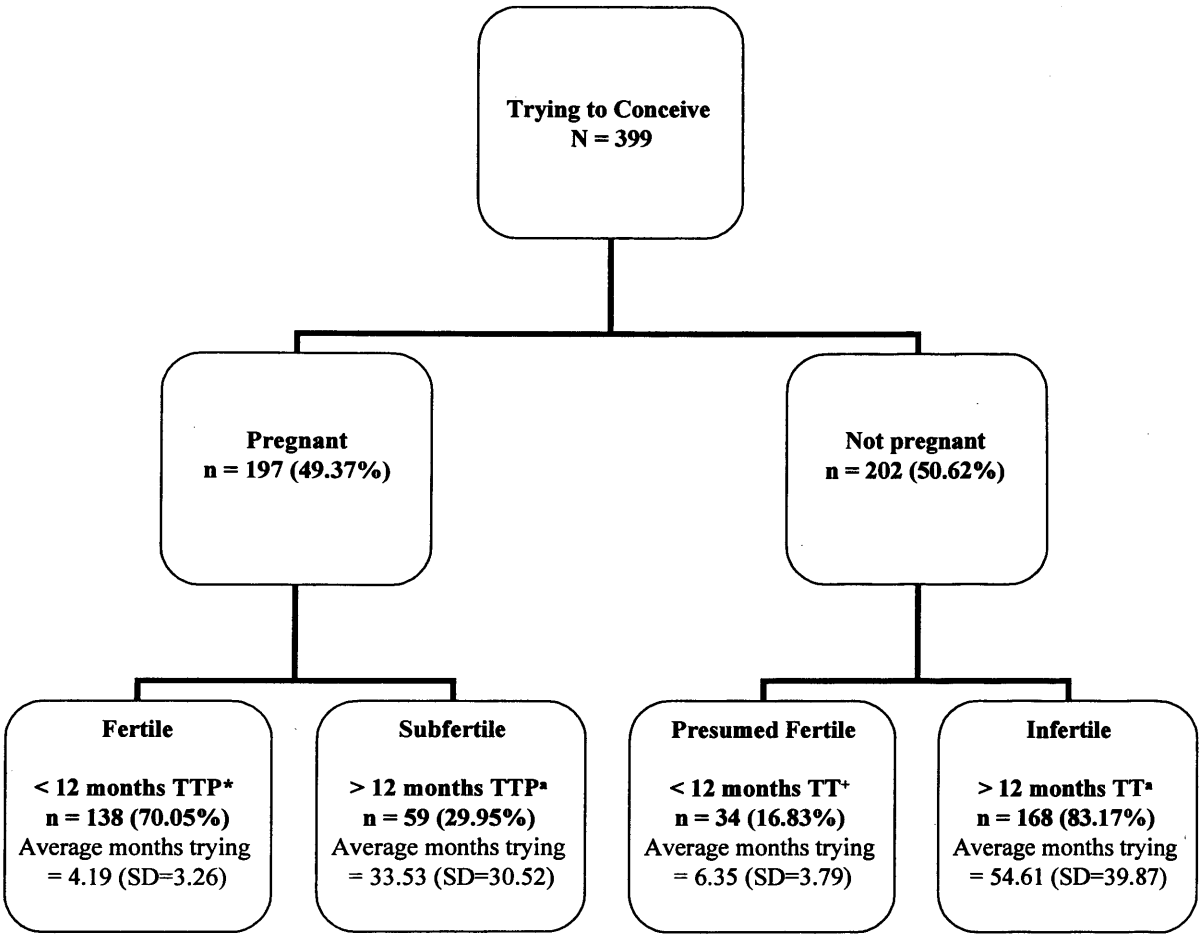
Factors	< 12 months n = 172	> 12 months[a] n = 227	Univariate analysis Infertility Status[bc]	CI[d]	Multivariate analysis Infertility Status[bc]	CI[d]
Time to pregnancy (SD)[e]	4.54 (3.44)	49.13 (38.73)				
Demographic						
Age (SD)	29.72 (4.90)	31.43 (5.65)	1.06**	1.02, 1.10	1.11***	1.05, 1.17
Reproductive, n (%)						
Period pains	37 (21.51)	81 (35.84)	2.04**	1.29, 3.21	1.97*	1.05, 3.70
Endometriosis	5 (2.92)	20 (9.09)	3.32*	1.22, 9.04	4.04[t]	0.90, 18.11
Pelvic Inflammatory Disease (PID)	5 (2.98)	8 (3.54)	1.20	0.38, 3.72	0.48	0.10, 2.30
Menstrual cycle less than 21 days	15 (8.82)	9 (3.98)	0.43[t]	0.18, 1.00	0.65	0.20, 2.10
Menstrual cycle more than 35 days	33 (19.76)	41 (18.47)	0.92	0.55, 1.53	0.60	0.27, 1.32
Menstrual cycle irregular	42 (24.56)	96 (42.67)	2.29***	1.48, 3.54	3.74***	1.88, 7.46
Period	10 (5.88)	19 (8.64)	0.88	0.68, 3.34	3.38*	1.09, 10.55
Pelvic surgery	16 (9.30)	39 (17.49)	2.07*	1.11, 3.84	1.44	0.62, 3.35
Sexually Transmitted Disease (STD)	16 (9.41)	28 (12.56)	1.38	0.72, 2.65	1.16	0.46, 2.92
Lifestyle, n (%)						
Overweight	36 (21.69)	68 (31.19)	1.64*	1.03, 2.61	1.42	0.80, 2.52
Unprotected sexual intercourse with multiple partners	18 (10.53)	61 (27.23)	3.18***	1.80, 5.63	3.53**	1.57, 7.91
Stress	10 (5.99)	40 (18.18)	3.49***	1.69, 7.21	4.05**	1.41, 11.60
Class A drug ever	17 (10.06)	26 (11.45)	1.16	0.61, 2.21	0.56	0.21, 1.51
Alcohol	12 (7.02)	16 (7.17)	1.02	0.47, 2.23	0.83	0.29, 2.37
Smoke	24 (14.46)	24 (10.71)	0.71	0.39, 1.30	0.77	0.31, 1.92
Caffeine	8 (4.71)	18 (7.96)	1.75	0.74, 4.13	1.08	0.31, 3.74
Marijuana	6 (3.55)	7 (3.13)	0.88	0.29, 2.66	0.99	0.19, 5.16
Anabolic steroid[f]	1 (0.59)	2 (0.88)				
					P = 0.001[g]	

[a]Or 6 months if the woman is > 35 years. [b]DV = 0 (Fertile), 1 (Infertile) . [c]Fertile refers months trying to conceive < 12 months, Infertile refers to months trying > 12 months or >34 and months trying > 6 months. [d]CI = Confidence Intervals. [e]For not pregnant time to pregnancy = months trying to conceive. [f]Anabolic Steroid was excluded from univariate and multivariate analysis due to low frequency. [g]Overall multivariate model significance level. [t]P< 0.10. *P< 0.05. **P<0.01. ***P<0.001

Secondary Analysis Between Lifestyle Factors and Fertility Indicators

One question raised by the results of the logistic regressions was why some of the negative lifestyle factors were unexpectedly associated with increased odds of pregnancy (or decreased odds of infertility). One explanation may be that women who have been trying for some time but are not yet pregnant modify their lifestyle habits to increase their odds of pregnancy. To further explore this possibility women were categorised according to both pregnancy and infertility status (see Figure 5.2.1) using similar fertility categories as used in the risk research (Olsen, 1991; Stanton & Gray, 1995; Hassan & Killick, 2004; Ramlau-Hansen et al., 2007). Figure 5.2.1 shows sample sizes according to the fertility categories (e.g., fertile, subfertile, presumed fertile and infertile). Of those who were currently pregnant, 70.05% (n = 138) achieved a pregnancy within 12 months of trying to conceive and were labelled 'fertile', whereas 30.0% (n = 59) of pregnant women took more than 12 months to conceive and were labelled as 'subfertile'. For the women not yet pregnant 16.83% (n = 34) had been trying for less than 12 months and were therefore labelled 'presumed fertile' whereas the remaining 83.17% (n = 168) had been trying to get pregnant for more than 12 months and were labelled 'infertile'. The groups did not differ on education (χ^2=12.95, df = 9, P = 0.17).

Figure 5.2.1. Breakdown of fertility status in women trying to conceive (n = 399).



Note.

*TTP refers to time to pregnancy

+TT refers to time trying to get pregnant

[a]Or 6 months if the woman is > 35 years

Table 5.2.5 reports the frequency for each of the 19 risk factors according to the fertility categories. Individual ANOVA and chi-square tests were conducted on each factor revealing significant differences between groups on eight of the 19 risk factors. Of particular relevance for the secondary analysis is the pattern of scores on the negative lifestyle factors that had produced unexpected results in the logistic regressions (i.e., alcohol, smoking, caffeine and marijuana). As shown in Table 5.2.5 within the pregnant women those who had taken longer to conceive (subfertile) reported higher frequencies on all negative lifestyle factors, as predicted, when compared to the pregnant women who had taken less time to conceive (fertile). This pattern was the same for the not yet pregnant women. That is, the women who had been trying the longest (infertile) reported greater frequencies on these negative lifestyle factors than those who had been trying for less than 6 months (presumed fertile). The two exceptions were smoking and marijuana use where the pattern is reversed in the not pregnant women, that is, the presumed fertile reported greater consumption than the infertiles.

Table 5.2.5. *Differences of each risk factor according to fertility category.*

Factors	Pregnant (n = 197)		Not Pregnant (n = 202)		F statistic
Fertility category	Fertile < 12 months (n = 138)	Subfertile > 12 months (n = 59)	Presumed fertile < 12 months (n = 34)	Infertile > 12 months (n = 168)	
Months trying to conceive (SD)	4.19 (3.26)[a]	33.53 (30.52)[b]	6.35 (3.79)[c]	54.61 (39.87)[d]	80.93***
Previous birth (%)	44.93[a]	44.07[a]	44.12[a]	14.97[b]	38.99***
Risk Factors					
Demographic					
Age (SD)	30.01 (5.07)[a]	31.78 (6.05)[b]	28.39 (3.85)[a]	31.30 (5.51)[b]	4.16**
Reproductive	%	%	%	%	χ^2
Period pains	21.01[a]	32.20	23.53	37.13[b]	10.20*
Endometriosis	0.73[a]	5.08[b]	11.76[b]	10.56[b]	13.82**
Pelvic Inflammatory Disease (PID)	2.22	1.69	6.06	4.19	2.17
Menstrual cycle less than 21 days	9.56	6.78	5.88	2.99	5.74
Menstrual cycle more than 35 days	18.52	15.25	25.0	19.63	1.35
Menstrual cycle irregular	20.44[a]	44.07[b]	41.18[b]	42.17[b]	19.26***
Period	4.41	6.78	11.76	9.32	3.60
Pelvic surgery	7.25[a1]	5.08[a]	17.65[b]	21.95[b]	18.19***
Sexually Transmitted Disease (STD)	7.35	12.07	17.65	12.73	3.88
Lifestyle					
Overweight	19.40[a]	19.30[a]	31.25	35.40[b]	11.68**
Unprotected sexual intercourse with multiple partners	7.23[a]	13.79[a]	23.53[b]	31.93[b]	30.23***
Stress	6.77[a]	14.29	2.94[a]	19.51[b]	13.91**
Class A drug	1.48	1.69	0	0.60	1.21
Anabolic steroids	0.70	1.70	0	0.60	1.01
Alcohol	8.76	12.07	0	5.45	6.01
Smoke	14.29	18.64	15.15	7.88	5.92
Caffeine	5.88	8.47	0	7.78	3.25
Marijuana	3.68[c2]	10.17[a]	3.03	0.61[b]	12.52**

Note. Number or percent with different superscripts are significantly different. [1]Trend reported for fertile compared to presumed fertile (P = 0.06). [2]Trend reported for fertile and subfertile (P = 0.07) and fertile and infertile (P = 0.06). *P< 0.05. **P<0.01. ***P<0.001.

Discussion

The main finding of the current study has been demonstrating that it is possible to generate a significant multivariate model of correlates of female fertility status. The model discriminated between currently pregnant and non-pregnant women and between fertile and infertile women. The most important univariate correlates were endometriosis, unprotected sexual intercourse with multiple partners and irregular menstrual cycles. These univariate correlates were also the most important when all the factors were considered as a group with stress and amenorrhea also emerging as important correlates. The pattern of results also demonstrated that women may modify their lifestyle to increase their chances of conceiving. These findings lend further support for the development of a tool to assess personal fertility potential.

The first aim of the present study was to replicate the associations between individual risk factors and indicators of female fertility. The results support past research in showing that risk factors such as endometriosis, previous pelvic surgery, period pains, irregular menstrual cycles, overweight, unprotected intercourse with multiple partners and stress were all associated with a lower likelihood of pregnancy and a time trying to conceive of more than 12 months. Endometriosis was associated with the largest odds ratio in the likelihood of pregnancy (OR 0.20, CI = 0.09, 0.41) and stress was associated with the largest odds ratio in time trying to conceive (OR 3.49, CI = 1.69, 7.21). Age was found to have the weakest significant association on time trying to conceive (OR 1.06, CI = 1.02, 1.10) and for pregnancy status (OR 0.95, CI = 1.02, 1.10). PID and STD were not consistently significant but were in the right direction for both pregnancy (OR below 1) and fertility (OR above 1). These results were unexpected considering that STD and PID had the largest averaged odds ratios for fertility difficulties in the empirical literature (see Table 5.1.4, page 170). A

possible explanation for the inconsistency may be the low frequency of STD and PID in the present sample. Indeed only 13 women reported suffering from PID. Cohen and Cohen (1983) report that correlations will be underestimated where the proportion of cases is highly skewed in dichotomous variables, as was the case in the present study.

The only set of reproductive risk factors to show an inconsistent pattern of results was the menstrual set. Shorter menstrual cycles were (unexpectedly) associated with better fertility, longer cycles with both reduced pregnancy and increased fertility, amenorrhea with both reduced pregnancy and increased fertility (but reduced fertility in multivariate analysis), and irregular cycles were (as predicted) associated with reduced fertility potential (both reduced pregnancy and increased infertility). Previous research has found that self-reported menstrual cycle length can be problematic due to individual variation in response to menstrual cycle questions (e.g., when does it start? how long is the bleed?) and therefore self-report may not provide the most accurate data (Jukic et al., 2007). The lack of consistency among menstrual questions within this study and between this study and past research (e.g., Jukic et al., 2007) may reflect this lack of clarity. More pilot testing might have provided a better fit between the meaning of menstrual cycle questions between researcher and participant.

The pattern of results with lifestyle factors was more complex. When focusing on pregnancy status (pregnant versus not pregnant women) the results were the exact opposite to the predicted direction for drinking alcohol, smoking (tobacco and marijuana) and caffeine consumption, that is, all these factors were associated with an *increased* chance of pregnancy. This was surprising given that these have all shown significant associations with lack of pregnancy in numerous other studies (Wilcox et al., 1988; Hatch & Bracken, 1993; Olsen et al., 1997; Hakim et al., 1998; Hull et al.,

2000; Hassan & Killick, 2004; Axmon et al., 2006). There is isolated evidence for the benefit of some of these lifestyle factors. For example caffeine consumption has been associated with increased sperm motility (Sobreiro, Lucon, Pasqualotto, Hallak, Athayde & Arap, 2005). However, the overall pattern of association across *different* lifestyle risk factors would argue for a more systematic account for the findings.

There are two possible explanations for this surprising finding: pregnant women may be risk seekers or non-pregnant women may be risk averse. It may well be that the pregnant women in the present sample were risk takers in general, that is that they were drinking more, smoking more and potentially, that this risk taking extended to their sexual life and led to the current pregnancy. Indeed such level of high risk taking is seen in some young teenage mothers (Stevens-Simon, Kelly & Kulick, 2001), perhaps representing a subgroup of women that are obscuring the expected pattern of results. However, if this were true then one would expect to find that these risky behaviours were mirrored in a number of the other risk factors such as unprotected sexual intercourse, younger age, and higher incidence of STD's. However none of these risk factors were higher in the pregnant women, quite the opposite in fact (age was indeed younger in the pregnant women but comparable to national age at first birth, Office of National Statistics, 2004). In addition, the incidence of lifestyle factors in the pregnant women was not greater than the population values (see Table 5.2.2, page 194). Thus, it seems unlikely that the pregnant women represent a highly 'risky' group of women.

Alternatively, and perhaps a more plausible explanation, is that the not pregnant women were risk averse, and perhaps even actively modified their lifestyle habits over time because they were trying to get pregnant leading to lower risk

activity. If true this would create a spurious positive association between negative lifestyle factors and pregnancy. Efforts to influence chances of conception among women has been noted in other contexts, for example taking relaxation sessions to increase success of treatment (Domar, Zuttermeister, Seibel & Benson, 1992) or abstaining in sexual activity to improve sperm quality (De Jonge, LaFromboise, Bosmans, Pharm, Ombelet, Cos & Nijs, 2004). Chapter 4 highlighted that people are aware of a number of lifestyle factors that are associated with a detrimental effect on female fertility; therefore people may attempt to modify these behaviours when they do not get pregnant. Research on lifestyle change in men and women diagnosed with cancer suggests that adapting lifestyle habits (e.g., diet, exercise) may induce a sense of personal control over their situation (Patterson, Neuhouser, Hedderson, Schwartz, Standish, & Bowen, 2003). The factors with unexpected results (smoking, alcohol and caffeine consumption) were also the easiest factors for people to control and modify. They can all be almost immediately reduced with little adverse effect (depending on the level of dependency of the drug). Other lifestyle factors showing the expected pattern of results can also be modified (e.g., weight) but may take longer to achieve and involve more effort and commitment (e.g., change in diet, exercise regime) or could not be changed as they had already occurred (e.g., previous misuse of Class A drugs).

When the groups were examined in more depth in secondary analyses the expected negative association between risk and fertility was observed since the women who had been trying the longest to conceive (subfertile and infertile) had the highest frequency of negative lifestyle factors when compared to women who had been trying for a lesser amount of time (fertile and presumed fertile). The pattern of results presented here suggests a complex relationship between these lifestyle factors

and fertility potential. In order to adequately test this hypothesis one would have to conduct a prospective study to follow women from the moment they start trying to conceive to see whether lifestyle habits do change over time and, if so, at what point this change begins.

The second aim of the current study was to examine whether a multifactorial approach to assessment of risk factors would identify areas of overlap among reproductive and lifestyle factors in their association with fertility indicators. On the whole, the majority of the risk factors were significantly associated with female fertility potential in both the univariate and multivariate analyses. This pattern of results indicates that each risk factor was an independent risk factor associated to fertility due to its own unique aspects rather than because it correlated to some other fertility risk. Where there was change in significance, the reduction appeared mainly due to a change in power rather than a change in actual importance of the factor, as the majority of the OR's did not change direction but reduced in size. The original power calculations recommended recruitment of over 1000 women, indeed this sample size was achieved, however, once exclusions were made due to selection criterion the sample size was greatly reduced by more than 300 women. Future studies should therefore aim to increase initial recruitment in order to maximise frequencies of all the risk factors.

Methodological Implications and Limitations

The main methodological issue arising from the present results is the use of cross-sectional data. While the methodology is cost effective and very useful in highlighting potential factors associated with female fertility difficulties it cannot lead to cause and effect. For example, in the present study a large odds ratio was found for

the effect of stress on chance of pregnancy. Such a result may be due to the fact that stress reduces the chance of pregnancy as suggested by prospective research (Stoleru et al., 1993; Hjollund et al., 1999). Conversely it could be due to the fact that as failure to conceive persists, stress increases. Only prospective research could further support the argument that the correlates identified here are also predictors of fertility, and this research would be essential to correctly advise women about the impact such a factor may have on the chances of achieving a successful pregnancy.

The recruitment method was successful with a large number of women being recruited over a short period of time. One noteworthy limitation with the sample size was the fact that while a large number of women were recruited not all were planning to conceive and this markedly reduced the sample size in the infertility status analysis (due to no data on TTP in the unplanned pregnancies), reducing the chance of achieving a large sample size for the low frequency factors (e.g., anabolic steroids). This criterion was used to index exposure (i.e., time to pregnancy) but in the current sample over half (63%) of pregnant women (n = 532) stated that the pregnancy was not planned. Previous data suggests that around 40 – 50% of all pregnancies are unplanned (Ray, Singh & Burrows, 2004; WHO, 2005; Lakha & Glasier, 2006; Mohllajee, Curtis, Morrow & Marchbanks, 2007), and future studies should take into account this ratio in recruitment in order to maximise the prevalence of the low frequency events such as anabolic use or PID.

Due to the software used to develop the online survey there was no way of ascertaining drop out in the internet sample, as participation could only be recorded once the participant had submitted their response. In the clinic sample the participation rate was 32.41% (33% return rate from the antenatal units, 35% from the

fertility unit and 28% from the abortion clinic). This is lower than a review of nearly 200 published studies on medical mail surveys where the average response rate was 60% (Asch, Jedrziewski & Christakis, 1997). However, this average did include a number of studies where written and telephone reminders were used, which was found to increase participation rate. In the present study it is difficult to judge whether the people with less favourable habits (e.g., drug use, past STD) declined to participate because disclosure of such behaviours was necessary. However, as the prevalence of all the risk factors was similar to those found in the population it seems likely that the sample was representative.

Finally, the present study did not take into account factors that affect male fertility potential. This may have introduced unknown bias into the results as female fertility depends on male fertility. The development of future research needs to assess female, male and couple risk factors in order to exercise more control over this.

Clinical Implications and Future Directions

The present study has demonstrated that a multivariate model of risk correlates assessing fertility potential is possible. Current statistics and research shows individual risk factors are on the increase in Western societies, and thus people need to be made aware of the potential impact these factors may have on a woman's fertility potential. The results from the present study may provide some evidence that people are adopting changes in some of their lifestyle habits (e.g., alcohol consumption) but it is unclear at what point these changes (if any) may begin to occur. Further not all factors that can be changed appeared to be targeted (e.g., overweight) suggesting that people may not be behaving in the most optimal way even when it is

possible and even when they have been trying to conceive for many months and even years.

Future research needs to employ prospective designs that can provide causal data between the risk factors, pregnancy and fertility status over time to adequately assess the factors predictive of reduced fertility potential. Such data would be especially valuable in providing more accurate effect sizes for each of the risk factors, which would contribute to better understanding of the factors to target when people cannot conceive. General Practitioners receive clear guidance about which factors to treat and in which order when it comes to reproductive risk factors (through the use of guidelines published by organisations such as NICE) and it might be beneficial to do the same at a personal level. This may be of importance when one considers that people may modify lifestyle factors that are not as important as others. For example, it may be more beneficial for an overweight woman to attempt to lose weight than for her to modify other less important lifestyle factors such as alcohol consumption (although they may be related). Further, if people are modifying factors that have no or minimal impact on fertility potential then people may be unnecessarily delaying when they should be seeking medical advice regarding their situation. Finally, people need to be informed of the importance of these factors prior to trying to conceive so that they become more aware of, and have the option to prevent, change and/or modify their current habits in order to reduce the potential impact they may have on their future life goals of becoming a parent.

Notwithstanding the issues surrounding the use of cross-sectional data the present study has established the importance of a number of reproductive and lifestyle factors that can be addressed in women thinking about having children now or in the

future in order to reduce the impact that these factors can have on female fertility potential.

Chapter 6
General Discussion

The aim of the studies presented in this thesis was to better understand help seeking behaviour in the context of fertility problems, establish risk factors associated with fertility potential, and identify targets for public health campaigns to improve fertility health related behaviour. The current chapter will present an overview of the main findings, discuss the clinical implications of these findings, and identify areas for future research.

Help Seeking Behaviour in the Context of Fertility Problems

Infertility is a prevalent problem in society, affecting 72 million couples worldwide (Chapter 2), yet perhaps unexpectedly and most importantly the present set of results revealed that uptake of medical treatment is much lower than expected with a similar rate between more and less developed nations. The low uptake of fertility medical services was an unanticipated finding given the documented importance of parenthood as a central life goal desired by the majority of young men and women in all societies around the world. Thus one would have expected to see this desire mirrored by high uptake rates of medical services under the premise that such action would assist couples in achieving their parenting goal when faced with difficulties conceiving. In addition, one would have also expected to see higher rates of treatment seeking behaviour given that the high success rates of fertility treatment make treatment a very viable option to resolve the fertility problem.

This research showed that taking steps to seek treatment was also dependent on psychological factors and this confirmed previous empirical research and theoretical predictions and provided support for the application of help seeking

theories in decision making for fertility health issues. Specifically, these centre mainly on perceived susceptibility that a problem actually exists, a fear of diagnosis as a result of seeking advice, attitudes towards treatment (e.g., is medical treatment unnatural?) and the mechanics of actively seeking out medial care (e.g., knowing how to and where to access medical help).

Three issues arising from the present studies warrant further investigation. First, there is a pressing need for more up-to-date data on the prevalence of infertility and demand for fertility medical services. A number of the studies reviewed were more than a decade old and there appeared to be a distinct lack of prevalence research from the less developed nations, especially with regard to the demand for medical services. Data should be collected through population-based prospective and cross-cultural designs that take a multidisciplinary approach due to the established importance of psychological, social and cultural factors. Further, it would be especially valuable to generate better estimates of those seeking advice, of those seeking treatment and of those actually receiving treatment since the latter stages might be the ones to differentiate according to developmental status. For example, in a recent world report on the availability of assisted reproductive technologies, the number of cycles per million varied considerably, with a 1000-fold difference between countries with the highest (Israel, 3263 cycles) and lowest (Guatemala, 2 cycles) values (Adamson et al., 2006).

In accordance with the conclusions made by Schmidt and Münster (1995) in their review of prevalence a key issue prior to the undertaking of these prospective studies is the need for better consistency between researchers on the operational definitions for infertility and the most appropriate time frames of exposure to be

assessed since comparisons between data is made much more difficult when different definitions have been employed. In 2006 The International Committee Monitoring Assisted Reproductive Technologies (ICMART) published a glossary of Assisted Reproductive Technologies (ART) terminology which included a definition of infertility (failure to conceive after at least one year of unprotected coitus) (Zegers-Hochschild et al., 2006). However, there is little current prevalence data so it is not possible to establish yet whether this definition is being actively used. Perhaps the reason why consensus in prevalence research has not been achieved is that the debate on what the agreed definition should be has yet to be fully resolved (Habbema et al., 2004; Homburg, 2005; Larsen, 2005).

Second, there is a need for more in-depth information about why people are not seeking treatment as the present research only explored a limited number of variables. Of particular interest would be to establish whether inaction is a result of decisions to actively remain childless, or a result of a lack of knowledge about how to seek medical help or lack of access to medical help. In addition, there may be other psychological and cultural beliefs and values that impact on decision making that warrant further investigation (e.g., religion). A more in-depth understanding of the importance of the factors associated with decision making will help establish ways in which barriers to seeking medical help (for those who wish to access it) can be overcome. The present results also lend support to the need for more cross-cultural research because there would seem to be far more 'behind' the similarity in the numbers of couples seeking medical help that warrants explaining. Further, the methods used to recruit women trying to conceive (i.e., internet sampling) were not very successful in reaching people of other cultures, or a wider range of educational levels. A clearer understanding of any cultural factors that influence decision making

will impact on the formulation of help provided to couples faced with difficulties conceiving. For example, access to fertility treatments has been shown to be more limited in less developed nations (Adamson et al., 2006) which could go towards explaining the low numbers of treatment uptake found in the review for these countries. Conversely in more developed nations the low uptake of treatment could reflect a broader change in parenting interests in men and women. Changes in Western society (e.g., women remaining in education for longer) may impact on decision making when difficulties trying to conceive occur, as couples may decide that they have other life goals that could be pursued (e.g., career progression and development) instead of seeking medical help.

To better inform on the factors that impact on decision making prospective research is now needed in order to identify more conclusively on the causal mechanisms identified in the present research (e.g., attitudes, perceived susceptibility, and fear) so that one could be more confident of manipulating these factors to facilitate help seeking in people who want treatment. This would have to be conducted in an ethical way as by doing so it might be misconstrued as undue pressure on people to submit to pronatalist norms, which is to do absolutely everything possible to conceive a child (Remennick, 2000; K. Park, 2002). However, it is also important to recognise that for at least 20% of women who had a strong need for parenthood action had not occurred despite trying for nearly two years (Chapter 3). This inaction appeared to be associated with a fear of finding out whether a fertility problem existed and the consequences of such a diagnosis (e.g., fear of being labelled infertile).

Third, the present studies did not address decision making taking into account the medical provider. This is an important area needing further investigation as past research does provide some evidence that provider delay can impact on whether couples who seek initial medical help are referred to the appropriate specialist to get that help (Gunnell & Ewings, 1994). Further, an assessment of whether guidelines developed for use by general practitioners when people present with fertility difficulties (e.g., NICE, 2004) are being effectively implemented needs to be undertaken, so that all people who want medical help and treatment are provided with accurate information in a consistent manner in order to aid their decision making.

Deciding on a course of action when suspecting fertility difficulties might also be helped by decision support technologies (DST) that would guide decision making about treatment seeking behaviour. DSTs are designed to aid decision making through providing people with detailed information on the different options available to them and the likelihood of certain outcomes occurring (e.g., chances of pregnancy) depending on particular courses of action (e.g., seeking medical treatment). They have been developed and extensively used for a variety of health conditions and treatments that involve complex decision making (e.g., deciding whether or not to take an amniocentesis test, Durand, Boivin, & Elwyn, 2008). The development of the tools rely on both quantitative and qualitative research methodologies to form an inclusive representation of the processes involved in decision making when someone is faced with a specific problem. One would hope that through the use of such approaches men and women faced with a fertility problem can come up with decision making strategies that provide individuals with all the relevant information needed to find solutions to the problem, future research could benefit from the development of such a tool informed by both patients and general medical practitioners.

A final consideration of the present research is the lack of male data. Men were not intentionally excluded from this research, but recruitment of men may have been hindered by the use of predominately female orientated websites (e.g., gettingpregnant.co.uk). Previous literature does suggest that it is the female partner who takes the prominent role in decision making regarding reproductive impairment (Greil et al., 1988) with men less likely in general to initiate seeking medical help when they are ill (Banks, 2001). Nevertheless fertility impairments involve both partners so exploring factors associated with decision making from a male perspective warrants future examination.

Risk Factors Associated with Fertility Potential

The second part of this thesis took a comprehensive approach to establishing the factors associated with reduced female fertility potential. A thorough literature review and consultation with medical and reproductive experts produced a critical list of risk factors associated with female fertility. These 14 risk factors were then successfully shown to be associated with fertility status (i.e., pregnant/not pregnant) replicating previous findings, and further emphasising their importance. Perhaps more importantly the present research is the first in the literature to assess so comprehensively not only the unique contribution of these factors on female fertility but also their shared contribution, providing valuable data to show these risk factors retain their individual importance even when assessed in a multifactorial way. Further, the present research demonstrated that young people were aware of many of these 14 risk factors, and that in fact those trying to get pregnant may even try to increase fertility potential by modifying some of the risk factors (e.g., alcohol consumption).

These findings have important implications for future research. The next step in this research would be to determine whether these risks can *predict* individual fertility status. In addition conducting a prospective study affords unique opportunities to explore more possible risk factors that have received limited research to date (e.g., ethnicity). As was the case for the future research on prevalence, prospective studies would need to reach consensus on the use of operational definitions (e.g., infertility) as the research reviewed showed variations on associations depending on whether the research focused on pregnancy status or infertility status. These data could also confirm proposals made here, for example, that people change risk behaviour (e.g., alcohol consumption) to increase fertility potential.

