CARDIFF UNIVERSITY

Modelling Disease Progression and Treatment Pathways for Depression

by

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Summary

Modelling Disease Progression and Treatment Pathways for Depression

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Depression is a global public health issue which affects and is affected by many life factors. The burden of depression has an impact on an individual's quality of life as well as on healthcare costs. Studies have shown that the condition is complex and healthcare providers are struggling to meet the demand.

Building on the existing studies of model-based economic evaluation and a stepped care treatment recommendation, the study aims to develop a model which incorporates disease progression and treatment pathways. It seeks to investigate: the impact of depression on healthcare services; the relationship between different levels of service provision and depression progression, and its related burden of disease.

The literature review shows there is a gap in the application of a hybrid simulation in mental health care. This research endeavours to fill that gap by combining Agent Based Modelling and System Dynamics approaches to describe depression progression and related treatment pathways.

Data obtained from different sources inform the parameters for running the experimentation at different service levels. The results indicate that an increase in service provision tends to reduce inpatient care use, the deterioration of depression, and relapse cases. Such an increase in service use may also increase healthcare costs, however treating more people with depression could avoid a detrimental effect.

The research addresses the development of a hybrid simulation model applied in a healthcare problem where disease progression and treatment pathways are important elements that cannot be separated. The developed model can be used to answer questions relating to disease progression, resource utilisation, and implications for the burden of disease and health policy. Further research should consider a multi disciplinary study including experts from different fields: Operational Research, Data Science, and Public Health.

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This thesis is the result of my own independent work, except where otherwise stated, and the views expressed are my own. Other sources are acknowledged by explicit references. The thesis has not been edited by a third party beyond what is permitted by Cardiff University's Use of Third Party Editors by Research Degree Students Procedure.

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WORD COUNT Approx. 49,410 of 63,667.

To Kevin, Nabil, David, and Aishah.

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The last sentence has been typed. I feel relief and gratitude to the Lord Who bestowed upon me the ability and the power to complete my study. This is the thesis. A culmination of effort in seeking knowledge supported by an abundance of encouragement, sacrifices, patience, and trust from the wonderful people around me. No words will ever be enough to express my gratitude.

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Presentations

Conference and Workshop Presentations

Modelling Mental Health Patient Pathways: In the Process of Understanding the System - Brice S.N., *PhD Seminar*, University of Adelaide, November 2016.

Modelling Mental Health Services: Capturing Human Behaviour - Brice S.N., Harper P., Gartner D., *OR and Stats Group Seminar*, Cardiff School of Mathematics, December 2017.

Modelling Disease Progression and Treatment Pathways for Depression, Brice S.N., Harper P., Gartner D., Behrens D., *OR60*, Lancaster University, September 2018.

Modelling Disease Progression and Treatment Pathways for Depression, Brice S.N., Harper P., Gartner D., Behrens D., *SWORDS Seminar*, Cardiff School of Mathematics, October 2018.

Modelling Depression Progression and Treatment Pathways, Brice S.N., Harper P., Gartner D., Behrens D., *DECHIPHer Forum*, Cardiff School of Social Sciences, January 2019.

Modelling Depression Progression and Treatment Pathways, Brice S.N., Harper P., Gartner D., Behrens D., *Healthcare Modelling Group*, Cardiff School of Mathematics, February 2019.

Modelling Disease Progression and Treatment Pathways for Depression, Brice S.N., Harper P., Gartner D., Behrens D., *System Dynamics Mini Conference*, Cardiff Business School, March 2019.

Hybrid Simulation Modelling of Disease Progression and Treatment Pathways for Depression, Brice S.N., Harper P., Gartner D., Behrens D., *NHS Wales Modelling Collaborative: From Macro to Micro Health Simulation*, Cardiff, June 2019.

Poster Presentation

Modelling Mental Health Care Pathways and Services for Capacity Planning and Policy Decisions, Brice S.N., Harper P., Gartner D., Behrens D., *ORAHs*, University of Bath, August 2017.

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Abbreviations

ABM	**A**gent **B**ased **M**odelling
ABMUHB	**A**bertawe **B**ro **M**organnwg **U**niversity **H**ealth **B**oard
ABUHB	**A**neurin **B**evan **U**niversity **H**ealth **B**oard
CAT	**C**are **A**nd **T**reatment plan
CBT	**C**ognitive **B**ehavioural **T**herapy
CCBT	**C**omputerised **C**ognitive **B**ehavioural **T**herapy
CLD	**C**ausal **L**oop **D**iagram
CMHT	**C**ammunity **M**ental **H**ealth **T**eam
CRHTT	**C**risis **R**esolution **H**ome **T**reatment **T**eam
CPP	**C**omplex **P**atient **P**athway
DALY	**D**isability **A**djusted **L**ife **Y**ear
DES	**D**iscrete **E**vent **S**imulation
DGH	**D**istrict **G**eneral **H**ospital
DSM	**D**iagnostic and **S**tatistical **M**anual
ECT	**E**lectro **C**onvulsive **T**herapy
ED	**E**mergency **D**epartment
GCBT	**G**roup **C**ognitive **B**ehavioural **T**herapy
GDP	**G**ross **D**omestic **P**roduct
GP	**G**eneral **P**ractitioner
ICC	**I**ntermediate **C**are **C**entre
ICD	**I**nternational **C**lassification of **D**iseases
IP	**I**nterpersonal **T**herapy
LD	**L**earning and **D**isability
LHB	**L**ocal **H**ealth **B**oard

LPMHSS	**L**ocal **P**rimary **M**ental **H**ealth **S**upport **S**ystem
MDD	**M**ajor **D**epressive **D**isorder
MHSS	**M**ental **H**ealth **S**hort **S**tay
NGO	**N**on **G**overnmental **O**rganisation
OAH	**O**lder **A**dult **H**ospital
OECD	**O**rganisation for **E**conomic **C**o-operation and **D**evelopment
OOH	**O**ut **O**f **H**our service
OR	**O**perational **R**esearch
PICU	**P**sychiatric **I**npatient **C**are **U**nit
PTSD	**P**ost **T**raumatic **S**tress **D**isorder
QALY	**Q**uaility **A**djusted **L**ife **Y**ear
SD	**S**ystem **D**ynamics
SSRI	**S**elective **S**erotonin **R**euptake **I**nhibitor

Chapter 1

Introduction

1.1 Why mental health?

Mental health is a global issue which affects hundreds of millions of people and is regarded as one of the leading causes of disability (World Health Organization (2001)). It continues to affect the population globally in significant numbers. The determinant factors are manifold, covering social, economical, as well as an individual's physical health condition. People affected by mental health conditions not only suffer from stigma (Crowe et al. (2016)), which may lead to disadvantages in life, but also can experience premature death due to suicide (Twenge et al. (2019)). The effect of mental health on the economy has been found to be significant due to loss of productivity and incurred associated healthcare costs (Parsonage and Saini (2018)).

The complexity related to mental health has multi layers. This includes a wide spectrum of conditions; the unknown true size of prevalence; and the provision of healthcare services dedicated to people with mental health problems.

Globally, depression is considered as a common mental health condition which has different levels of severity. It starts with a mild condition which, if untreated, can progress to a more severe condition. The significance of depression not only affects a large number of the world's population, but has also been found to be comorbid with many chronic physical as well as mental health conditions (example found in Shen et al. (2010)). This issue, among others, affects the accuracy of detecting mental health and leads to issues of under diagnosis and under treatment (Daveney et al. (2019)).

Public health services continue to improve the provision of healthcare for people suffering from mental health conditions. The provision of a mental health service has undergone a transformation from a specialist service to a more general health service. Nowadays, the care is provided at many levels ranging from primary to tertiary care, with more emphasis on community care. However, the diversity of service providers means a fragmenting of care which creates complex treatment pathways.

The provision of mental healthcare varies across the globe. In many countries, it suffers from a lack of available resources; human as well as financial (World Health Organization (2018c)). This may be due to the difficulty in estimating the true demand for health services, and the complexity of treatment pathways. Although a recommendation on treatment pathways (such as stepped care) is available, its application in practice is not well known.

1.2 Study context

The variety of healthcare services for treating mental health conditions across the globe makes it impossible to generalise any model of care service. In order to give some description of current mental health service provision we studied two different systems: the healthcare system in Wales (UK) and the healthcare system in South Australia. The two countries were chosen as their experts are collaborating partners in the current study.

During the first and second year of study, we spent a year in South Australia, where we learnt about the provision of mental health care with the experts (psychiatrists, GP, and people who have been part of SA health). Our intention was to develop a model based on the problems in South Australia, hence we did not have any engagement with the local experts in Wales. During this visit, we developed a Causal Loop Diagram, which will be explained in more detail in Chapter 4, as a means of communication with the experts as well as a tool to explore the problems related to mental health care. Despite this purpose, we did not develop our hybrid model based on the description found in the Causal Loop Diagram model.

Following the visit to South Australia, we started developing a hybrid model using a combination of Agent Based Modelling and System Dynamics. We followed every procedure for ethical approval to get the necessary data from the SA health. Unfortunately, the acquisition of data, which would involve transferring health data across the continent, did not materialise. The rest of the study was carried out in the UK. During this time, we had a chance to engage with the local experts from the Aneurin Bevan Health Board. We were able to get local data, albeit very little that could be used for our hybrid model. Nonetheless, the local health board data helped in getting the picture of patient flow within the inpatient facilities in Wales.

The description of the two different geographical contexts, South Australia and Wales, provides interesting insights into the provision of mental healthcare relative to: prevalence, healthcare financing, and networks of healthcare providers. It is not meant to be a comparative study, rather the two contexts complement each other in illustrating the complexity of the healthcare system.

Existing studies on complex healthcare systems have used several different methods. However, the literature search on Operational Research methods applied in mental healthcare highlights three points. Firstly, Markov models are frequently applied and predominantly used in the area of medical decision making and treatment evaluation. Analytical approaches, such as queueing theory and mathematical modelling, are used very infrequently.

Secondly, the application of simulation methods (Discrete Event Simulation, System Dynamics, and Agent Based Modelling) is not frequent. The areas of study include: system operation, policy evaluation, medical decision and treatment evaluation, as well as epidemiology. Studies on systems operation focus on evaluating the resource utilisation and patient waiting time, while studies on policy evaluation focus on finding better strategies in providing an efficient mental health care.

Thirdly, the applications of simulation methods in mental health related areas are mainly done singularly. Although hybrid simulations have been applied in other healthcare related issues, their application in mental health is not yet to be found. Why is this so? It could be due to many factors, such as the complex mental health conditions, the associated treatment pathways, the nature of the problem being investigated, or the preferred method for solving the problem. Furthermore, studying a complex system requires detailed data, ample knowledge of the system, and a good collaboration from different experts. All of the above factors may contribute to the choice of approach in modelling mental health related problems.

Considering the points highlighted in the literature search, the current research attempts to demonstrate the use of hybrid simulation in addressing a problem related to a mental health condition and its associated treatment pathways. In particular, it utilises a combination of two simulation approaches the framework of which has not been explicitly outlined.

1.3 Project aim and objectives

The project aims to develop a hybrid simulation model which addresses disease progression and related treatment pathways. The developed model will be used to answer the following research questions:

1. How can we build a hybrid simulation model which addresses depression progression and its related treatment pathways?

2. Using a recommended treatment model, how can the prevalence of depression affect healthcare services?

3. How can different levels of service coverage affect the progression of depression?

4. What recommendations can be made to healthcare providers to reduce the burden of depression?

The objectives are classified into two. The first classification concerns the development of a hybrid simulation model which addresses the aim of the study and research question 1. This includes the following:

- To develop an Agent Based (AB) model which represents the progression of depression.
- To develop a System Dynamics (SD) model which represents the recommended treatment pathways for depression.
- To combine the two developed models, AB and SD, into one hybrid simulation model which runs synchronously.

The second classification of objectives concerns the use of the developed model and addresses research questions 2, 3, and 4. This includes:

- To estimate the population suffering from depression and the related health service needs.
- To evaluate the relationship between different levels of service coverage and depression progression.
- To investigate the best strategy which should be implemented for the mental healthcare service by estimating the burden of depression related to healthcare costs and to the Disability Adjusted Life Years (DALYs).

1.4 Study contributions

The study evaluates the relationship between the health service provision and the progression of a disease using a hybrid simulation model. It seeks to contribute to the following:

1. To fill the gap in the body of literature on hybrid simulation models applied in healthcare in general and in mental health care in particular.

2. To share with wider audiences the relevance and advantages of a hybrid simulation model in tackling problems where disease progression and treatment pathways are two interrelating elements to be studied.

3. To make recommendations, based on the model building experience, on how to build a better simulation model for future research.

4. To make recommendations, based on simulation results, on strategies in providing mental health care to reduce the burden of disease.

1.5 Thesis outline

The thesis consists of seven chapters in total, the current chapter summaries the context, aim, and objectives of the study.

The second chapter provides the background to the study. It divides the discussion into three main sections. The first section discusses mental health as a global phenomenon. The issues highlighted in this section include: the prevalence of mental health globally; how mental health conditions affect the quality of life; and the challenges faced by the health service in providing care and treatment for people affected by mental health illnesses.

The second section discusses depression as one of the common mental health problems. The discussion covers factors influencing the development of depression, the prevalence of depression globally, the global burden of depression, the challenges in accessing mental health services, and the mainstream treatment for depression.

The third section describes the mental health care system. The author used two contexts, Wales and South Australia, to explore the provision of care for people suffering with mental health in general. There is no specific discussion for the system of care for depression. This is due to the fact that the mental health care system encompasses the care for depression.

The third chapter is dedicated to the literature review. The focus of the literature review is on simulation modelling applied in mental health care. By simulation we mean the Discrete Event, the Agent-Based, and the System Dynamics (whether applied individually or in any combination of the three). The aim is to highlight the existing literature on the topic and identify any gaps in the literature.

The fourth chapter describes the development of the simulation model. The discussion is divided into four main sections: the framework for developing a hybrid simulation model; the discussion on developing the Agent Based model; the discussion on developing the System Dynamics model; and the discussion on connecting the two models to serve as a hybrid model. This chapter provides an answer to research question 1 and addresses the first classification of objectives.

The fifth chapter has two main sections. The first section describes the parameters needed for the developed model and the sources. The discussion starts with Wales's population profile, where we try to extract any useful values to be used in the model. It will highlight the challenges in obtaining the parameter values for the model and how the decision on using particular values may affect the overall result of the experimentation.

The second section describes the process of testing the developed model. This is deemed important to mention, as the development of the model is not a straight forward endeavour.

The sixth chapter provides the results from running the simulation model. This chapter answers research question 2, 3, and 4 and fulfils the second classification of research objectives.

The last chapter, chapter seven, provides a discussion of the results and a conclusion to the study. The description includes: the issues and challenges in developing the model; what contributions the current study presents; and some suggestions for future studies.

Chapter 2

Background

2.1 Introduction

Mental health is a public health issue which affects healthcare systems around the world. The discourse around mental health not only covers the myriad conditions but also the effect it inflicts on many life factors. Its significance can be seen from the magnitude of the prevalence and the burden of disease.

The purpose of this chapter is to explore the significance of mental health and how the healthcare is provided to answer the need of people with mental health conditions. The discussion is divided into four main sections; the issues around the mental health as a global concern, the issues around depression as a common mental health condition, the issues around mental healthcare system, and the reason why the Operational Research (OR) methods are needed for studying a mental healthcare system.

2.2 Mental health as a global phenomenon

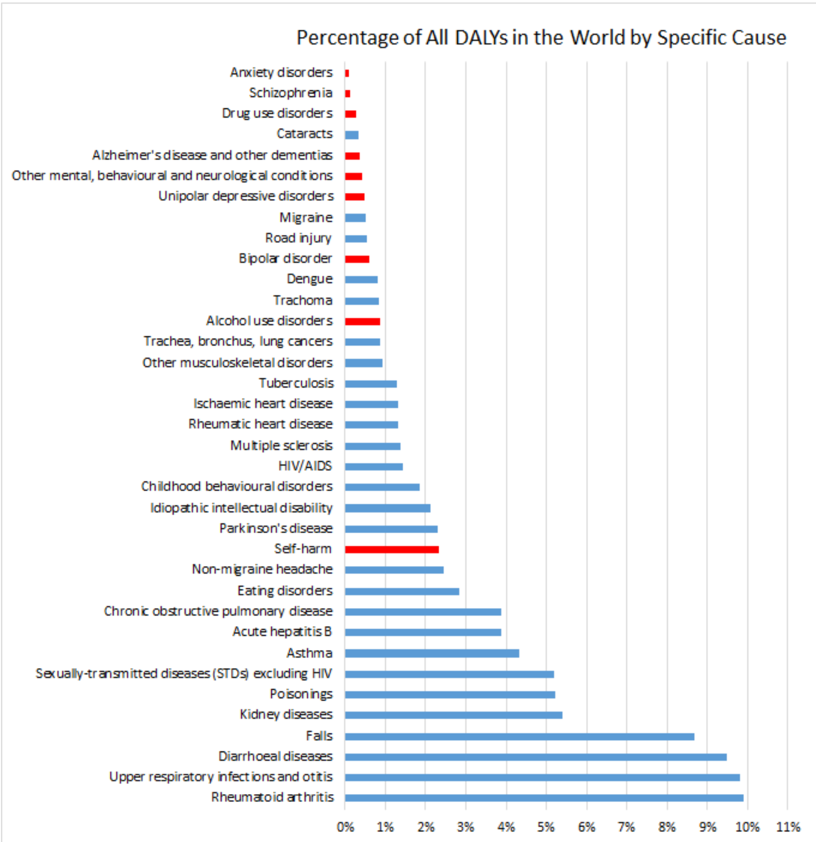
Mental health is regarded as "an integral part of health and well-being" where an individual's health status is defined as complete well-being, encompassing physical, mental and social functioning (World Health Organization, 2001, p.3). Mental health can be impacted by various factors in life such as individual physical disease (Prince et al. (2007)), socio-economical, cultural, believe, political and environmental factors as well as individual psychological and biological immune systems (World Health Organization (2001) and Hungerford et al. (2012)).

Globally, mental health illnesses affect hundreds of millions of people and the number of people suffering from depression and anxiety has increased between 1990 to 2013 (World Health Organization (2016c)). The disease is associated with premature death. The World Health organization estimated, in 2016, the average suicide rate in the European region reached 15.4 per 100,000 population, while the figure for the United Kingdom was 8.9. This regional average rate is higher than the rate for countries from the Western Pacific region (10.2). However, Australia's suicide rate accounted for 13.2 per 100,000 population which was considerably higher than the UK rate (World Health Organization (2018e)).

It is argued that mental disorders are a major contributor to the burden of disease (Duckett and Willcox (2011)) which affects various factors from carers to health care providers due to stigma (Cottler (2011)), from the cost of treatment (example in UK context can be seen in King's Fund (2008)), to the quality of life due to burden of disease (Eaton (2012)). Mental health conditions are risk factors for the development of physical illnesses, contributory factors to intentional and unintentional injury, and leading factors to long-term disability (Prince (2011)). Figure 2.1 summarises the disability-adjusted life years (DALYs) for selected cause in the world. The data was estimated for 2012 and the percentage is taken from the total DALYs.

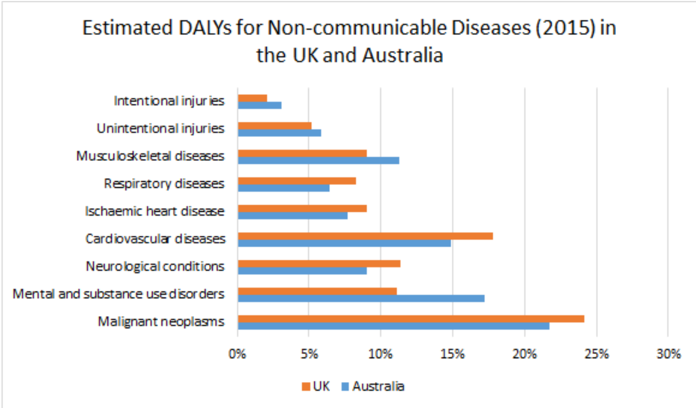
The contributory factors related to mental health conditions are highlighted in red. These include anxiety disorders, drug use disorders, Alzheimer's disease and other dementias, mental health conditions related to behaviour and neurological conditions, unipolar and bipolar depressive disorders, and self harm. Although in some cases eating disorders relate to mental health, its care is often separated from the treatment for mental health conditions, and so is not highlighted here. The highlights are not to suggest that these are the only contributing factors to mental health conditions. Other physical conditions may also be contributing factors to mental health disorder which will be explored later.

FIGURE 2.1: Disability-Adjusted Life Years (DALYs) by Selected Cause in the World for All Ages, 2012; Source: World Health Organization (2018b).



In a specific context, figure 2.2 presents proportion of DALYs caused by a non-communicable disease for the UK and Australia. In the UK, over 11% of all non-communicable diseases is contributed by mental health diseases and over 2% is accounted for intentional injuries. Whereas in Australia, 17.19% of non-communicable diseases DALYs is due to mental and substance use disorders, and over 3% is accounted for due to intentional injuries.

FIGURE 2.2: Percentage Disability-Adjusted Life Years (DALYs) in the UK and Australia for All Ages, 2015; Source: World Health Organization (2016b).



Some mental health illnesses, i.e. those categorised as chronic conditions, require long term treatment which leads to a high cost of healthcare. The provision of mental health services varies from country to country and the proportion of people, affected by mental health conditions, accessing the service has been found to correspond to the countries' spending on health (Wang et al. (2007)). Although the severity of illness relates to the probability of using mental health service, there is still a high level of unmet need for mental health treatment worldwide which leads to a delay in treatment (Wang et al. (2005), The WHO World Mental Health Survey Consortium et al. (2004)). This delay in seeking treatment is associated with many factors such as the age of the patients, culture and socio-demographic profiles, and is reported as to having a median duration of 8 years (Wang et al. (2005)).

Another crucial factor that leads to resistance in seeking help is related to stigma (Crowe et al. (2016)). People suffering from a mental health illness often become vulnerable to some disadvantages such as stigmatization and discrimination (Logie et al. (2013)) which can lead to a violation of their human rights which puts them in the margins of society (World Health Organization (2013)).

The issue of unmet demand also relates to the scarcity of resource availability. The Mental Health Atlas 2017 provides a description on the availability of mental health resources across nations in the world. With respect to human resources, it is estimated that there is only one psychiatrist per 100,000 population globally. The gap in the availability of psychiatrists is huge between the low-income countries (0.1) and the high-income countries (12.7) per 100,000 population. This gap continues to the availability of mental health beds either in the mental health hospitals or in general hospitals. Not to mention that the admission rates for mental health facilities are much higher than the available beds across the globe, and the global median for discharge rate within one year is 80%. Ultimately the gap of the resource availability between the high-income and low-income countries reflects the rate of treated illness. Except for the high-income countries, the treated prevalence of psychosis is higher than the treated prevalence of depression (World Health Organization (2018c)).