Another issue that showed variations in associations was in regard to a lack of consistency on the critical thresholds associated with risk. If smoking 10 cigarettes a day is the critical threshold for a detrimental effect of tobacco smoking on fertility then what happens if someone reduces to nine cigarettes a day? Further, is nine cigarettes smoked with more depth and longer duration of inhalation healthier than 10 cigarettes smoked more lightly? This specificity has been established in other research focusing on people trying to reduce their exposure to nicotine by restricting cigarette intake (Shields, 2002), and in settings where individuals have to smoke a cigarette quickly (e.g., short smoking breaks in working environment, Chapman, Haddad, & Sindhusake, 1997). Thus, even though a behaviour change in smoking habits may occur through increased awareness about the risk of the behaviour on subsequent disease, the individual may actually fail to reduce their risk in any way.

As was the case in help seeking research, future prospective data needs to take a multifactorial approach. The current research is the first of its kind to assess all 14

risk factors together. The literature reviewed revealed that only 19% of studies took a multifactorial approach to the assessment of risk factors, but even these only assessed a few of the risk factors. These studies did find evidence for mediating and moderating factors (Stanton & Gray, 1995; Tolstrup et al., 2003), an issue that was not explored in the thesis but worthy of future investigation. This would be especially important when one considers how people may perceive themselves to be 'at risk' when an individual has some risk factors, but not others. For example, knowing that you are not at risk for one factor may provide one with a false sense of security about other factors even though the factors may be related. For example, Strychar et al. (1998) assessed the impact of dietary change in men receiving blood cholesterol test results and reported that the men who received a low cholesterol test result but ate foods high in saturated fat falsely believed it would be ok to continue eating such fatty foods because they had low cholesterol. In relation to risk associated with infertility, people who have unprotected sex but do not have an STI may be given a false sense of security that unprotected sexual intercourse is in fact safe. If the future of this research is to educate people about their risk of fertility difficulties it would be imperative to establish the exact risk.

Taken together with other research there is converging evidence supporting associations with these 14 factors and fertility impairment. Evidence also shows that young people were aware of a number of the risks, yet these risks do not appear to be reducing in the general population, quite the contrary, with research demonstrating that the majority of the negative lifestyle risks (e.g., obesity, smoking) and reproductive risks (e.g., STD) associated with fertility are on the rise. Perhaps the future of this research lies in personalising information. The NHS is now actively encouraging people to take more control over their own health and wellbeing by

providing them with specific knowledge about the risks associated with a detrimental impact on their health (Department of Health, 2006). Therefore these fertility risk factors could be targeted. During the past five years there has been some increase in raising awareness bout fertility health issues (ASRM, 2006), however, as yet no personalised fertility campaign has been conducted to raise personal fertility awareness, and perhaps this is the direction that future research needs to explore.

The debate regarding informing people about risks centres on a balance between increasing awareness to better educate, reduce fear and motivate change where needed compared to provoking unnecessary fear and worry. The arguments for increasing awareness appear to outweigh the arguments against, providing that people are educated in an appropriate way, that is by giving accurate knowledge that aids effective decision making (e.g., to reduce one's risk of developing lung disease one should cut down or stop smoking), and giving support when change is required (e.g., free nicotine replacement patches, support counselling). In the context of fertility health it remains to be established as to whether providing young people with such information would result in active behaviour change when needed (e.g., reduction in smoking).

Finally, poor participation rates of men in studies 3 and 4 resulted in the decision to only review and test the risk factors associated with female infertility. However, successful conception is dependent on both female and male fertility potential and the data provided in the present thesis is therefore only presenting half of the story. In future research the same process involved in the identification of risks using the female FRFS should be applied to identify risks for male fertility. Such studies would have to address ways in which men can be recruited. However, there

are male orientated websites that could be a place to target men. A pilot study (conducted in the same laboratory) using a preliminary internet version of a male FRFS recruited nearly 200 men in one month; therefore such future studies may well be feasible.

Key methodological Issues

Through the completion of the set of studies presented in this thesis two common methodological issues have arisen, that warrant further discussion. The first is in regards to sampling issues and the second is in regards to the measurement of individual constructs.

Sampling issues.

Having a representative sample is a main aim when conducting research, that is, that the characteristics and behaviours measured in the participant pool are an accurate reflection of those found in the population (Heiman, 1999), thus minimising any potential biases that may impact on any assumptions or conclusion drawn (e.g., education, socio-economic status, age). The benchmark for obtaining a representative sample would be through population-based surveys that access everyone in a specified population using, for example, a local electoral role. However, in the present set of studies such a design could not be implemented, therefore one has to question whether the samples obtained for the studies presented, and thus the conclusions drawn, accurately represent, and are applicable to a wider community. Indeed the majority of the women employed in the studies conducted were recruited via the internet, which as already discussed does have limited accessibility to all. However, unlike previous studies that also did not use population based surveys but relied on recruiting couples once registered in the medical system (thus are prone to biases concerning only those

who seek treatment ~50% of couples), the internet offers the opportunity to recruit women at all stages of trying to conceive. Indeed this was achieved when one looks at the ranges of months trying to conceive in Chapters 3 (0 – 132 months) and 5 (0 – 204 months). Further, the average age of women in these Chapters was similar to the national average at first birth in the United Kingdom. In addition, population comparisons were made in the sample recruited in study 5.2, which showed a good level of agreement between the frequencies of factors reported in the recruited sample and those reported in the general population.

Such results lend support that the samples recruited in the studies presented showed good representation compared to the population in terms of reproductive matters (e.g., age at first birth). However, there was an over-representation of highly educated samples and further, no attempts were made to assess the socio-economic status of participants. Therefore it is unknown to what extent the participant's sampled are representative in different socio-economic categories. In addition, the majority of respondents from Chapter 3 onwards were from more developed nations (mainly UK and USA) and therefore one has no way of assessing whether the current issues addressed are applicable across developmental status. Future research must therefore look to validate the data collected to date in population based samples that will ensure a representative sample from all socio-economic backgrounds, with an emphasis on collecting data from less developed nations.

Another sampling issue concerns the size of samples recruited, more specifically the size of sub-samples used. For example, while a projected sample size calculation was conducted for study 5.2, of which it was achieved, when the sample was broken down into sub-groups for analysis (e.g., pregnant, not pregnant, intended

pregnancy) over one third of the sample were excluded from the majority of the analysis (unplanned pregnancy). This is problematic when one wants to look at individual effects or interactive effects on specific variables when the frequencies of such variables are very low. For example, it would be hard to examine the impact of illegal drug use and smoking tobacco in pregnant women who tried to conceive compared to not yet pregnant women, when there were less than 5 women in each group who reported partaking in both activities. While these comparisons would be very useful to look in more detail at any relationships between risk factors, with small sub-sample sizes they become near impossible to conduct, and thus future research may benefit from setting a minimum sample size for any proposed sub-groups prior to the start of recruitment.

One also has to be cautious when reviewing samples obtained from different studies which may impact on the interpretation of the results reported. For example, in Chapter 2 a comprehensive review of the prevalence literature was conducted on studies using population based samples. These prevalence ratings were then compared and averaged to estimate the prevalence of current and lifetime infertility in couples in more and less developed nations. However, one important issue is any differences between the samples reviewed, that may impact on the interpretation of the prevalence rates reported. For example, when one compares the prevalence rating for the Gunnell and Ewring's (1994) study (26.4% lifetime prevalence) to the Schmidt et al. (1995) study (15.7% lifetime prevalence) there appears to be quite a difference between the two numbers reported. A possible explanation for the difference in numbers is concerning the samples used. For example, in the Gunnell and Ewring (1994) study they sampled all women, that is, women who stated they were voluntarily and involuntarily childless. Whereas in the Schmidt et al. (1995) study they only sampled

women who stated they were involuntarily childless. Therefore, the estimate from the Gunnell and Ewring (1994) study includes more women, even though the intentions of the women categorised as 'infertile' may be for different reasons (e.g., no intention to try to conceive). However, while this could account for some difference between the two prevalence scores previous research suggests that the estimated number of voluntarily childless women is relatively small (Chancey, 2006).

Perhaps a more plausible explanation for the divergence in the prevalence ratings concerns the age of the samples recruited. In the Gunnell and Ewring (1994) study the sample selected for analysis aged 36 – 50 years old compared to 15 – 44 years old in the Schmidt et al. (1995) sample. Indeed the Schmidt et al. (1995) study does provide a breakdown of the number of infertile women according to age, reporting a 22.1% prevalence rate for women aged 35 – 44, which is much more similar to that reported by Gunnell and Ewrings (1994). Differences in the characteristics of samples reviewed are important issues to consider for future research in order to make accurate comparisons between studies that will not impact on the interpretation of results.

A final sampling issue is the emphasis of the current research to focus only on female infertility. This exclusion was not meant to encourage the idea that infertility only concerns females and is not a couple problem, but more of a consequence of a lack of male participation. If the ultimate goal of this body of work is to raise better awareness about fertility health issues it would be futile to believe that fertility health only concerns females and that only one person (the female) is important in achieving reproductive success. While it is important to ascertain individual information about reproductive and lifestyle habits in order to better educate people about how their

behaviours now (e.g., unprotected sexual intercourse with multiple partners, illegal drug misuse) may impact on future life goals of becoming a parent, it is also important to ascertain a couples risk. For example, if a woman is trying to get pregnant one cannot just base the chances of conceiving on responses only about her reproductive, medical and lifestyle history, as the partner's reproductive, medical and lifestyle history will also impact on the chances of success. Only considering individuals and not couples may also impact on the way feedback and advice is provided concerning being 'at risk' when one is trying to conceive. For example, if a couple are trying to conceive and the women does not consume alcohol, smoke tobacco or take illegal drugs, she would be deemed at low risk for these negative factors impacting on her chances of successful conception. Therefore the information she may be provided in an attempt to raise awareness about her fertility health would reflect her responses concerning negative lifestyle habits. However, her partner may well partake in all these negative habits and thus may be impacting on their chances of conceiving. As already discussed, future research needs to make more of an effort in attempting to recruit men into psychological studies concerning fertility research in order to better understand the male decision making processes associated with unsuccessful attempts when trying to conceive, and the factors associated with having a detrimental impact on male fertility potential. Further, these issues also need to be explored from the couple's perspective as well.

Measurement of individual constructs.

The second methodological issue surrounds the way in which constructs were measured in each study conducted. The majority of the studies presented in the thesis have attempted to take multifactoral approaches throughout. For example, in Chapter 3 this involved the amalgamation of a number of constructs from different decision-

making theories, models and previous empirical literature. Taking such an approach has allowed for the testing of multiple constructs and variables associated with the question in hand (e.g., decision making about help-seeking behaviour, the effect of all lifestyle factors on fertility potential). However, one issue with such an approach is that it may lead to an over simplification of the measurement of individual constructs. That is, through such a design do individual effects get lost, and are constructs being adequately assessed. For example, in Chapter 4 and 5 to measure stress one sentence was used ("I am experiencing levels of stress that I cannot cope with"). While this is a valid measure to ascertain extreme levels of stress, it may not fully capture the underlying processes of dealing with stressful situations. Indeed in the case of infertility it is often referred to as a low-control stressor, that is, a stressful situation in which the infertile couple can do little to alter any possible causes or outcomes of their situation (Schmidt, Holstein, Christensen & Boivin, 2005). Thus, measuring stress in one question may not adequately reflect the complex nature of the stressor involved. Further, some effects may be a general response to everyday situations (e.g., stable coping mechanisms) while others may have some specificity to a certain situation (e.g., infertility) which may make measuring coping styles as a 'snap shot' and not a process difficult to apply to all situations. For example, couples who enter fertility treatment are often encouraged to be optimistic about their chances for a successful outcome (Schmidt et al., 2005). This may lead to more 'wishful' thinking about the situation ("wished for a miracle to happen"). However, such wishful thinking can often be categorised as a type of escapism coping (Terry & Hynes, 1998), which may be interpreted as the individual not adequately coping with the situation in hand.

An additional issue with measuring multiple factors is that some factors have established modes of action, for example smoking in women has been linked to a reduction in the number of viable oocytes, leading to an earlier onset of the menopause (Zavos & Zarmakoupis_Zavos, 1998) but also modes of action which may reflect correlated attributes, for example marijuana effects may reflect smoking. However, measuring and analysing such relationships can be complicated, especially when testing so many variables, of which many may be correlated.

Therefore, a potential draw back of a multifactoral approach employed in the present studies is that it may not fully capture the individual processes of each construct measured (e.g., stress, coping, smoking). However, this may not just be a problem associated with taking a multifactorial approach, but perhaps is more concerned with the use of retrospective designs. While the present studies have provided a wealth of knowledge about the issues addressed, what is really needed now to better understand decision making and risk associated with fertility potential (e.g., risky behaviours over time) is prospective longitudinal data that will be able to disentangle cause and effect, that will offer the advantage to assess the processes of certain constructs measured over time.

Finally, another possible set of influences (e.g., genetics) have not been taken into account in the present research that may impact on the results obtained, and warrant consideration in future research. For example, there is now a large body of evidence to suggest that genetic influences may predispose people's behaviours towards alcohol consumption (Devor & Cloninger, 1989). This may have an impact on one's tolerance and biological reaction towards alcohol consumption, which may in turn impact on the effect alcohol consumption, could have on fertility potential.

Further, such genetic influences may interact with other factors, such as ethnicity, which may impact on the ways in which raising awareness can be applicable to all or just specific groups of people.

The research presented in this thesis does provide a better understanding of help seeking behaviour in the context of fertility problems and has established a set of risk factors associated with female fertility potential. A key message from the present research is the need for better awareness about one's fertility health and fertility potential. Further, as will be presented in the next section, this research has highlighted the potential targets for such fertility awareness campaigns. However, what is now needed is prospective research that takes into consideration the key methodological themes discussed in the current section. Only through the validation of the results found in the present set of studies bearing in mind these methodological issues (e.g., population based studies to ensure good socio-economic representation) can this research move forward to the next step, that is, increasing personal and public awareness about fertility health issues, making sure that the information provided is relevant and useful in helping all people (female, male and couples) realise their parenting goals.

Targets for Public Health Campaigns to Improve Fertility Health Related Behaviour

The present research has identified two potential groups that may benefit from future public health campaigns to improve fertility health related behaviour. First, public health campaigns could take a preventative approach targeting factors identified in the current research, on the understanding that through the prevention of the risk factors fewer women (and men) would be faced with fertility difficulties in the future. Indeed the factors shown to have some of the largest negative impacts on

fertility status (e.g., PID, STD) are easily preventable, and thus young people especially need to be informed about such risks in order for them to realise that their actions now can severely impact on their future fertility potential. A second goal of preventative strategies would be to empower women to become more aware of their fertility (e.g., what is your menstrual cycle, is it what it should be?). The increase in personal awareness about one's fertility may also help young people become more attuned to changes that may warrant appropriate action to be taken (e.g., sudden increase in menstrual cramping), to prevent worsening of the condition (e.g., treatment for endometrial scarring). Ultimately, providing people with information about the risks allows that individual to make informed decisions about their own future fertility.

While the preventative public health campaigns would hope to reduce risks and thus reduce the number of couples affected by infertility some couples would still be faced with difficulties conceiving. Thus a second public health campaign should target couples trying to conceive. The emphasis for these targets would not just be prevention of risks (although this would be important) but would focus more on effective decision making when faced with a difficulty conceiving, so that timely action could be taken, if warranted.

Such a campaign would take two approaches to effectively tackle the main barriers that appear to inhibit effective action. First, people need to be better informed about treatment seeking behaviour and the options available to them if a fertility problem occurs. Namely, people need to know what to do when conception does not occur. There has been some attempt to tackle these issues. The Assisted Conception Taskforce (2006) released a pamphlet detailing the pathways towards seeking medical

advice and getting treatment. The pamphlet provided a step by step guide for couples trying to conceive in an attempt to help them understand every step from the initial first attempts at trying to conceive, through the initial consultation with a general practitioner to the more complex treatment options available, thus providing them with accurate information about the treatment seeking process from which they can make decisions based on informed choice. While such a pamphlet provides couples with invaluable advice about the treatment process, it was unfortunately not widely advertised.

A second approach to tackle barriers associated with inaction would involve the active reduction of fear associated with seeking medical help. That is, the fear that through seeking advice (or treatment) one may face being told the worst fear, which is that one, cannot have children. Fear has been shown to be a major cause of delay in other health areas (e.g., detection of a lump in the breast or testicle; Facione, 1993; Oliveria et al., 1999; Carney et al., 2002; Grunfeld et al., 2002; Bish et al., 2005; Smith et al., 2005; Facione & Facione, 2006). From this research it is believed that through effective public awareness campaigns that promote early detection (e.g., improved prognosis: Hillis et al., 1993) and better awareness about the main signs and symptoms of illness result in a reduction in delay due to fear. This idea brings one back to the need to raise awareness about the risks associated with infertility but also highlights the need for people to make timely decisions about their situations. For example, if a couple have been trying unsuccessfully for many years without seeking any medical help, this inaction may impact on future chances of conceiving for two reasons. First, this inaction may have resulted in more disease progression of the underlying cause of the infertility (e.g., underlying untreated STD which has resulted in the development of tubal factor infertility). Second, this inaction will have resulted

in the couple increasing risk of age related infertility. Current estimates of age at first birth in the United Kingdom (mean 27.1, Office for National Statistics, 2000) suggest that a delay of 2 – 3 years would put couples in an age bracket where their fertility would start to decline. Thus persistent inaction for couples who wish to become parents may be increasing the chances that they will remain involuntary childless.

Only through a systematic approach of increasing awareness about the risks associated with infertility and tackling the main barriers associated with inaction when couples are faced with fertility difficulties can people make informed choices.

Conclusions

The present research comes at time when the importance of fertility health issues is ever-increasing. Indeed infertility has been recognised as a public health issue worldwide by the World Health Organisation (WHO) (Vayena et al., 2001), and has been prioritised on both public health and social policy agendas by the European Union (Evans, 2007). The research presented in this thesis could help to provide the foundational groundwork for public health campaigns to increase awareness about fertility health issues and further, maintain infertility as an important public health issue that warrants continual investigation. Ultimately the research presented in this thesis proposes that the future of fertility health care should be centred on providing people with information leading to informed choice about all aspects of their own fertility health.

References

Abbasi, F., Brown, B. W. Jr., Lamendola, C., McLaughlin T., & Reaven G. M. (2002). Relationship between obesity, insulin resistance, and coronary heart disease. *Journal of the American College of Cardiology, 40(4),* 937-943.

Adamson, G.D., de Mouzon, J., Lancaster, P., Nygren, K. G., Sullivan, E., & Zegers-Hochschild, F. (2006). World collaborative report on in vitro fertilization, 2000. *Fertility and Sterility, 85(6),* 1586-1622.

Adashi, E. Y., Cohen, J., Hamberfer, L., Jones, H. W., de Krestser, Jr. D. M., Lunenfeld, B., Rosenwaks, Z., & Van Sterteghem, A. (2000). Public Perception on infertility and its treatment: an international survey. *Human Reproduction, 15(2),* 330-334.

Agurto, I., Bishop, A., Sánchez, G., Betancourt, Z., & Robles, S. (2004). Perceived barriers and benefits to cervical cancer screening in Latin America. *Preventive Medicine, 39(1),* 91-98.

Ajzen, I. (1991). The Theory of Planned Behavior. *Organizational Behavior and Human Decision Processes, 50(2),* 179-211.

Akande, V. A., Hunt, L. P., Cahill, D. J., & Jenkins, J. M. (2004). Differences in time to natural conception between women with unexplained infertility and infertile women with minor endometriosis. *Human Reproduction, 19(1),* 96-103.

Alm-Roijer, C., Fridlund, B., Stagmo, M., & Erhardt, L. (2006). Knowing your risk factors for coronary heart disease improves adherence to advice on lifestyle changes and medication. *Journal of Cardiovascular Nursing, 21(5),* E24-34.

American Society for Reproductive Medicine (ASRM). 2006. *Infertility: An Overview. Patient Information Series* [Brochure].

Andersen, A. M. N., Wohlfhart, J., Christens. P., Olsen, J., & Melbye, M. (2000). Maternal age and fetal loss: population based register linkage study. *British Medical Journal, 320,* 1708-1712.

Angrad, N. T. (1999). Diagnosis Infertility: These treatments can help couples achieve pregnancy. *AWHONN Lifelines, 3(3),* 22-29.

Armitage, C. J., & Arden, M. A. (2002). Exploring discontinuity patterns in the transtheoretical model: an application of the theory of planned behaviour. *British Journal of Health Psychology, 7,* 89-103.

Armitage, C. J., & Conner, M. (2000). Social cognition models and health behaviour: a structured review. *Psychology and Health, 15,* 173-189.

Arnett, J. J. (2000). Emerging adulthood. A theory of development from the late teens through the twenties. *American Psychologist, 55(5),* 469-480.

Arslanian, S., & Suprasongsin, C. (1997). Testosterone treatment in adolescents with delayed puberty: changes in body composition, protein, fat, and glucose metabolism. *Journal of Clinical Endocrinology and Metabolism, 82(10),* 3213-3220.

Asch, D. A., Jedrziewski, M. K., & Christakis, N. A. (1997). Response rates to mail surveys published in medical journals. *Journal of Clinical Epidemiology, 50(10),* 1129-1136.

Assisted Conception Taskforce (2006). *The ACT Pathway, your step-by-step guide to achieving a pregnancy.* http://www.assistedconception.ca/english/

Audit Commission. *Managing the financial implications of NICE guidance.* Health National report September 2005.

Augood, C., Duckitt, K., & Templeton, A. A. (1998). Smoking and female infertility: a systematic review and meta-analysis. *Human Reproduction, 13,* 1532-1539.

Axmon, A., Rylander, L., Albin, M., & Hagmar, L. (2006). Factors affecting time to pregnancy. *Human Reproduction, 21(5),* 1279-1284(6).

Baird, D. D., & Wilcox, A. J. (1985). Cigarette smoking associated with delayed conception. *Journal of the American Medical Association, 253(20),* 2979-2983.

Baird, D. D., Weinberg, C. R., & Rowland, A. S. (1991). Reporting errors in time-to-pregnancy data collected with a short questionnaire. Impact on power and estimation of fecundity ratios. *American Journal of Epidemiology, 133(12),* 1282-1290.

Bakeo, A. C. (2004). Trends in live births by mother's country of birth and other factors affecting low birthweight in England and Wales, 1983-2001. *Health Statistics Quarterly, 23,* 25-33.

Banks, I. (2001). No man's land: men, illness, and the NHS. *British Medical Journal, 323,* 1058-1060.

Barden-O'Fallon, J. (2005). Associates of self-reported fertility status and infertility treatment-seeking in a rural district of Malawi. *Human Reproduction, 20(8),* 2229-2236.

Barlow, D. H. (2003). The design, publication and interpretation of research in subfertility medicine: uncomfortable issues and challenges to be faced. *Human Reproduction, 18(5),* 899-901.

Barnett, J., Timotijevic, L., Shepherd, R., & Senior, V. (2007). Public responses to precautionary information from the Department of Health (UK) about possible health risks from mobile phones. *Health Policy, 82(2),* 240-250.

Basaria, S., Wahlstrom, J. T., & Dobs, A. S. (2001). Anabolic-androgenic steroid therapy in the treatment of chronic diseases. *The Journal of Clinical Endocrinology & Metabolism, 86,* 5108-5117.

Bass, S. B. (2003). How will Internet use affect the patient? A review of computer network and closed Internet-based system studies and the implications in understanding how the use of the Internet affects patient. *Journal of Health Psychology, 8(1),* 25-38.

Basso, O., Juul, S., & Olsen, J. (2000). Time to pregnancy as a correlate of fecundity: differential persistence in trying to become pregnant as a source of bias. *International Journal of Epidemiology, 29,* 856-861.

Beaglehole, R., Bonita, R., & Kjellström, T. (2006). *Basic epidemiology.* 2nd Edition. Geneva: World Health Organisation.

Bellaby, P. (2001). Evidence and risk: the sociology of health care grappling with knowledge and uncertainty. *In Evidence based patient choice. Inevitable or impossible?* Eds. A. Edwards, & G. Elwyn. Oxford University Press.

Bennet, P., & Murphy, S. (1997). *Psychology and Health Promotion.* Open University Press.

Berry, D. (2004). *Risk, communication and health psychology.* Open University Press, New York: McGraw-Hill.

Bewley, S., Davies, M., & Braude, P. (2005). Which career first? *British Medical Journal, 331,* 588-589.

Bish, A., Ramirez, A., Burgess, C., & Hunter, M. (2005). Understanding why women delay in seeking help for breast cancer symptoms. *Journal of Psychosomatic Research, 58,* 321-326.

Blake, D., Smith, D., Bargiacchi, A., France, M., & Gudex, G. (1997). Fertility awareness in women attending a fertility clinic. *Australian and New Zealand Journal of Obstetrics and Gynaecology, 37(3),* 350-352.

Bland, J. M., & Altman, D. G. (2000). Statistics Notes: The odds ratio. *British Medical Journal, 320,* 1468.

Blenner, J. L. (1990). Passage through infertility treatment: a stage theory. *Image: Journal of Nursing Scholarship, 22(3),* 153-158.

Boholm, A. (1998). Comparative studies of risk perception: A review of twenty years of research. *Journal of Risk Research, 1(2),* 135-163.

Boivin, J., Scanlan, L.C., & Walker, S. M. (1999). Why are infertile patients not using psychosocial counselling? *Human Reproduction, 14(5),* 1384-1391.

Boivin, J., & Schmidt, L. (2005). Infertility-related stress in men and women predicts treatment outcome 1 year later. *Fertility and Sterility, 83(6),* 1745-1752.

Bolch, O. H., & Warren, J. C. (1973). Induction of premature menstruation with anabolic steroids. *American Journal of Obstetrics and Gynecology, 117(1),* 121-125.

Bolumar, F., Olsen, J., Rebagliato, M., & Bisanti, L. (1997). Caffeine intake and delayed conception: a European multicenter study on infertility and subfecundity. *Obstetrical & Gynecological Survey, 52(8),* 487-488.

Bolumar, F., Olsen, J., Rebagliato, M., Saez-Lloret, I., & Bisanti, L. (2000). Body mass index and delayed conception: a European multicenter study on infertility and subfecundity. *American Journal of Epidemiology, 151(11),* 1072-1079.

Botting, B., & Dunnell, K. (2000). Trends in fertility and contraception in the last quarter of the 20th century. *Population Trends, 100,* 32-39.

Bowen, D. J., Meischke, H., & Tomoyasu, N. (1994). Preliminary evaluation of the processes of changing to a low-fat diet. *Health Education Research, 9,* 85-94.

Buckett, W., & Bentick, B. (1997). The epidemiology of infertility in a rural population. *Acta Obstetricia et Gynecologica Scandinavica, 76,* 233-237.

Bundorf, M. S., Wagner, T. H., Singer, S. J., & Baker, L. C. (2006). Who searches the internet for health information? *Health Services Research, 41(3), Part I,* 819 – 836.

Buchholz, T., & Thaler, C.J. (2003). Inherited Thrombophilia: impact on human reproduction. *American Journal of Reproductive Immunology, 50,* 20-32.

Brand, A. (2005). iPsychExpts: Web Experiments for Psychologists. http://www.ipsychexpts.com.

Callan, V. J., Kloske, B., Kashima, Y., & Hennessey, J. F. (1988). Toward understanding women's decisions to continue or stop in vitro fertilization - the role of social, psychological, and background factors. *Journal of in Vitro Fertilization and Embryo Transfer, 5(6),* 363-369.

Calman, K. C. (1998). *The potential for health: how to improve the nation's health.* Oxford. Oxford University Press.

Carney, R., Fitzsimons, D., & Dempster, M. (2002). Why people experiencing acute myocardial infarction delay seeking medical assistance. *European Journal of Cardiovascular Nursing, 1(4),* 237-242.

Castellanos, J., & Axelrod, D. (1990). Effect of habitual knuckle cracking on hand function. *Annals of the Rheumatic Diseases, 49,* 308-309; doi:10.1136/ard.49.5.308.

Cates, R. T., Rolfs, W., & Aral, S. O. (1990). Sexually transmitted diseases, pelvic inflammatory disease, and infertility: an epidemiologic update. *Epidemiology Review, 12(1),* 199-220.

Cates, W., Farley, T. M., & Rowe, P. J. (1985). Worldwide patterns of infertility: is Africa different? *The Lancet, 14(2),* 596-8.

Cates, W. Jr., & Stone, K. M. (1992). Family planning, sexually transmitted diseases and contraceptive choice: a literature update part I. *Family Planning Perspectives, 24(2),* 75-84.

Chabbert Buffet, N., Djakoure, C., Christin Maitre, S., & Bouchard, P. (1998). Regulation of the human menstrual cycle. *Frontiers in Neuroendocrinology, 19,* 151-186.

Chancey, L. (2006). *Voluntary childlessness in the United States: recent trends by cohort and period.* Master of Arts Thesis. Louisiana State University.

Chandra, A., & Stephen, E. H. (1998). Impaired fecundity in the United States: 1982-1995. *Family Planning Perspectives, 30(1),* 34-42.

Chapman, S., Haddad, S., & Sindhusake, D. (1997). Do work-place smoking bans cause smokers to smoke "harder"? Results from a naturalistic observational study. *Addiction, 92(5),* 607-610.

Chappell, R., Pearce, D., Carlos-Bovagnet, F., & Till, D. (2005). *Focus on people and migration.* Chapter 10: The UK population in the European context.

Che, Y., & Cleland, J. (2002). Infertility in Shanghai: prevalence, treatment seeking and impact. *Journal of Obstetrics and Gynaecology, 22,* 643-648.

Clark, A. M., Thornley, B., Tomlinson, L., Galletley, C., & Norman, R. J. (1998). Weight loss in obese infertile women results in improvement in reproductive

outcome for all forms of fertility treatment. *Human Reproductive, 13,* 1502-1505.

Clarke, V. A., & Savage, S. A. (1999). Breast self-examination training: A brief review. *Cancer Nursing, 22(4),* 320-326.

Cohen, J. (1992). A power primer. *Psychological Bulletin, 112(1),* 155-159.

Cohen, J., & Cohen, P. (1983). *Applied multiple regression/correlation for the behavioural sciences.* 2nd Edition. L. Erlbaum Associates. Hillsdale, N. J.

Collins, A., Freeman, E. W., Boxer, A. S., & Tureck, R. (1992). Perceptions of infertility and treatment stress in females as compared with males entering in vitro fertilization treatment. *Fertility and Sterility, 57(2),* 350-356.

Collins, H., & Evans, R. (2007). *Rethinking expertise.* Chicago: University of Chicago Press.

Collins, J. (2002). An international survey of the health economics of IVF and ICSI. *Human Reproduction Update, 8(3),* 265-277.

Conner, M., & Norman, P. (1996). The Role of Social Cognition in Health Behaviours. In M. Conner & P. Norman (Eds.), *Predicting Health Behaviour* (1 ed., pp. 1-22): Open University Press.

Consedine, N. S., Magai, C., Krivoshekova, Y. S., Ryzewicz, L., & Neugut, A. L. (2004). Fear, Anxiety, Worry, and Breast Cancer Screening Behavior: A Critical Review. *Cancer Epidemiology, Biomarkers & Prevention, 13(4),* 501-510.

Consedine, N. S., Morgenstern, A. H., Kudadjie-Gyamfi, E., Magai, C., & Neugut, A. L. (2006). Prostate cancer screening behaviour in men from seven ethnic groups: the fear factor. *Cancer Epidemiology, Biomarkers & Prevention, 15,* 228-237.

Crossman, S. H. (2006). The challenge of pelvic inflammatory disease (disease/disorder overview). *American Family Physician, 73(5),* 859-865.

Curry, S. J., Kristal, A. R., & Bowen, D. J. (1992). An application of the stage model of behaviour change to dietary fat reduction. *Health Education Research, 7,* 97-105.

Daniluk, J. C. (2001). *The infertility survival guide: everything you need to know to cope with the challenges while maintaining your sanity, dignity and relationships.* Oakland, Calif: New Harbinger.

Davies, H. T., Crombie, I. K., & Tavakoli, M. (1998). When can odds ratios mislead? *British Medical Journal, 316,* 989-91.

De Crée, C. (1998). Sex steroid metabolism and menstrual irregularities in the exercising female: a review. *Sports Medicine, 25(6),* 369-406.