The WHO Mental Health Action Plan 2013-2020 developed four major objectives, one of which is to provide comprehensive, integrated and responsive mental health and social care services in community-based settings (World Health Organization (2013)). This objective is set in response to the global phenomena that demand for mental health care is still higher than the provision of service. Mental health services are in urgent need of improvement to become a service that can deliver high quality of care to those in need (Mental Health Australia (2016)).

2.3 Depression as a common mental health problem

Mental disorders have many different types which are classified into broad range such as mood, anxiety, alcohol use, and psychotic. Mood disorders can further be divided into depression, dysthymia, and bipolar disorder. There are variations in referring to certain mood disorders. Depression is also known as unipolar depressive disorders or major depressive disorders (MDD). It mainly involves only depressive symptoms. Bipolar is a term given where people are affected by both depression and manic symptoms. Whereas dysthymia is a type of persistent depression (Hooley et al. (2017)).

The symptoms vary from one type of mental illness to another, but they are mainly characterised by problems relating to emotions, ways of thinking, and how people behave and relate to each other in society. Some mental health problems are also comorbid with one or more mental health conditions such as depression and anxiety. One of the common mental health problems is depression which, it has been estimated, affects around 300 million (4.4%) of the world's population (World Health Organization (2017)). Although mental health illnesses encompass many different types, for the purpose of the current study, we limit our discussion to depression and its related issues. Figure 2.3 captures the influencing factors from the literature search used in the subsequent subsections.

FIGURE 2.3: Determinants associated with depression

2.3.1 Diagnosis for depression

Depression is an illness that affects mood, ways of thinking, physical functioning, and social behaviour. Current common diagnosis frameworks are provided in ICD-10 and DSM-V. ICD-10 stands for International Classification of Diseases; a guideline developed by the World Health Organisation. DSM stands for Diagnostic and Statistical Manual developed by the American Psychiatric Association. In order to be classified as having a depressive episode, one has to have a minimum of four out of ten symptoms (according to ICD-10) or five out of nine (according to

DSM-V). The list of symptoms is provided in table 2.1. Depending on the severity of the symptoms, the episode can be classified further into mild, moderate or severe. The term depression is mainly used in ICD-10 whereas DSM-V uses major depression to describe a similar case (Cowen et al. (2018)).

The category of mild requires at least two of the most typical symptoms and at least two of the common symptoms for a minimum of 2 weeks. A moderate episode needs at least two of the typical should be present and at least three of the common symptoms for minimum duration of 2 weeks. Severe episode requires all of the three from the most typical symptoms and at least four from the common ones with severe intensity (World Health Organization (1992)).

TABLE 2.1: Comparison of symptoms between ICD-10 and DSM-V for depressive episode

ICD-10 [a]	**DSM-V**[b]
Most typical symptoms	
Depressed mood	Depressed mood or feeling sad
Loss of interest and enjoyment	Decreased interest or pleasure once enjoyed
Reduced energy and decreased activity	Changes in appetite
Common symptoms	Sleep problems
Reduced concentration	Increase in purposeless physical activity
Reduced self-esteem and confidence	Fatigue or loss of energy
Ideas of guilt and unworthiness	Feeling of guilt or worthlessness
Pessimistic thoughts	Diminished concentration
Ideas of self-harm	Thoughts of death or suicide
Disturbed sleep	
Diminished appetite	

[a] Source: (World Health Organization, 1992, p.119)
[b] Source: American Psychiatric Association (2018)

Depression is a long term disease the onset of which could start as early as childhood. The diagnosis of depression depends on symptom detection and until the symptoms are apparent, it is difficult to know if a person is suffering with the illness. Coupled with variability of individuals, this leads to the sensitivity issue in diagnosing the depression. Studies on depression diagnosis in primary care (such as Vermani et al. (2011)) have found that the rate of positively detected depression by a physician is only 34.1%. This gives no doubt that a large proportion of people with depression could be missed by clinicians especially when depression is comorbid with other physical illnesses.

Undetected depression leads to an untreated condition and can have a detrimental effect of progressing to a more severe condition. It has been found that people with untreated depression have a statistically significant challenge in obtaining access to primary care and in receiving a comprehensive range of available services (Druss et al. (2008)).

2.3.2 Factors influencing depression

Depression is a complex illness influenced by many different factors encompassing biological, environmental and social factors. The subsequent sub sections describe some factors related to mental health development.

2.3.2.1 Sociodemographic factors

Women are more prone to have depression biologically. A relationship between menopausal and depressive symptoms has been investigated and the influencing direction is both ways (Gonçalves et al. (2013)). Women with a history of miscarriages or other types of pregnancy loss are at risk to experiencing depression and post traumatic stress disorder (Giannandrea et al. (2013)).

Being a mother can also lead to maternal depression (Gjesfjeld et al. (2010), Redshaw and Henderson (2013)). Although both men and women can experience similar depression symptoms due to being parents (Shafer and Pace (2015)). A population study in America has found that a 12 months prevalence of major depression among mothers was over 10%; and the risk of developing depression was found to be higher in mothers of unmarried status, low education attainment, or low financial status (Ertel et al. (2011)).

Prevalence of depression in older women was also found to vary from men. As women aged they were more likely to report their poor health problems (Ried and Planas (2002)). Gender and ethnic discrimination has also contributed to development of depression for African females who were affected by HIV (Logie et al. (2013)).

2.3.2.2 Social and economic challenges

A cross cultural study by Brailovskaia et al. (2018) found that resilience and social support have a significant negative association with depression, anxiety and stress symptoms. The authors assumed that the negative environment where people live or adverse life events do not necessarily have an impact on mental health when people are resilient and have good support.

Work related environment factor such as repetitive job strain (Stansfeld et al. (2012)) or job strain and bullying are significantly related to development of depression which lead to absenteeism and loss in productivity (McTernan et al. (2013)), which ultimately affects the economic cost (Cocker et al. (2014)). Experiencing economic hardship, such as job loss, can put people at risk of developing a depressive illness (Leung et al. (2014)), and unemployed people at higher risk of contemplating suicide than those in employment (Hiswls et al. (2015)).

Social life factor can be contributed by stressful events affected by the condition of country people live in. People who undergo displacement due to war are vulnerable to experiencing major depression or post traumatic stress disorder (Tekeli-Yesil et al. (2018)).

2.3.2.3 Comorbidity with physical illnesses

The complexity of depression is also due to its comorbidity with other physical problems. Obesity is one of the common problems which comorbids with depression (Svenningsson et al. (2012)). However, both obesity and underweight problems increased the risk of depression by 30% and 40% respectively (Chen et al. (2009)). In some cases obesity was not only associated with development of major depression, but also with thoughts about and attempt at suicide (Carpenter et al. (2000)).

Depression has been found to have a positive association with chronic illnesses such as Chronic Obstructive Pulmonary Disease (Horita et al. (2013)). Other chronic conditions which were found high in prevalence that comorbid with depression are diabetes, heart disease, and hypertension by Shen et al. (2010). The study used a large administrative data of women veterans and found that the depression prevalence was 27% of which 60% was classified with minor depression and 40% was major depression. Although the sample was a specific cohort, it does not rule out the possibility that similar cases exist in the general population. An example is a study that looked at depression prevalence in heart failure patients in an outpatient setting (Brouwers et al. (2014), Dekker et al. (2009)).

Musculoskeletal pain was also found to be comorbid with depression in a of study involving a large sample of people attending outpatient clinics (George et al. (2011)). The authors of the study concluded that a high prevalence of depressive symptoms were found among women with chronic condition and who had surgery for their condition.

In another study, by Airila et al. (2014), the possibility of different paths for development of musculoskeletal pain and depressive symptoms was investigated. The findings suggested that the factors contributing to depression were symptoms related to job demand which, in this case, included mental workload, poor interpersonal skills with others, lifestyle related problems and sleeping problems, and feeling less optimistic in life. Factors contributing to development of musculoskeletal pain related more to lifestyle problems, alcohol consumption, and sleeping problems (Airila et al. (2014)).

The prevalence of depression among patients affected with HIV/AIDS and substance-use disorders is as high as 72.9% according to a study by Berger-Greenstein et al. (2007). This study did not find a significant difference between male and female participants nor ethnicity differences which contradicted the study by Logie et al. (2013).

The association of chronic disease with the prevalence of depression is not a one way trajectory of influence, but vice versa may happen. Having a history of depression or a persistent type of depression suggests an increased risk of developing diabetes of almost double (Hasan et al. (2014)); or with development of obesity in a certain ethnic group (Needham et al. (2010)).

2.3.3 Prevalence of depression

In epidemiological studies, prevalence refers to the counts of people who are affected by a disease at any given point in time. It can be estimated from three different points. The first one refers to point prevalence where the count of affected people is only conducted at a specific point in time. This will not include anyone who has been affected and cured. The second one measures the number of people affected by a disease during the past 12 months. This is called 12-month prevalence. The last one refers to the lifetime prevalence where it quantifies all people who have been recorded as having a disease. Another measurement relates to the counts of new cases; this is called incidence (Hooley et al., 2017, p.36-37).

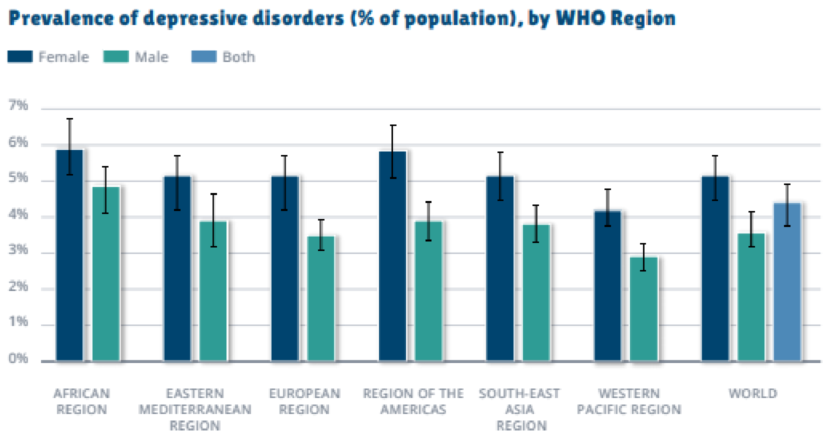
Across the globe, depression is estimated to affect 300 million people, 4.4% prevalence rate, in World Health Organization (2017). This rate is not uniform for all countries due to several reasons. The differences may be due to the difference in study design or inaccuracy in recording of people affected by depression. Self reported studies will differ from clinical diagnosis based studies. Self reported studies may suffer from recall bias, and clinical diagnosis based studies may underdetect depression due to other physical issues experienced by the patients. Low income countries will have difficulty in accurately recording their population affected by depression due to low access of health service use.

The variation in reported results on depression prevalence is also contributed to by the fact that many studies only investigate the prevalence on a certain subgroup of the population. For example, prevalence of depression is most often reported as a comorbidity with other physical illnesses; or on specific gender related issues such as issues pertaining to women. Further, studies that use population based surveys are rare especially in low income countries.

A recent systematic review and meta analysis by Lim et al. (2018) investigated depression prevalence in 30 countries. The number of included studies was 91, covering those published between 1994 and 2014. The results highlighted three different rates for prevalence. The aggregated point prevalence from 68 studies was estimated as 12.9% (95% CI: 11.1% - 15.1%). The aggregated one year prevalence was reported as 7.2% (95% CI: 4.8% - 10.6%) from 9 studies. While the aggregated lifetime prevalence from 13 studies gave 10.8% (95% CI: 7.8% - 14.8%).

All the three rates investigated in Lim et al. (2018) were reported as having a significantly high variability between each of the included studies. The variability is not only detected among the group of the studies but also between the three rates of prevalence. The point prevalence is reported higher than one year prevalence. The authors found that the mediators contributing to high variability included gender, the year the studies were conducted, and whether the survey was self-reporting or interview based. They argued that possible reasons that the point prevalence was reported more than the one year prevalence include recall bias, possibility of remission, and missing formal diagnosis.

FIGURE 2.4: Prevalence of depression; figure is taken from World Health Organization (2017).



The results from the study by Lim et al. (2018) also indicated that women have a higher prevalence of depression than men, and the life time prevalence is higher than the one year prevalence. In a large population study, the prevalence of depression among older women aged 65 and over was estimated as 5.9% and a lifetime prevalence of 12.3% (McGuire et al. (2008)).

In the context of the UK, the self-reported 12-month prevalence of depression based on European Health Interview Survey 2014 estimated as 7.7%, with a female and male prevalence of 10.4% and 7.3% respectively (OECD (2017)). This rate is higher than the aggregated rate reported by Lim et al. (2018) but similar to the aggregated rate in Wales for the year 2016-2017 based on the recorded health record which will be described later in Chapter 5.

2.3.4 Global burden of disease of depression

Depression affects the functioning status of individuals especially when coupled with other physical problems. In patients with heart failure, depression has been found to mediate the association between the physical symptoms and the ability to performing physical activities (Song et al. (2009)). The challenge in body functioning lowers the quality of life experienced by the affected individuals.

According to the World Health Organization (2016a), the UK Years Lost due to Disability (YLD) in 2015 are estimated as 186,000 YLD for all depressive types of illness, and 174,700 YLD for depression only. This accounts for 25.7% and 20.37% of all mental and substance use disorders (723,700) YLD respectively. In comparison, for Australia, the YLD was estimated as 100,200 (27.03%) for all depressive illnesses and 84,400 (22.77%) YLD for depression only.

DALYs measurement gives a higher percentage. For 2015, depressive illness accounted for 28.23% of all DALYs from mental health and substance use disorders in the UK; and 29.31% in Australia (World Health Organization (2016a)). This is understandable since DALYs measurement is a sum of Years Lived with Disability (YLD) and Years Lived Lost due to premature death (YLL).

There are no mortality rates specifically due to depression reported in World Health Organization (2018a). However, overall mortality rates due to mental health and substance use disorders were estimated as 5.2 for UK and 6.0 for Australia per 100,000 population. It has been found that depression relates to premature deaths, e.g. in Twenge et al. (2019) and Kyron et al. (2019), which is categorised as self harm. While the death rates due to intentional injuries were 8.9 for the UK and 12.8 for Australia per 100,000 population. Out of these rates, 91.41% were categorised as self harm in Australia compared to 85.39% in the UK (World Health Organization (2018a)). In comparison, in the OECD recent report, suicide rates in 2015 for Australia and the UK were estimated as 12.8 per 100,000 population and 7.5 respectively (OECD (2018d)).

The burden of disease also affects the economic cost due to absence from work. The impact of sickness and productivity loss due to depression has been investigated by McTernan et al. (2013). The results estimated, for those employees with mild depression, the cost of absence and loss in productivity was as high as $1850 AUD; and for moderate and severe depression was $3870 and $3975 per annum respectively. In the UK context, the estimated cost for loss in productivity due to the mental health related burden at work amounted to £34.9 billion during 2016-2017 according to a report by Parsonage and Saini (2018).

2.3.5 Access barrier to seeking help

Access to a mental health care service is a common issue across the globe. Despite the availability of treatment, a large proportion of people affected with mental disorders do not receive treatment (Campion et al. (2017)). A community adults survey conducted in 2001 - 2003 by the World Health Organization reported that between 35.5% and 50.3% of severe mental health problems did not receive any treatment 12 months prior to the survey in developed countries. The treatment gap is even wider for developing countries, which was estimated between 76.3% and 85.4% (The WHO World Mental Health Survey Consortium et al. (2004)).

Depression prevalence is regarded as common in countries such as South Africa and even then only 28% of people with moderate or severe cases received treatment in the last 12 months (Williams et al. (2008)). The rate of seeking treatment was much lower (3.4%) in metropolitan China (Sehn et al. (2006)).

The issue with accessing the service is not just about the rate of the service use, but also which services were accessed. An adult population survey in New Zealand revealed that only 45% of those affected by major depression sought treatment in the past 12 months, with one year as the median of the delay in seeking treatment (Oakley Browne et al. (2006)). The authors of the study also reported that only 10.5% of those with depression contacted psychiatrists, 44.1% contacted a general practitioner, and 22% contacted other mental health specialists.

In Japan, the mental health service use is low. A study by Ishikawa et al. (2016) reported that a large proportion (61.3%) of people with mood disorders, including depression, received no treatment; and of those who sought treatment, 27.3% contacted mental health specialists and only 12.6% contacted general practitioners.

Having access to a mental health care service not only gives the opportunity to be treated early but also to prevent detrimental effects caused by the disease. The decision to access treatment can be influenced by the available service. It has been found that although there is no significant association between the service coverage in the community based service with suicide, but an increase in the community based service has decreased the rate in inpatient treatment due to suicide attempts (Machado et al. (2018)).

Help seeking behaviour displayed by affected individuals does not always lead to an improvement in the condition. A factor such as quality of health service also plays an important role in determining the treatment outcome. However, the quality of service received varies from service to service and from country to country. A service that is not standardised may influence to the deterioration of the outcome. The disparity in receiving service may lead to the perceived unmet mental health care need. A study by Ali et al. (2018) found that for people with mental health condition and attempted suicide, the rate who perceived the unmet mental health care need is as high as 35%. The authors added that this rate is the overall rate including both those people who have and have not been in contact with the service. They also found that the rate was higher (46%) among affected individuals who have been in contact with the service in the past year.

2.3.6 Treatment for depression

Treatments for depression can be divided into three; those involving using medication (refered to as pharmachotheraphy), those using alternative biological treatments, and those using psychotheraphy. Treatments categorised as part of pharmacotherapy include antidepressant, mood-stabilizing, and antipsychotic drugs. Alternative biological treatments can be Electroconvulsive therapy (ECT), Transcranial magnetic stimulation (TMS), deep brain stimulation, bright light therapy. Whereas psychotherapy includes Cognitive-Behavioural Therapy (CBT), Behavioural Activation treatment, Interpersonal Therapy (IP), and family and marital therapy (Hooley et al., 2017, p.276-282).

Cognitive-behavioural therapy is a treatment the main aim of which is to help patients in developing a skill to help themselves in solving their problems. The focus is to enable patients to recognise the source of their problems and help them to change their behaviour to what they desire. CBT requires not only the therapist but also the patients to be actively involved in designing and implementing the treatment (Hawton et al., 1989, p.13). The psychotherapy treatment can also be provided online and the efficacy of such a service in improving the coverage has been examined in Lokkerbol et al. (2014). A detailed discussion of the various treatment types is not within the scope of the current study.

2.3.7 The NICE guideline for treatment and management of depression.

The National Institute for Health and Care Excellence (NICE) produced a guideline for the treatment and management of depression, which is currently called the National Clinical Practice Guideline 90. The guideline was developed by the National Collaborating Centre for Mental Health (NCCMH). The rest of the explanation in this section is based on National Collaborating Centre for Mental Health (2010).

The developed recommendation treatment pathways is based on a stepped care model. This model assumes that, regardless of the severity of the condition, the treatment should start with a low intensity treatment which does not involve medication or inpatient care unless there is a risk to life. Treatment may progress to a more intense one when there is no improvement or when the condition deteriorates.

The model suggests that the treatment involves four steps. At the lower end, step one, treatment is dedicated to the recognition of the condition along with assessment and initial care management.

Initial recognition of depression manifestation can be carried out by any health practitioner. If depression is detected, assessment for mental health should follow and be performed by a competent practitioner. This assessment can either be conducted by the patient's GP or by a mental health professional if the GP cannot carry out the assessment.

At the first step, risk to life of the affected individual or others may be detected. If this is the case, then referral to a more specialist mental health service has to be made urgently.

The second step is dedicated to people whose depression has been detected. This includes people with mild depression who may recover with or without intervention. The follow up assessment should be arranged within 2 weeks to monitor the progress of depression.

The treatments or interventions offered in step two are for those with persistent depression or for those with a mild to moderate condition. At this stage, low intensity interventions include individual cognitive behavioural therapy (CBT), computerised cognitive behavioural therapy (CCBT), and a structured group physical activity programme.

For patients who choose CBT, the recommended duration of treatment is between 9 to 12 weeks consisting of 6 to 8 sessions. A similar duration is recommended for CCBT. As for the physical activity programme, the duration is between 10 to 14 weeks with 3 session per week. Another type of intervention is group based CBT. This treatment is offered for 12 to 16 weeks consisting of 10 to 12 meetings.

Treatment at step two also includes offering medication. The recommendation suggests to offer medication only to those with a past history of moderate or severe depression, or to those with a long period of depression symptoms of at least 2 years.

The step three treatments are dedicated for those with persistent subthreshold depression symptoms; people with mild to moderate depression who do not show improvement with initial treatments; and those with moderate to severe condition.

The types of treatments include: medication with antidepressants (selective serotonin reuptake inhibitor - SSRI); high intensity psychological intervention (either CBT or interpersonal therapy - IP); or a combination of medication and therapy.

There are many types of antidepressant available for treating depression. Neither the detail of the type of medication nor the detail of therapy are within the scope of this study.

When patients are considered to take medication, the first 4 weeks are the monitoring weeks. Depending on the patients' progress, they can either switch medication or continue for a certain prescribed duration.

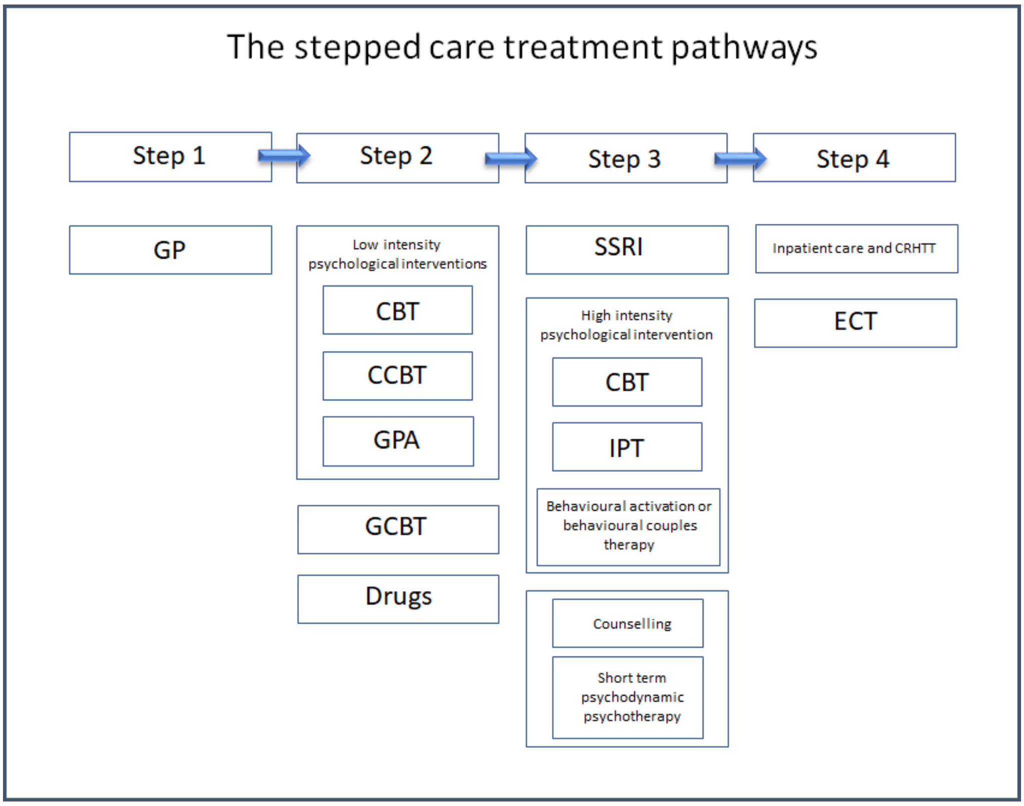
There are different types of psychological intervention in this step, including CBT, IPT, and behavioural activation (the detail of each therapy is not within the scope of this project). All of the therapies could take from 3 to 4 months with 16 to 20 sessions. The follow up sessions are three or four within 3 to 6 months.