De Jonge, C., LaFromboise, M., Bosmans, E., Pharm, D., Ombelet, W., Cox, A., & Nijs, M. (2004). Influence of the abstinence period on human sperm quality. *Fertility and Sterility, 82(1),* 57-65.

Decarli, A., Calza, S., Masala, G., Specchia, C., Palli, D., & Gail, M. H. (2006). Gail model for prediction of absolute risk of invasive breast cancer: independent evaluation in the Florence-European prospective investigation into cancer and nutrition cohort. *Journal of the National Cancer Institute, 98(23),* 1686-1693.

Delgado-Rodriguez, M., Gómez-Olmedo, M., Bueno-Cavanillas, A., & Gálvez-Vargas. (1997). Unplanned pregnancy as a major determinant in inadequate use of prenatal care. *Preventive Medicine, 26(6),* 834-838.

DeNooijer, J., van Assema, P., De Vet, E., & Brug, J. (2005). How stable are stages of change for nutrition behaviors in the Netherlands. *Health Promotion International, 20(1),* 27-32.

Department of Health (2006). Our health, our care, our say: a new direction for community services. Cm 6737. http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4127453.

Dewalt, D. A., Berkman, N. D., Sheridan, S., Lohr, K. N., & Pignone, M. P. (2004). Literacy and health outcomes. A systematic review of the literature. *Journal of General Internal Medicine, 19,* 1228-1239.

Dick, M. L. B., Bain, C. J., Purdie, D. M., Siskind, V., Molloy, D., & Green, A. C. (2003). Self-reported difficulty in conceiving as a measure of infertility. *Human Reproduction, 18(12),* 2711-2717.

DiClemente, C. C. (2005). A premature obituary for the transtheoretical model: a response to West. *Addiction, 100(8),* 1046-1048.

DiClemente, C. C., & Prochaska, J. O. (1985). Processes and stages of change: Coping and competence in smoking behavior change. In S. Shiffman & T. A. Wills (Eds.), *Coping and substance use* (pp. 319 - 342): Academic Press.

DiClemente, C. C., Fairhurst, S. K., Velasquez, M. M., Prochaska, J. O., Velicer, W. F., & Rossi, J. S. (1991). The Process of Smoking Cessation - an Analysis of Precontemplation, Contemplation, and Preparation Stages of Change. *Journal of Consulting and Clinical Psychology, 59(2),* 295-304.

Domar, A. D., Zuttermeister, P. C., Seibel, M., & Benson, H. (1992). Psychological improvement in infertile women after behavioural treatment: a replication. *Fertility and Sterility, 58,* 144-147.

Ducot, B., Spira, A., Thonneau, P., Toulemon, L., & Leridon, H. (1991). Difficulties in conceiving. Discussion about methodology concerning the INED-INSERM survey carried out in France in 1988 on 3,181 women aged between 18 and 49.

Journal of Gynaecology Obstetrics and Biological Reproduction (Paris), 20, 643-650.

Dunson, D. B., Baird, D. D., & Colombo, B. (2004). Increased infertility with age in men and women. *Obstetrics & Gynecology, 103,* 51-56.

Durand, M. A., Boivin, J., & Elwyn, G. (2008). A review of decision support technologies for amniocentesis. *Human Reproduction Update, 14(6), 659*-668.

Dyer, S. J., Abrahams, N., Hoffman, M., & van der Spuy, Z. M. (2002). Infertility in South Africa: women's reproductive health knowledge and treatment-seeking behaviour for involuntary childlessness. *Human Reproduction, 17(6),* 1657-1662.

Dyer, S. J. (2008). Infertility-related reproductive health knowledge and help-seeking behaviour in African countries. *Human Reproduction,* doi:10.1093/humrep/den148.

Edwards, A., Elwyn, G., & Mulley, A. L. (2002). Explaining risks: turning numerical data into meaningful pictures. *British Medical Journal, 324,* 827-830.

Edwards, R. (2004). The problem of tobacco smoking. *British Medical Journal, 328,* 217-219.

Egger, M., Low, N., Smith, G. D., Lindblom, B., & Herrmann, B. (1998). Screening for chlamydial infections and the risk of ectopic pregnancy in a county in Sweden: ecological analysis. *British Medical Journal, 316,* 1776-1780.

Eggert, J., Theobald, H., & Engfeldt, P. (2004). Effects of alcohol consumption on female fertility during an 18-year period. *Fertility and Sterility, 81(2),* 379-383.

Elliot, D. L., & Goldberg, L. (2000). *Women and anabolic steroids.* In Yesalis, C. E. (Ed.) Anabolic steroids in sport and exercise, 2nd Edition. Human Kinetics, Champaign, pp. 225-246.

Elton, P. J., Ryman, A., Hammer, M., & Page, F. (1994). Randomised controlled trial in northern England of the effect of a person knowing their own serum cholesterol concentration. *Journal of Epidemiology and Community Health, 48,* 22-25.

Ericksen, K., & Brunette, T. (1996). Patterns and predictors of infertility among African women: a cross-national survey of twenty-seven nations. *Social Science and Medicine, 42,* 209-220.

Eschenbach, D. A. (1999). Pelvic infections and sexually transmitted diseases. In J. R. Scott, P. J. Di Saia, C. B. Hammond, & W. N. Spellacy (Eds.), *Danforth's Obstetrics and Gynecology* (8th ed. pp. 579 - 600). Philadelphia. Lippincott Williams & Wilkins.

ESHRE Capri Workshop Group 2001. Social determinants of human reproduction. *Human Reproduction, 16,* 1518-1526.

ESHRE Good clinical treatment in assisted reproduction. An ESHRE position paper. June 2008.

Etter, J. (2005). Theoretical tools for the industrial era in smoking cessation counselling: a comment on West. *Addiction, 100(8),* 1041-1042.

Evans, J. (2007). Infertility – The need for policy update. *Pharmaceuticals Policy and Law, 9,* 9-12.

Facione, N. C. (1993). Delay versus help seeking for breast cancer symptoms: a critical review of the literature on patient and provider delay. *Social Science & Medicine, 36(12),* 1521-1534.

Facione, N. C., & Facione, P. A. (2006). The cognitive structuring of patient delay in breast cancer. *Social Science & Medicine, 63(12),* 3137-3149.

Far, H. R. M., Ågren, G., Lindqvist, AS., Marmendal, M., Fahlke, C., & Thiblin. I. (2006). Administration of the anabolic androgenic steroid nandrolone decanoate to female rats causes alterations in the morphology of their uterus and a reduction in reproductive capacity. *European Journal of Obstetrics & Gynecology and Reproductive Biology, 131,* 189-197.

Fathalla, M. F., & Fathalla, M. M. F. (2004). *A practical guide for health researchers.* WHO Regional Publications Eastern Mediterranean Series 30. ISBN: 92-9021-363-9.

Faul.F, & Erdfelder, E. (1992).GPOWER: A priori, post-hoc, and compromise power analyses for MS-DOS [Computer program].

Fenster, L., Quale, C., Waller, K., Windham, G., Elkin, E., Benowitz, N., & Swan, S. Caffeine consumption and menstrual function. *American Journal of Epidemiology, 149(6),* 550-557.

Fenton, K. A., Korovessis, C., Johnson, A., McCadden, A., McManus, S., Wellings, K., Mercer, C., Carder, C., Copas, A., & Nanchahal, K. (2001). Sexual behaviour in Britain: reported sexually transmitted infections and prevalent genital infection. *The Lancet, 358(9296),* 1851-1854.

Fenton, K. A., & Lowndes, C. M. (2004). Recent trends in the epidemiology of sexually transmitted infections in the European Union. *Sexually Transmitted Infections, 80,* 255-263.

Fidler, A. T., & Bernstein, J. (1999). Infertility: from a personal to a public health problem. *Public Health Reports, November – December; 114(6),* 494-511.

Field, A. *Discovering statistics using SPSS.* 2nd Edition. Sage Publications, London. 2005.

Fischhoff, B., Bostrom, A., & Quadrel, M. J. (1993). Risk Perception and Communication. *Annual Review of Public Health, 14,* 183-203.

Fishbein, M., & Yzer, M. C. (2003). Using theory to design effective health behavior interventions. *Communication Theory, 13(2),* 164-183.

Folkman, S., & Lazarus, R. S. (1988). Manual for the ways of coping questionnaire. Consulting Psychologist Press, Palo Alto, CA.

Fontes, M., & Roach, P. (2007). Predictors and confounders of unprotected sex: a UK web-based study. *The European Journal of Contraception & Reproductive Health Care, 12(1),* 36-45.

Frank, O. (1983). Infertility in Sub-Saharan Africa: estimates and implications. *Population and Development Review, 9(1),* 137-144.

Freundenberg, N., Picard Bradley, S., & Serrano, M. (2007). Public health campaigns to change industry practices that damage health: an analysis of 12 case studies. *Health Education & Behavior,* doi:10.1177/1090198107301330.

Fries, J. F., Koop, C. E., Sokolov, J., Beadle, C. E., & Wright, D. (1998). Beyond health promotion: reducing need and demand for medical care. *Health Affairs, 17(2),* 70-84.

Fuentes, A., & Devoto, L. (1994). Infertility after 8 years of marriage: a pilot study. *Human Reproduction, 9,* 273-278.

Gail, M. H., Brinton, L. A., Byar, D. P., Corle, D. K., Green, S. B., Schairer, C., & Mulvihill, J. J. (1989). Projecting individualized probabilities of developing breast cancer for white female who are being examined annually. *Journal of the National Cancer Institute, 81(24),* 1879-1886.

Garcia, K., & Mann, T. (2003). From 'I wish' to 'I will': social cognitive predictors of behavioural intentions. *Journal of Health Psychology, 8*, 347-360.

Gannon, K., Glover, L., & Abel, P. (2004). Masculinity, infertility, stigma and media reports. *Social Science and Medicine, 59,* 1169-1175.

Geelhoed, D. W., Nayembil, D., Asare, K., Schagen van Leeuwen, J. H., & van, R. J. (2002). Infertility in rural Ghana. *International Journal of Gynaecology and Obstetrics, 79,* 137-142.

Gersh, E. S., & Gersh, I. (1981). *The Biology of Women.* University Park Press.

Gesink Law, D. C., Maclehose, R. F., & Longnecker, M. P. (2007). Obesity and time to pregnancy. *Human Reproduction, 22(2),* 414-420.

Gigerenzer, G., & Edwards, A. (2003). Simple tools for understanding risks: from innumeracy to insight. *British Medical Journal, 327,* 741-744.

Glanz, K., Patterson, R.E., Kristal, A., DiClemente, C. C., Heimendinger, J., Linnan, L., & McLerran, D. F., (1994). Stages of change in adopting healthy diets: fat, fiber, and correlates of nutrient intake. *Health Education & Behavior, 21,* 499-519.

Gleicher, N., Vanderlaan, B., Karande, V., Morris, R., Nadherney, K., & Pratt, D. (1996). Infertility treatment dropout and insurance coverage. *Obstetrics and Gynecology, 88,* 289-293.

Gleicher, N., & Barad, D. (2006). Unexplained infertility: does it really exist? *Human Reproduction, 21(8),* 1951-1955.

Gnoth, C., Godehardt, D., Godehardt, E., Frank-Herrmann, P., & Freundl, G. (2003). Time to pregnancy: results of the German prospective study and impact on the management of infertility. *Human Reproduction, 18(9),* 1959-1966.

Gnoth, C., Godehardt, E., Frank-Herrmann, P., Friol, K., Tigges, J., & Freundl, G. (2005). Definition and prevalence of subfertility and infertility. *Human Reproduction, 20(5),* 1144-1147.

Goddard, E. (2006), *General Household Survey. Smoking and Drinking among Adults, 2005*, Office for National Statistics, London.

Gordley, L. B., Lemasters, G., Simpson, S. R., & Yiin, J. H. (2000). Menstrual disorders and occupational, stress, and racial factors among military personnel. *Journal of Occupational & Environmental Medicine, 42(9),* 871-881.

Gosling, S. D., Vazire, S., Srivastava, S., & John, O. P. (2004). Should we trust web-based studies? A comparative analysis of six preconceptions about internet questionnaires. *American Psychologist, 59(2),* 93-104.

Green, B. B., Weiss, N. S., & Daling, J. R. (1988). Risk of ovulatory infertility in relation to body weight. *Fertility and Sterility, 50(5),* 721-726.

Green, K. C., Armstrong, J. S., & Graefe, A. (2007). *Methods to elicit forecasts from groups: Delphi and prediction markets compared.* Munich Personal RePEc Archive.

Greenhall, E., & Vessey, M. (1990). The prevalence of subfertility: A review of the current confusion and a report of two new studies. *Fertility and Sterility, 54,* 978-83.

Greening, L., Chandler, C. C., Stoppelbein, L., & Robison, L. J. (2006). Risk perception: using conditional versus general base rates for risk communication. *Journal of Applied Social Psychology, 35(10),* 2094-2122.

Greenlee, A. R., Arbuckle, T. E., & Po-Huang, C. (2003). Risk factors for female infertility in an agricultural region. *Epidemiology, 14(4),* 429-236.

Greil, A.L. (1997). Infertility and psychological distress: A critical review of the literature. *Social Science and Medicine, 45(11),* 1679-1704.

Greil, A. L., Leitko, T. A., & Porter, K. L. (1988). Infertility: His and Hers. *Gender and Society, 2(2),* 172-199.

Greil, A. L., & McQuillan, J. (2004). Help-seeking patterns among subfecund women. *Journal of Reproductive and Infant Psychology, 22(4),* 305-319.

Grodstein, F., Goldman, M. B., & Cramer, D. W. (1994). Body mass index and ovulatory infertility. *Epidemiology, 5,* 247-250.

Gronbaek, M., Mortensen, E. L., Mygind, K., Andersen, A. T., Becker, U., Gluud, C., & Sorensen, T. I. (1999). Beer, wine, spirits and subjective health. *Journal of Epidemiology and Community Health, 53,* 721-724.

Grunfeld, E. A., Hunter, M. S., Ramirez, A. J., & Richards, M. A. (2003). Perceptions of breast cancer across the lifespan. *Journal of Psychosomatic Research, 54,* 141-146.

Grunfeld, E. A., Ramirez, A. J., Hunter, M. S., & Richards, M. A. (2002). Women's knowledge and beliefs regarding breast cancer. *British Journal of Cancer, 86,* 1373-1378.

Gunnell, D. J., & Ewings, P. (1994). Infertility prevalence, needs assessment and purchasing. *Journal of Public Health Medicine, 16(1),* 29-35.

Haagen, E. C., Tuil, W., Hendriks, J., de Bruijn, R. P. J., Braat, D. D. M., & Kremer, J. A. M. (2003). Current Internet use and preferences of IVF and ICSI patients. *Human Reproduction, 18(10),* 2073-2078.

Habbema, J. D. F., Collins, J., Leridon, H., Evers, J. L. H., Lunenfeld, B., & te Velde, E. R. (2004). Towards less confusing terminology in reproductive medicine: a proposal. *Human Reproduction, 19(7),* 1497-1501.

Hakim, R. B., Gray, R. H., & Zacur, H. (1998). Alcohol and caffeine consumption and decreased fertility. Fertility and Sterility, 70(4), 632-637.

Hamilton, B. E., Martin, J. A., & Sutton, P. D. (2004). *Births: preliminary data for 2003.* National vital statistics reports. 53(9), November 23rd 2004.

Hammond, C. B., & Riddick, D. H. (1999). Pelvic infections and sexually transmitted diseases. In J. R. Scott, P. J. Di Saia, C. B. Hammond, & W. N. Spellacy (Eds.), *Danforth's Obstetrics and Gynecology* (8th ed. pp. 601-614). Philadelphia. Lippincott Williams & Wilkins.

Hammond, C. B., & Stillman, R. J. (1999). Infertility and assisted reproduction. In J. R. Scott, P. J. Di Saia, C. B. Hammond, & W. N. Spellacy (Eds.), *Danforth's Obstetrics and Gynecology* (8th ed. pp. 601-614). Philadelphia. Lippincott Williams & Wilkins.

Harlow, S. D., & Ephross, S. A. (1995). Epidemiology of menstruation and its relevance to women's health. *Epidemiologic Reviews, 17(2),* 265-286.

Hartgens, F., & Kuipers, H. (2004). Effects of endrogenic-anabolic steroids in athletes. *Sports Medicine, 34(8),* 513-554.

Harwood-Lejeune, A. (2000). Rising Age at Marriage and Fertility in Southern and Eastern Africa. *European Journal of population, 17,* 261-280.

Hassan, M., & Killick, S. R. (2003). Effect of male age on fertility: evidence for the decline in male fertility with increasing age. *Fertility and Sterility, 79(Suppl 3),* 1520-1527.

Hassan, M., & Killick, S. R. (2004). Negative lifestyle is associated with a significant reduction in fecundity. *Fertility and Sterility, 81(2),* 384-392.

Hatch, E. E., & Bracken, M. B. (1993). Association of delayed conception with caffeine consumption. *American Journal of Epidemiology, 138(12),* 1082-1092.

Hawkins, N. A., Berkowitz, Z., & Peipins, L. A. (2007). What does the public know about preventing cancer? Results from the Health Information National Trends Survey (HINTS). *Health Education and Behavior,* doi:10.1177/1090198106296770.

Hay, J., Shuk, E., Cruz, G., & Ostroff, J. (2005). Thinking through cancer risk: characterizing smokers' process of risk determination. *Qualitative Health Research, 15(8),* 1074-1085.

Health Protection Agency. *All new episodes seen at GUM clinics: 1997-2006.* United Kingdom and country specific tables. July 2007.

Heatherley, S. V., Mullings, E. L., Tidbury, M. A., & Rogers, P. J. (2006). Caffeine consumption among a sample of UK adults. *Appetite, 47,* 266.

Hecht, S. S. (1999). Tobacco smoke carcinogens and lung cancer. *Journal of the National Cancer Institute, 91(14),* 1194-1210.

Heiman, G. W. (1999). *Research methods in psychology.* 2nd Edition. New York. Houghton Mifflin Company.

Hepworth, S. J., Schoemaker, M. J., Muir, K. R., Swerdlow, A. J., van Tongeren, M. J. A., & McKinney, P. A. (2006). Mobile phone use and risk of glioma in adults: case-control study. *British Medical Journal, 332,* 883-887.

Hill, D., White, V., Jolley, D., & Mapperson, K. (1988). Self examination of the breast: is it benefical? Meta-analysis of studies investigating breast self examination and extent of disease in patients with breast cancer. *British Medical Journal, 297,* 271-275.

Hillis, S. D., Joesoef, R., Marchbanks, P. A., Wasserheit, J. N., Cates, W. Jr., & Westrom, L. (1993). Delayed care of pelvic inflammatory disease as a risk factor for impaired fertility. *American Journal of Obstetrics & Gynecology, 168(5),* 1503-1509.

Hillis, S. D., Owens, L. M., Marchbanks, P. A., Amsterdam, L. E., & Mac Kenzie, W. R. (1997). Recurrent chlamydial infections increase the risks of hospitalization for ectopic pregnancy and pelvic inflammatory disease. *American Journal of Obstetrics and Gynecology, 176,* 103-107.

Hjollund NH, Jensen TK, Bonde JP, Henriksen TB, Andersson AM, Kolstad HA, Ernst E, Giwercman A, Skakkebaek NE, & Olsen J. (1999). Distress and reduced fertility: a follow-up study of first-pregnancy planners. *Fertility and Sterility, 72(1),* 47-53.

Homan, G. F., Davies, M., & Norman, R. (2007). The impact of lifestyle factors on reproductive performance in the general population and those undergoing infertility treatment: a review. *Human Reproduction Update, 13(3),* 209-223; doi:10.1093/humupd/dml056.

Homburg, R. (2005). Towards less confusing terminology in reproductive medicine. A counter proposal. *Human Reproduction, 20(2),* 316-319.

Home Office (2007). *Tackling drugs.* Changing lives: turning strategy intro reality.

House of Commons Health Committee. *Health - Third Report.* Publications on the internet. Health Committee Publications. 8 March 2005. http://www.parliament.the-stationery-office.com/pa/cm200405/cmselect/cmhealth/252/25202.htm.

Hull, M. G. R., Glazener, C. M. A., Kelly, N. J., Conway, D. I., Foster, P. A., Hinton, R. A., Coulson, C., Lambert, P. A., Watt, E. M., & Desai, K. M. (1985).

Population study of causes, treatment, and outcome of infertility. *British Medical Journal, 291,* 1693-1697.

Hull, M. G. (1992). Infertility treatment: relative effectiveness of conventional and assisted conception methods. *Human Reproduction, 7(6),* 785-796.

Hull, M. G., North, K., Taylor, H., Farrow, A., & Ford, W. C. (2000). Delayed conception and active and passive smoking. The Avon Longitudinal Study of Pregnancy and Childhood Study Team. *Fertility and Sterility, 74(4),* 725-33.

Human Fertilisation & Embryology Authority (HFEA). *Infertility the HFEA guide.* Annual report 2007/2008. [Brochure].

Jamieson, D. J., & Steege, J. F. (1996). The prevalence of dysmenorrhea, dyspareunia, pelvic pain, and irritable bowel syndrome in primary care practices. *Obstetrics & Gynecology, 87,* 55-58.

Janz, N. K., & Becker, M. H. (1984). The health belief model: a decade later. *Health Education Quarterly, 11(1),* 1-47.

Jensen, T. K., Hjollund, N. H., Henriksen, T. B., Scheike, T., Kolstad, H., Giwercman, A., Ernst, E., Bonde, J. P., Skakkebaek, N. E., & Olsen, J. (1998). Does moderate alcohol consumption affect fertility? Follow up study among couples planning first pregnancy. *British Medical Journal, 22; 317(7157),* 505-10.

Joesoef, M. R., Beral, V. Aral, S. O., Rolfs, R. T., & Cramer, D. W. (1993). Fertility and use of cigarettes, alcohol, marijuana and cocaine. *Annals of Epidemiology, 3(6),* 592-594.

Joffe, M. (1997). Time to pregnancy: a measure of reproductive function in either sex. *Occupational and Environmental Medicine, 54,* 289-295.

Joffe, M., Villard, L., Li, Z., Plowman, R., & Vessey, M. (1993). Long-term recall of time-to-pregnancy. *Fertility and Sterility, 60(1),* 99-104.

Joffe, M., Villard, L., Li, Z., Plowman, R., & Vessey, M. (1995). A time to pregnancy questionnaire designed for long term recall: validity in Oxford, England. *Journal of Epidemiology and Community Health, 49,* 314-319.

Joffe, M., Key, J., Best, N., Keiding, N., Scheike, T., & Jensen, T. K. (2005). Studying time to pregnancy by use of a retrospective design. *American Journal of Epidemiology, 162(2),* 115-124.

Jones, R. E. (1997). *Human Reproductive Biology.* 2nd Edition. Academic Press Limited, London.

Juhl, M., Olsen, J., Nybo Anderson, A., & Grønbæk. (2003). Intake of wine, beer and spirits and waiting time to pregnancy. *Human Reproductive, 18(9),* 1967-1971.

Jukic, A. M. Z., Weinberg, C. R., Wilcox, A. J., McConnaughey, D. R., Hornsby, P., & Baird, D. D. (2007). *American Journal of Epidemiology, 167,* 25-33.

Julian-Reynier, C., Welkenhuysen, M., Hagoel, L., Decruyenaere, M., & Hopwood, P. (2003). Risk communication strategies: state of the art and effectiveness in the context of cancer genetic services. *European Journal of Human Genetics, 11,* 725-736.

Juul, S., Karmaus, W., & Olsen, J. (1999). Regional differences in waiting time to pregnancy: pregnancy-based surveys from Denmark, France, Germany, Italy and Sweden. *Human Reproduction, 14(5),* 1250-1254.

The 1996 Kaiser Family Foundation Survey on teens and sex: what they say teens today need to know, and who they listen to. Princeton Survey Research Associates. Menlo Park, California, Henry J. Kaiser Family Foundation, 1996 Jun. 22 p.

Kaplan, B., Nahum, R., Yairi, Y., Hirsch, M., Pardo, J., Yogev, T., & Orvieto, R. (2005). Use of various contraceptive methods and time of conception in a community-based population. *European Journal of Obstetrics & Gynecology and Reproductive Biology, 123,* 72-76.

Karmaus, W., & Juul, S. (1999). Infertility and Subfecundity in population-based samples from Denmark, Germany, Italy, Poland and Spain. *European Journal of Public Health, 9(3),* 229-235.

Kemkes-Grottenthaler, A. (2003). Postponing or rejecting parenthood? Results of a survey among female academic professional. *Journal of Biosocial Science, 35.* 213-226.

Kent, A. (2000). Raising awareness or spreading fear? *British Medical Journal, 321,* 247.

Khadem, N., & Mazlouman, S. J. (2004). Study of endometriosis related infertility, a comparative study. *Acta Medica Iranica, 42(5),* 383-389.

Khan, K. S., Riet, G., Popay, J., Nixon, J., & Kleijnen, J. (2001). Study quality assessment. In: K. S. Khan, G. Riet, J. Glanville, A. J., Sowden, & J. Kleiknen (Eds.). *Undertaking systematic reviews of research on effectiveness: CRD's guidance for those carrying out or commissioning reviews.* CRD Report number 4 (2nd ed.) (pp. 1 – 20). University of York: NHS Centre for Reviews and Dissemination.

Kinney, A., Kline, J., Kelly, A., Reuss, M. J., & Levin, B. (2007). Smoking, alcohol and caffeine in relation to ovarian age during the reproductive years. *Human Reproduction, 22(4),* 1175-1185; doi:10.1093/humrep/del496.

Kleinbaum, D. G., Kupper, L. L., & Morgenstern, H. (1982). *Epidemiologic research: Principles and quantitative methods.* New York; Van Nostrand Reinhold.

Koff, E., Rierdan, J., & Stubbs, M. (1990). Conceptions and misconceptions of the menstrual cycle. *Women and Health, 16(3-4),* 119-136.

Kolstad, H. A., Bonde, J. P., Hjøllund, N. H., Jensen, T. K., Henriksen, T. B., Ernst, E., Giwercman, A., Skakkebaek, N. E., & Olsen, J. (1999). Menstrual cycle pattern and fertility: a prospective follow-up study of pregnancy and early embryonal loss in 295 couples who were planning their first pregnancy. *Fertility and Sterility, 71(3),* 490-496.

Korkia, P., & Stimson, G. V. (1997). Indications of prevalence, practice and effects of anabolic steroid use in Great Britain. *International Journal of Sports Medicine, 18(7),* 557-562.

Kuang, B., Mahutte, N., Heyman, K., & Ouhilal, S. (2006). Fertility and infertility: What do students at an Ivy League college really know? *Fertility and Sterility, 86(3),* S24-S24.

Kuhn, C. M. (2002). Anabolic steroids. *Recent Progress in Hormone Research, 57,* 411-434.

Künzel, W., & Drife, J. (2004). Editors' highlights. *European Journal of Obstetrics Gynecology and Reproductive Biology, 130(2),* 145-147.

Kutscher, E. C., Lund, B. C., & Perry, P. J. (2002). Anabolic steroids a review for the clinician. *Sports Medicine, 32(5),* 285-296.

La Rochebrochard, E., & Thonneau, P. (2003). Paternal age ≥ 40 years: an important risk factor for infertility. *American Journal of Obstetrics and Gynecology, 189(4),* 901-905.

Lakha, F., & Glasier, A. (2006). Unintended pregnancy and use of emergency contraception among a large cohort of women attending for antenatal care or abortion in Scotland. *The Lancet, 368,* 1782-1787.

Lalos, O. (1988). Risk factors for tubal infertility among infertile and fertile women. *European Journal of Obstetrics & Gynecology and Reproductive Biology, 29,* 129-136.

Lamb, E. J., & Leurgans, S. (1979). Does adoption affect subsequent fertility? *American Journal of Obstetrics and Gynecology, 134(2),* 138-44.

Lamb, R., & Joshi, M. S. (1996). The stage model and processes of change in dietary fat reduction. *Journal of Human Nutrition and Dietetics, 6,* 43-53.

Lampic, C., Svanberg, A. S., Karlström, P., & Tydén, T. (2006). Fertility awareness, intentions concerning childbearing, and attitudes towards parenthood among female and male academics. *Human Reproduction, 21(2),* 558-564.

Lampman, C., & Dowling-Guyer, S. (1995). Attitudes toward voluntary and involuntary childlessness. *Basic and Applied Social Psychology, 17(1&2),* 213-222.

Land, J. A., & Evers, J. L. (2002). Chlamydia infection and subfertility. *Clinical Obstetrics & Gynaecology, 16(6),* 901-912.

Lancastle, D., & Boivin, J. (2005). Dispositional optimism, trait anxiety, and coping: unique or shared effects on biological response to fertility treatment? *Health Psychology, 24(2),* 171-8.

Langdridge, D., Connolly, K., & Sheeran, P. (2000). Reasons for wanting a child: a network analytic study. *Journal of Reproductive and Infant Psychology, 18(4),* 321-338.

Langdridge, D., Connolly, K., & Sheeran, P. (2005). Understanding the reasons for parenthood. *Journal of Reproductive and Infant Psychology, 23(2),* 121-133.

Lansac, L. (1995). Delayed parenting. Is delayed childbearing a good thing? *Human Reproduction, 10(5),* 1099-1036.

Larsen, U. (2000). Primary and secondary infertility in sub-Saharan Africa. *International Journal of Epidemiology, 29,* 285-291.

Larsen, U. (2005). Research on infertility: which definition should we use? *Fertility and Sterility, 83,* 846-852.

Larsson, M., Eurenius, K., Westerling, R., & Tydén, T. (2004). Emergency contraceptive pills in Sweden: evaluation of an information campaign. *International Journal of Obstetrics and Gynaecology, 111,* 820-827.

Last, J. M. (1995). *A dictionary of epidemiology.* 3rd Edition. A handbook sponsored by the I.E.A. Oxford University Press.

Lauver, D., & Tak, Y. (1995). Optimism and coping with a breast cancer symptom. *Nursing Research, 44,* 202-207.

Lebo, H. (2004). First Release of Findings from the UCLA World Internet Project shows significant 'digital gender gap' in many countries; at: http://newsroom.ucla.edu/portal/ucla/First-Release-of-Findings-From-4849.aspx?RelNum=4849 (last accessed September 2008).

Lipkus, I. M., & Hollands, J. G. (1999). The visual communication of risk. *Journal of the National Cancer Institute Monographs, 25,* 149-163.

Litt, D. M., Tennen, H., & Affleck, G. (1992). Coping and cognitive factors in adaptation to in vitro fertilization failure. *Journal of Behavioral Medicine, 15,* 171-187.

Liu, J., Larsen, U., & Wyshak, G. (2005). Prevalence of primary infertility in China: in-depth analysis of infertility differentials in three minority province/autonomous regions. *Journal of Biosocial Science, 37,* 55-74.

Lockwood, P. (2003). Drawbacks and benefits of cardiovascular risk tools. *Cardiology in general practice, 10(2),* 155-158.

Lunenfeld, B., & Van Steirteghem, A. (2004). Infertility in the third millennium: implications for the individual, family and society: Condensed Meeting Report from the Bertarelli Foundation's Second Global Conference. *Human Reproduction Update, 10(4),* 317-326.

Maheshwari, A., Hamilton, M., & Bhattacharya, S. (2008). Effect of female age on the diagnostic categories of infertility. *Human Reproduction, 23(3),* 538-542.

Mohllajee, A. P., Curtis, K. M., Morrow, B., & Marchbanks, P. A. (2007). Pregnancy intention and its relationship to birth and maternal outcomes. *Obstetrics and Gynecology, 109(3),* 678-689.

Mahoney, C. A., Thombs, D. L., Ford, O. J. (1995). Health belief and self-efficacy models: their utility in explaining college student condom use. *AIDS Education and Prevention, 7(1),* 32-49.

Mahmood, T. A., & Templeton, A. (1991). Prevalence and genesis of endometriosis. *Human Reproduction, 6(4),* 544-549.

Maibach, E. W., Abroms, L. C., & Marosits, M. (2007). Communication and marketing as tools to cultivate the public's health: a proposed "people and places" framework. *BioMed Central Public Health, 7(88),* doi:10.1186/1471-2458-7-88.

Malcolm, C. E., & Cumming, D. C. (2004). Follow-up of infertile couples who dropped out of a specialist fertility clinic. *Fertility and Sterility, 81(2),* 269-270.

Malik, A., Jain, S., Hakim, S., Shukla, I., & Rizvi, M. (2006). Chlamydia trachomatis infection & female infertility. *Indian Journal of Medical Research, 123,* 770-775.

Mann, C. J. (2003). Observational research methods. Research design II: cohort, cross sectional, and case-control studies. *Emergency Medicine Journal, 20,* 54-60.

Marchbanks, P. A., Peterson, H. B., Rubin, G. L., & Wingo, P. A. (1989). Research on infertility: definition makes a difference. *American Journal of Epidemiology, 130(2),* 259-267.

Marteau, T. M., & Lerman, C. (2001). Genetic risk and behavioural change. *British Medical Journal, 322,* 1056-1059.

McClure, J. B. (2002). Are biomarkers useful treatment aids for promoting health behaviour change? An empirical review. *American Journal of Preventive Medicine, 22(3),* 200-207.

McGlothlin, W. H. (1972). Marijuana: an analysis of use, distribution and control. *Contemporary Drug Problems, 1,* 467-500.

McGlothlin, W. H. (1975). Drug use and drug abuse. *Annual Review of Psychology, 26,* 45-64.

McClenahan, C., Shevlin, M., Adamson, G., Bennett, C., & O'Neill, B. (2007). Testicular self-examination: a test of the health belief model and the theory of planned behaviour. *Health Education Research, 22(2),* 272-284.

McCormack, W. M. (1994). Pelvic inflammatory disease. *New England Journal of Medicine, 330,* 115-119.

Meheus, A., Reniers, J., & Colletet, M. (1986). Determinants of infertility in Africa. *African Journal of Sexually Transmitted Diseases, 2,* 31-35.

Miller, S. M. (1987). Monitoring and blunting; validation of a questionnaire to assess styles of information-seeking under threat. *Journal of Personality and Social Psychology, 52,* 345-353.

Miller, W. C., Ford, C. A., Morris, M., Handcock, M. S., Schmitz, J. L., Hobbs, M. M., Cohen, M. S., Harris, K. M., & Udry, J. R. (2004). Prevalence of chlamydial ad gonococcal infections among young adults in the United States. *Journal of the American Medical Association, 291(18),* 2229-2236.

Miller, W. R., & Rollnick, S. *Motivational interviewing preparing people for change.* 2nd edition. New York: Guildford Press, 2002.

Ministry of Agriculture, Fisheries and Food (MAFF) (1998). *Survey of caffeine and other methylxanthines in energy drinks and other caffeine containing products* (updated). Food Surveillance Information Sheet No. 144 (No. 103 revised). London

"The Misuse of Drugs Act 1971 (Modification)(No. 2) Order 2003 (SI 2003 No. 3201)". Statutory Instrument. Ministry of Justice (2003-12-10). Retrieved on 29/08/08.

Mobile phone use 'linked to tumour'. (2:10AM GMT 26 Jan 2007). *The Telegraph.* http://www.telegraph.co.uk/news/uknews/1540496/Mobile-phone-use-'linked-to-tumour'.html.

Molteni, N., Caraceni, M. P., Bardella, M. T., Ortolani, S., Gandolini, G. G., & Bianchi, P. (1990). Bone mineral density in adult celiac patients and the effect of gluten-free diet from childhood. *American Journal of Gastroenterology, 85(1),* 51-53.

Morgan, J. F. (1999). Eating disorders and reproduction. *The Australian and New Zealand Journal of Obstetrics and Gynaecology, 39(2),* 167-173.

Morice, P., Josset, P., Chapron, C., & Dubuisson, J. B. (1995). History of Infertility. *Human Reproduction Update, 1(5),* 497-504.

Mosher, W. D., & Aral, S. O. (1991). Testing for sexually transmitted diseases among women of reproductive age: United States, 1988. *Family Planning Perspectives, 23(5),* 216-21.

Mosher, W. D., & Bachrach, C. A. (1996). Understanding U.S fertility: continuity and change in the National Survey of Family Growth, 1988-1995. *Family Planning Perspectives, 28(1),* 4-12.

Mueller, B. A., Daling, J. R., Weiss, N. S., & Moore, D. E. (1990). Recreational drug use and the risk of primary infertility. *Epidemiology, 1(3),* 195-200.

Nachtigall, R.D., Becker, G., & Wozny, M. (1992). The effects of gender-specific diagnosis on men's and women's response to infertility. *Fertility and Sterility, 57,* 113-121.

National Cancer Institute (1997). Changes in cigarette-related disease risks and their implications for prevention and control. *Smoking and Tobacco Control Monograph 8,* Rockville, Maryland.

National Health Service (NHS) centre for reviews and dissemination (1998). Effective Health Care. *Cholesterol and coronary heart disease: screening and treatment*, Volume 4 (no 1), University of York. Pages 1 – 16. ISSN: 0965-0288.

Newton, C. R., Sherrard, W., & Glavac, I. (1999). The fertility problem inventory: measuring perceived infertility-related stress. *Fertility and Sterility, 72(1),* 54-62.

Newcomb, P. A., & Carbone, P. P. (1992). The health consequences of smoking. Cancer. *The Medical clinics of North America, 76(2),* 305-31.

New Zealand Herpes Foundation (2007). *Herpes – Myth vs. Fact.* http://www.herpes.org.nz/patient/myths.htm).

Ng, T. P., Tan, N. C., & Wansaicheong, G. K. (1992). A prevalence study of dysmenorrhoea in female residents aged 15-54 years in Clementi Town, Singapore. *Annals of the Academy of Medicine, 21(3),* 323-327.

Nguyen, R. H. N., & Wilcox, A. L. (2005). Terms in reproductive and perinatal epidemiology: I. Reproductive terms. *Journal of Epidemiology and Community Health, 59,* 916-919.

National Institute for Clinical Excellence (NICE): Clinical Guideline (2003). Antenatal Care.

National Institute for Clinical Excellence (NICE): Clinical Guideline (2004). *Fertility: assessment and treatment for people with fertility problems.*

Nielsen/NetRatings Inc, authors. Internet usage statistics for the month of December 2001 (United Kingdom). [2008 September 15]. http://www.nielsen-netratings.com/resources.jsp?section=pr_netv&nav=1.

Noar, S. M. (2006). A 10-year retrospective of research in health mass media campaigns: where do we go from here? *Journal of Health Communication, 11,* 21-42.

Office for National Statistics (ONS). *Average age of mother at childbirth: Social Trends 33.* ST33219. 2000. National Statistics: London.

Office for National Statistics (ONS). *Average age of mother at childbirth: Social Trends 34.* ST340221. 2004. National Statistics: London.

Office for National Statistics (ONS)a. *Annual Population Survey (2004).* National Statistics: London.

Office for National Statistics (ONS)b. *Cancer statistics registrations: Registrations of cancer diagnosed in 2004, England.* Series MB1 No.35, National Statistics: London.

Office for National Statistics (ONS). *Survey of psychiatric morbidity among adults in Great Britain,* 2006. National Statistics: London.

Office for National Statistics (ONS). *Level of Highest Qualification Held by Adults: England,* 2008. National Statistics: London.

Okoli, C., & Pawlowski, S. D. (2004). The Delphi method as a research tool: an example, design considerations and applications. *Information and Management, 42(1),* 15-29.

Okonofua, F. E. (June, 2003). Desiring children in poorly resourced countries (Abstract). *Human Reproduction 18 xviii49 Supp. 1,* June 2003.

Okonofua, F. E., Harris, D., Odebiyi, A., Kane, T., & Snow, R. C. (1997). The social meaning of infertility in Southwest Nigeria. *Health Transition Review 7,* 205-220.

Olive, D. L., & Schwartz, L., B. (1993). Medical Progress: Endometriosis. *The New England Journal of Medicine, 328(24),* 1759-1769.

Oliveria, S. A., Christos, P. J., Halpern, A. C., Fine, J. A., Barnhill, R., & Berwick, M. (1999). Patient knowledge, awareness, and delay in seeking medical attention for malignant melanoma. *Journal of Clinical Epidemiology, 52(11),* 1111-1116.

Olsen, J. (1991). Cigarette smoking, tea and coffee drinking, and subfecundity. *American Journal of Epidemiology, 133(7),* 734-739.

Olsen, J., KuppersChinnow, M., & Spinelli, A. (1996). Seeking medical help for subfecundity: A study based upon surveys in five European countries. *Fertility and Sterility, 66(1),* 95-100.

Olsen, J., Bolumar, F., Boldsen, J., & Bisanti, L. (1997). Does moderate alcohol intake reduce fecundability? A European multicenter study on infertility and

subfecundity. *Alcoholism: Clinical and Experimental Research, 21(2),* 206-212.

Olsen, J., Basso, O., Spinelli, A., & Kuppers-Chinnow, M. (1998). Correlates of care seeking for infertility treatment in Europe. *European Journal of Public Health, 8,* 15-20.

Olsen, J., Juul, S., & Basso, O. (1998). Measuring time to pregnancy. Methodological issues to consider. *Human Reproduction, 13(7),* 1751-1756.

Orchard, J. W., Fricker, P. A., White, S. L., Burke, L. M., & Healey, D. J. (2006). The use and misuse of performance-enhancing substances in sport. *The Medical Journal of Australia, 184(3),* 132-136.

Park, K. (2002). Stigma management among the voluntarily childless. *Sociological Perspectives, 45(1),* 21-45.

Park, B., McPartland, J. M., & Glass, M. (2004). Cannabis, cannabinoids and reproduction, *Prostaglandins, Leukotrienes and Essential Fatty Acids, 70(2),* 189-197.

Patterson, R. E., Neuhouser, M. L., Hedderson, M. M., Schwartz, S. M., Standish, L. J., & Bowen, D. J. (2003). Changes in diet, physical activity, and supplement use among adults diagnosed with cancer. *Journal of the American Dietetic Association, 103(3),* 323-328.

Peterman, T. A., Lin, L. S., Newman, D. R., Kamb, M. L., Bolan, G., Zenilman, J., Douglas, J. M., Rogers, J., & Malotte, C. K. (2000). Does measured behavior reflect STD risk?: an analysis of data from a randomised controlled behavioural intervention study. *Sexually Transmitted Diseases, 27(8),* 446-451.

Petrie, A., & Sabin, C. (2000). *Medical statistics at a glance.* Oxford. Blackwell Science Ltd.

Petticrew, M., & Roberts, H. (2006). *Systematic reviews in the social sciences. A practical guide.* Oxford. Blackwell Science Ltd.

Peronace, L. A., Boivin, J., & Schmidt, L. (2007). Patterns of suffering and social interactions in infertile men: 12 months after unsuccessful treatment. *Journal of Psychosomatic Obstetrics & Gynecology, 28(2),* 105-114.

Pescosolido, B. A. (2007). *Help-seeking. In Blackwell Encylopedia of Sociology.* Ed. G. Ritzer. Malden, MA; Oxford: Blackwell Publishing. Page 2104-2107.

Philippov, O. S., Radionchenko, A. A., Bolotova, V. P., Voronovskaya, N. I., & Potemkina, T. V. (1998). Estimation of the prevalence and causes of infertility in western Siberia. *Bulletin of the World Health Organization, 76(2),* 183-7.

Pinborg, A., Schmidt, L., & Nyboe Andersen, A. (2007). Crude 5-year follow-up on delivery and adoption rates among 1338 new couples treated with ART (abstract). *Human Reproduction, 22(Suppl. 1)*:i30.

Poikolainene, K., & Vartiainen, E. (1999). Wine and good subjective health. *American Journal of Epidemiology, 150(1),* 47-50.

Population Council; Macro International (1997a). Central African Republic 1994-1995: results from the Demographic and Health Survey (DHS]). *Studies in Family Planning, 28(1),* 62-66.

Population Council; Macro International (1997b). Eritrea 1995: results from the Demographic and Health Survey (DHS]). S*tudies in Family Planning, 28(4),* 336-340.

Population Council; Macro International (1997c). Mali 1995-1996: results from the Demographic and Health Survey (DHS]). *Studies in Family Planning, 28(4),* 341-345.

Povey, R., Conner, M., Sparks, P., James, R., & Shepherd, R. (1999). A critical examination of the application of the Transtheoretical Model's stages of change to dietary behaviours. *Health Education Research, 14(5),* 641-651.

Prochaska, J. O., DiClemente, C. C., Velicer, W. F., Ginpil, S., & Norcross, J. C. (1985). Predicting change in smoking status for self-changers. *Addictive Behaviors, 10,* 395-406.

Prochaska, J. O., DiClemente, C. C., & Norcross, J. C. (1992). In search of how people change. Applications to addictive behaviors. *American Psychologist, 47(9),* 1102-1114.

Pullon, S., Reinken, J., & Sparrow, M. (1988). Prevalence of dysmenorrhoea in Wellington women. *The New Zealand Medical Journal, 101(839),* 52-54.

Quinn, M., Babb, P., Kirby, E.A., & Brock, A. (2000). Registrations of cancer diagnosed in 1994-1997, England & Wales in Health Statistics Quarterly. Office for National Statistics. *Health Statistics Quarterly, 7,* 71-82.

Ramlau-Hansen, C. H., Thulstrup, A. M., Nohr, E. A., Bonde, J. P., Sorensen, T. I. A., & Olsen, J. (2007). Subfecundity in overweight and obese couples. *Human Reproduction, 22(6),* 1634-1637.

Randolph, W. & Viswanath, K. (2004). Lessons learned from public health mass media campaigns: marketing health in a crowded media world. *Annual Review of Public Health, 25,* 419-437.

Ranke, M. B., & Bierich, J. R., (1986). Treatment of growth hormone deficiency. *Clinics in Endocriniology and Metabolism, 15(3),* 495-510.

Ratzan, S. C. (2008). Communicating and advancing health with research. *Journal of Health Communication, 13,* 105-106.

Ray, J. G., Singh, G., & Burrows, R. F. (2004). Evidence of suboptimal use of periconceptional folic acid supplements globally. *British Journal of Obstetrics and Gynaecology, 111,* 399-408.

Ray, K. (2006). Chlamydia trachomatis & infertility. Commentary. *Indian Journal of Medical Research, 123,* 730-734.

Remennick, L. (2000). Childless in the land of imperative motherhood: stigma and coping among infertile Israeli women. *Sex Roles, 43,* 821-841.

Rhoton-Vlasak, A. (2000). Infections and infertility. *Primary Care Update Obstetrics and Gynecology, 7(5),* 200-206.

Rice, F., Lewis, A., Harold, G., van den Bree, M., Boivin, J., Hay, D. F., Owen, M. J., & Thapar, A. Agreement between maternal report and antenatal records for a range of pre and peri-natal factors: the influence of maternal and child characteristics. *Early Human Development, 83,* 497-504.

Rich-Edwards, J. W., Golman, M. B., Willett, W. C., Hunter, D. J., Stampfer, M. J., Colditz, G. A., & Manson, J. E. (1994). Adolescent body mass index and infertility caused by ovulatory disorder. *General Obstetrics and Gynecology, 171(1),* 171-177.

Richards, M. A., Smith, P., Ramirez, A. J., Fentiman, I. S., & Rubens, R. D. (1999). The influence of survival of delay in the presentation and treatment of symptomatic breast cancer. *British Journal of Cancer, 79,* 858-864.

Richards, M. A., Westcombe, A. M., Love, S. B., Littlejohns, P., & Ramirez, A. J. (1999). Influence of delay on survival in patients with breast cancer: a systematic review. *The Lancet, 353,* 1119-1126.

Rimm, E. B., Stampfer, M. J., Giovannucci, E., Ascherio, A., Spiegelman, D., Colditz, G. A., & Willett, W. C. (1995). Body size and fat distribution as predictors of coronary heart disease among middle-aged and older US men. *American Journal of Epidemiology, 141(12),* 1117-1127.

Ristvedt, S. L., & Trinkaus, K. M. (2005). Psychological factors related to delay in consultation for cancer symptoms. *Psycho-oncology, 14(5),* 339-50.

Rizk, B., Atterbury, J. L., & Groome, L. J. (1996). Reproductive risks of cocaine. *Human Reproduction Update, 2(1),* 43-55.

Row, S., & Man, L. (2006). *Drug misuse declared: findings from the 2005/2006 British Crime Survey.* Home Office Statistics Bulletin. ISSN 1358-510X.

Rowland, A. S., Baird, D. D., Long, S., Wegienka, G., Harlow, S. D., Alavanja, M., & Sandler, D. (2002). Influence of medical conditions and lifestyle factors on the menstrual cycle. *Epidemiology, 13(6),* 668-674.

Rosenstock, I. (1990). The health belief model: explaining health behavior through expectancies. In K. Glanz, F. M. Lewis, B. Rimers (Eds.), *Health Behavior and Health Education.* San Francisco, CA, Jossey-Bass.

Rosenthal, R., Rosnow, R. L., & Robin, D. B. (1999). *Contrast and Effect Sizes in Behavioural Research: A Correlational Approach:* Cambridge University Press.

Ross, J. (2008). PID. *British Medical Journal Clinical Evidence, 3,* 1606-1618.

Rostad, B., Schei, B., & Sundby, J. (2006). Fertility in Norwegian women: results from a population-based health survey. *Scandinavian Journal of Public Health, 34,* 5-10.

Roth, L. K., & Taylor, A. H. (2001). Risks of smoking to reproductive health: Assessment of women's knowledge. *American Journal of Obstetrics and Gynecology, 184(5),* 934-939.

Rowe, G., & Wright, G. (1999). The Delphi technique as a forecasting tool: issues and analysis. *International Journal of Forecasting, 15,* 353-375.

Rowe, P. J., Comhaire, F. H., Hargreave, T. B., & Mellows, H. J. (1993). *WHO manual for the standard investigation and diagnosis of the infertile couple.* Cambridge: Cambridge University Press, 1993.

Rowland, A. S., Baird, D. D., Long, S., Wegienka, G., Harlow, S. D., Alavanja, M. & Sandler, D. P. (2002). Influence of medical conditions and lifestyle factors on the menstrual cycle. *Epidemiology, 13(6),* 668-674.

Royal Commission on New Reproductive Technologies (1993). *Proceed with Care: Final Report of the Royal Commission on New Reproductive Technologies.* Ministry of Government Services Canada, Ottawa. (P 179-198).

Ryan, G., Maassen, R., Dokras, A., Syrop, C., & VanVoorhis, B. (2005). A majority of women delay childbearing in both fertile and infertile groups despite understanding the risks of ageing on fertility. *Fertility and Sterility, 84,* S73-S73.

Ryan, R., Hill, S., Broclain, D., Horey, D., Oliver, S., & Prictor, M. Cochrane consumers and communication review group. Study Quality Guide. March 2007. www.latrobe.edu.au/cochran/resources.html (last accessed 28 September 2008).

Sabates, R., & Feinstein, L. *Education, training and the take-up of preventative health care.* June 2004. Wider Benefits of Learning Research Report No. 12.

Sallam, H. N. (2008). Infertility in developing countries: funding the project. *Human Reproduction, 10(6),* doi: 10.1093/humrep/den144.

Sander W (1995) Schooling and quitting smoking. *Review of Economic Statistics 77(1),* 191-199.

Scheier, M. F., & Carver, C. S. (1985). Optimism, Coping, and Health - Assessment and Implications of Generalized Outcome Expectancies. *Health Psychology, 4(3),* 219-247.

Scheier, M. F., & Carver, C. S. (1987). Dispositional optimism and physical well-being: The influence of generalized outcome expectancies on health. *Journal of Personality, 55(2),* 169-210.

Schenken, R. S. (1999). Endometriosis. In J. R. Scott, P. J. Di Saia, C. B. Hammond, & W. N. Spellacy (Eds.), *Danforth's Obstetrics and Gynecology* (8th ed. pp. 669 – 676). Philadelphia. Lippincott Williams & Wilkins.

Schmidt, L., & Munster, K. (1995). Infertility, involuntary infecundity, and the seeking of medical advice in industrialized countries 1970-1992: a review of concepts, measurements and results. *Human Reproduction, 10(6),* 1407-1418.

Schmidt, L., Munster, K., & Helm, P. (1995). Infertility and the seeking of infertility treatment in a representative population. *British Journal of Obstetrics and Gynaecology, 102(12),* 978-984.

Schmidt, L., Holstein, B. E., Christensen, U., & Boivin, J. (2005). Communication and coping as predictors of fertility problem stress: cohort study of 816 participants who did not achieve a delivery after 12 months of fertility treatment. *Human Reproduction, 20(199),* 3248-3256.

Schenker, J. G., Meirow, D., & Schenker, E. (1992). Stress and human reproduction. European *Journal of Obstetrics Gynecology and Reproductive Biology, 16; 45(1),* 1-8.

Scholes, D., Stergachis, A., Heidrich, F. E., Andrilla, H., Holmes, K. K., & Stamm, W. E. (1996). Prevention of pelvic inflammatory disease by screening for cervical chlamydial infection. *The New England Journal of Medicine, 334,* 1362-1366.

Sciarra, J. J. (1997). Sexually transmitted diseases: global importance. *International Journal of Gynecology and Obstetrics, 58,* 107-119.

Scott, I. Interpreting risks and ratios in therapy trials. *Australian Prescriber, 31(1),* 12-16.

Senderowitz, J. (1999). *Making reproductive health services youth friendly.* Research, Program and Policy Series. February, 1999. Focus on Young Adults, Washington.

Sher, K., & Mayberry, J. (1994). Female fertility, obstetric and gynaecological history in coeliac disease: a case control study. *Gastroenterology, 55,* 243-246.

Sheeran P & Abraham C (1996) The health belief model. In M. Conner & P. Norman (Eds.), *Predicting Health Behaviour*. Buckingham, UK: Open University Press, 1996, pp. 23-61.

Shields, P. G. (2002). Molecular epidemiology of smoking and lung cancer. *Oncogene, 21,* 6870-6876.

Siahpush, M., McNeill, A., Hammond, D., & Fong, G. T. (2006). Socioeconomic and country variations in knowledge of health risks of tobacco smoking and toxic constituents of smoke: results from the 2002 International Tobacco Control (ITC) Four Country Survey. *Tobacco Control, 15(3),* 65-70.

Sin, J., & Reid, H. (1999). Statistical inference by confidence intervals: issues of interpretation and utilization. *Physical Therapy, 79(2),* 186-195.

Sjöberg, L. (1997). Explaining risk perception: an empirical evaluation of cultural theory. *Risk Decision and Policy, 2(2),* 113-130.

Sjöberg, L. (2000). Factors in risk perception. *Risk Analysis, 20(1),* 1-12.

Skoog Svanberg, A., Lampic, C., Karlström, P., & Tydén, T. (2006). Attitudes toward parenthood and awareness of fertility among postgraduate students in Sweden. *Gender Medicine, 3(3),* 187-195.

Speroff, L., Glass, H., & Kase, G. (1994). *Clinical gynecologic endocrinology and infertility.* (5th edition). Baltimore: Williams & Wilkins.

Small, C. M., Manatunga, A. K., Klein, M., Feigelson, H. S., Dominguez, C. E., Mcchesney, R., & Marcus, M. (2006). Menstrual cycle characteristics: associations with fertility and spontaneous abortion. *Epidemiology, 17(1),* 52-60.

Smeenk, J. M. J., Verhaak, C. M., Eugster, A., van Minnen, A., Zielhuis, G. E., & Braat, D. D. M. (2001). The effect of anxiety and depression on the outcome of in-vitro fertilization. *Human Reproduction, 16(7),* 1420-1423.

Smith, L. K., Pope, C., & Botha, J. L. (2005). Patients' help-seeking experiences and delay in cancer presentation: a qualitative synthesis. *The Lancet, 366,* 825-831.

Snyder, L. (2007). Health communication campaigns and their impact on behavior. *Journal of Nutrition Education and Beahvior, 39(2),* S32-S40.

Sobreiro, B. P., Lucon, A. M., Pasqualotto, F. F., Hallak, J., Athayde, K. S., & Arap, S. (2005). Semen analysis in fertile patients undergoing vasectomy: reference values and variations according to age, length of sexual abstinence,

seasonality, smoking habits and caffeine intake. *Sao Paulo Medical Journal, 123,* 161-166.

Stanton, C. K., & Gray, R. H. (1995). Effects of caffeine consumption on delayed conception. *American Journal of Epidemiology, 142(12),* 1322-1329.

Stein, Z., & Susser, M. (2000). The risks of having children in later life. *The Western Journal of Medicine, 173(5),* 295–296.

Stephen, E. H., & Chandra, A. (1998). Updated projections of infertility in the United States: 1995-2025. *Fertility and Sterility, 70(1),* 30-34.

Stephen, E. H., & Chandra, A. (2000). Use of infertility services in the United States: 1995. *Family Planning Perspectives, 32(3),* 132-137.

Stephen, E. H., & Chandra, A. (2006). Declining estimates of infertility in the United States: 1982-2002. *Fertility and Sterility, 86(3),* 516-523.

Steptoe, P. C., & Edwards, R. G. (1978). Birth after the reimplantation of a human embryo. *The Lancet, ii,* 366.

Stevens-Simons, C., Kelly, L., & Kulick, R. (2001). A village would be nice but...it takes a long-acting contraceptive to prevent repeat adolescent pregnancies. *American Journal of Preventive Medicine, 21(1),* 60-65.

Stewart, A. L., Hays, R. D., & Ware, J. E. (1988). The MOS short form general health survey: Reliability and validity in a patient population. *Medical Care, 26,* 724-735.

Stoleru, S., Teglas, J. P., Fermanian, J., & Spira, A. (1993). Psychological factors in the aetiology of infertility: a prospective cohort study. *Human Reproduction, 8(7),* 1039-1046.

Strauss, R. H., Liggett, M. T., & Lanese, R. R. (1985). Anabolic steroid use and perceived effects in ten weight-trained women athletes. *Journal of American Medical Association, 253,* 2871-2873.

Strauss, R. H., & Yesalis, C. E. (1991). Anabolic steroids in the athlete. *Annual Review of Medicine, 42,* 449-457.

Straus, S. E., & Sackett, D. L. (1998). Getting research findings into practice. Using research findings in clinical practice. *British Medical Journal 317,* 339-342.

Stretcher, V. (2007). Internet methods for delivering behavioral and health-related interventions (eHealth). *Annual Review of Clinical Psychology, 3,* 53-76.

Strychar, I. M., Champagne, F., Ghadirian, P., Bonin, A., Jenicek, M., & Lasater, T. M. (1998). Impact of receiving blood cholesterol test results on dietary change. *American Journal of Preventive Medicine, 14,* 103-110.

Sundby, J., Mboge, R., & Sonko, S. (1998). Infertility in the Gambia: Frequency and health care seeking. *Social Science and Medicine, 46(7),* 891-899.

Survey Tracker for Windows, Training Technologies Inc, Cincinnati, Ohio, 2007.

Sutton, S. (1998). How ordinary people in Great Britain perceive the health risks of smoking. *Journal of Epidemiology and Community Health, 52,* 338-339.

Svanberg, L., & Ulmsten, U. (1981). The incidence of primary dysmenorrhea in teenagers. *Archives of Gynecology and Obstetrics, 230(3),* 173-177.

Swasdio, K., Rugpao, S., Tansathit, T., Uttavichai, C., Jonqusuk, P., Vutayavanich, T., Oranratanachai, A., Pruthitada, N., Peerakom, S., Ittipunkul, W., Rowe, P. J., & Ward, M. E. (1996). The association of chlamydia trachomatis/gonococcal infection and tubal factor infertility. *The Journal of Obstetrics and Gynaecology Research, 22(4),* 331-340.

Synder, L. B. (2007). Health communication campaigns and their impact on behvaior. *Journal of Nutrition Education and Behavior, 39,* S32-S40.

Tabachnick, B. G., & Fidell, L. S. (2001). *Using multivariate statistics.* Allyn and Bacon, University of Michigan.

Talih, F., fatal, O., & Malone, J. R. (2007). Anabolic steroid abuse: psychiatric and physical costs. *Cleveland Clinic Journal of Medicine, 74(5),* 341-352.

Taylor, A. (2003). ABC of subfertility: Extend of the problem. *British Medical Journal, 327,* 434-436.

Taylor, E., & Gomel, V. (2008). The uterus and fertility. *Fertility and Sterility, 89(1),* 1-16.

Taylor, P. J., & Collins, J. A. (1992). *Unexplained infertility.* Oxford Medical Publications. Oxford. Oxford University Press.

Templeton, A., Fraser, C., & Thompson, B. (1990). The Epidemiology of Infertility in Aberdeen. *British Medical Journal, 301(6744),* 148-152.

Terry, D. J., & Hynes, G. J. (1998). Adjustment to a low-control situation: Re-examining the role of coping responses. *Journal of Personality and Social Psychology, 74(4),* 1078-1092.

Te Velde, E. R., Eijkemans, R., & Habbema. (2000). Variation in couple fecundity and time to pregnancy, an essential concept in human reproduction. *The Lancet, 355(3),* 1928-1929.

Te Velde, E. R., & Pearson, P. L. (2002). The variability of female reproductive ageing. *Human Reproduction Update, 8(2),* 141-154.

Thonneau, P., Quesnot, S., Ducot, B., Marchand, S., Fignon, A., Lansac, J., & Spira, A. (1992). Risk factors for female and male infertility: results of a case-control study. *Human Reproduction, 7(1),* 55-58.

Tinker, T. L. (1996). Recommendations to improve health risk communication: lessons learned from the U.S. public health service. *Journal of Health Communication, 1,* 197-217.

Tjønneland, A., Grønbæk, M., Stripp, C., & Overvad, K. (1999). Wine intake and diet in a random sample of 48763 Danish men and women. *American Journal of Clinical Nutrition, 69,* 49-54.

Tolstrup, J. S., Kjær, S. K., Holst, C., Sharif, H., Munk, C., Osler, M., Schmidt, L., Nybo Andersen, A., & Grønbæk, M. (2003). Alcohol use as predictor for infertility in a representative population of Danish women. *Acta Obstetricia et Gynecologica Scandinavica, 82(8),* 744-749.

Tussing, L., & Chapman-Novakosfski, C. (2005). Osteoporosis prevention education: behaviour theories and calcium intake. *Journal of the American Dietetic Association, 105(1),* 92-97.

Tversky, A. A., & Kahneman, D. (1981). The framing of decisions and the psychology of choice. *Science, 211,* 453-458.

Tyden, T., Svanberg, A. S., Karlstrom, P. O., Lihoff, L., & Lampic, C. (2006). Female university students' attitudes to future motherhood and their understanding about fertility. *European Journal of Contraception and Reproductive Health Care, 11(3),* 181-9.

Unisa, S. (1999). Childlessness in Andhra Pradesh, India: Treatment-Seeking and Consequences. *Reproductive Health Matters, 7,* 54-64.

Urbach, D. R., Marrett, L. D., Kung, R., & Cohen, M. M. (2001). Association of perforation of the appendix with female tubal infertility. *American Journal of Epidemiology, 153(6),* 566-571.

Vayena, E., Rowe, P. J., & Griffin, P. D. (Eds.) (2001 September) *Medical, ethical & social aspects of assisted reproduction. Current practices & controversies in assisted reproduction:* Report of a WHO meeting, 2001: Geneva, Switzerland.

van Balen, F. (2005). Late parenthood among subfertile and fertile couples: motivations and educational goals. *Patient Education and Counseling, 59,* 276-282.

van Balen, F., Verdurmen, J., & Ketting, E. (1997a). Age, the desire to have a child and cumulative pregnancy rate. *Human Reproduction, 12(3),* 623-627.

van Balen, F., Verdurmen, J., & Ketting, E. (1997b). Choices and motivations of infertile couples. *Patient Education and Counselling, 31(1),* 19-27.

van Balen, F., & Verdurmen, J. (1999). Medical anxiety and the choice for treatment: The development of an instrument to measure fear of treatment. *Psychology and Health, 14(5),* 927-935.

van den Brink, G. R., van den Boogaardt, D. E., van Deventer, S. J., & Peppelenbosch, M. P. (2002). Feed a cold, starve a fever? *Clinical Diagnostic Laboratory Immunology, 9(1),* 182-183.

van Goor, H. (2007). Consequences and complications of peritoneal adhesions. *Colorectal Disease 9(s2),* 25–34 doi:10.1111/j.1463-1318.2007.01358.x.