Step four focuses on treatment for those with severe depression or those who suffer from depression which is comorbid with other mental or physical illnesses. At this stage, the treatment can be a combination of medication and a high-intensity psychological intervention.

At the fourth step, where the depression condition is complex, the treatment involves a team of mental health specialists. The crisis resolution and home treatment teams (CRHHT) provide responses to treat people with severe depression who are in crisis in their home environment. They also provide the service for people who are treated in inpatient care who can benefit from early discharge and continue care at home.

The stepped care model also acknowledges the need for the inpatient service. People with depression who show a risk of suicide or potential harm to themselves and others will be treated in inpatient care where close monitoring is possible. The types of treatment offered comprises: medication; electroconvulsive theraphy (ECT); and transcranial magnetic stimulation (TMS).

Figure 2.5: Recommended treatment pathways for depression; summarised from NICE guideline CG90 in National Collaborating Centre for Mental Health (2010).



2.4 Mental health care systems

This section provides a discussion on mental health care in general in the context of the UK and Australia. The discussion is limited to the general population demographic, the national expenditure on health care, the health funding system, and the structure of mental health care delivery.

The estimate of population size, in 2015, in the UK and Australia is 65,397,000 and 23,800,000 respectively (United Nations, Department of Economic and Social Affairs, Population Division (2017)). This estimate will grow to 67,334,000 and 25,398,000 in 2020 for the two countries respectively. The life expectancy from birth in the UK is 81.2 years (female: 83.0, male: 79.4) and for Australia in general is 82.5 years (female: 84.6, male: 80.4) (OECD (2018c)).

Total health expenditure as a percentage of Gross Domestic Product (GDP) for the UK in 2017 was estimated as 9.687% ($ 4,262 per capita), whereas for Australia was 9.133% ($4,543 per capita) according to the OECD (2018a) report. The estimate also indicated that for Australia, the spending in 2017 had increased from 2013 spending (8.774%) by 0.359%, whereas for the UK the 2017 spending had slightly decreased from 2013 spending (9.772%) by 0.085%.

In the UK, healthcare is mainly funded by the government through taxation. This is different to Australia where a mix between government funding and private insurance is the main method for health care funding. The UK central government expenditure in health and social care reached £121,939 million for 2017-2018, and this accounted for almost 20% of total government expenditure (UK Government (2018)).

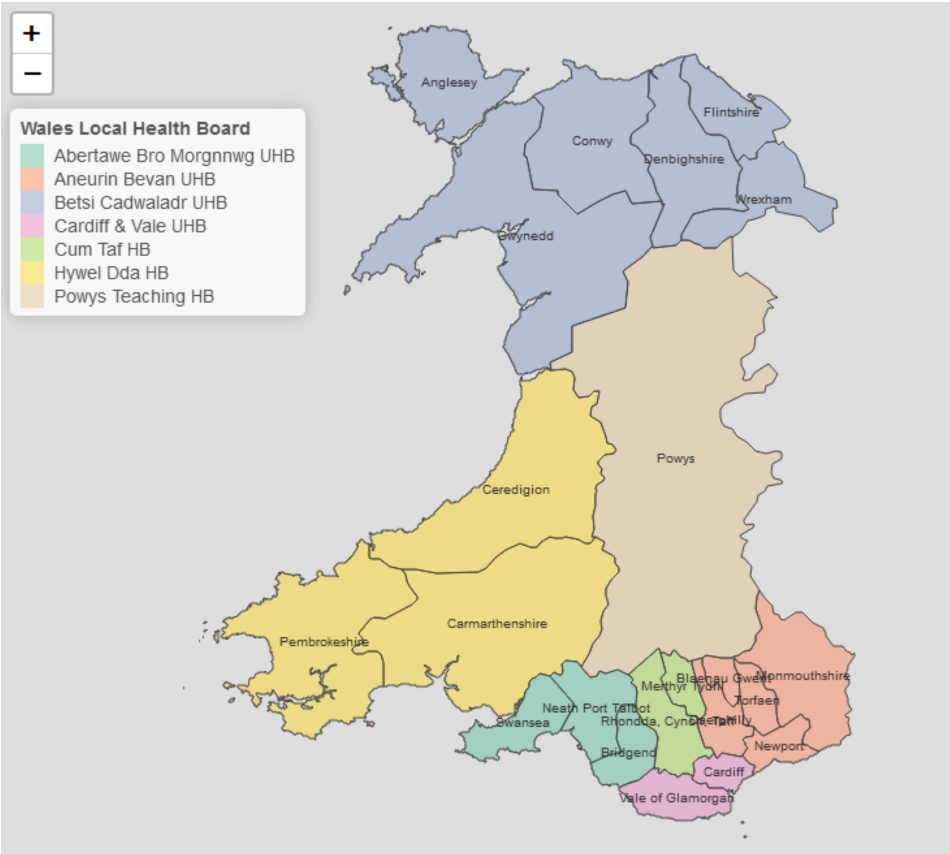
According to the OECD (2018b) report, the psychiatric hospital beds availability in the UK for 2015 was 0.42 per 1000 population, which is around 16% of all hospital care beds (2.61 per 1000 population). In comparison to Australia, the report suggested that the figure is not much different (0.41 per 1000 population). However, for Australia, this figure means that the availability of psychiatric hospital beds is less than 11% of total hospital beds, 3.82 per 1000 population.

2.4.1 Mental healthcare in Wales

In general, the healthcare in Wales is provided by the National Health Service Wales (NHS Wales) free for all the population in Wales. NHS Wales is comprised of seven local health boards (LHB) and three NHS Trusts which are responsible for delivering the health service for the population of Wales. The three NHS Trusts are the Welsh Ambulance Services, Velindre NHS Trust, and Public Health Wales. The 7 LHBs are Aneurin Bevan University Health Board (ABUHB), Abertawe Bro Morgannwg University Health Board (ABMUHB), Cardiff & Vale University Health Board, Hywel Dda Health Board, Cwm Taf health Board, Betsi Cadwaladr

Univeristy Health Board, and Powys Teaching Health Board. Figure 2.6 illustrates the geographical boundary for each local health board.

FIGURE 2.6: Geographical division of Wales local health boards



The change in treatment landscape from institution to more community settings also happened in the UK and hence Wales. The three main laws which provide the framework for the mental health service in Wales comprise the Mental Health Act 1983 (revised in 2016), the Mental Capacity Act 2005, and the Mental Health (Wales) Measure 2010.

The Mental Capacity Act (2005) provides a definition of what constitutes lack of mental capacity in a person. It aims to protect people's dignity and encourage people to make their own decisions. In relation to mental health care, point 28 gives independence and power to people who are affected by mental disorders to determine and choose their treatment (Department of Health, 2005, p.17).

The Mental Health Act 1983 provides a comprehensive framework for the provision of a mental health service in Wales which promotes equality and safety focusing on patients and their carers' needs. It gives guidance not only for professionals on how to provide the treatment, but also for patients and their families and carers on how to collaborate in making decisions about the patients' treatment (Welsh Government (1983)).

The Mental Health Measure (2010) (Welsh Government (2010)) provides law that defines the duty of local health boards and the local authority in delivering the mental health service from assessment to treatment. The Mental Health Measure has four parts. The first part regulates the establishment of a mental health support system which supports the primary care. The support system is called the Local Primary Mental Health Support System (LPMHSS). Patients who may be detected as having a mental health episode by their GP might be referred to LPMHSS in order to get an assessment from mental health specialists and to determine what treatment should be given.

Part two of the Measure relates to the provision of Care and Treatment Plan (CAT) for all patients who have been treated in the secondary care (inpatient). The regulation places the duty of this provision on both the local authority and the local health boards.

Part three ensures the provision of assessment of the former users of the secondary care. People who have been admitted in the inpatients and discharged will be given easier access to go back to the inpatients should their conditions require them to access the service without having to go through the initial process of assessment in the primary care.

The last part of the measure relates to the provision of an independent support system for patients with mental health problems. Patients who require further support, such as social support which can provide help in managing a patient's daily activities, are able to request such support.

The policy and strategy to deliver the mental health services in Wales are outlined in "Together for Mental Health" (developed by Welsh Government (2012)). This strategy recognises the burden of mental health to the society and healthcare costs, as well as the potential positive impact on health and economic when a population's mental wellbeing is improved. Its focus is not only to improve individual mental health wellbeing, but also to establish an integrated network of care. It brings together services that provide medical treatment, and other services which support the population's needs such as social care and employment.

The strategy document in Welsh Government (2012) states that there is a need for investment in mental health services to be transparent, and service providers are expected to make efficiency. They need to continuously review their resource use to accommodate the increasing mental health needs and the change in population demographic profile.

Mental health adult services in Wales are provided in community and hospital settings. Hospitals can have both inpatient and day care facilities which offer different types of services. General and community type hospitals can offer acute assessment and admission, a Psychiatric Inpatient Care Unit (PICU), a rehabilitation centre or other open wards for low security.

Day care hospitals offer a range of services which mainly facilitate treatment without having to keep patients in the hospital overnight. The services are delivered by multi-specialists and can include: Community Mental Health Teams (CMHTs), Assertive Outreach, a Crisis Resolution Home Treatment Team (CRHTT), Criminal justice, Psychiatric liaison, etc.

More specialist services are dedicated for a certain group of the population. This includes mental health services for older adults, a service for those affected by substance misuse, and mental health services dedicated for forensics. Across Wales, mental health services are provided by at least 17 hospitals with psychiatric wards (one of which is a specialist psychiatric hospital), 3 community hospitals for the elderly, and 4 hospitals which offer services for those with learning disability.

The total number of admissions for mental health facilities in Wales in 2016-2017 reached 8,723 according to StatsWales (2018a). Patients were not only served by the hospitals administered by the local health board but also by independent hospitals (2.84% of total admissions). Apart from one local health board (Cwm Taf) all other health boards experienced a reduction in the number of admissions from the year 2015-16 to 2016-17 (see table 2.2). However, for the period from 2013 to 2017, the only increase was experienced by Aneurin Bevan University Health Board by 1.46%. Overall, the number of mental health patient admissions were reduced by about 15% from 2013 to 2017 for the whole Wales.