Verhaak, C. M., Smeenk, J. M. J., van Minnen, A., Kremer, J. A. M., & Kraaimaat, F. W. (2005). A longitudinal, prospective study on emotional adjustment before, during and after consecutive fertility treatment cycles. *Human Reproduction, 20(8),* 2253-2260.

Velicer, W. F., Prochaska, J. O., DiClemente, C. C., & Brandenburg, N. (1985). Decisional Balance Measure for Assessing and Predicting Smoking Status. *Journal of Personality and Social Psychology, 48(5),* 1279-1289.

Virtala, A., Kunttu, K., Huttunen, T., & Virjo, I. (2006). Childbearing and the desire to have children among university students in Finland. *Acta Obstetricia et Gynecologica Scandinavica, 85(3),* 312-316.

Wang, X., Chen, C., Wang, L., Chen, D., Guang, W., French, J., & the Reproductive Health Study Group. (2003). Conception, early pregnancy loss, and time to clinical pregnancy: a population-based prospective study. *Fertility and Sterility, 79(3),* 577-584.

Wang, B., & Davidson, P. (2006). Sex, Lies and Videos in Rural China: A Qualitative Study of Women's sexually Debut and Risky Sexual Behavior. *Journal Sex Research 43(3),* 227-235.

Wang, S. L., Charron-Prochownik, D., Sereika, S. M., Siminerio, L., & Kim, Y. (2006). Comparing three theories in predicting reproductive health behavioural intention in adolescent women with diabetes. *Pediatric Diabetes, 7(2),* 108-115.

Ware, J. E. Jr., Snow, K. K., Kosinski, M., & Gandek, B. *SF-36 health survey manual and interpretation guide.* Boston, MA: New England Medical Center, The Health Institute, 1993.

Ware, J. E. Jr. (2000). SF-36 health survey update. *SPINE, 25(24),* 3130-3139.

Warner, L., Newman, D. R., Austin, H. D., Kamb, M. L., Douglas, J. M., Malotte, C. K., Zenilman, J. M., Rogers, J., Bolan, G., Fishbein, M., Kleinbaum, D. G., Macaluso, M., & Peterman, T. A. (2004). Condom effectiveness for reducing transmission of gonorrhea and chlamydia: the importance of assessing partner infection status. *American Journal of Epidemiology, 159(3),* 242-251.

Webb, S., & Holman, D. (1992). A survey of infertility, surgical sterility and associated reproductive disability in Perth, Western Australia. *Australian Journal of Public Health, 16,* 376-381.

Weinstein, N. D. (1980). Unrealistic optimism about future life events. *Journal of Personality and Social Psychology, 39(5),* 806-820.

Weinstein, N. D. (1999). What does it mean to understand a risk? Evaluating risk comprehension. *National Cancer Institute Monographs, 25,* 15-20.

Weissman, A., Gotlieb, L., Ward, S., Greenblatt, E., & Casper, R. F. (2000). Use of the Internet by infertile couples. *Fertility and Sterility, 73(6),* 1179-1182.

West, R. (2005). What does it take for a theory to be abandoned? The transtheoretical model of behaviour change as a test case. *Addiction, 100(8),* 1048-1050.

Westhoff, C., Murphy, P., & Heller, D. (2000). Predictors of ovarian follicle number. *Fertility and Sterility, 74,* 624-628.

Weström, L. V. (1993). Sexually transmitted disease and infertility. *Sexually Transmitted Diseases, 21(2),* S32-S37.

Weston, G., & Vollenhoven, B. (2002). Is IVF becoming a band aid for social infertility? *Australian and New Zealand Journal of Obstetrics and Gynaecology, 42(5),* 476-477.

White, A. K., & Johnson, M. (2000). Men making sense of their chest pain – niggles, doubts and denials. *Journal of Clinical Nursing, 9,* 534-541.

White, L., McQuillan, J., & Greil, A. L. (2006). Explaining disparities in treatment seeking: the case of infertility. *Fertility and Sterility, 85(4),* 853-857.

Whiteford, L. M., & Gonzalez, L. (1995). Stigma: The hidden burden of infertility. *Social Science and Medicine, 40(1),* 27-36.

WHO (1983). A prospective multi-centre trial of the ovulation method of natural family planning - III Characteristics of the menstrual cycle and of the fertile phase. *Fertility and Sterility, 40,* 773-78.

WHO. Ottawa Charter for Health Promotion. Geneva, 1986.

WHO. *Global prevalence and incidence of selected curable sexually transmitted infections overview and estimates.* World Health Organization: Geneva. 2001.

WHO. *Infertility: A tabulation of available data on prevalence of primary and secondary infertility.* Programme on Maternal and Child Health and Family Planning, Division of Family Health. World Health Organization: Geneva. 1991.

WHO. *Global InfoBase Online.* World Health Organization: Geneva. Retrieved February 28, 2008, from http://www.who.int/ncd_surveillance/infobase/web/InfoBaseCommon/Help/HelpList.aspx?Type_Code=hp.tc.001.

WHO. *Defining and assessing risks to health.* The World Health Report World Health Organization: Geneva. 2002.

WHO. *Obesity: preventing and managing the global epidemic.* Report of a WHO consultation. WHO Technical Report Series 894. World Health Organization: Geneva. Geneva. 2000.

WHO. *Chapter 3: Make every mother and child count.* The world health report 2005. World Health Organization: Geneva.

WHO. *Obesity and overweight fact sheet.* http://www.who.int/dietphysicalactivity/publications/facts/obesity/en/.Volume , DOI: World Health Organization: Geneva. September 2006.

Wiesenfeld, H. C., Hillier, S. L., Krohn, M. A., Amortegui, A. J., Heine, R. P., Landers, D. V., & Sweet, R. L. (2002). Lower genital tract infection and

endometritis: insight into subclinical pelvic inflammatory disease. *Obstetrics and Gynecology, 100,* 456-463.

Wilcox, A., Weinberg, C., & Baird, D. (1988). Caffeinated beverages and decreased fertility. *The Lancet, 2,* 1453-1455.

Wilson, P. W. F., D'Agostino, R. B., Levy, D., Belanger, A. M., Silbershatz, H., & Kannel, W. B. (1998). Prediction of coronary heart disease using risk factor categories. *Circulation, 97,* 1837-1847.

Wilson, C. A., & Keye, W. R. Jr. (1989). A survey of adolescent dysmenorrhea and premenstrual symptom frequency. A model program for prevention, detection, and treatment. *Journal of Adolescent Health Care, 10(4),* 317-322.

Wilson, D. K., Purdon, S. E., & Wallston, K. A. (1988). Compliance to health recommendations: a theoretical overview of message framing. *Health Education Research, 3(2),* 161-171.

Wolfe, B. E., (2005). Reproductive health in women with eating disorders. *Journal of Obstetric, Gynecologic, and Neonatal Nursing, 34(2),* 255-263.

Wollin, S. D., & Jones, P. J. (2001). Alcohol, red wine and cardiovascular disease. *Journal of Nutrition, 131,* 1401-1404.

World Fertility Awareness Month (2006). *What you never know about fertility* [Brochure].

Wulff, M., Hogberg, U., & Stenlund, H. (1997). Infertility in an industrial setting - A population-based study from northern Sweden. *Acta Obstetricia Et Gynecologica Scandinavica, 76(7),* 673-679.

Wyshak, G. (2001). Infertility in American college alumnae. *International Journal of Gynecology and Obstetrics, 73(3),* 237-242.

Zarger, A. H., Wani, A. L., Masoodi, S. R., Laway, B. A., & Salahuddin, M. (1997). Epidemiologic and etiologic aspects of primary infertility in the Kashmir region of India. *Fertility and Sterility, 68,* 637-643.

Zegers-Hochschild, F., Nygren, K. G., Adamson, G. D., de Mouson, J., Lancaster, P., Mansour, R., & Sullivan, E. (2006). The international committee monitoring assisted reproductive technologies (ICMART) glossary on ART terminology. *Fertility and Sterility, 86,* 16-19.

Zielhuis, G. A., Hulscher, M. E. J. L., & Florack, E. I. M. (1992). Validity and reliability of a questionnaire on fecundability. *International Journal of Epidemiology, 21(6),* 1151-1156.

Zinaman, M. J., Clegg, E. D., Brown, C. C., O'Connor, J., & Selevan, S. G. (1996). Estimates of human fertility and pregnancy loss. *Fertility and Sterility, 65,* 503-509.

Zondervan, K. T., Yudkin, P. L., Vessey, M. P., Dawes, M. G., Barlow, D. H., & Kennedy, S. H. (1998). The prevalence of chronic pelvic pain in women in the United Kingdom: a systematic review. *British Journal of Obstetrics and Gynaecology, 105,* 93-99.

Appendices:

Appendix A: Medline search for prevalence of infertility and demand for fertility treatment

Prevalence of infertility

Search History in Medline/PubMed (1990 to 2006). Search conducted 25.05.08

#1 Infertility/epidemiology [Majr:NoExp] OR Infertility [Majr:NoExp] AND

epidemiological studies (85 references found)

#2 Infertility, Female [Mesh] AND Prevalence [Mesh]

(122 records, 9 reviews)

#3 Infertility[Mesh] AND Infertility [Title/abstract] AND

Infertility/epidemiology [MeSH] (563 records, 40 reviews)

Need and demand for fertility treatment

Search History in Medline/PubMed (1990 to 2006). Search conducted 25.05.08

#1 Infertility [MeSH] AND Patient Acceptance of Health Care [MeSH]

(141 records, 15 reviews)

#2 Infertility [Title/Abstract] AND Patient Acceptance of Health Care [MeSH]

(135 records/ 14 reviews)

#3 Infertility [Title/Abstract] AND treatment-seeking [MeSH]

(9 records/ 1 review)

#4 Infertility [MeSH] AND treatment-seeking [MeSH]

(9 records/ 1 review)

Appendix B: Treatment Decision Making Questionnaire (TDMQ) Ethical Approval

03/11/2005

The School of Psychology Ethics Committee has considered and approved your proposal: Intentions to seek medical advice when efforts to conceive are unsuccessful (EC.05.12.06.615). Please note that if any changes are made to the above proposal then the Ethics Committee will need to be made aware of them.

Regards, Dominique Bird

Secretary to the Ethics Committee

Appendix C: Items in the Treatment Decision Making Questionnaire (TDMQ) matched to constructs in the theoretical framework

Table A1.
Items in the Treatment Decision Making Questionnaire (TDMQ) matched to constructs in the theoretical framework.

TDMQ Question	Theory of Planned Behaviour	Transtheoretical Model	Health Belief Model	Help-Seeking Model for Infertility
Background Information (11 items)				
Gender				
Country of residence	External variables		Demographic & socioeconomic	Predisposing and Enabling conditions
Age	External variables		Demographic & socioeconomic	Life course factors
Relationship status	External variables		Demographic & socioeconomic	Life course factors
Years together (months)				
Age of partner				
Parity (yes/no)	Behavioural intention		Demographic & socioeconomic	Life course factors
Education level (Partner education level) 0 = None, 1 = Primary, 2 = Secondary, 3 = Trade/technical, 4 = College/university	External variables		Demographic & socioeconomic	Predisposing and Enabling conditions
General health 1 = Poor, 2 = Fair, 3 = Good, 4 = Very good, 5 = Excellent	Perceived behavioural control		Cues to action	Predisposing and Enabling conditions
Your Fertility (3 items)				
How fertile do you believe you are? 1 = Not at all, 2 = Slightly, 3 = Moderately, 4 = Very, 5 = Extremely	Perceived behaviour control	Contemplation, Precontemplation	Perceived susceptibility	Predisposing conditions, symptom salience

Table A1.
Items in the Treatment Decision Making Questionnaire (TDMQ) matched to constructs in the theoretical framework (continued).

TDMQ Question	Theory of Planned Behaviour	Transtheoretical Model	Health Belief Model	Help-Seeking Model for Infertility
Well Being (34 items)				
Need for parenthood (6 items) 1 = Strongly disagree, 2 = Somewhat disagree, 3 = Neither, 4 = Somewhat agree, 5 = Strongly agree	Behaviour intention	Contemplation	Perceived benefits, Barrier identification	Symptom salience, Individual and social cues
How optimistic are you (Life Orientation Test, 12 items) 0 = Strongly disagree, 1 = Disagree, 2 = Neutral, 3 = Agree, 4 = Strongly agree	Personality variables	Personality variables	Personality variables	Personality variables
Coping style (THWC, 16 items) 0 = Not used, 1 = Used somewhat, 2 = Used quite a bit, 3 = Used a great deal	Personality variables	Personality variables	Personality variables	Personality variables
Engagement in Medical Treatment (32 items)				
Have you sought medical services? (yes/no)		Action		
What contributes (a)/contributed (b) to seeking medical advice (16 items) 1 = Contributes not at all, 2 = Slightly, 3 = Moderately, 4 = Very, 5 = Extremely				
Awareness of a problem	Behavioural intention, Perceived behavioural control	Contemplation	Perceived susceptibility, Cues to action	Symptom salience

Table A1.
Items in the Treatment Decision Making Questionnaire (TDMQ) matched to constructs in the theoretical framework (continued).

TDMQ Question	Theory of Planned Behaviour	Transtheoretical Model	Health Belief Model	Help-Seeking Model for Infertility
Engagement in Medical Treatment (32 items) ***(continued).***				
Told about a fertility problem Being labelled Scared of what doctor might say Embarrassment discussing private topic Disrupt relationship Talk confidentially about fertility concerns Reassurance nothing wrong For/against medical interventions Success of medical treatment Worry about medical treatments going wrong High-tech procedure Medical treatment invasive	Behavioural attitude	Contemplation	Barrier identification	Predisposing and Enabling conditions
Complicated/easy to get help How to get help Cost of treatment	Perceived behavioural control	Contemplation, Preparation	Barrier identification	Life course factors, Predisposing and Enabling conditions

Table A1.
Items in the Treatment Decision Making Questionnaire (TDMQ) matched to constructs in the theoretical framework (continued).

TDMQ Question	Theory of Planned Behaviour	Transtheoretical Model	Health Belief Model	Help-Seeking Model for Infertility
Engagement in Medical Treatment (32 items) ***(continued).***				
How does each consequence make you feel (9 items) 3 = Extremely good, 2 = Quite good, 1 = Slightly good, 0 = Neither, -1 = Slightly bad, -2 = Quite bad, -3 = Extremely bad Treatment would lead to: Becoming a mother Finding out if something is wrong Disrupting social life and work commitments Disrupting relationship with partner Visiting the doctors Financially worse off Taking drugs and undergoing procedures Happier relationship and marriage Talking to someone about fertility concerns	Behavioural attitude	Contemplation	Perceived susceptibility, Perceived threat	Predisposing and Enabling conditions
How strongly do you agree with the following: People important to me (2 items) Partner important to me (2 items) 3 = Strongly agree, 2 = Somewhat agree, 1 = Slightly agree, 0 = Neither, -1 = Slightly disagree, -2 = Somewhat disagree, -3 = Strongly disagree	Subjective norms, Normative beliefs, Motivation to comply	Preparation	Cues to action	Individual and social cues
How comfortable are you confiding in family and friends 1 = Not very comfortable, 2 = Somewhat uncomfortable, 3 = Neither, 4 = Somewhat comfortable, 5 = Very comfortable	Subjective norms, Normative beliefs, Motivation to comply	Preparation	Cues to action	Individual and social cues

Appendix D: Treatment Decision Making Questionnaire (TDMQ)

Decision-Making about Fertility Issues

This web survey was programmed by iΨ Expts

Introduction

We are interested in understanding decision-making around fertility issues. The majority of couples will conceive without using medical treatment. However, a small percentage of people will need fertility treatment. We are interested in people's perceptions and reasons for and against seeking medical help because many people who could benefit from treatment do not seek help or do not get the medical help they need.

We are interested in the opinions of all who are trying to conceive, even those who do not need medical treatment.

In order to find out more about this process we are asking people who are currently trying to conceive to complete a questionnaire. The questions concern your fertility, your perceptions of the medical process and your well being.

The questionnaire takes between 10 - 15 minutes to complete and you can omit any questions you do not wish to complete.

Your participation would be very valuable in helping us better understand decision-making around fertility issues, especially about engaging in the medical process.

This study is being conducted by Laura Bunting with the supervision of Dr Jacky Boivin from Cardiff University who can be contacted via the following email address: boivin@cardiff.ac.uk.

Participation in this study is anonymous and will not involve any known risks. Data gathered in the study will be for research purposes only. We will not be able to trace responses to individual participants. Note, however that there is a possibility that someone could intercept your responses on the way to us but this risk is negligible.

You are free to withdraw from the study at any time without penalty or loss of benefits to which you are otherwise entitled.

This study has been approved by the Ethics Committee of the School of Psychology, Cardiff University, which can be reached via Judy McPherson (mcpherson@cardiff.ac.uk).

If you are 18 or over, understand the statement above and freely consent to participate in this study then click on the "I Agree" button to begin the study.

I Agree

I Do Not Agree

Background Information

1. Your country of residence:

2. Your gender:

3. Your age: Years old

4. Your partner's age: Years old

5. Your highest educational qualification:

6. Your partner's highest educational qualification:

7. How long have you and your partner been living together? Years: Months:

8. Do you or your partner have any children?

If YES then Tick all that apply:

☐ I have a child/children with my current partner.

☐ I have a child/children with a previous partner.

☐ My partner has a child/children with a previous partner.

9. In general would you say your health is:

Continue

Your Fertility

1. How fertile do you believe you are?

2. Please rate how confident you are that you (or your partner) will become pregnant.

(Note: 0% = Not Confident at All, 100% = Completely Confident)

3. Please indicate how long you have been trying to conceive/get pregnant?

Years: Months:

Continue

Engaging in Medical Treatment

The majority of couples will conceive without using medical treatment. However, a small percentage of people will need fertility treatment. We are interested in people's perceptions and reasons for and against seeking medical help. In particular, we want to know about your decision making and plans *if* your efforts to conceive are unsuccessful.

1 a. Have you consulted a doctor about trying to conceive/get pregnant?

Continue

Engaging in Medical Treatment Continued

1 b. How long would you now wait before consulting a doctor? Years: [ ] Months: [ ]

---

2. Below you will find various reasons for and against seeking medical advice and/or treatment. Please read each reason and indicate to what extent it would contribute to your own decision to seek medical advice and/or treatment:

a. I would go if I felt I had a fertility problem or was at risk. [ ]

b. I would be worried that medical treatments would go wrong. [ ]

c. It would give me the chance to talk to someone confidentially about my fertility concerns. [ ]

d. I would not want to be labelled infertile. [ ]

e. Seeking medical advice would give me reassurance that nothing was wrong and I was doing everything correctly. [ ]

f. I would feel awkward and embarrassed discussing such a private topic with someone I did not know. [ ]

Continue

Engaging in Medical Treatment Continued

h. I am against medical interventions to conceive.

i. I would not want to be told I had a fertility problem.

j. I do not think medical treatments are successful.

k. I would not know how to get help.

l. I would be worried about how much treatment would cost.

m. It would be too complicated to get help.

n. I would be afraid that treatment would involve very high-tech procedures.

o. I would be too scared of what the doctor could tell me.

p. Seeking medical advice would disrupt my relationship.

Other consequences: please specify below:

Continue

Engaging in Medical Treatment Continued

3. Seeking medical advice could have various different consequences. Please rate how each consequence below would make you feel (if it were to happen to you):

a. I could become a mother/father.

b. I could find out if there is anything wrong.

c. Treatment could disrupt my social life and work commitments.

d. Treatment could cause friction between me and my spouse.

e. Treatment would involve me having to go to the doctors.

f. We could be financially worse off.

g. I could have to take drugs and undergo high-tech procedures.

h. I could have a happier relationship and marriage with my partner.

i. I could talk to someone about my fertility concerns.

Other reasons: please specify below:

Continue

Engaging in Medical Treatment Continued

4. The following statements refer to how you think the people closest to you would want you to behave *if* your attempts to conceive were unsuccessful. Please indicate on each scale how strongly you agree or disagree with each statement:

a. I think most people who are important to me would want me to seek medical advice:

Strongly Agree	Moderately Agree	Somewhat Agree	Neutral	Somewhat Disagree	Moderately Disagree	Strongly Disagree
O	O	O	O	O	O	O

b. Generally speaking, I want to do what most people who are close to me think I should do:

Strongly Agree	Moderately Agree	Somewhat Agree	Neutral	Somewhat Disagree	Moderately Disagree	Strongly Disagree
O	O	O	O	O	O	O

c. I think *my partner* would want us to seek medical advice:

Strongly Agree	Moderately Agree	Somewhat Agree	Neutral	Somewhat Disagree	Moderately Disagree	Strongly Disagree
O	O	O	O	O	O	O

d. Generally speaking, I want to do what *my partner* thinks is best:

Strongly Agree	Moderately Agree	Somewhat Agree	Neutral	Somewhat Disagree	Moderately Disagree	Strongly Disagree
O	O	O	O	O	O	O

---

5. How comfortable are you about confiding in family and friends regarding trying for a child:

Very Comfortable				Not Very Comfortable
O	O	O	O	O

Continue

Well Being

Now, we would like some feedback concerning how you are feeling about becoming a parent and about your attitude towards life in general.

1. Please indicate on the scale below to what extent you agree with the following statements:

a. Having a child is the most important thing in life.

b. Its hard for me to imagine a life without children.

c. Having a child is not necessary for my happiness.

d. Couples without a child are just as happy as those with children.

e. Being a parent is one of the most important things a person can do.

f. There is a certain freedom without children that appeals to me.

Continue

Well Being Continued

2. The following questions are concerned with your attitudes towards life in general. There are no right or wrong answers. Please be as honest and as accurate as you can, and try not to let your answers to one question influence your answers to other questions.

a. In uncertain times, I usually expect the best.

Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
O	O	O	O	O

b. It's easy for me to relax.

Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
O	O	O	O	O

c. If something can go wrong for me, it will.

Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
O	O	O	O	O

d. I always look on the bright side of things.

Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
O	O	O	O	O

Continue

Well Being Continued

e. I'm always optimistic about my future.

Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
○	○	○	○	○

f. I enjoy my friends a lot.

Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
○	○	○	○	○

g. It's important for me to keep busy.

Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
○	○	○	○	○

h. I hardly ever expect things to go my way.

Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
○	○	○	○	○

i. Things never work out the way I want them to.

Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
○	○	○	○	○

Continue

Well Being Continued

j. I don't get upset too easily.

Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
O	O	O	O	O

k. I'm a believer in the idea that "every cloud has a silver lining".

Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
O	O	O	O	O

l. I rarely count on good things happening to me.

Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
O	O	O	O	O

Continue

Well Being Continued

This is the final question set in the questionnaire and consists of 16 items:

3. Listed below are statements that describe different ways people have of handling a problem. Please read each statement and indicate to what extent you have used each statement when dealing with a problem:

a. Got busy with other things to keep my mind off the problem.

Not Used	Used Somewhat	Used Quite a Bit	Used a Great Deal
O	O	O	O

b. Daydreamed or imagined a better time or place than the one I was in.

Not Used	Used Somewhat	Used Quite a Bit	Used a Great Deal
O	O	O	O

c. Thought about what steps to take to deal with the problem.

Not Used	Used Somewhat	Used Quite a Bit	Used a Great Deal
O	O	O	O

Continue

Well Being Continued

d. Talked with friends about how I was feeling.

Not Used	Used Somewhat	Used Quite a Bit	Used a Great Deal
○	○	○	○

e. Tried to think of ways of dealing with the problem.

Not Used	Used Somewhat	Used Quite a Bit	Used a Great Deal
○	○	○	○

f. Hoped a miracle would happen.

Not Used	Used Somewhat	Used Quite a Bit	Used a Great Deal
○	○	○	○

g. Talked with a spouse or other relatives about how I was feeling.

Not Used	Used Somewhat	Used Quite a Bit	Used a Great Deal
○	○	○	○

h. Wished I could change the situation.

Not Used	Used Somewhat	Used Quite a Bit	Used a Great Deal
○	○	○	○

Continue

Well Being Continued

i. Considered several alternatives for handling the problem.

Not Used	Used Somewhat	Used Quite a Bit	Used a Great Deal
○	○	○	○

j. Avoided being with people in general.

Not Used	Used Somewhat	Used Quite a Bit	Used a Great Deal
○	○	○	○

k. Made light of the situation; refused to get too serious about it.

Not Used	Used Somewhat	Used Quite a Bit	Used a Great Deal
○	○	○	○

l. Tried to see the positive side of the situation.

Not Used	Used Somewhat	Used Quite a Bit	Used a Great Deal
○	○	○	○

Continue

Well Being Continued

m. Let my feelings out somehow.

Not Used	Used Somewhat	Used Quite a Bit	Used a Great Deal
○	○	○	○

n. Tried to step back from the situation and be more objective.

Not Used	Used Somewhat	Used Quite a Bit	Used a Great Deal
○	○	○	○

o. Set some goals for myself to deal with the problem.

Not Used	Used Somewhat	Used Quite a Bit	Used a Great Deal
○	○	○	○

p. Kept my feelings to myself.

Not Used	Used Somewhat	Used Quite a Bit	Used a Great Deal
○	○	○	○

Continue

Your Comments

Before providing you with additional information about the purpose of the study, we invite you to make any comments about decision-making about fertility issues in the box below:

Now to submit all your data to the researcher and be debriefed click on the submit button.

Submit

Decision-Making about Fertility Issues

This web survey was programmed by iΨ Expts

Debrief

Thank you for taking the time to complete this important questionnaire.

Many individuals can benefit from seeking medical advice in order to conceive. However, many couples are either not seeking advice or are not receiving the medical help or treatment they require. We are interested in people's perceptions and reasons for and against seeking medical help. Specifically we are concerned with people's intentions to seek medical advice and/or treatment if conception is unsuccessful. Two theories have proposed ways in which people change or adopt new behaviours, and have been used to predict and understand peoples' decision making in other health areas, such as the decision to quit smoking or the decision to start (or increase) exercising on a daily basis. These theories predict that an individual's belief about medical treatment, their evaluations about what medical treatment can achieve and their perceptions and values of the people close to them will have an influence on whether or not they would seek medical advice. Other theories suggest that decision-making is determined by a process of stages. Such theories predict that an individual must progress through each of the stages in order to achieve success in adopting a new behaviour. There is no time limit for each stage and some individual's may progress through certain stages quicker than others. Such a theory may be able to account for why a number of individuals are not seeking medical advice when conception is unsuccessful. In this study we were examining which theory is most useful in the context of fertility.

Thank you again for your time, and we would like to assure you that the data you have just provided us will be held anonymously.

If you have any further questions about this research then please contact boivin@cardiff.ac.uk.

Continue

Appendix E: Factors Affecting Fertility Scale (FAFS) Ethical Approval

10/07/2006

The School of Psychology Ethics Committee has considered and approved your postgraduate project proposal - Risk factors and infertility (EC.06.08.15.864/942). Please note that if any changes are made to the above proposal then the Ethics Committee will need to be made aware of them.

Regards, Dominique Bird

Secretary to the Ethics Committee

Appendix F: Factors Affecting Fertility Scale (FAFS)

Factors that affect Fertility

This web survey was programmed by [*i* Ψ Expts]

Introduction

We are interested in how you think various factors affect female and male fertility.

The study takes between 10 - 15 minutes to complete and you can omit any questions you do not wish to complete.

This study is being conducted by Laura Bunting with the supervision of Dr Jacky Boivin from Cardiff University who can be contacted via the following email address: boivin@cardiff.ac.uk.

Participation in this study is anonymous and will not involve any known risks. Data gathered in the study will be for research purposes only. We will not be able to trace responses to individual participants. Note, however that there is a possibility that someone could intercept your responses on the way to us but this risk is negligible.

You are free to withdraw from the study at any time without penalty or loss of benefits to which you are otherwise entitled.

This study has been approved by the Ethics Committee of the School of Psychology, Cardiff University, which can be reached via Dominique Bird (birdd3@cardiff.ac.uk).

If you are 18 or over, understand the statement above and freely consent to participate in this study then click on the "I Agree" button to begin the study.

[I Agree]

[I Do Not Agree]

Background Information

1. Your gender:

2. Your age: Years old

3. Your highest educational qualification:

Continue

Instructions

We are interested in the factors that may have an effect on fertility. By fertility we mean you or your partner getting pregnant.

We will present you a list of factors. Beside the list of factors is a scale that goes from 0 women to 100 women. Imagine that 100 women were trying to get pregnant. On average we would expect 50 women to achieve this goal within three months.

We would like to know whether you believe any of the factors listed would affect this fertility rate.

If you think the factor would DECREASE the chance of getting pregnant then click on a number BELOW 50 women, if you think the factor would INCREASE the chance of getting pregnant click on a number ABOVE 50 women. How much below or above 50 you put your dot depends on how much you think the factor affects fertility. If you think the factor has no effect on the chance of getting pregnant then keep the dot on 50. Consider each factor individually.

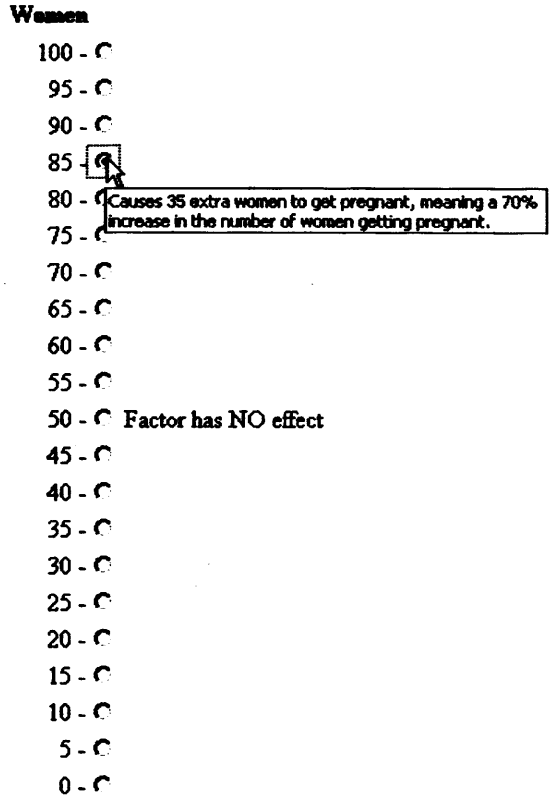
Continue

Instructions

Here is an example:

Eating 10 strawberries a day will...

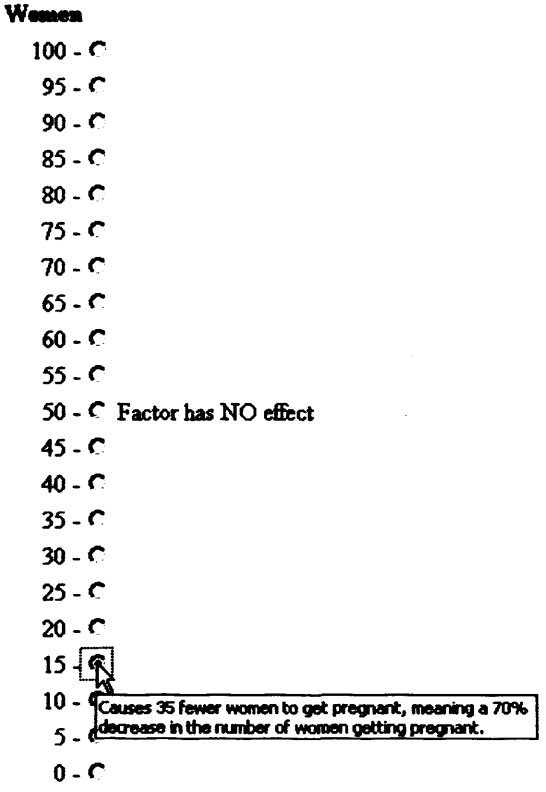
If you place your dot on 85 women, it means you think an extra 35 women (above the 50) would get pregnant, meaning a 70% increase in the number of women getting pregnant due to eating strawberries (see example below).



Continue

Instructions

If instead you placed your dot on 15 women, it means you think 35 fewer women would get pregnant, meaning a 70% decrease in the number of women getting pregnant due to eating strawberries.



Note, hovering over a point on the scale with the mouse will show a pop-up text caption that provides more information about what the point means. Also note that this pop-up text caption may take a few seconds to appear.

Continue

Please rate the effect that adopting a baby will have on a woman's fertility and then click on the continue button below.

Women

100 - ○
95 - ○
90 - ○
85 - ○
80 - ○
75 - ○
70 - ○
65 - ○
60 - ○
55 - ○
50 - ◉ **Factor has NO effect**
45 - ○
40 - ○
35 - ○
30 - ○
25 - ○
20 - ○
15 - ○
10 - ○
5 - ○
0 - ○

Continue

Factors that affect Fertility

This web survey was programmed by *i*Ψ Expts

Debrief

Thank you for taking the time to complete this important questionnaire.

The majority of couples will get pregnant after trying for 12 months. However, for a small number of couples it may take longer. Current government guidelines (NICE) recommend couples to seek medical advice if they have been trying for longer than 12 months without success. A number of studies however, have highlighted that many couples are either not seeking advice or are not receiving the medical help or treatment they require. Furthermore, previous research has revealed that peopleís knowledge of fertility and the factors that can have a negative effect on it is limited. This could help to explain why some couples are not seeking help. We therefore want to determine what people believe are risk factors for fertility and whether the general populations' beliefs about fertility correspond with the current literature and research in the area.

We are also interested to see if changing the way in which information is presented in the response scales would have an effect on a participant's rating of each factor. In the current study there were three scales that varied in the way information was presented to each participant. You would have only had one of the three response scales presented to you. One scale presented information in frequencies (e.g., [risk factor]...causes 35 extra women to get pregnant); another in percentages (e.g., ...causes 75% increase in the number of women getting pregnant) and the other presented information in frequencies and percentages (e.g., ...causes 35 extra women to get pregnant. This means a 75% increase in the number of women getting pregnant). We wanted to determine whether varying the way information was presented to a participant would have an impact on their ratings of each factor. It is important to provide response scales in such a way as to provide relevant information (i.e., what the numbers mean in terms of an increase or a decrease in the number of pregnancies) without influencing what a participant decides about a risk factor (i.e., whether and how much of an effect it has).

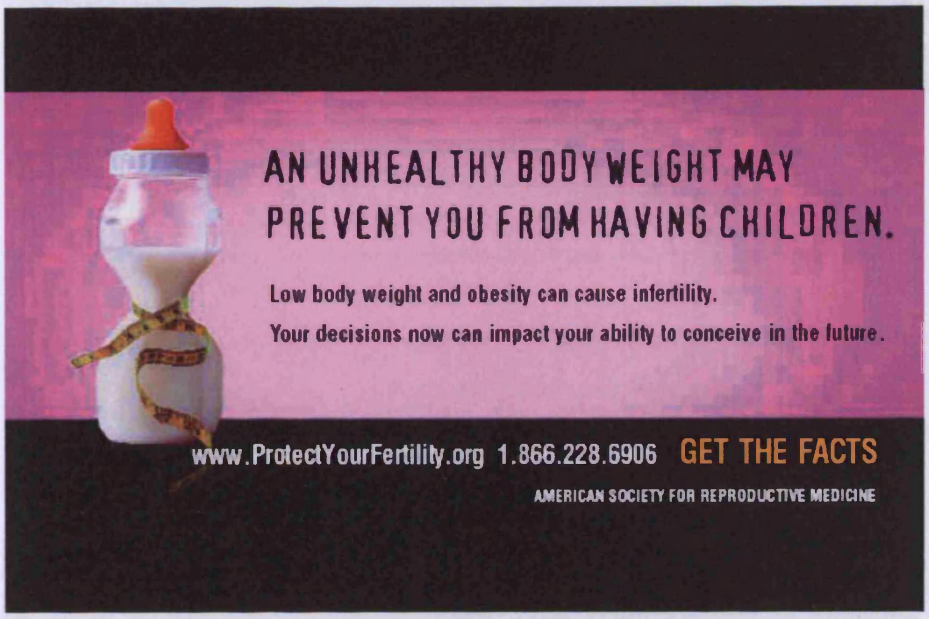
Thank you again for your time, and we would like to assure you that the data you have just provided us will be held anonymously.

If you have any further questions about this research then please contact boivin@cardiff.ac.uk.

Continue

Appendix G: American Society for Reproductive Medicine fertility awareness campaign

Reproduced without permission from http://www.protectyourfertility.org/ (last accessed 22 August 2008).



Reproduced without permission from http://www.protectyourfertility.org/ (last accessed 22 August 2008).

Appendix H: Medline search for risk factors for study 5.1

Search History in Medline/PubMED (1978 to 2008)

Search conducted 25.05.08

#1 Female Infertility	(19,026 records/ 2,335 reviews)
Female Infertility AND:	
#2 Risk Factors	(600 records, 157 reviews)
#3 Population Characteristics	(1,500 records/ 189 reviews)
#4 Age Factors	(648 records/ 92 reviews)
#5 Ethnic Groups	(56 records/ 3 reviews)
#6 Occupation	(15 records)
#7 Environmental Exposure	(81 records/ 19 reviews)
#8 Reproductive History	(232 records/ 11 reviews)
#9 Endometriosis	(1587 records/ 331 reviews)
#10 Menstrual Cycle	(1395 records/ 147 reviews)
#11 Dysmenorrhea	(135 records/ 20 reviews)
#12 Amenorrhea	(877 records/ 85 reviews)
#13 Oligomenorrhea	(91 records/8 reviews)

#14 Pelvic Inflammatory Disease (782 records/ 104 reviews)

#15 Polycystic Ovary Syndrome (830 records/ 185 reviews)

#16 Sexually Transmitted Diseases (536 records/ 87 reviews)

#17 Chlamydia (356 records/ 42 reviews)

#18 Gonorrhea (53 records/ 13 reviews)

#19 Lifestyle (54 records/ 21 reviews)

#20 Alcohol Drinking (28 records/ 8 reviews)

#21 Alcohol-Related Disorders (15 records/ 2 reviews)

#22 Caffeine (17 records/ 6 reviews)

#23 Contraceptive Agents (320 records/ 61 reviews)

#24 Exercise (27 records/ 11 reviews)

#25 Coitus (142 records/ 18 reviews)

#26 Substance-Related Disorders (32 records/ 5 reviews)

#27 Cocaine (2 records)

#28 N-Mthyl-3,4-methylenedioxyamphetamine (Esctasy/LCD) (0 records)

#29 Amphetamine (0 records)

#30 Heroin (diacetylmorphine) (1record)

#31 Marijuana, Smoking (1 record)

#32 Tobacco Use Cessation (5 records)

#33 Tobacco (25 records/ 10 reviews)

#34 Stress (33 records/ 12 reviews)

#35 Stress, Psychological (115 records/ 20 reviews)

#36 Chemotherapy, Adjuvant (19 records/ 7 reviews)

#37 Radiotherapy (107 records/ 40 reviews)

#38 Coeliac (13 records/ 2 reviews)

#39 Diabetes Insipidus (8 records)

#40 Diabetes Mellitus (96 records/ 28 reviews)

#41 Epilepsy (20 records/ 8 reviews)

#42 Heart Diseases (57 records/ 12 reviews)

#43 Kidney Diseases (58 records/ 10 reviews)

#44 Lupus Erythematosus, Systemic (18 records/ 9 reviews)

#45 Appendicitis/Appendectomy (15 records/ 1 review)

#46 Perforation of the appendix (4 records)

#47 Anti-depressive Agents (6 records/ 2 reviews)

#48 Antidepressants (17 records/ 2 reviews)

#49 Anti-Inflammatory Agents (48 records/ 10 reviews)

#50 Asthma (5 record)

#51 Asthma Medicine (1 record)

#52 Hormone Replacement Therapy (47 records/ 21 reviews)

#53 Anemia, Sickle Cell (3 records)

#54 Thrombophilia (13 records/ 3 reviews)

Appendix I: Medical and Reproductive Reviewers

11/12/2006

Ms Sandra K Dill	ESHRE PLF, ICSI, ACCESS Australia
Ms Beverly Hanck	Infertility Awareness Association of Canada
Dr Andrea Borini	Tecnobios Procreazione, Italy
Dr Jacky Boivin	Psychologist, School of Psychology, Cardiff University, UK
Ms Chantal Seror-Ramogida	Follow Up, France
Dr Thomas Hahn	Institut für IVF and Reproduktionsmedizin, Germany
Mr Conrad Engler	Advocacy AG/Verein Kinderwunsch, Switzerland
Dr Richard Porter	IVF Australia
Dr Micheal Schenk	Kinderwunsch Institut, Austria
Ms Geertrui De Cock	Fertility Association of Belgium
Prof. Petra De Sutter	Ghent University Hospital, Belgium
Dr Albert Yuzpe	Genesis Fertility Centre, Canada
Dr David Rumpik	Clinic of Reproductive Medicine and Gynecology, Czech Republic
Dr Petra Thorn	Patient Representative, Wunschkind, Counsellor, Germany
Mr Declan Keane	Human Assisted Reproduction Ireland (HARI)
Ms Helen Hayes-Browne	National Infertility Support & Information Group (NISIG), Ireland
Ms Donatella Caione	Associazione Mammeonline. Italy
Prof. Karl-Gösta Nygren	Sophiahemmet Hospital, Sweden
Mr Robert Forman	Centre for Reproductive Medicine, UK
Mrs Susan Seenan	Infertility Network UK

Appendix J: Summary of design characteristics of each study

Table A2. *Summary of design characteristics of each study.*

Authors	Risk factor	Bias	Control	Outcome	Definitions	Sample
Retrospective						
Akande et al.(2004)	Endometriosis	Selection, drop out	Yes	Reduced conception rate	Infertility ≥ 12 months unprotected sexual intercourse	117 unexplained infertile women & 75 women with laparoscopic diagnosed endometriosis (< 40), questionnaire & 3 year follow-up United Kingdom 1985 - 1995
Axmon et al. (2006)	Menstrual, Age, Alcohol, smoking, stress	Selection	Yes	Increased TTP	Excluded women ≥ 12 months unprotected sexual intercourse	1,578 women (23 - 39), randomly selected from general population, questionnaire, recall menstrual cycle length every 3 months of trying to conceive, Sweden, 2000
Bolũmar et al. (1997)	Caffeine	Selection	Yes	Increased TTP ≥ 9.5 months	Excluded women ≥ 12 months unprotected sexual intercourse	3,187 women (25 - 44) randomly selected from general population, interview, Europe 1991 - 1993
Bolũmar et al. (2000)	Weight	No information available	Yes	Increased TTP	Excluded women ≥ 12 months unprotected sexual intercourse, clinical pregnancy	2,587 pregnant women at least 20 weeks gestation (25-44), prenatal care unit, questionnaire or interview, Europe 1992
Eggert et al. (2004)	Alcohol	No information available	No, did not ascertain information on lifestyle factors other than alcohol	Risk of infertility	Medical diagnosis/hospital admission	7,393 (18 - 28) randomly selected women from general population, questionnaire, Sweden, 1969
Gesink Law et al. (2007)	Weight	No information available	Yes	Increased TTP	Censored at 13 months unprotected sexual intercourse, clinical pregnancy	7,327 pregnant women median gestation 16 weeks, interview, United States 1959 - 1965
Green et al. (1988)	Weight	Misclassification, recall	Yes	Risk of ovulatory infertility	Diagnosis of ovulatory infertility	380 infertile cases & 1,520 demographic & socioeconomic-matched controls given birth same year (20 - 39), interview, US 79 -81

Table A2. *Summary of design characteristics of each study (continued).*

Authors	Risk factor	Bias	Control	Outcome	Definitions	Sample
Retrospective *(continued)*						
Greenlee et al. (2003)	Alcohol, smoking, weight	No information available	Yes	Risk of infertility	Infertility ≥ 12 months unprotected sexual intercourse	322 primary infertile cases & 322 age-matched pregnant (during 1st trimester) controls (18 - 35), interview, Canada 1997 - 2001
Gordley et al. (2000)	Stress	Selection, measurement error	No information available	Menstrual irregularities	Menstrual irregularities defined	170 women employed by the US Air Force (18 - 41), questionnaire about menstrual patterns in preceding 3 months , United States
Grodstein et al. (1994)	Alcohol, caffeine, weight	Interviewer bias	Yes	Risk of tubal infertility & Risk of ovulatory infertility	Infertility ≥ 12 months unprotected sexual intercourse, live birth	1,050 infertile women & 3,833 women admitted for delivery of pregnancy, interview, United States & Canada 1981 - 1983
Hassan & Killick (2003)	Age	No information available	Yes	Increased TTP > 12 & 24 months	Infertility ≥ 12 months unprotected sexual intercourse	1,976 pregnant women (25 - 44), antenatal units, questionnaire, United Kingdom 2000 - 2001
Hassan & Killick (2004)	Alcohol, caffeine, drug use, smoking, weight	Sample size within groups	Yes	Increased TTP	Infertility ≥ 12 months unprotected sexual intercourse	1,976 pregnant women (25 - 44) antenatal units, questionnaire, United Kingdom 2000 - 2001
Hatch & Bracken (1993)	Caffeine,	Misclassification	Yes	Increased TTP	Infertility ≥ 12 months unprotected sexual intercourse	1,909 pregnant women antenatal unit, interview, United States 1980 - 1982
Hillis et al. (1997)	STD	Under-representation of all chlamydia cases	Yes, but for a number of lifestyle factors no information ascertained	Risk of PID	Diagnosis of PID	11,000 women known to have had chlamydia trachomatis (10 - 44), medical records of registered hospitalisation for PID, United States 1985 - 1992
Hull et al. (2000)	Smoking	Recall, selection	Yes	Increased TTP 6 & 12 months	Infertility ≥ 12 months unprotected sexual intercourse, clinical pregnancy	8,515 pregnant women at least 18 weeks gestation, questionnaire, United Kingdom 1991 - 1992

Table A2. *Summary of design characteristics of each study (continued).*

Authors	Risk factor	Bias	Control	Outcome	Definitions	Sample
Retrospective *(continued)*						
Juhl et al. (2003)	Alcohol	Sample size within groups	Yes & Power calculations	Increased TTP > 12 months & shorter TTP	Infertility ≥ 12 months unprotected sexual intercourse, clinical pregnancy	29,844 pregnant women at least 12 weeks gestation (14 - 44), national birth cohort, interview, Denmark 1997 - 2000
Joesoef et al. (1993)	Drug use	Limited information	Yes	Shorter TTP	Infertility ≥ 12 months unprotected sexual intercourse, live birth	1,818 infertile cases & 2,817 controls given birth same year, interview, United States & Canada 1981 - 1983
Kaplan et al. (2005)	Age, weight	No information available	No information available	Increased TTP > 3 & > 6 months	Infertility ≥ 12 months unprotected sexual intercourse	798 pregnant women (20 - 40), antenatal unit, questionnaire, Israel 2003
Khadem & Mazlouman (2004)	Endometriosis, menstrual	Selection	No information available	Risk of infertility	Infertility ≥ 12 months unprotected sexual intercourse	100 infertile women & 120 fertile age-matched controls (19 - 39), laparoscopy performed & medical records, Iran
Lalos (1988)	Endometriosis, pelvic surgery, STD, PID	Small sample size	No information available	Risk of tubal infertility & infertility	Tubal infertility confirmed	120 infertile cases & 126 pregnant controls with no history of infertility (18 - 43), questionnaire & medical records, Sweden 1978 - 1982
La Rochebrochard & Thonneau (2003)	Age	Selection & recall	Yes	Risk of infertility	Infertility ≥ 12 months unprotected sexual intercourse	6,188 women (25 - 44), randomly selected from census registers, interview, Europe 1991 - 1993
Maheshwari et al. (2008)	Age	Change in diagnostic methods over time	Yes & Power calculations	Risk of tubal & unexplained infertility	Infertility ≥ 12 months unprotected sexual intercourse	7,172 infertile women (20 - 50), medical records based on first clinic visit, United Kingdom 1993-2006

Table A2. *Summary of design characteristics of each study (continued).*

Authors	Risk factor	Bias	Control	Outcome	Definitions	Sample
Retrospective *(continued)*						
Malik et al. (2006)	STD	No information available	No information available	Risk of infertility	Infertility ≥ 12 months unprotected sexual intercourse	110 primary & secondary infertile cases & 30 healthy term pregnant controls (18 - 40), hysterosalpingography performed on all patients, India 2003 - 2004
Mueller et al. (1990)	Drug use	Response & Recall	Yes	Risk of primary tubal infertility & Risk of ovulatory infertility	Infertility ≥ 12 months unprotected sexual intercourse, live birth	84 infertile cases & demographic & socioeconomic-matched controls given birth same year (20 - 39), interview, United States 1979 - 1981
Olsen (1991)	Caffeine	Recall	Yes	Increased TTP > 12 months	Infertility ≥ 12 months unprotected sexual intercourse, clinical pregnancy	10,886 pregnant women at 36th week of gestation, questionnaire, Denmark 1984 - 1987
Olsen et al. (1997)	Alcohol	Selection & Recall	Yes	Increased TTP > 9.5 months	Clinical pregnancy	2,587 pregnant women at least 20 weeks gestation & those just given birth (25 - 44), interview, Europe, 1992
Ramlau-Hansen et al. (2007)	Weight	No information available	Yes	I ncreased TTP > 12 months	Infertility ≥ 12 months unprotected sexual intercourse, clinical pregnancy	47,835 pregnant women at least 16 weeks gestation (15-44), two telephone interviews during & after pregnancy, Denmark 1996 - 2002
Rich-Edwards et al. (1994)	Weight	Selection, recall	Yes	Risk of infertility	Infertility ≥ 12 months unprotected sexual intercourse, clinical pregnancy	2,527 infertile women & 46,718 women whose first pregnancy lasted > 6 months with no history of infertility (25 - 42), questionnaires, United States 1989 - 1995
Rowland et al., (2002)	Menstrual	Selection	Yes	Risk of infertility	Infertility ≥ 12 months unprotected sexual intercourse	3,941 women (21 - 40), questionnaire, United States 1994 - 1996

Table A2. *Summary of design characteristics of each study (continued).*

Authors	Risk factor	Bias	Control	Outcome	Definitions	Sample
Retrospective *(continued)*						
Stanton & Gray (1995)	Caffeine	Selection	Yes	Increased TTP > 12 months	Infertility ≥ 12 months unprotected sexual intercourse	2,501 pregnant women employed at semioconductor plants, interview, United States, 1989 - 1990
Swasdio et al.(1996)	STD	No information available	Yes	Risk of tubal infertility	Tubal infertility confirmed	55 primary infertile confirmed tubal damage cases & 59 postpartum controls, past infections assessed measuring serum IgG antibodies, Thailand 1990 - 1992
Thonneau et al.(1992)	Pelvic surgery, STD, PID	Recruitment	Yes	Risk of primary infertility & secondary	Infertility ≥ 12 months unprotected sexual intercourse, live birth	301 infertile cases & 380 controls who had just given birth, interview, France 1988 - 1989
Urbach et al. (2001)	Endometriosis, PID, Age, smoking	Selection, recall, cases not aged matched	Yes & Power calculations	Risk of tubal infertility	Clinical pregnancy	121 primary infertile cases & 490 clinically pregnant controls (20 - 44), questionnaires, Canada 1998
Wiesenfeld et al. (2002)	STD	No information available	Yes	Risk of subclinical PID	Diagnosis of subclinical PID	556 women (15- 30) with lower genital tract infections or determined at risk of such infections, sexual & reproductive health clinics, endometrial sampling for histologic analysis, United States 1998 - 2000
Augood et al. (1998) (11 studies were retrospective, 1 prospective)	Smoking	Publication, self-report, recall, misclassification, selection	Yes, in all studies reviewed	8 studies - longer TTP, 4 studies risk of infertility	Infertility ≥ 12 months unprotected sexual intercourse (6 studies), excluded women ≥ 12 months unprotected sexual intercourse (1 study), no definition (2 studies), pregnant (1 study), clinical (2)	Meta analysis of 12 cohort and case-control studies in the general population 1985 - 1997

Table A2. *Summary of design characteristics of each study (continued).*

Authors	Risk factor	Bias	Control	Outcome	Definitions	Sample
Prospective						
Dunson et al. (2004)	Age	No information available	No information available	Risk of infertility	Infertility ≥ 12 cycles unprotected sexual intercourse	782 women (18 - 40), randomly selected, daily fertility & menstrual characteristics recorded, Europe 1992 - 1996
Fenster et al. (1999)	Stress	Selection	Yes	Short menstrual cycle < 24 days & Risk of anovulation ≥ 36 days	Menstrual irregularities defined	403 women (18 - 39) daily menstrual characteristics, urine samples & interviews, United States 1990 - 1991
Hakim et al. (1998)	Alcohol	Recall & sample size	Yes	Reduced conception rate	Conception	124 women (23 - 41), daily urine samples & reports of lifestyle habits, United States 1989 - 1991
Hjollund et al. (1999)	Stress	Planning	Yes	Reduced conception rate	Infertility ≥ 12 months unprotected sexual intercourse, clinical pregnancy	390 women (20 - 35) monthly questionnaires for 6 menstrual cycles or until clinical pregnancy, Denmark 1992 - 1995
Jensen et al. (1998)	Alcohol, caffeine	Recruitment & Selection	Yes	Reduced conception rate	Clinical pregnancy	423 women (20 - 35), monthly questionnaires for 6 menstrual cycles or until clinical pregnancy, Denmark 1992 - 1995
Kolstad et al.(1999)	Menstrual	Selection	Yes	Reduced conception rate	Conception	295 trade union women (20 - 35), daily urine samples for 5 menstrual cycles or until conception, Denmark 1992 - 1995
Liu et al. (2004)	Alcohol, smoking	Selection	Yes	Short follicicular phase & menstrual irregularities	Menstrual irregularities defined	338 women (20 - 44), daily urine samples & reports of lifestyle habits, United States 1989 - 1991
Small et al. (2006)	Menstrual	Sample size	Yes	Reduced conception rate	Infertility ≥ 12 months unprotected sexual intercourse, clinical pregnancy	470 women employed by government (< 40), interview, urine collection 2 days per cycle for year or until a clinical preg, US 90 - 94

Table A2. *Summary of design characteristics of each study (continued).*

Authors	Risk factor	Bias	Control	Outcome	Definitions	Sample
Prospective *(continued)*						
Stoleru et al. (1993)	Stress	Selection	Yes	Risk of infertility	Infertility ≥ 12 months unprotected sexual intercourse	63 women (20 - 35) trying to conceive, questionnaire at 1 & 12.8 months, France
Tolstrup et al. (2003)	Alcohol	Recruitment	No control for variables developing over time (e.g., endometriosis)	Risk of infertility	Medical diagnosis through hospital or registration on the Danish Infertility Cohort Register	7,760 women (20 - 29), randomly selected from general population, interview, Denmark 1991 - 1993
Westrom (1993)	PID	No information available	Yes	Risk of infertility	Diagnosed with tubal factor infertility	1,966 women all diagnosed with acute salpingitis (15 - 34), laparoscopy & follow-up interviews, Sweden 1960 - 1989
Wilcox et al. (1988)	Caffeine	No information available	Yes, but did not measure all lifestyle factors	Risk of infertility	Infertility ≥ 12 months unprotected sexual intercourse, clinical pregnancy	104 women , daily menstrual characteristics recorded & interviews at 0, 3, 6, 12 & 24 months or until clinical pregnancy, United States

Appendix K: Categories of excluded factors from study 5.1

The following factors have all been associated with fertility potential. After review and consultation with the medical and reproductive experts it was decided that they should be removed from the development of the Fertility Risk Factors Scale (FRFS) for the following reasons:

Factors do not have an independent impact on fertility potential (5 factors)

- Exercise (lifestyle)
- Underweight (BMI <19)
- Ethnicity (Demographic)
- PCOS (Reproductive)
- Epilepsy (medical)

Evidence for factors impact on fertility is contradictory (4 factors)

- Contraception use (lifestyle)
- Occupation and environmental exposures (demographic)
- Asthma medication (medical)
- Prescribed drug use (medical)

Factors associated with an impact on fertility after conception (3 factors)

- Heart disease (medical)
- Coeliac (medical)
- Thrombophilia/ Deep Venous Thrombosis (medical)

Exclusion of all non-reproductive medical factors (5 factors)

Low prevalence (2 factors)

- Sickle cell anaemia
- Lupus Erythematosus SLE

Previous knowledge (3 factors)

- Cancer, Chemotherapy and Radiotherapy
- Diabetes
- Kidney disease and transplantation

Appendix L: Calculation of odds ratios for study 5.1

Dunson, D.B., Baird, D.D., Columbo, B. (2004). Increased infertility with age in men and women. *Obstetrics & Gynecology*, 103, 51-56.

	(0) Age (1)		
Pregnant	19-26	27-34	Total
Yes	92	86.5	178.5
No	8	13.5	21.5
Total	100	100	400

[92 x 13.5] / [8 x 86.5] = 1.79
(1242) (692)

	(0) Age (1)		
Pregnant	19-26	27-34	Total
Yes	92	82	174
No	8	18	26
Total	100	100	400

[92 x 18] / [8 x 82] = 2.52
(1656) (656)

Kaplan, B., Nahum, R, Yairi, Y., Hirsch, M., Pardo, J., Yogev, Y., Orvieto, R. (2005). Use of various contraceptive methods and time of conception in a community-based population. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, 123, 72-76.

3 months trying

	(0) BMI (1)		
Pregnant	<25	>25	Total
Yes	44	37	81
No	56	63	119
Total	100	100	400

[44 x 63] / [56 x 37] = 1.34
(2772) (2072)

6 months trying

	(0) BMI (1)		
Pregnant	<25	>25	Total
Yes	74	54	128
No	25	46	72
Total	100	100	400

[74 x46] / [26 x 54] = 2.42
(3404) (1404)

Khadem, N., & Mazlouman, S. J. (2004). Study of endometriosis related infertility, a comparative study. *Acta Medica Iranica*, 42, 383 – 388.

	% Infertile	
Dyspareunia	Yes	No
Yes	12	3
No	88	97

[12 x 97] / [88 x 3] = 4.41
(1164) (264)

	% Infertile	
Endometriosis	Yes	No
Yes	38	11.6
No	62	88.4

[38 x 88.4] / [62 x 11.6] = 4.67
(3359.2) (719.2)

	% Infertile	
Pelvic Pain	Yes	No
Yes	28	3
No	72	97

[28 x 97] / [72 x 3] = 12.57
(2716) (216)

	% Infertile	
Dysmenorrhea	Yes	No
Yes	55	31.7
No	45	96.3

[55 x 96.3] / [45 x 31.7] = 3.71
(5296.5) (1426.5)

Kolstad, H.A., Bonde, J.P., Hjollund, N.H., Jensen, T.K., Henrikden, T.B., Ernst, E., Giwercman, A., Skakkebaek, N.E., Olsen, J. (199). Menstrual cycle pattern and fertility: a prospective follow-up study of pregnancy and early embryonal loss in 295 couples who were planning their first pregnancy. *Fertility and Sterility*, 71, 490-496.

	Cycle length	
Pregnant	< 40	>40
Yes	16	11
No	84	89
Total	100	100

[16 x 89] / [84 x 11] = 1.54
(1424) (924)

Lalos, O. (1988). Risk factors for tubal infertility among infertile and fertile women. *European Journal of Obstetrics & Gynecology and Reproductive Biology, 29,* 129-136.

	% Infertile	
Gonorrhoea	Yes	No
Yes	13	2
No	87	98

[13 x 98] / [27 x 2] = 7.32
(1274) (174)

	% Infertile	
Previous Surgery	Yes	No
Yes	59	25
No	41	75

[59 x 75] / [41 x 25] = 4.32
(4425) (1025)

	% Infertile	
Endometriosis	Yes	No
Yes	10	3
No	90	97

[10 x 97] / [90 x 3] = 3.59
(970) (270)

	% Infertile	
PID	Yes	No
Yes	41	14
No	59	86

[41 x 86] / [59 x 14] = 4.27
(3526) (826)

Appendix M: Fertility Risk Factors Survey (FRFS) Ethical Approval

University Ethical Approval

24/04/2007

Extract from the unconfirmed University Research and Ethics Committee (UREC) meeting minutes of 24 April 2007 follows:

"128 PROJECT REFERRAL Received paper 06/1026B, 'School of Psychology, Cardiff University Ethics Proforma '.

NOTED

.1 That UREC's approval has been sought for a PSYCH student research project in view of the nature of the study.

RESOLVED

.2 That the research project is in an important and valid academic area and scientifically robust; .3 That the research subjects will be totally anonymised and safeguarded and that participation in the study is entirely voluntary; .4 That the project be approved by this Committee."

Dr Kathryn Pittard Davies confirmed that using the University notice board would not be a problem.

Dr Kathryn J Pittard Davies

Head of Research Policy and Management, Research and Commercial Division, Cardiff University.

NHS South East Wales Research Ethics Committee Ethical Approval

24/04/2007

NHS WALES GIG CYMRU

Cardiff and Vale NHS Trust | Ymddiriedolaeth GIG Caerdydd a'r Fro

University Hospital of Wales
Ysbyty Athrofaol Cymru

Heath Park, Cardiff CF14 4XW
Phone 029 2074 7747
Minicom 029 2074 3632

Parc Y Mynydd Bychan, Caerdydd CF14 4XW
Ffôn 029 2074 7747
Minicom 029 2074 3632

Eich cyf/Your ref
Ein cyf/Our ref
Welsh Health Telephone Network 1872
Direct line/Llinell uniongyrchol

Tel: 029 20743742
Fax: 029 20745311

From: Professor MF Scanlon
Trust R&D Director
Radnor House
University Hospital of Wales
Cardiff
CF14 4XW

E-mail: Research.Development@cardiffandvale.wales.nhs.uk

02 July 2007

Dr Jacky Boivin
School Of Psychology
Cardiff University, Tower Building
Park Place Cardiff CF10 3AT

Dear Dr Boivin

Project ID : 07/RPM/3999 : Survey Of Fertility Health Issues

Thank you for your recent communication regarding the above project, which was reviewed on 29 June 2007 by the Joint Trust/University Risk Review Committee.

I am pleased to inform you that the project has been approved and that Cardiff University will act as research Sponsor under the Research Governance Framework for Health and Social Care. Cardiff & Vale NHS Trust is therefore happy for the project to begin, subject to:

1) Approval from the appropriate NHS Research Ethics Committee
2) Honorary Contracts, where required, being in place before the research begins.

Please ensure that the appropriate Research Ethics Committee have a copy of this letter. Once you have gained ethical approval, please forward a copy of the approval letter to the Research and Development Office at the above address.

May I take this opportunity to wish you success with the project and remind you that as Principal Investigator you are required to:

- Inform the Trust R&D Office if any external or additional funding is awarded for this project in the future.
- Inform the Trust R&D Office of any amendments relating to the protocol, including personnel changes and amendments to the actual or anticipated start / end dates.

- Complete any documentation sent to you by the Trust R & D Office or University Research & Commercial Division regarding this project.
- Ensure that adverse event reporting is in accordance with Cardiff and Vale NHS Trust Policy and Procedure for Reporting Research-Related Adverse Events (Refs 164 & 174) and the Trust Incident Reporting and Investigation Procedure (Ref 108).
- Undertake the project in accordance with ICH-GCP.
- Adhere to the protocol as approved by the Research Ethics Committee.
- Ensure the research complies with the Data Protection Act 1998.