Table 2.2: Mental health admissions in Wales by local health boards[a]

Local Health Board	**2013-14**	**2014-15**	**2015-16**	**2016-17**	**% Increase** 13-14 to 16-17
Betsi Cadwaladr UHB	1,835	1,709	1,525	1,262	-31.23%
Powys Teaching HB	333	326	323	319	-4.20%
Hywel Dda UHB	925	957	902	768	-16.97%
Abertawe Bro Morgannwg UHB	2,945	2,351	2,530	2,367	-19.63%
Cwm Taf University HB	1,154	1,296	952	1,145	-0.78%
Aneurin Bevan UHB	1,436	1,562	1,535	1,457	1.46%
Cardiff and Vale UHB	1,361	1,266	1,216	1,157	-14.99%
Independent hospitals	285	296	314	248	-12.98%
Wales	10,274	9,762	9,297	8,723	-15.10%

[a] Data source: StatsWales (2018a).
Figures for 2017-18 are not available yet.

The mental health care system in Wales also includes those non-governmental organisations, such as charities, which are run by families of affected people or health care professionals. An example of this third sector service is a sanctuary house which offers consultation for people who do not want to go to formal settings such as a GP or a hospital. Discussion of third sector services however is not within the scope of this project.

The Mental Health Measure 2010 provides a national service model which focuses on supporting local primary care. Included in the support it provides is carrying out individual assessment which identifies the local primary treatment or other services which might improve the patient's mental health. Referral to other mental health services include the community mental health services, secondary mental health services, other primary care which might provide the identified treatment, a more specific service for children, other social services such as housing or well-being services, and education and training (Welsh Government, 2010, p.10).

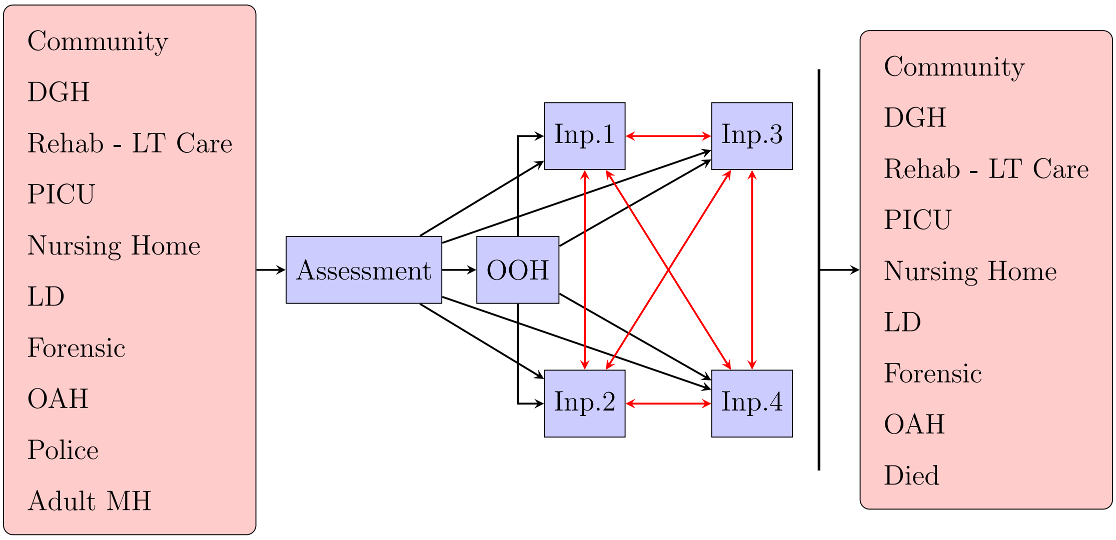
The Measure provides a framework for an ideal patient pathway where patients start their treatment journey in primary care before they can access a more specialist service. However, in reality, this is not always the case. Patients affected by mental health problems might access the care service by consulting their GP or other primary health care providers; and depending on the condition and severity of the illness, the GP might then make referral to a more specialist setting. But some patients might access a specialist service, such as the hospital, prior to consulting their GP. This might happen when the patient is admitted due to other physical health problems or in emergency situations.

The provision of mental health care which comprises different levels and settings, contributes to the complexity of the patient pathways. Our investigation on one of the local health board's inpatient data in Wales highlighted that patients admitted to the inpatient care can come from any source. This includes a GP, general hospitals, other mental health hospitals, a nursing home, the police, or even self-referral.

Figure 2.7 describes the complexity of the mental health patient pathway within one of Wales' local health boards. The data used to generate the pathway came from mental health inpatient data provided by Aneurin Bevan University Health Board for the three financial years 2014-2017. Admission to mental health inpatient care can come from any service within the health care system or other systems. These different services include district general hospitals (DGH), Psychiatric Intensive Care Unit (PICU) special care for severe mental health problems, learning and disability (LD), older adult hospitals (OAH), forensic, police, nursing home, rehabilitation centres, as well as community care.

The pathway is not always a straight forward pathway where patients are admitted from one institution and then discharged to another. During the patients' stay in inpatient care, some patients experience multiple transfers between inpatient care services for one reason or another. The black arrows, in Figure 2.7, represent a one way path, whereas the red arrows represent two ways paths.

FIGURE 2.7: Mental health patient pathways within ABUHB



Data source: ABUHB inpatient data 2014-2017.

The mental health inpatient facilities captured in Figure 2.7 are Adferiad which is part of St Cadoc's Hospital serving the population in Newport; Carn-y-Cefn in Ysbyty Aneurin Bevan which serves tyhe population in Blaenau Gwent; Talygarn in Talygarn County Hospital which serves the population in Torfaen; and Ty Cyfannol in Ysbyty Ystrad Fawr which serves the population in Caerphilly. The out of hour (OOH) service is located in Talygarn County Hospital. The data analysis further revealed that the four inpatient units served not only the population from their geographical location, but also from other parts of Wales as well as England and Scotland in some cases.

2.4.2 Mental health care in Australia

The Australian National Health Survey 2014-2015 reported that around 4 million people (17.5%) suffered from long-term mental and behavioural conditions. During the survey period, around one in nine (11.7%) adults experienced high and very high levels of psychological distress (Australian Bureau of Statistics (2015)). The report also stated that anxiety and mood affective disorders were the most frequently reported illnesses that affected 2.6 and 2.1 million people respectively, and that 1 in 3 people with mental and behavioural conditions aged 15-64 were not in the labour force compared with 1 in 5 people who did not suffer the conditions.

The total government spending for mental health services is estimated over A$8 billion in 2013-2014 with South Australia spent nearly A$400 million. Out of A$8 billion, just over A$4.8 billion came from the state and territory government, A$2.9 billion from the Australian government, and about A$309 million from private health insurance (Australian Institute of Health and Welfare (2015)). This high cost will only increase if the number of sufferers increases even if other aspects of health services remain unchanged.

Although the provision of mental health services in Australia had undergone some reforms in the 1950s, the contemporary service in South Australia was started in the 1960s (Meadows et al. (2007)) . It was marked by de-institutionalisation which was based on the principle that patients should be treated in the community which was seen as a better environment for the patients to be in (World Health Organization (2001)). This movement involved the development of community-based services including community mental health centres, community housing, psychiatric units in public general hospitals for outpatient and acutely ill patients (Willis et al. (2012)). This de-institutionalisation caused the number of specialist hospitals to be reduced from 59 psychiatric hospitals in 1989-1990 to 20 in 2014-2015 (AIHW (2017)). The reason for such a massive reduction was as a result of the advancement of medication which allowed patients to be treated in the community and the integration of services in general acute hospitals (Duckett and Willcox (2011)).

The provision of mental health services is based on the national mental health strategy which consists of a mental health policy, plan, and a statement of rights and responsibility. The first strategy and plan covered 1992-1997 and focused on mainstreaming the services that involve relocating the psychiatric services to be embedded in general hospitals, and integrating the service to better coordinate between the community services and the hospitals, there by ensuring the continuation of patients' care (Meadows et al. (2007) and Willis et al. (2012)).

Since then the mental health plan has undergone revisions and the current mental health service is based on the fifth national mental health plan which focuses on the integrated services which incorporate medical and mental health care. The integration is between the Primary Health Networks and the Local Hospital Networks (Australian Government Department of Health (2016)).

Public funded mental health care providers come in different types. In general settings, the mental health service can be provided by General Practitioners, Psychiatrists, Psychologists, public acute hospitals and private hospitals, and other allied mental health services. In specialist settings, the service can be provided by community mental health care, public acute hospitals, public psychiatric hospitals, private hospitals and residential mental health care (Duckett and Willcox (2011)). Other types of setting include forensics, prisons, the police, and ambulances.

The Australian health care model has shifted toward a more market oriented model which regards patients as consumers who can determine which service they want to choose. The provision of care is less reliant on government services and is provided through NGOs, primary care (GPs), and allied health services. This customer oriented movement has increased the reliance on informal carers such as family, friends and community (Willis et al. (2012)). Although this model has given the power and freedom of choosing care to the individuals, not everyone in the population is in a position to choose. For the majority of population, the question remains on how well the government provides the care to its population in need.

In formal settings, the most accessed services by mental health patients are the GPs and the community mental health services which act as the gate keepers of specialised services. However, the de-institutionalisation of mental health services, which aims to improve care for mental health patients, still has some issues such as the accessibility and quality of service especially in community settings (Australian

Government department of Health (2015)). The community-based services do not always receive enough support to accommodate and manage the care of mental health patients (Duckett and Willcox (2011)). This issue creates a service which tends to focus more on the crisis and lack of attention to the prevention in the first place (Australian Government department of Health (2015)).

Mental illnesses are classified by their clinical symptoms. Black and Andreasen (2011) explain that the obvious and severe symptoms can be found such as in psychosis, and the more subtle one can be found in personality disorders. They also state that the study of mental illnesses is the territory of psychiatry which is a branch of medicine that deals with understanding the human mind, spirit and human brain. In dealing with people with mental illnesses, the psychiatrist will study patients' behaviour in relation to their social life settings such as living environment, socio-economic conditions, past experience, and social network. Furthermore, the psychiatrist will try to understand the factors influencing the emergence of symptoms which then can be used to choose better and more suitable treatments (Black and Andreasen (2011)). Since each individual patient is different, the treatment journey may vary depending on the diagnosis related to the individual. A treatment journey for any particular patient may involve several different settings.

According to mental health experts in South Australia (SA), different care providers will have different models of treatment which will often be influenced by the type of condition. For example the Emergency Department (ED) and psychiatry inpatient unit in a general hospital are designed to treat episodic and acute illnesses. They added that the type of treatment received in an ED and acute inpatient is different from the one received in a community-based or other specialist hospitals. Patients with mental health episodes presenting to ED or acute hospitals will only be treated until their conditions are stable and the follow up care will be managed and provided by the community-based services. In the integrated care model, a strong network and collaboration between service providers are crucial to determine the accessibility and quality of care (Fallon and Faddon (1993)). However, in reality this is not always the case. The SA experts further explained, that often hospital inpatient units have no connection with other services in the community setting in the sense that they do not provide post hospital care.

The Australian government recently published its response on these issues in Australian Government department of Health (2015). It called for reforming the mental healthcare system to provide a better service that focuses on early intervention, is based on a stepped care treatment model, addresses individual patient need, and better utilises an innovative approach in its delivery.