Yours sincerely,

Professor MF Scanlon
Chair of the Joint Trust/University Peer & Risk Review Committee

CC Chris Shaw, Research and Commercial Division, Cardiff University
CC **R&D Lead Professor A Fiander**

L:\study folders\3999RD Letters\07-RPM-3999 Risk Review Approval Letter 02-07-2007.doc

Canolfan Gwasanaethau Busnes
Business Services Centre

South East Wales Research Ethics Committee Panel B

Telephone: 02920 376823
Facsimile: 02920 376835
Email: Carl.phillips@bsc.wales.nhs.uk

Dr Jacky Boivin
School of Psychology
Cardiff University
Psychology Building, Park Place
Cardiff
CF10 3AT

1 October 2007

Dear Dr Boivin

Full title of study: **Survey of fertility health issues**
REC reference number: **07/WSE02/77**

Thank you for your letter of 25 September 2007, responding to the Committee's request for further information on the above research, and for submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation [as revised].

Ethical review of research sites

The Committee has designated this study as exempt from site-specific assessment (SSA).

There is no requirement for [other] Local Research Ethics Committees to be informed or for site-specific assessment to be carried out at each site.

Conditions of approval

The favourable opinion is given provided that you comply with the conditions set out in the attached document.

You are advised to study the conditions carefully.

Canolfan Gwasanaethau Busnes
Ty Churchill
17 Ffordd Churchill
Caerdydd, CF10 2TW
Ffôn: 029 20 376820 WHTN: 1809
Ffacs: 029 20 376826

Business Services Centre
Churchill House
17 Churchill Way
Cardiff, CF10 2TW
Telephone: 029 20 376820 WHTN: 1809
Fax: 029 20 376826

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Application	5.4	07 August 2007
Investigator CV	J Boivin	07 August 2007
Investigator CV	L Bunting	25 September 2007
Protocol	1	06 August 2007
Letter from Sponsor	Cardiff University	26 June 2007
Peer Review	Joint Trust/University Peer & Risk Review Committee	02 July 2007
Compensation Arrangements	UMAL	01 August 2007
Questionnaire: Survey of fertility health issues	1	07 August 2007
Letter of invitation to participant	2 - Evans	25 September 2007
Letter of invitation to participant	2 - Penketh	25 September 2007
Participant Information Sheet	1 - James	07 August 2007
Participant Information Sheet	1 - Jose	07 August 2007
Participant Information Sheet	1 - Evans	07 August 2007
Response to Request for Further Information		25 September 2007

R&D approval

All researchers and research collaborators who will be participating in the research at NHS sites should apply for R&D approval from the relevant care organisation, if they have not yet done so. R&D approval is required, whether or not the study is exempt from SSA. You should advise researchers and local collaborators accordingly.

Guidance on applying for R&D approval is available from http://www.rdforum.nhs.uk/rdform.htm.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

Feedback on the application process

Now that you have completed the application process you are invited to give your view of the service you received from the National Research Ethics Service. If you wish to make your views known please use the feedback form available on the NRES website at:

https://www.nresform.org.uk/AppForm/Modules/Feedback/EthicalReview.aspx

We value your views and comments and will use them to inform the operational process and further improve our service.

07/WSE02/77	Please quote this number on all correspondence

With the Committee's best wishes for the success of this project

Yours sincerely

Carl Phillips
Executive Officer
South East Wales Research Ethics Committees

Enclosures: Standard approval conditions SL-AC2

Copy to: R&D office for Cardiff University

R&D office for Cardiff & Vale NHS Trust

Canolfan Gwasanaethau Busnes
Business Services Centre

South East Wales Research Ethics Committee Panel B

Tel: 02920 376822/6823
Fax: 02920 376835

25 January 2008

Dr Jacky Boivin
Reader
School of Psychology, Cardiff University
Psychology Building, Park Place
Cardiff
CF10 3AT UK

Dear Dr Boivin

Study title: **Survey of fertility health issues**
REC reference: **07/WSE02/77**
Amendment number: **Amendment No. 1**
Amendment date: **16 January 2007**

Thank you for submitting the above amendment, which was received on 25 January 2008. I can confirm that this is a valid notice of a substantial amendment and will be reviewed by the Sub-Committee of the South East Wales REC – Panel B at its next meeting.

Documents received

The documents to be reviewed are as follows:

Document	Version	Date
Questionnaire: Survey of reproductive health issues	2	16 January 2007
Protocol	2	16 January 2008
Participant Information Sheet	2	16 January 2007
Notice of Substantial Amendment (non-CTIMPs)	Amendment No. 1	16 January 2007
Letter of invitation to participant	3	16 January 2007

Notification of the Committee's decision

The Committee will issue an ethical opinion on the amendment within a maximum of 35 days from the date of receipt.

Canolfan Gwasanaethau Busnes
Ty Churchill
17 Ffordd Churchill
Caerdydd, CF10 2TW
Ffôn: 029 20 376820 WHTN: 1809
Ffacs: 029 20 376826

Business Services Centre
Churchill House
17 Churchill Way
Cardiff, CF10 2TW
Telephone: 029 20 376820 WHTN: 1809
Fax: 029 20 376826

NHS WALES GIG CYMRU

rhan o Addysgu Bwrdd Iechyd Lleol Powys / part of Powys Teaching Local Health Board

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval for the research.

07/WSE02/77:	Please quote this number on all correspondence

Yours sincerely

Mrs Jagjit Sidhu
Committee Co-ordinator

E-mail: jagit.sidhu@bsc.wales.nhs.uk

Copy to: *R&D office for Cardiff University*
R&D office for Cardiff and Vale NHS Trust

Canolfan Gwasanaethau Busnes
Business Services Centre

South East Wales Research Ethics Committee Panel B

Tel: 02920 376823
Fax: 02920 376835
E-mail: Carl.phillips@bsc.wales.nhs.uk

Dr Jacky Boivin
School of Psychology
Cardiff University
Psychology Building, Park Place
Cardiff
CF10 3AT

14 February 2008

Dear Dr Boivin

Study title:	**Survey of fertility health issues**
REC reference:	**07/WSE02/77**
Amendment number:	**Amendment No. 1**
Amendment date:	**16 January 2007**

The above amendment was reviewed at the meeting of the Executive Sub-Committee of Panel B of the South East Wales Research Ethics Committees held on 13 February 2008.

Ethical opinion

The members of the Committee present gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Membership of the Committee

The members of the Committee who were present at the meeting are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

[redacted]

Approved documents

The documents reviewed and approved at the meeting were:

[redacted]	[redacted]	[redacted]
Questionnaire: Survey of reproductive health issues	2	16 January 2007
Protocol	2	16 January 2008
Participant Information Sheet	2	16 January 2007
Notice of Substantial Amendment (non-CTIMPs)	Amendment No. 1	16 January 2007
Letter of invitation to participant	3	16 January 2007

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

07/WSE02/77: Please quote this number on all correspondence

Yours sincerely

Carl Phillips
Executive Officer
South East Wales Research Ethics Committee

Enclosures — List of names and professions of members who were present at the meeting and those who submitted written comments

Copy to: R&D office for Cardiff University

R&D office for Cardiff and Vale NHS Trust

South East Wales Research Ethics Committee Panel B

Attendance at Sub-Committee of the REC meeting on 13 February 2008

Mrs A Dowden	Chair and Lay Member	Lay
Dr I J Kerby	Consultant Oncologist	Expert

NHS WALES GIG CYMRU

Cardiff and Vale NHS Trust | Ymddiriedolaeth GIG Caerdydd a'r Fro

University Hospital of Wales
Ysbyty Athrofaol Cymru

Heath Park, Cardiff CF14 4XW
Phone 029 2074 7747
Minicom 029 2074 3632

Parc Y Mynydd Bychan, Caerdydd CF14 4XW
Ffôn 029 2074 7747
Minicom 029 2074 3632

Eich cyf/Your ref
Ein cyf/Our ref
Welsh Health Telephone Network 1872
Direct line/Llinell uniongyrchol

Tel: 029 20743742
Fax: 029 20745311
Research.Development@cardiffandvale.wales.nhs.uk

From: Professor MF Scanlon
Trust R&D Director
Radnor House
University Hospital of Wales
Cardiff
CF14 4XW

07 April 2008

Dr Jacky Boivin
School Of Psychology
Cardiff University, Tower Building
Park Place Cardiff CF10 3AT

Dear Dr Boivin

Project ID : 07/RPM/3999 : Survey Of Fertility Health Issues

REC Reference: 07/WSE02/77
Amendment Number: 1
Amendment Date: 16/01/08

The above amendment has been received by the Joint Trust/University Peer and Risk Review Committee.

The documents reviewed were:-

Document	Version	Date
Protocol	2	16/01/08
Patient Invitation Letter	2	16/01/08
Survey of Reproductive Health Issues	2	16/01/08
Patient Information Sheet	2	16/01/08
South East Wales REC approval Letter		14/02/08

I can confirm that the above support documentation has been approved and that you may continue with this study accordingly.

Please ensure that the appropriate Research Ethics Committee have a copy of this letter.

May I take this opportunity to wish you success with the project and remind you that as Principal Investigator you are required to:

- Inform the Trust R&D Office if any external or additional funding is awarded for this project in the future.
- Inform the Trust R&D Office of any further amendments relating to the protocol, including personnel changes and amendments to the actual or anticipated start / end dates.
- Complete any documentation sent to you by the Trust R & D Office or University Research & Commercial Division regarding this project.
- Adhere to the protocol as approved by the Research Ethics Committee.
- Ensure the research complies with the Data Protection Act 1998.

Yours sincerely,

Professor MF Scanlon
Chair of the Joint Trust/University Peer & Risk Review Committee

CC **R&D Lead Prof Alison Fiander**
Chris Shaw, Research and Commercial Division, Cardiff University
Miss Laura Elizabeth Bunting

C:\my documents\lisa\databases\study folders\3999\RD Letters\07-RPM-3999 Amendments After Approval 07-04-2006.doc

Research and Commercial Division
Director Geraint W Jones
Adran Ymchwil a Masnach
Cyfarwyddwr Geraint W Jones

Cardiff University
7th Floor
30 - 36 Newport Road
Cardiff CF24 0DE
Wales UK

Tel *Ffôn* +44(0)29 2087 5834
Fax *Ffacs* +44(0)29 2087 4189

Prifysgol Caerdydd
Llawr 7
30 - 36 Heol Casnewydd
Caerdydd CF24 0DE
Cymru Y Deyrnas Gyfunol

26 June 2007

Dr Jacky Boivin
PSYCH
Cardiff University

Dear Dr Boivin

Survey of Fertility Health Issues

I understand that you are acting as Academic Supervisor for the above *PhD* project to be conducted by Laura Bunting.

I confirm that Cardiff University agrees in principle to act as Sponsor for the above project, as required by the Research Governance Framework for Health and Social Care.

Final acceptance of Sponsorship responsibilities is dependent on the project receiving approval from:

- the joint Cardiff and Vale NHS Trust / University Peer and Risk Review Committee (JTUPeRR)[1];
- the appropriate Research Ethics Committee(s);

Once RACD has received evidence of the above approvals, the University is considered to have accepted Sponsorship.

Prior to submitting your COREC application form for review by an NHS Research Ethics Committee, you will be required to contact RACD to arrange signature of the 'Declaration by the Sponsor Representative' (Part B, section 7 of the COREC application form).

May I take this opportunity to remind you that, as Principal Investigator, you are required to:

- ensure you are familiar with your responsibilities under the Research Governance Framework for Health and Social Care;
- undertake the Trial in accordance with Cardiff University's Research Governance Framework and the principles of Good Clinical Practice;
- ensure the Research complies with the Data Protection Act 1998;
- inform the Research and Commercial Division (RACD) of any amendments to the protocol or Trial design, including changes to start / end dates;
- co-operate with any audit inspection of the project files or any requests from RACD for further information.

You should quote the following unique reference number in any correspondence relating to sponsorship for the above project:

SPON 404-07

This reference number should be quoted on all documentation associated with this project.

Yours sincerely

Dr K J Pittard Davies
Head of Research Policy & Management

Appendix N: Online Fertility Risk Factors Survey (FRFS)

Online FRFS (Pregnant women)

Survey of fertility health issues

Public health surveys help doctors to learn about many health issues, for example heart disease and diabetes in the community. Such surveys help find out how common or rare a symptom is and whether a symptom can identify whether a person might or might not develop a disease. Such information also helps to develop campaigns to keep people healthy.

Many community surveys have been carried out for arthritis, asthma, heart disease and other common ailments. However, we do not know as much about fertility health issues. The purpose of this survey is to collect more information on factors that may or may not affect fertility.

You will be asked to state how many statements apply to you. The questions will ask for general information about yourself (e.g., age), your lifestyle habits (e.g., smoking, alcohol consumption) and reproductive history (e.g., menstrual cycle). Please be as honest as possible, all answers will remain anonymous.

We will not be able to trace any responses to individual participants. Note, however, that there is a possibility that someone could intercept your responses on the way to us but this risk is negligible.

You are free to omit any questions you do not wish to answer or withdraw from the study at any time by closing the window.

The project has received ethical approval from UREC, Cardiff University. If you have any questions about this project then please contact the principal investigator Dr Jacky Boivin at boivin@cardiff.ac.uk.

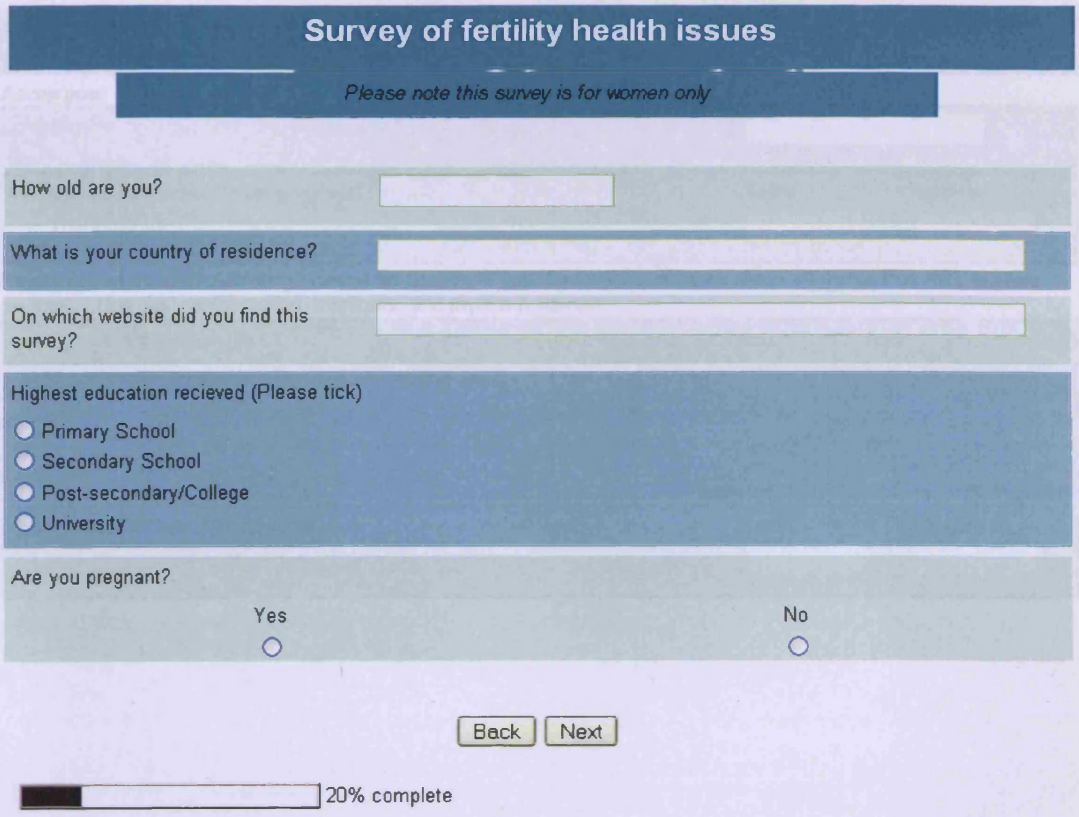
If you are 18 or over, understand the statement above and freely consent to participate in this study please tick 'YES' and continue by clicking 'Next' below. If you do not want to complete the survey please close this window now *(this survey is for women only)*.

Yes

○

Next

0% complete



Survey of fertility health issues

About you:

How many weeks pregnant are you?

How long did it take you to get pregnant? Years Months

Please tick which of the following statements applies to you. By contraception we mean **all forms** that ACT to prevent pregnancy (e.g. oral contraception, condoms, and rhythm methods).

Prior to my pregnancy I was...

- 1. Sexually active and always used contraception.
- 2. Sexually active, not using contraception and trying to get pregnant.
- 3. Sexually active, not using contraception but not particularly intending or trying to get pregnant.
- 4. Not sexually active.

If you ticked answer 2 or 3 above:
How long had you been having unprotected sex? Years Months

Survey of fertility health issues

Your reproductive history: Please answer the questions as they applied to you **before** your current pregnancy.

I had previously given birth	Yes ○	No ○
I suffered from severe period pains	Yes ○	No ○
I suffered from endometriosis	Yes ○	No ○
I had previously had pelvic inflammatory disease (PID)	Yes ○	No ○

On average my menstrual cycle was unpredictable when not using contraceptives *(My period often came more than 5 days earlier or later than expected.)*

- ○ Yes
- ○ No
- ○ I did not have a period

When not using contraception my menstrual cycle was on average:

- ○ Less than 21 days
- ○ Between 21 and 35 days
- ○ More than 35 days
- ○ I did not have a period

My male partner had mumps after puberty	Yes ○	No ○	Don't know ○	No partner ○
My partner had (or previously had) undescended testicles	Yes ○	No ○	Don't know ○	No partner ○

I had had pelvic surgery	Yes ○	No ○
If YES, describe the type of surgery		

Survey of fertility health issues

Your lifestyle: Please answer the questions as they applied to you **before** your current pregnancy.

I had unprotected sex with multiple partners	Yes ○	No ○
I was more than 13 kilos (28 pounds/2 stone) overweight	Yes ○	No ○
How much did you weigh? (Answer in either stones & pounds or kilos.)	Stones	Pounds / Kilos
My height was: *(Answer in either feet & inches or centimeters.)*	Feet	Inches / Centimeters
I was experiencing levels of stress that I could not cope with	Yes ○	No ○
I had previously had a sexually transmitted infection	Yes ○	No ○
If YES, what infection did you have?		
Had you ever taken class-A drugs? *(e.g., heroin, cocaine, ecstasy)*	Yes ○	No ○
If YES, which drug(s)?		
If YES, was this within the 12 months prior to your pregnancy?	Yes ○	No ○
Myself and/or my partner had taken anabolic steroids in the previous 12 months	Yes ○	No ○
If YES, which steroid(s)?		
I drank more than 14 units of alcohol **per week** *(1 unit = small glass of wine, 1/2 pint of beer, 1 single measure of a spirit)*	Yes ○	No ○
I was a smoker who regularly smoked ten or more cigarettes **per day**	Yes ○	No ○
I drank more than 7 units of caffeine **per day** *(1 unit = cup of coffee. 1/2 unit = cup of tea or can of soft drink such as cola)*	Yes ○	No ○
I smoked marijuana frequently *(more than four times a week)*	Yes ○	No ○

Survey of fertility health issues

Finally, this section is for everyone to fill out. Please would you write how much on average you consumed of the following before your current pregnancy. If you did not consume any please put a zero in the box:

How many units of alcohol did you drink **per week**? *(1 unit = small glass of wine, 1/2 pint of beer, 1 single measure of a spirit)*	
How many cigarettes did you smoke **per day**?	
How many **cups of coffee** did you drink **per day**?	
How many **cups of tea** did you drink **per day**?	
How many **cups/cans of soft drink such as cola** did you drink **per day**?	
How many times had you used class-A drugs in the past **12 months?**	
How much marijuana did you smoke **per week**?	

Additional comments:

Thank you for participating in this survey!

Back Next

40% complete

Survey of fertility health issues

Thank you for your time in completing this survey
Below is some more information about our research

One of the most important issues in determining health behaviour is how we perceive our own health and illness (Berry 2004). Successful public health campaigns have used a strategy of increasing public awareness of certain illnesses by researching the relevant health indicators for each illness, ensuring most people are aware of the signs and symptoms of such diseases (e.g., cancer, heart disease). Such research has highlighted the effectiveness of health indicators; health indicators can be used to monitor needs for health care, and evaluate the effectiveness and impact of health care programs (Temmerman et al., 2006).

The majority of couples will get pregnant after trying for 12 months. However, for a small number of couples it may take longer. There has been little research highlighting the main indicators for those that might have difficulties getting pregnant. Further to this relatively few people know the signs of reproductive disease or the risk factors for fertility difficulties (Dyer et al., 2002). With reference to the success of other health campaigns/surveys we wanted to examine the frequency of a number of factors that might or might not be important predictors of fertility. We hope to use the information provided to develop campaigns to keep people healthy. At the end of the project we will post a brief report on this website.

It was important to ask a range of personal questions about your lifestyle and reproductive history and we would like to assure you that all the data you have provided us is anonymously, that is, it is impossible to trace back to you.

If you have concerns about your health please contact your family doctor or local GP.

If you have any further questions about this research then please contact the principal investigator:

Dr Jacky Boivin
School of Psychology
Cardiff University
Tower Building, Park Place
Cardiff, Wales
CF10 3AT
boivin@cardiff.ac.uk

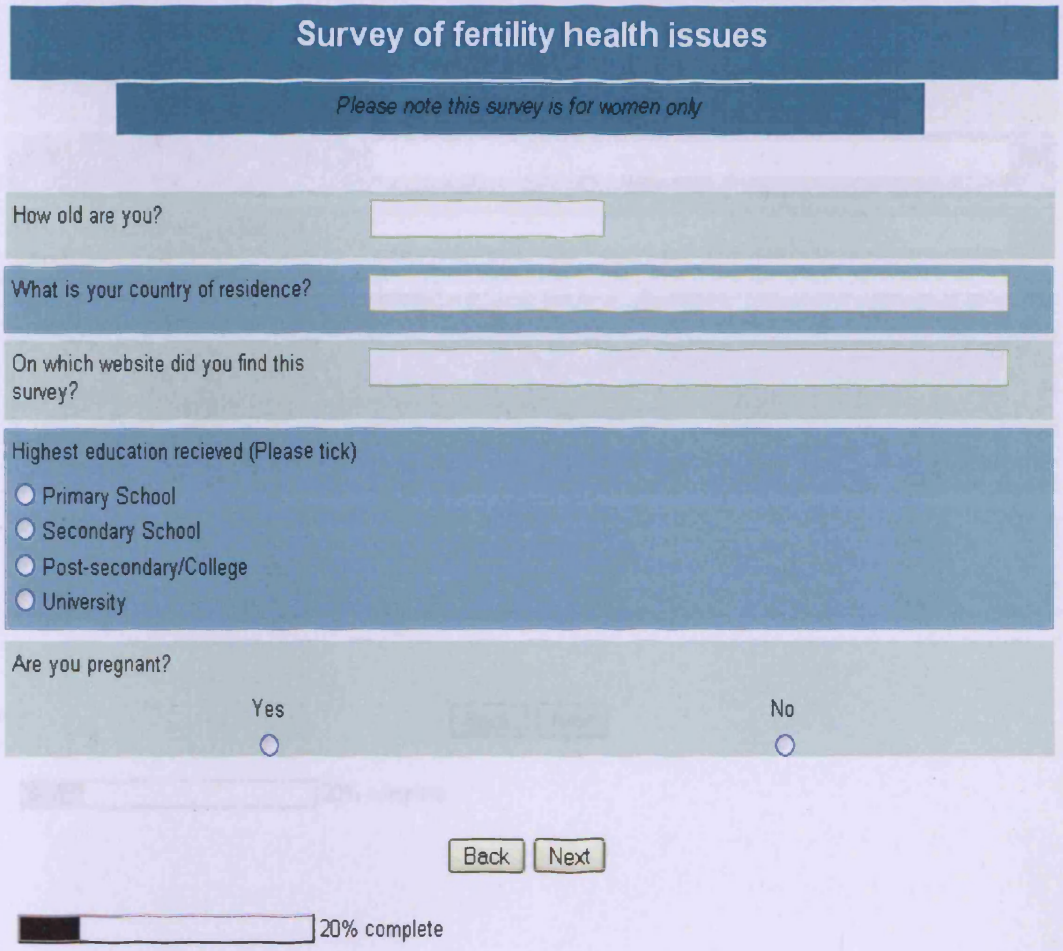
Dr Jacky Boivin is interested in the psychosocial aspects of reproductive health. She has conducted many studies in this area on issues such as the link between stress and fertility, differences between men and women in emotional reactions to fertility problems, whether counselling helps people cope with fertility problems, how children conceived with fertility treatment develop, and much more.

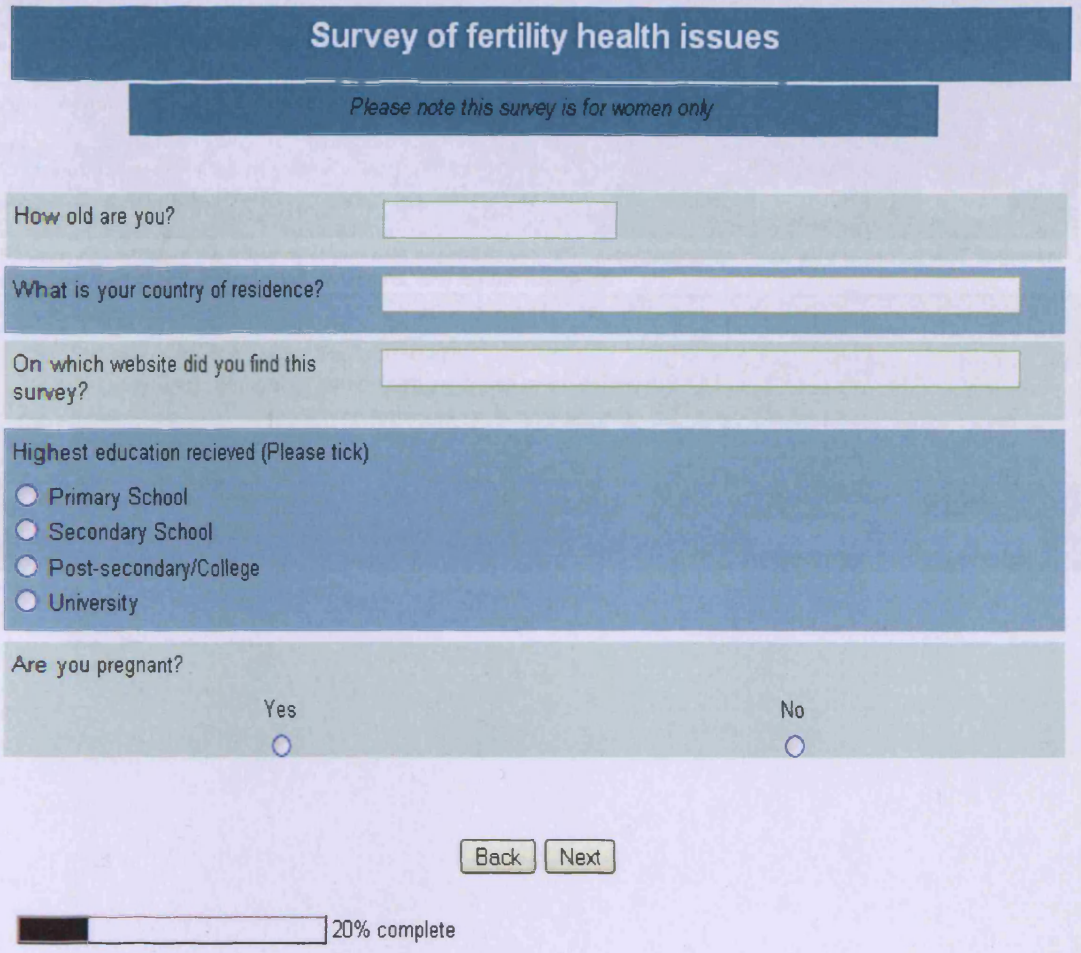
This research has been carried out with the help of women from many countries worldwide. You can see some of the published reports of this work on Dr Boivin's website at the School of Psychology, Cardiff University; http://www.cardiff.ac.uk/psych/home/boivin/indexmain.html

Back Submit

80% complete

Online FRFS (Not pregnant women)





Survey of fertility health issues

Please note this survey is for women only

How old are you?

What is your country of residence?

On which website did you find this survey?

Highest education recieved (Please tick)

- Primary School
- Secondary School
- Post-secondary/College
- University

Are you pregnant?

Yes | No

Back | Next

20% complete

Survey of fertility health issues

About you:

Are you currently **trying** to get pregnant?	Yes ○	No ○

If YES, how long have you been trying to get pregnant?	Years	Months

Please tick which of the following statements applies to you. By contraception we mean **all forms** that ACT to prevent pregnancy (e.g. oral contraception, condoms, and rhythm methods).

I am currently...

- ○ 1. Sexually active and always use contraception.
- ○ 2. Sexually active, not using contraception and trying to get pregnant.
- ○ 3. Sexually active, not using contraception but not particularly intending or trying to get pregnant.
- ○ 4. Not sexually active.

If you ticked answer 2 or 3 above: How long had you been having unprotected sex?	Years	Months

Survey of fertility health issues

Your reproductive history:

I have previously given birth	Yes ○	No ○
I suffer from severe period pains	Yes ○	No ○
I suffer from endometriosis	Yes ○	No ○
I have had pelvic inflammatory disease (PID)	Yes ○	No ○

On average my menstrual cycle is unpredictable when not using contraceptives *(My period often comes more than 5 days earlier or later than expected.)*

- ○ Yes
- ○ No
- ○ I do not have a period

When not using contraception my menstrual cycle is on average:

- ○ Less than 21 days
- ○ Between 21 and 35 days
- ○ More than 35 days
- ○ I do not have a period

My male partner had mumps after puberty	Yes ○	No ○	Don't know ○	No partner ○
My partner has (or has had) undescended testicles	Yes ○	No ○	Don't know ○	No partner ○

I have had pelvic surgery	Yes ○	No ○
If YES, describe the type of surgery		

Survey of fertility health issues

Your lifestyle:

I have had unprotected sex with multiple partners	Yes ○	No ○
I am more than 13 kilos (28 pounds/2 stone) overweight	Yes ○	No ○
How much do you weigh? *(Answer in either stones & pounds or kilos.)*	Stones	Pounds / Kilos
What is your height? *(Answer in either feet & inches or centimeters.)*	Feet	Inches / Centimeters
I am experiencing levels of stress that I cannot cope with	Yes ○	No ○
I have had a sexually transmitted infection	Yes ○	No ○
If YES, what infection did you have?		
Have you ever taken class-A drugs? *(e.g., heroin, cocaine, ecstasy)*	Yes ○	No ○
If YES, which drug(s)?		
If YES, was this within the last 12 months?	Yes ○	No ○
Myself and/or my partner has taken anabolic steroids in the previous 12 months	Yes ○	No ○
If YES, which steroid(s)?		
I drink more than 14 units of alcohol **per week** *(1 unit = small glass of wine, 1/2 pint of beer, 1 single measure of a spirit)*	Yes ○	No ○
I am a smoker who regularly smokes ten or more cigarettes per day	Yes ○	No ○
I drink more than 7 units of caffeine per day (1 unit = cup of coffee. 1/2 unit = cup of tea or can of soft drink such as cola)	Yes ○	No ○
I smoke marijuana frequently (more than four times a week)	Yes ○	No ○

Survey of fertility health issues

Finally, this section is for **everyone** to fill out. Please would you write how much you consume **on average** of the following. If you did not consume any please put a zero in the box:

How many units of alcohol do you drink **per week?** *(1 unit = small glass of wine, 1/2 pint of beer, 1 single measure of a spirit)*	
How many cigarettes do you smoke **per day?**	
How many **cups of coffee** do you drink **per day?**	
How many **cups of tea** do you drink **per day?**	
How many **cups/cans of soft drink** such as cola do you drink **per day?**	
How many class-A drugs have you taken in the past **12 months?**	
How much marijuana do you smoke **per week?**	

Additional comments:

Thank you for participating in this survey!