2.4.2.1 South Australia's mental health care system

South Australia's health administration is divided into six divisions which comprise the SA Ambulance Service, the Women's and Children Health Network, the Country Health South Australia Local Health Network, the Southern Adelaide Local Health Network (SALHN), the Northern Adelaide Local Health Network (NALHN), and the Central Adelaide Local Health Network (CALHN). Mental health services are provided throughout these six administrative divisions. Organisationally, SA health has a structure where the Mental Health & Substance Abuse Division works directly under System Performance and Service Delivery, which is accountable to the Interim Chief Executive SA Health who is responsible to three Ministers, namely the Minister for Health, the Minister for Ageing, and the Minister for Mental Health and Substance Abuse (SA Health (2016)).

Prior to the 1980s South Australia had three psychiatric hospitals: Glenside, Hillcrest, and Enfield. The de-institutionalisation in SA resulted in the closure of Enfield hospital in 1981 (Meadows et al. (2007)). Currently only Glenside still operate and is under the Central Adelaide Local Health Network, which serves statewide.

Following the mainstreaming of mental health care, the provision of service in South Australia is shared with other settings such as the general teaching hospitals and community-based services. The five general hospitals which provide mental health services are the Royal Adelaide Hospital, Flinders Medical Centre, the

Queen Elizabeth Hospital, Lyell McEwin Hospital, and Modbury Hospital. In the primary setting, the service is provided by GPs. The community-based services are provided by teams of health professionals who are either co-located with general hospitals, GPs, or other stand alone community health clinics.

Currently, South Australia's public mental health service is provided by at least 7 general hospitals and 17 community-based centres with more specialized services dedicated to elderly people, women and children, and forensics (Government of South Australia (2016)). Other types of settings include Police, Prison, Ambulance, and Hospital at Home, as well as Non-Governmental Organisations (NGOs).

Some issues or challenges outlined by Meadows et al. (2007) include the difficulty in provision of integrated services, the fact that community-based services are still under-supported as there is more demand than the available capacity, and the lack of provision of housing support which is suitable for people with mental health conditions. The authors also suggested that South Australia's mental health services need to better integrated and coordinated between regions. The recent Government's response, in Australian Government department of Health (2015), highlighted that these issues persist today.

2.4.2.2 South Australia's mental health services

The discussion on mental health services in South Australia is the result of a conversation with experts. The description is very context specific to the South Australian system. However, it will not be surprising if other regions in Australia find similarities with their system.

The provision of mental health care in each health network consists of GPs, hospitals, community-based, allied mental health professionals, and Non-Governmental Organisations (NGOs). More specific services such as for women and children or forensics are statewide services. Although GPs, NGOs, and other allied health professionals are not part of the government body, it is important to mention their roles in the discussion about mental health services in South Australia.

General Practitioners (GPs) provide an initial assessment for mental health conditions in the primary care setting. GPs are not part of public mental health services in the sense that they are provided privately. However, GPs commence their services with a medicare agreement which is funded by the Federal government. GPs may have collaboration with other services, such as allied health professionals, to provide joint programmes or referral for their patients who experience mental health conditions and need more specialist care. The current system allows people, with a recommendation from their GP, to choose which service they want to access. This includes the choice of using private services at the expense of either private insurance or people's own money.

A community-based setting is another type of primary care which provides services mostly without the need for beds. The types of service provided by community-based services are different from those provided by the hospitals. The services are mostly provided through outpatient clinics with various programmes, which generally focus on areas of promotion of health, treatment and maintenance, and prevention (Clinton and Nelson (2004)). The duration of service also varies according to the condition of each patient. At any time during the treatment period, if necessary, the community team can refer their patient to hospital services. GPs can refer people to the community-based services. Both GPs and community-based services act as the main portal to the mental health care system. One of the concerns around community-based services is that there are lots of people registered in the system who are actually reasonably stable in maintenance care, but they are not discharged for several reasons including that the system relies on court orders before discharging patients.

Also provided by the community-based services are residential and rehabilitation services. Residential is a type of community-based service that provides beds but is outside the hospital setting. The beds are funded by the Federal government through the State/Territory government. Patients using these services tend to stay for shorter periods of time than those using the community-based services. The residential services are provided by the Intermediate Care Centres (ICC) and the patient's length of stay is expected to be between 5 and 15 days. In some respect, the residential services are also called the sub-acute services and were originally developed to serve those patients who needed a longer stay after hospital inpatient care.

The rehabilitation services, on the other hand, are for a long episode of care. One example of such a service is provided by Elpida House. In the rehabilitation services, a patients' length of stay is expected to be between 3 and 12 months. This type of service is also called Community Rehabilitation Centre. Both residential and rehabilitation services interface with the inpatient hospital care. So there is a link between the service from the inpatient hospital to the community residential and rehabilitation service, characterised by mutual referrals between them. In some cases, such as in Flinders Medical Centre, the link is one way in the sense that the inpatient care may refer patients to the community-based care but not vice versa. Moreover, the hospital team does not have any involvement with a patient's care in the community setting. This is one area for improvement in the system where the relationship between the community-based and the inpatient services can be strengthened.

Hospital based services provide treatment for more acute conditions. A teaching hospital such as Flinders Medical Centre has inpatient units that provide a service for patients with mental health conditions. Their inpatient unit comprises acute and intensive care wards. The acute facility is also called the open ward which is dedicated to patients with moderate mental health conditions. The intensive care, however, is called the closed ward and this is dedicated to those patients with more severe mental health conditions where close monitoring is essential. There are two ways for movement of patients between the acute and the intensive care units. The transfer of patients between acute and intensive care does not only occur within a hospital, but also between different hospitals. An example is the collaboration of patients' care between Flinders Medical Centre and Noarlunga Hospital in the Southern network.

Patients do not arrive in hospital inpatient facilities unless they have been referred from other services. The ideal system would have patients come to any acute or intensive care unit from either a GP or a community-based team. However, patients often arrive in hospital inpatient units from the hospital emergency department (ED). Mainly, there are two types of patient who access the hospital via ED. The first type of patient is one with genuine emergency conditions such as in crisis because of a suicide attempt or accident. Another type of patient is one who is not classified as a real emergency case. Patients of either type could be known to the system as they may have registered in the community services or non-government organisations (NGOs) and be actively receiving the service. For those with no real emergency condition and who are known to the system, their access to the emergency service is seen as taking a short cut into the system. Some health professionals have hypothesised that this phenomenon occurs because of a lack of facility and support in the upper stream, i.e. community-based, services.

Another reason why many people with mental health conditions access ED to get to the hospital is that these people have physical comorbidities which necessitate them to have medical treatment. However, these patients are not classified as mental health patients while they are receiving medical treatment. In some cases, patients have mental health conditions as well as physical comorbidities. These comorbidities of illness require both teams, i.e. a mental health and a medical team, to collaborate. Patients with mental health comorbidities have been found to tend to stay longer in the inpatient units compared to those patients without mental health comorbidities (as also found in Jansen et al. (2018)). These patients will stay in medical wards and will be seen by psychiatric liaison officers who are contacted by the doctors if their expertise is needed.

To help with the overcrowding in ED for mental health patients, some hospitals, such as Flinders Medical Centre and the Royal Adelaide Hospital, set up a Mental Health Short Stay (MHSS) facility next to their ED. Patients who are considered to need a longer stay from the one provided by ED, will be transferred to MHSS where they will wait for their condition to stabilise before being discharged or continuing their journey to the inpatient units. The mental health patients who stay in MHSS are seen by psychiatric liaison officers. This proactive mode of care aims to speed up the process of treatment or the patient's transfer to the next facility. A concern with respect to patients in MHSS is the boundary of power over the patients between the psychiatric and the medical health professionals. While the location of MHSS is neither within the psychiatric nor the medical unit, there is a question of co-provision of treatment, to what extent the liaison psychiatric officer can claim that the patient is theirs and hence they can start the process of the treatment. This is one of the issues in hospital management that still needs exploring.

Another type of mental health service (which is not classified as a public mental health service) is the one provided by non-government organisations (NGOs). The services provided by the NGO are different from the ones provided by the community-based service. They are not for profit organisations and are funded by the government. The purpose of NGOs is to provide support for patients with mental health conditions in areas such as social inclusion, community support housing, housing support, and employment.

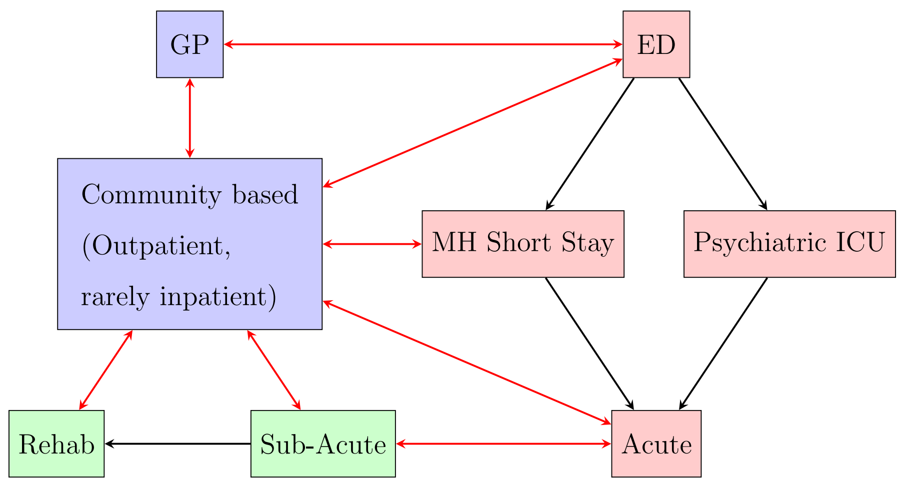
People need access to mental health services often in the time outside the normal working hours. In the case of an emergency, support is provided by a type of triage service which is staffed by health professionals without the need to go to hospital in the first instance. SA Health Mental Health Emergency Triage Service is a telephone based triage system which provides information on crisis or emergency incidence. It can refer people to hospital acute or crisis teams if necessary. The opening hour of this service is 7 days a week and 24 hours a day, ensures the provision of service to whoever needs intervention outside the normal working hours.

The Emergency Triage Service also links to the Ambulance service which is divided into two, according to the geographical location it serves: the Ambulance service dedicated to people living in metropolitan Adelaide, and the service that caters for people living in the country. The Ambulance service in the country has fewer health professionals compared to the one in metropolitan Adelaide.

The myriad of aforementioned mental health care services does not work in isolation. Each of these services is a subsystem of a whole mental health care system which itself is a subsystem of the health care system. Although some of the settings may overlap in providing treatment or services, each will have different characteristics. Within the mental health system, they are the elements of the whole system which interlink and influence one another, and one cannot determine the whole mental health system behaviour in isolation from the others. In other words, the whole mental health system performance is a product of all its elements acting together.

Mental health care is a complex system of care and studying each element in the system is not an easy task, let alone studying the whole system. Describing the whole system of care can be done by describing patient flow in the system. Patient flow has been argued as a useful way to study the utilisation of health delivery systems (Bhattacharjee and Ray (2014)). Figure 2.8 provides a hypothesis on South Australia's mental health system based on patient flow. The figure is not a comprehensive representation of the system as it excludes prison, forensics, and other types of services. It is a description of some part of the system based on public general hospitals, community-based, and GP services. The links between any two services are hypothesised by experts in the system. These links can be confirmed should the linkage data processed by South Australia Health, which captures the patient's movement in the system, become available.

FIGURE 2.8: Mental Health patient flow in SA.



The diagram was produced following consultation with the experts.