Back Next

60% complete

Survey of fertility health issues

Thank you for your time in completing this survey
Below is some more information about our research

One of the most important issues in determining health behaviour is how we perceive our own health and illness (Berry 2004). Successful public health campaigns have used a strategy of increasing public awareness of certain illnesses by researching the relevant health indicators for each illness, ensuring most people are aware of the signs and symptoms of such diseases (e.g., cancer, heart disease). Such research has highlighted the effectiveness of health indicators; health indicators can be used to monitor needs for health care, and evaluate the effectiveness and impact of health care programs (Temmerman et al., 2006).

The majority of couples will get pregnant after trying for 12 months. However, for a small number of couples it may take longer. There has been little research highlighting the main indicators for those that might have difficulties getting pregnant. Further to this relatively few people know the signs of reproductive disease or the risk factors for fertility difficulties (Dyer et al., 2002). With reference to the success of other health campaigns/surveys we wanted to examine the frequency of a number of factors that might or might not be important predictors of fertility. We hope to use the information provided to develop campaigns to keep people healthy. At the end of the project we will post a brief report on this website.

It was important to ask a range of personal questions about your lifestyle and reproductive history and we would like to assure you that all the data you have provided us is anonymously, that is, it is impossible to trace back to you.

If you have concerns about your health please contact your family doctor or local GP.

If you have any further questions about this research then please contact the principal investigator:

Dr Jacky Boivin
School of Psychology
Cardiff University
Tower Building, Park Place
Cardiff, Wales
CF10 3AT
boivin@cardiff.ac.uk

Dr Jacky Boivin is interested in the psychosocial aspects of reproductive health. She has conducted many studies in this area on issues such as the link between stress and fertility, differences between men and women in emotional reactions to fertility problems, whether counselling helps people cope with fertility problems, how children conceived with fertility treatment develop, and much more.

This research has been carried out with the help of women from many countries worldwide. You can see some of the published reports of this work on Dr Boivin's website at the School of Psychology, Cardiff University; http://www.cardiff.ac.uk/psych/home/boivin/indexmain.html

Back Submit

80% complete

Appendix O: Clinic Fertility Risk Factors Survey (FRFS)

Clinic FRFS (Antenatal unit)

Eich cyf/Your ref
Ein cyf/Our ref
Welsh Health Telephone Network 1872
Direct line/Llinell uniongyrchol

Cardiff and Vale NHS Trust
Ymddiriedolaeth GIG
Caerdydd a'r Fro

University Hospital of Wales
Ysbyty Athrofaol Cymru

Heath Park,
Cardiff CF14 4XW
Phone 029 2074 7747
Minicom 029 2074 3632

Parc Y Mynydd Bychan,
Caerdydd CF14 4XW
Ffôn 029 2074 7747
Minicom 029 2074 3632

Dear Patient,

We are currently trying to find out more information about factors that may or may not affect fertility. To meet this goal we would like patients to answer a short survey about their reproductive history and lifestyle.

We are inviting all women attending the clinic to take part in a research study. Participation in the study is voluntary and if you do not wish to complete the survey please place it in the box labelled "Survey Responses" or alternatively return to the reception desk. A decision to withdraw at any time or a decision not to take part, will not affect the standard of care you will receive.

If you would like to take part please fill out the short survey in this pack. The questions will ask you general information about yourself, your lifestyle habits and reproductive history. We need to ask these questions to represent all the people in the community and all factors that may impact on fertility. Please be assured that we have no way of tracing the responses back to you. The survey asks you to tick as many of the statements as apply to you. Completing the attached survey should take about 5 minutes of your time and would be very helpful in developing a greater knowledge on the indicators of fertility health. Participation is completely anonymous so please **do not put your name on any of the forms.**

Once you have completed the survey, simply fold it and put it in the box labelled "Survey Responses" which you will find in the waiting room. Alternatively, if you would like to fill the survey out elsewhere then please use the prepaid freepost envelope provided in your pack to send it back to us once completed.

Thank you very much for helping us with this project.

Sincerely,

Richard Penketh

Director,
Cardiff and Vale Antenatal Clinic
NHS Trust

Mary James
Clinical lead midwife
Cardiff and Vale Antenatal Clinic
NHS Trust
Llandough hospital

Survey of fertility health issues

We are interested in the frequency of reproductive and fertility health issues in the general population.
Please do not write your name anywhere on the survey as it is anonymous

About you:

How old are you?		
How many weeks pregnant are you?		
How long did it take you to get pregnant?	weeks	months

Please tick which of the following statements applies to you. By contraception we mean all forms that ACT to prevent pregnancy (e.g. oral contraception, condoms, and rhythm methods).

Prior to my pregnancy I was:

1. Always using contraception	YES	NO
2. Not using contraception and trying to get pregnant	YES	NO
3. Not using contraception but not particularly intending or trying to get pregnant	YES	NO
If you ticked yes to 2 or 3 above:		
How long had you been having unprotected sex?	years	months

Your reproductive history: please circle yes or no for all statements that applied to you before your current pregnancy.

I had given birth	YES	NO		
I suffered from severe period pains	YES	NO		
I suffered from endometriosis	YES	NO		
I had pelvic inflammatory disease (PID)	YES	NO		
My menstrual cycle lasted less than 21 days (When I was not using contraceptives)	YES	NO		
My menstrual cycle lasted more than 35 days (When I was not using contraceptives)	YES	NO		
My menstrual cycle was unpredictable. My period often came more than 5 days earlier or later than I expected (When I was not using contraceptives)	YES	NO		
I had periods (When I was not using contraceptives)	YES	NO		
My male partner had mumps after puberty	YES	NO	Don't know	No Partner
My partner has (or has had) undescended testicles	YES	NO	Don't know	No Partner
I had pelvic surgery	YES	NO		
If YES, describe the type of surgery				

Your lifestyle: please circle yes or no for all statements that applied to you before your current pregnancy.

I had unprotected sex with multiple partners		YES	NO
I was more than 13 kilos (28 pounds/2 stone) overweight		YES	NO
How much did you weigh before getting pregnant?	Stones or	Pounds or	Kilos
What is your height?	Feet and	inches or	Centimetres
I had sex less than twice a week		YES	NO
I had a sexually transmitted infection		YES	NO
If YES, what infection did you have?			
I was experiencing levels of stress that I could not cope with		YES	NO
Have you ever taken Class A drugs *(e.g., heroin, cocaine, ecstasy)*		YES	NO
If YES, was this within the 12 months prior to your pregnancy?		YES	NO
If YES, which drug(s)			
Myself and/or my partner had taken anabolic steroids in the previous 12 months		YES	NO
If YES, which steroid(s)?			
I had been drinking more than 14 units of alcohol per week *(1 unit = small glass of wine, ½ pint of beer, 1 single measure of a spirit)*		YES	NO
I was a smoker who regularly smoked ten or more cigarettes per day		YES	NO
I drank more than 7 units of caffeine per day *(1 unit = cup of coffee. ½ unit = cup of tea or can of soft drink such as cola)*		YES	NO
I smoked marijuana frequently *(more than four times a week)*		YES	NO

PLEASE TURN OVER

The final set of questions are for everyone to answer. Please would you write how much you consumed of the following before your current pregnancy *(If you did not consume any please put a zero in the box):*

How many units of alcohol did you drink ***per week?*** *(1 unit = small glass of wine, 1/2 pint of beer or 1 single measure of a spirit)*	
How many cigarettes did you smoke ***per day?***	
How many cups of coffee did you drink ***per day?***	
How many cups of tea did you drink ***per day?***	
How many cups/cans of soft drink such as cola did you drink ***per day?***	
How much marijuana did you smoke ***per week?***	

Highest education received (please tick)	
Primary School	
Secondary School	
Post-secondary/College	
University	

Thank you for the time you spent completing this survey.
Please place it in the box labelled fertility survey in the waiting room, alternatively you can send it back via post using the prepaid envelope provided in your pack.

NHS WALES GIG CYMRU

Cardiff and Vale NHS Trust
Ymddiriedolaeth GIG Caerdydd a'r Fro

University Hospital of Wales
Ysbyty Athrofaol Cymru

Heath Park,
Cardiff CF14 4XW
Phone 029 2074 7747
Minicom 029 2074 3632

Parc Y Mynydd Bychan,
Caerdydd CF14 4XW
Ffôn 029 2074 7747
Minicom 029 2074 3632

Eich cyf/Your ref
Ein cyf/Our ref
Welsh Health Telephone Network 1872
Direct line/Llinell uniongyrchol

INFORMATION SHEET FOR PATIENTS
Research project
Survey of fertility health issues

You are being invited to take part in a research study. Before you decide, it is important that you understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends and relatives if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Consumers for Ethics in Research (CERES), publish a leaflet entitled 'Medical Research and You'. This leaflet gives more information about medical research and looks at some questions you may want to ask. A copy is available on request for additional background reading.

Thank you for reading this.

What is the purpose of this study?
Public health surveys help doctors to learn about many health issues, for example heart disease and diabetes in the community. Such surveys help find out how common or rare a symptom is and whether a symptom can identify whether a person might or might not develop a disease. Such information also helps to develop campaigns to keep people healthy. Many community surveys have been carried out for arthritis, asthma, heart disease and other common ailments. However, we do not know as much about fertility health issues. The purpose of this survey is to collect more information on factors that may or may not affect fertility.

Why have I been chosen?
You have been chosen because we are inviting all women attending the Cardiff and Vale Trust Antenatal Clinics.

Do I have to take part?
No. it is up to you to decide whether or not to take part. If you decide to take part you will be given this information sheet to keep. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time or a decision not to take part, will not affect the standard of care you receive.

What will happen to me if I take part?
If you decide to take part we will ask you to complete one survey. The survey asks you to tick the number of statements that apply to you. There are three sections consisting of demographic (e.g., age), reproductive history (e.g., menstrual cycle), and current lifestyle questions (e.g., alcohol consumption, smoking). The survey will take 5 minutes and you can fill it in while waiting for your medical appointment. Alternatively, if you wish to complete the survey elsewhere please use the envelope provided in the pack. Postage has been paid in advance for the envelope. No participation fee will be offered. At the end of the study we will put a summary of the results on the notice board in the patient waiting room.

What do I have to do?
If you would like to participate please fill in the survey and return it in the box marked fertility survey study, which is in the patient waiting room. Alternatively, if you wish to complete the survey elsewhere please use the prepaid envelope provided in the pack. Please do not write your name anywhere on the survey as it is anonymous. If you do not finish the survey before your appointment, you can finish it after the appointment or return it at a later date using the prepaid envelope provided. This study does not require any changes to your treatment or lifestyle.

What will happen if I don't want to participate?
If you do not wish to participate, put the survey, without filling it, in the collection box marked fertility survey study, which is in the patient waiting room. Your decision not to participate will not affect your treatment in any way.

What are the side effects of taking part?
There are no side effects anticipated in this project as there are no drugs or invasive procedures being tested. However, if you feel any discomfort as a result of participation in the study then please contact Dr Jacky Boivin (see details below) who is a psychologist specialising in reproductive and fertility issues. If you feel worried about your health then contact your local GP.

What are the benefits of taking part in the study?
We cannot promise the study will help you but the information we get will be used to advance our understanding of reproductive health and fertility issues.

Will my taking part in the study be kept strictly confidential?
Our procedures for handling, processing, storage and destruction of your data are compliant with the Data Protection Act 1998. All information you will provide us is anonymous and cannot be traced back to you individually. The anonymous data will be retained for indefinitely in accordance with the Data Protection Act, and stored on a computer that is password-protected and belongs to Dr Jacky Boivin.

What if there is a problem?
If you have a concern about any aspect of this study, you should ask to speak with the researchers who will do their best to answer your questions (see contact details below). If you remain unhappy and wish to complain formally, you can do this through the NHS complaints procedure. Details can be obtained from the hospital.

What will happen to the results of this research study?
The results of this study will be published in peer reviewed fertility journals. You cannot be identified in any report or publications.

Who is organising and funding the research?
Dr Jacky Boivin, School of Psychology Cardiff University.

Who has reviewed the research?
The South East Wales Local Research Ethics Committee has reviewed and approved this study.

You will be given a copy of the Information sheet to keep for your records.

Contact Details
You can contact the research team for any question on:

Mary James
Clinical lead midwife
Cardiff and Vale Antenatal Unit
Llandough hospital
Tel: 02920 716 097

Dr Jacky Boivin
School of Psychology
Cardiff University
Tower Building, Park Place
Tel: 02920 875 289

Thank you very much for taking time to read this leaflet.

Clinic FRFS (Fertility unit)

NHS WALES GIG CYMRU

Eich cyf/Your ref
Ein cyf/Our ref
Welsh Health Telephone Network 1872
Direct line/Llinell uniongyrchol

Cardiff and Vale NHS Trust
Ymddiriedolaeth GIG Caerdydd a'r Fro

University Hospital of Wales
Ysbyty Athrofaol Cymru

Heath Park,
Cardiff CF14 4XW
Phone 029 2074 7747
Minicom 029 2074 3632

Parc Y Mynydd Bychan,
Caerdydd CF14 4XW
Ffôn 029 2074 7747
Minicom 029 2074 3632

Dear Patient,

We are currently trying to find out more information about factors that may or may not affect fertility. To meet this goal we would like patients to answer a short survey about their reproductive history and lifestyle.

We are inviting all women attending the clinic to take part in a research study. Participation in the study is voluntary and if you do not wish to complete the survey please place it in the box labelled "Survey Responses" or alternatively return to the reception desk. A decision to withdraw at any time or a decision not to take part, will not affect the standard of care you will receive.

If you would like to take part please fill out the short survey in this pack. The questions will ask you general information about yourself, your lifestyle habits and reproductive history. We need to ask these questions to represent all the people in the community and all factors that may impact on fertility. Please be assured that we have no way of tracing the responses back to you. The survey asks you to tick as many of the statements as apply to you. Completing the attached survey should take about 5 minutes of your time and would be very helpful in developing a greater knowledge on the indicators of fertility health. Participation is completely anonymous so please **do not put your name on any of the forms.**

Once you have completed the survey, simply fold it and put it in the box labelled "Survey Responses" which you will find in the waiting room. Alternatively, if you would like to fill the survey out elsewhere then please use the prepaid freepost envelope provided in your pack to send it back to us once completed.

Thank you very much for helping us with this project.

Sincerely,

Mrs Janet Evans

Director,
Cardiff Assisted Reproduction Unit
University Hospital Wales

Survey of fertility health issues

We are interested in the frequency of reproductive and fertility health issues in the general population.
Please do not write your name anywhere on the survey as it is anonymous
About you:

How old are you?		
How long have you been trying to get pregnant?	years	months

Your reproductive history:

I have given birth	YES	NO		
I suffer from severe period pains	YES	NO		
I suffer from endometriosis	YES	NO		
I have had pelvic inflammatory disease (PID)	YES	NO		
My menstrual cycle lasts less than 21 days (When I am not using contraceptives)	YES	NO		
My menstrual cycle lasts more than 35 days (When I am not using contraceptives)	YES	NO		
My menstrual cycle is unpredictable. My period often comes more than 5 days earlier or later than I expected (When I am not using contraceptives)	YES	NO		
When I am not using contraceptives I have periods	YES	NO		
My male partner has had mumps after puberty	YES	NO	Don't know	No Partner
My partner has (or has had) undescended testicles	YES	NO	Don't know	No Partner
I have had pelvic surgery	YES	NO		
If YES, describe the type of surgery				

Your lifestyle:

I have had unprotected sex with multiple partners			
I am more than 13 kilos (28 pounds/2 stone) overweight		YES	NO
How much do you weigh?	Stones or	Pounds or	Kilos
What is your height?	Feet and	inches or	Centimetres
I have sex less than twice a week			
I have had a sexually transmitted infection		YES	NO
If YES, what infection did you have?			
I am experiencing levels of stress that I cannot cope with		YES	NO
Have you ever taken Class A drugs *(e.g., heroin, cocaine, ecstasy)*			
If YES, was this within the last 12 months?		YES	NO
If YES, which drug(s)?			
Myself and/or my partner have taken anabolic steroids in the previous 12 months		YES	NO
If YES, which steroid(s)?			
I drink more than 14 units of alcohol per week *(1 unit = small glass of wine, ½ pint of beer, 1 single measure of a spirit)*		YES	NO
I am a smoker who regularly smokes ten or more cigarettes per day			
I drink more than 7 units of caffeine per day *(1 unit = cup of coffee. ½ unit = cup of tea or can of soft drink such as cola)*		YES	NO
I smoke marijuana frequently *(more than four times a week)*			

The final set of questions are for everyone to answer. *(If you did not consume any please put a zero in the box):*

How many units of alcohol do you drink **per week?** *(1 unit = small glass of wine, 1/2 pint of beer or 1 single measure of a spirit)*	
How many cigarettes do you smoke **per day?**	
How many cups of coffee do you drink **per day?**	
How many cups of tea do you drink **per day?**	
How many cups/cans of soft drink such as cola do you drink **per day?**	
How much marijuana do you smoke **per week?**	

PLEASE TURN OVER

Highest education received (please tick)	
Primary School	
Secondary School	
Post-secondary/College	
University	

Thank you for the time you spent completing this survey.
Please place it in the box labelled fertility survey in the waiting room, alternatively you can send it back via post using the prepaid envelope provided in your pack.

NHS WALES GIG CYMRU

Eich cyf/Your ref
Ein cyf/Our ref
Welsh Health Telephone Network 1872
Direct line/Llinell uniongyrchol

Cardiff and Vale NHS Trust
Ymddiriedolaeth GIG Caerdydd a'r Fro

University Hospital of Wales
Ysbyty Athrofaol Cymru

Heath Park,
Cardiff CF14 4XW
Phone 029 2074 7747
Minicom 029 2074 3632

Parc Y Mynydd Bychan,
Caerdydd CF14 4XW
Ffôn 029 2074 7747
Minicom 029 2074 3632

INFORMATION SHEET FOR PATIENTS
Research project
Survey of fertility health issues

You are being invited to take part in a research study. Before you decide, it is important that you understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends and relatives if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Consumers for Ethics in Research (CERES), publish a leaflet entitled 'Medical Research and You'. This leaflet gives more information about medical research and looks at some questions you may want to ask. A copy is available on request for additional background reading.

Thank you for reading this.

What is the purpose of this study?
Public health surveys help doctors to learn about many health issues, for example heart disease and diabetes in the community. Such surveys help find out how common or rare a symptom is and whether a symptom can identify whether a person might or might not develop a disease. Such information also helps to develop campaigns to keep people healthy. Many community surveys have been carried out for arthritis, asthma, heart disease and other common ailments. However, we do not know as much about fertility health issues. The purpose of this survey is to collect more information on factors that may or may not affect fertility.

Why have I been chosen?
You have been chosen because we are inviting all women attending the Cardiff Assisted Reproduction Unit.

Do I have to take part?
No. it is up to you to decide whether or not to take part. If you decide to take part you will be given this information sheet to keep. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time or a decision not to take part, will not affect the standard of care you receive.

What will happen to me if I take part?
If you decide to take part we will ask you to complete one survey. The survey asks you to tick the number of statements that apply to you. There are three sections consisting of demographic (e.g., age), reproductive history (e.g., menstrual cycle), and current lifestyle questions (e.g., alcohol consumption, smoking). The survey will take 5 minutes and you can fill it in while waiting for your medical appointment. Alternatively, if you wish to complete the survey elsewhere please use the envelope provided in the pack. Postage has been paid in advance for the envelope. No participation fee will be offered. At the end of the study we will put a summary of the results on the notice board in the patient waiting room.

What do I have to do?
If you would like to participate please fill in the survey and return it in the box marked fertility survey study, which is in the patient waiting room. Alternatively, if you wish to complete the survey elsewhere please use the prepaid envelope provided in the pack. Please do not write your name anywhere on the survey as it is anonymous. If you do not finish the survey before your appointment, you can finish it after the appointment or return it at a later date using the prepaid envelope provided. This study does not require any changes to your treatment or lifestyle.

What will happen if I don't want to participate?
If you do not wish to participate, put the survey, without filling it, in the collection box marked fertility survey study, which is in the patient waiting room. Your decision not to participate will not affect your treatment in any way.

What are the side effects of taking part?
There are no side effects anticipated in this project as there are no drugs or invasive procedures being tested. However, if you feel any discomfort as a result of participation in the study then please contact Dr Jacky Boivin (see details below) who is a psychologist specialising in reproductive and fertility issues. If you feel worried about your health then contact your local GP.

What are the benefits of taking part in the study?
We cannot promise the study will help you but the information we get will be used to advance our understanding of reproductive health and fertility issues.

Will my taking part in the study be kept strictly confidential?
Our procedures for handling, processing, storage and destruction of your data are compliant with the Data Protection Act 1998. All information you will provide us is anonymous and cannot be traced back to you individually. The anonymous data will be retained for indefinitely in accordance with the Data Protection Act, and stored on a computer that is password-protected and belongs to Dr Jacky Boivin.

What if there is a problem?
If you have a concern about any aspect of this study, you should ask to speak with the researchers who will do their best to answer your questions (see contact details below). If you remain unhappy and wish to complain formally, you can do this through the NHS complaints procedure. Details can be obtained from the hospital.

What will happen to the results of this research study?
The results of this study will be published in peer reviewed fertility journals. You cannot be identified in any report or publications.

Who is organising and funding the research?
Dr Jacky Boivin, School of Psychology Cardiff University.

Who has reviewed the research?
The South East Wales Local Research Ethics Committee has reviewed and approved this study.

You will be given a copy of the Information sheet to keep for your records.

Contact Details
You can contact the research team for any question on:

Mrs Janet Evans
Director
Cardiff Assisted Reproduction Unit
University Hospital Wales
Tel: 02920 874 446

Dr Jacky Boivin
School of Psychology
Cardiff University
Tower Building, Park Place
Tel: 02920 875 289

Thank you very much for taking time to read this leaflet.

Clinic FRFS (Abortion unit)

NHS WALES GIG CYMRU

Eich cyf/Your ref
Ein cyf/Our ref
Welsh Health Telephone Network 1872
Direct line/Llinell uniongyrchol

Cardiff and Vale NHS Trust
Ymddiriedolaeth GIG Caerdydd a'r Fro

University Hospital of Wales
Ysbyty Athrofaol Cymru

Heath Park,
Cardiff CF14 4XW
Phone 029 2074 7747
Minicom 029 2074 3632

Parc Y Mynydd Bychan,
Caerdydd CF14 4XW
Ffôn 029 2074 7747
Minicom 029 2074 3632

Dear Patient,

We are currently trying to find out more information about factors that may or may not affect **reproductive health.** To meet this goal we would like patients to answer a short survey about their reproductive history and lifestyle.

We are inviting all women admitted for a medical abortion procedure aged 18 and above to take part in a research study. Participation in the study is voluntary and if you do not wish to complete the survey please return it sealed in the envelope provided in the pack. A decision to withdraw at any time or a decision not to take part, will not affect the standard of care you will receive.

If you would like to take part please fill out the short survey in this pack. The questions will ask you general information about yourself, your lifestyle habits and reproductive history. **We need to ask these questions to represent all people in the community and all factors that may influence reproductive health. Please be assured that we have no way of tracing the responses back to you.** The survey asks you to tick as many of the statements as apply to you. Completing the attached survey should take about 5 minutes of your time and would be very helpful in developing a greater knowledge on the indicators of reproductive health. Participation is completely anonymous so please do not put your name on any of the forms.

Once you have completed the survey, **simply return it sealed in the envelope provided in the pack.**

Thank you very much for helping us with this project.

Sincerely,

Dr Caroline Scherf

Consultant,
Sexual and Reproductive Health
Department of Gynaecology
Llandough Hospital

Carolyn Alport

Ward Manager,
Sexual and Reproductive Health
Department of Gynaecology
Llandough Hospital

Survey of reproductive health issues

We are interested in the frequency of reproductive health issues in the general population.
Please do not write your name anywhere on the survey as it is anonymous
About you:

How old are you?	
How advanced is this pregnancy?	weeks

Please tick which of the following statements applies to you. By contraception we mean all forms that ACT to prevent pregnancy (e.g. oral contraception, condoms, and rhythm methods).
Prior to the pregnancy I was:

1. Always using contraception	YES	NO
2. Sometimes using contraception	YES	NO
3. Not using contraception and not trying to get pregnant	YES	NO
4. Not using contraception and not particularly intending to get pregnant	YES	NO
5. Not using contraception and trying to get pregnant	YES	NO
If you ticked yes to 2, 3, 4 or 5 above:		
How long had you been having unprotected sex?	years	months

Your reproductive history: please circle yes or no for all statements that applied to you before **you became pregnant.**

I had given birth				
I suffered from severe period pains	YES	NO		
I suffered from endometriosis				
I had pelvic inflammatory disease (PID)	YES	NO		
My menstrual cycle lasted less than 21 days (When I was not using contraceptives)				
My menstrual cycle lasted more than 35 days (When I was not using contraceptives)	YES	NO		
My menstrual cycle was unpredictable. My period often came more than 5 days earlier or later than I expected (When I was not using contraceptives)				
I had periods (When I was not using contraceptives)	YES	NO		
My male partner had mumps after puberty				
My partner has (or has had) undescended testicles	YES	NO	Don't know	No Partner
I had pelvic surgery				
If YES, describe the type of surgery				

Your lifestyle: please circle yes or no for all statements that applied to you before **you became pregnant.**

I had unprotected sex with multiple partners			
I was more than 13 kilos (28 pounds/2 stone) overweight		YES	NO
How much did you weigh before getting pregnant?	Stones or	Pounds or	Kilos
What is your height?	Feet and	Inches or	Centimetres
I had sex less than twice a week			
I had a sexually transmitted infection		YES	NO
If YES, what infection did you have?			
I was experiencing levels of stress that I could not cope with			
Have you ever taken Class A drugs *(e.g., heroin, cocaine, ecstasy)*		YES	NO
If YES, which drug(s)			
If YES, was this within the 12 months prior to the pregnancy?		YES	NO
Myself and/or my partner had taken anabolic steroids in the previous 12 months			
If YES, which steroid(s)?			
I had been drinking more than 14 units of alcohol per week *(1 unit = small glass of wine, ½ pint of beer, 1 single measure of a spirit)*			
I was a smoker who regularly smoked ten or more cigarettes per day		YES	NO
I drank more than 7 units of caffeine per day *(1 unit = cup of coffee. ½ unit = cup of tea or can of soft drink such as cola)*			

PLEASE TURN OVER

I smoked marijuana frequently *(more than four times a week)*	YES	NO

The final set of questions are for everyone to answer. Please would you write how much you consumed of the following before **you became pregnant** *(If you did not consume any please put a zero in the box):*

How many units of alcohol did you drink ***per week?*** *(1 unit = small glass of wine, 1/2 pint of beer or 1 single measure of a spirit)*	
How many cigarettes did you smoke ***per day?***	
How many cups of coffee did you drink ***per day?***	
How many cups of tea did you drink ***per day?***	
How many cups/cans of soft drink such as cola did you drink ***per day?***	
How much marijuana did you smoke ***per week?***	

Highest education received (please tick)	
Primary School	
Secondary School	
Post-secondary/College	
University	

Thank you for the time you spent completing this survey.
Please seal it in the envelope provided and leave it on your bedside locker.

NHS WALES GIG CYMRU

Eich cyf/Your ref
Ein cyf/Our ref
Welsh Health Telephone Network 1872
Direct line/Llinell uniongyrchol

Cardiff and Vale NHS Trust
Ymddiriedolaeth GIG Caerdydd a'r Fro

University Hospital of Wales
Ysbyty Athrofaol Cymru

Heath Park,
Cardiff CF14 4XW
Phone 029 2074 7747
Minicom 029 2074 3632

Parc Y Mynydd Bychan,
Caerdydd CF14 4XW
Ffôn 029 2074 7747
Minicom 029 2074 3632

INFORMATION SHEET FOR PATIENTS
Research project
Survey of fertility health issues

You are being invited to take part in a research study. Before you decide, it is important that you understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends and relatives if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Consumers for Ethics in Research (CERES), publish a leaflet entitled 'Medical Research and You'. This leaflet gives more information about medical research and looks at some questions you may want to ask. A copy is available on request for additional background reading.

Thank you for reading this.

What is the purpose of this study?
Public health surveys help doctors to learn about many health issues, for example heart disease and diabetes in the community. Such surveys help find out how common or rare a symptom is and whether a symptom can identify whether a person might or might not develop a disease. Such information also helps to develop campaigns to keep people healthy. Many community surveys have been carried out for arthritis, asthma, heart disease and other common ailments. However, we do not know as much about **reproductive** health issues. The purpose of this survey is to collect more information on factors that may or may not affect **reproductive health.**

Why have I been chosen?
You have been chosen because we are inviting all women at the Sexual and Reproductive Health Clinic admitted for a medical abortion procedure aged 18 and above.

Do I have to take part?
No. it is up to you to decide whether or not to take part. If you decide to take part you will be given this information sheet to keep. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time or a decision not to take part, will not affect the standard of care you receive.

What will happen to me if I take part?
If you decide to take part we will ask you to complete one survey. The survey asks you to tick the number of statements that apply to you. There are three sections consisting of demographic (e.g., age), reproductive history (e.g., menstrual cycle), and current lifestyle questions (e.g., alcohol consumption, smoking). The survey will take 5 minutes and you can fill it in while waiting **on the ward**. No participation fee will be offered. At the end of the study we will put a summary of the results on the notice board in the waiting room of the **Community Sexual Health (Family Planning Clinic).**

What do I have to do?
If you would like to participate please fill in the survey **and place it in the envelope provided and leave it on your bedside locker.** Please do not write your name anywhere on the survey as it is anonymous. This study does not require any changes to your treatment or lifestyle.

What will happen if I don't want to participate?
If you do not wish to participate, put the survey, without filling it, sealed, in the envelope provided in the pack and leave it on your bedside locker. Your decision not to participate will not affect your treatment in any way.

What are the side effects of taking part?
There are no side effects anticipated in this project as there are no drugs or invasive procedures being tested. However, if you feel any discomfort as a result of participation in the study then please contact Dr Jacky Boivin (see details below) who is a psychologist specialising in reproductive issues. If you feel worried about your health then contact your local GP.

What are the benefits of taking part in the study?
We cannot promise the study will help you but the information we get will be used to advance our understanding of reproductive health.

Will my taking part in the study be kept strictly confidential?
Our procedures for handling, processing, storage and destruction of your data are compliant with the Data Protection Act 1998. All information you will provide us is anonymous and cannot be traced back to you individually. The anonymous data will be retained for indefinitely in accordance with the Data Protection Act, and stored on a computer that is password-protected and belongs to Dr Jacky Boivin.

What if there is a problem?
If you have a concern about any aspect of this study, you should ask to speak with the researchers who will do their best to answer your questions (see contact details below). If you remain unhappy and wish to complain formally, you can do this through the NHS complaints procedure. Details can be obtained from the hospital.

What will happen to the results of this research study?
The results of this study will be published in peer reviewed fertility journals. You cannot be identified in any report or publications.

Who is organising and funding the research?
Dr Jacky Boivin, School of Psychology Cardiff University.

Who has reviewed the research?
The South East Wales Local Research Ethics Committee has reviewed and approved this study.

You will be given a copy of the Information sheet to keep for your records.

Contact Details
You can contact the research team for any question on:

Caroline Scherf
Consultant
Sexual and Reproductive Health
Department of Gynaecology
Llandough Hospital
Tel: 02920 716 121

Dr Jacky Boivin
School of Psychology
Cardiff University
Tower Building, Park Place
Tel: 02920 875 289

Thank you very much for taking time to read this leaflet.