Components of the system in red represent the services provided in a general hospital setting. The components of the system in blue are part of the primary care setting which serves the outpatient. The green components represent the inpatient facility in the community-based settings.

The flow of patients represented by the arrows also indicates the complex networks of the services. The arrows in black represent a one way flow system and those in red represent a two way flow. Experts have suggested that the initial flow, i.e. for people with mental health contacting the service, should start from the population to either GP or ED, but this is not always the case.

2.5 The need for Operational Research tools in system modelling

Operational Research (OR) has been defined as a field of study which offers modelling tools for studying a complex system such as health care (Pitt et al. (2016)). The roles of OR include problem structuring, the evaluation of possible choices of solutions, and at a strategic level for selecting the best possible choice for system reconfiguration (Monks (2016)).

Depending on the nature and level of issue to be studied, the tool required to model and analyse the system can be different from one problem to another. Among OR tools for system modelling are those suitable for modelling a dynamical system which is characterised by constant change and stochasticity. These include Discrete Event Simulation (DES), Agent-Based Modelling (ABM), and System Dynamics (SD) simulation. These approaches are useful in addressing challenging problems which involve: many different influencing factors, any feedback in the system, policies and their effect on the healthcare, and the necessary conditions to successful delivery (Langellier et al. (2018)). More discussion on these three modelling techniques will be covered in Chapter 3.

A healthcare system, such as mental health care, with its unpredictability and constant changing is one example of a dynamical system. In order to elaborate this claim, we use the SIMULATE check list developed by Marshall et al. (2015) to determine whether the mental health care system is better approached using dynamical system modelling.

- System. Although mental health care is a subsystem of the healthcare system, it can also be regarded as a system in itself which consists of interrelated multiple subsystems. In metropolitan Adelaide for example, the mental health system consists of services in the community, general hospitals, and rehabilitation centres.

- Interactions. The interrelationship between elements of the system displays a nonlinear relationship. This can be seen from the network of services in the system which capture the patient transfer from one service to another.

- Multilevel. A mental health care system can be said to be a multilevel system. At the top level, the system consists of decision makers who formulate the policy and strategy to be implemented. At the bottom level, where the policy and strategy are implemented at the point of delivery, is where the interaction between patients and the care system occurs.

- Understanding. The complex mental health care system has characteristics such as constant change and stochasticity. It is important to understand how the system operates in order to help to improve of the quality of service. A model of a complex mental health system can be used to gain understanding of the existing care delivery and help identify any possible improvement.

- Loops. The mental health system has feedback loops between elements in the system. The mental health condition that affects individuals affect the system of care and may suggest a new policy. The policy and strategy implemented to deliver the care system may in return affect the condition of the individuals.

- Agents. In mental health care deliveries multiple agents interact with each other and their environment. A patient's decision to choose where to access the care may influence the behaviour of the physicians deciding what treatment is appropriate for the patient.

- Time. The delivery of mental health care often involves the transfer of patients between services. This transfer is dynamic and time dependent. The service at the next level cannot be delivered until the previous stage is completed.

- Emergence. Any intervention applied in any system element of mental health care may affect other parts of the system or the whole system behaviour. For example, a limitation of the service coverage may pose a barrier for accessing the service. As a result, this may cause deterioration in a patient's health which, as a consequence, may lead to a greater need for the health service.

2.6 Conclusions

Mental health conditions have shown to be significant. Depression alone affects a considerably large number of the world population (4.4%). The burden of disease not only affects the physical, mental and social functioning of affected individuals, but also affects healthcare costs and the economy due to the loss of productivity in employment.

The complexity of a mental health condition is multi faceted. It covers many conditions, each one of which comes with different classifications. Furthermore, the conditions can affect and be affected by many factors including biological, social and economical. This phenomenon has implications on the complex mental health care which has to be tailored to the different conditions and the individual characteristics.

Globally, the provision of mental health care varies and is in need of improvement. The presentation of people affected by mental health condition, including depression, at the health service is still considerably low. The difficulty in accessing mental health services may predominantly be due to lack of the availability of resources which in turn is a result of the demand for the service not being fully understood. Furthermore, in the case of depression, it is often missed in diagnosis due to commorbidity with other physical health problems.

In order to understand the demand for a mental health service, Operational Research tools, such as Agent Based Modelling, System Dynamics, or Discrete Event Simulation, can be used to study mental health and its related care system. How OR tools are used in modelling the health system, in particular the complex mental health care system, will be explored in the next chapter.

Chapter 3

Literature Review

3.1 Introduction

Operational Research offers many techniques to study a system including healthcare. To understand how mental health care has benefited from OR techniques, in particular simulation techniques, is the focus of our literature review. By simulation we mean simulation as defined in (Robinson, 2014, p. 5):

> *"Experimentation with a simplified imitation (on a computer) of an operations system as it progresses through time, for the purpose of better understanding and/or improving that system."*

The purpose of this literature review is to explore the modelling techniques used in mental health care and to answer questions such as: What OR methods have been applied in mental health care; what area of application have been explored; what gaps can be identified from the current literature.

3.2 Strategy for the literature search

We consulted databases including Web of Science, Scopus, EBSCOhost, and Science Direct. Within EBSChost, we included CINAHL, MEDLINE, and Business

Source Complete. Since each database contains different types of publication from journal articles to book chapters, we limit our search to peered review journal articles written in English and available in full text.

Review papers on the application of simulation in mental health care are scarce. The most recently published papers are Long and Meadows (2018), and Langellier et al. (2018). Despite their similarity (both reviewed literature which reported simulation studies), the study by Long and Meadows (2018) is more broad in its inclusion of simulation methods applied compared to Langellier et al. (2018) which was limited only to ABM, SD, and DES approaches.

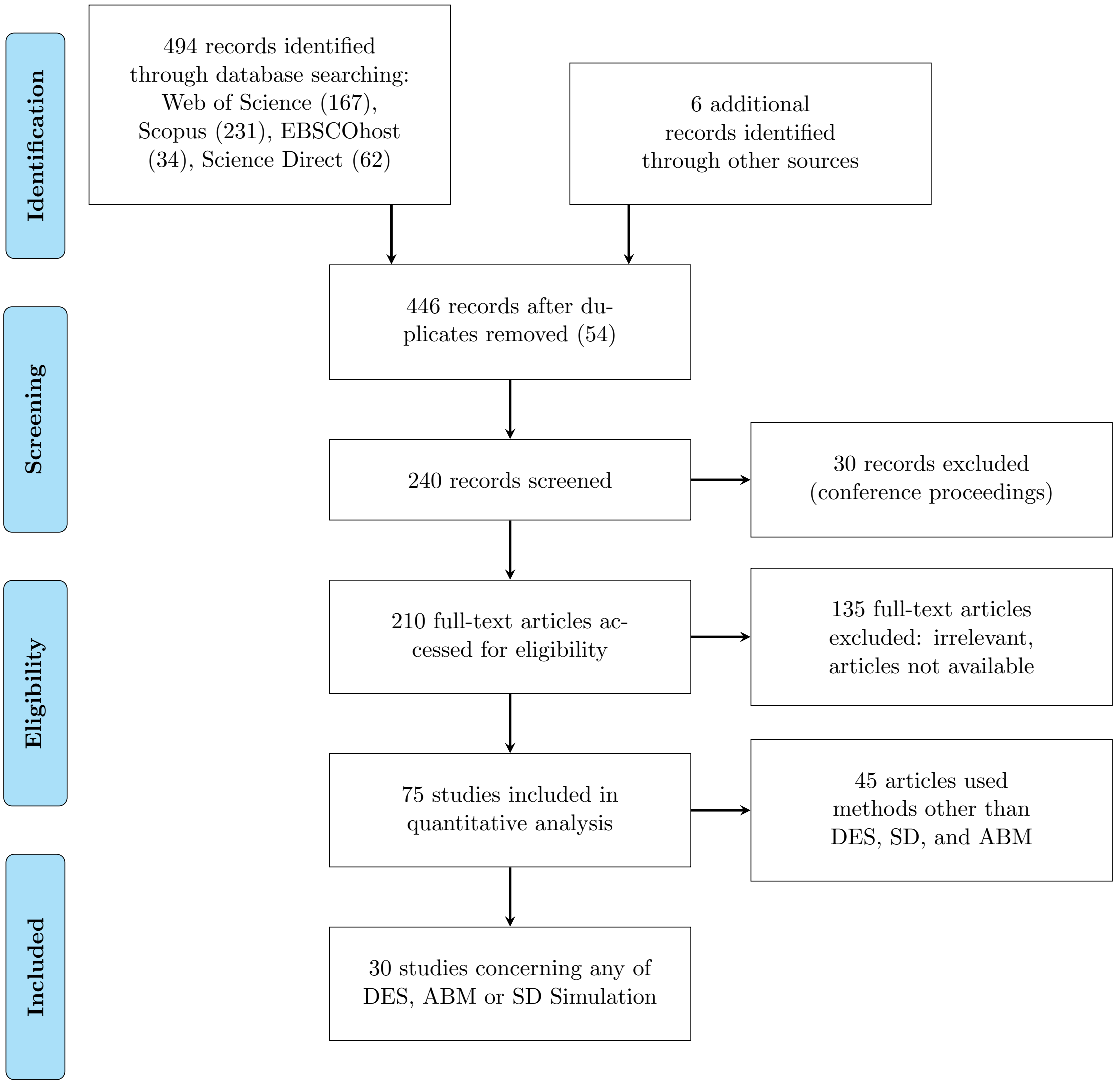
The current study has benefited from the methods used in these two reviews. We tried to emulate the steps taken to ensure the replication of similar results. We argue that any published review paper could become obsolete with time. With the possibility of a growing number of literature, it is not easy to get exactly the same result even if the exact same steps are followed. For the purpose of our study, we employed the keywords used in Long and Meadows (2018) and expanded them to include more simulation techniques such as linear programming, integer programming, queueing theory, and queueing network.

The strings used for searching within the abstract, title, and keywords are ('simulation model*' OR 'discrete event simulat*' OR microsimulat* OR 'markov model*' OR 'system dynamics model*' OR 'agent based model*' OR 'integer programming' OR 'linear programming' OR 'queueing theory' OR 'queueing network') AND ('mental health*' OR psychiatr*).

3.3 General results

Figure 3.1 presents the PRISMA 2009 diagram illustrating the literature search process. The first phase represents the identification of literature generated by the databases after using the filtering tool. The second phase represents the screening of literature by means of reading the title and the abstract. This phase includes removing any duplication or any texts which are not available in full. The third phase, eligibility, was conducted by reading the article in more detail to check the suitability based on the defined criteria. This phase includes checking the availability of the literature. Any text which is not available to be accessed is not included. The last phase filters the literature into two classifications: literature based on the three simulation methods (SD, DES, ABM); literature which uses other methods.

Figure 3.1: PRISMA 2009 Flow Diagram.



The defined criteria exclude any simulation outside the Operational Research tools. For example, any study using tangible simulation for medical purposes or computer simulation to aid medical students in learning processes. We also excluded any studies that employed stand alone statistical analyses such as time series or regression analysis.

We extracted 75 studies for quantitative analysis, 45 of which have reported using methods other than ABM, SD, or DES. The remaining 30 studies, have used either DES, SD or ABM and are analysed in detail in the next section.

Table 3.1 presents the summary of the findings based on the method used. The total is more than the actual number of included papers. This is due to the fact that two studies, by Koizumi et al. (2005) and Chepenik and Pinker (2017), reported using Queueing Theory and developed the models in DES. The application of SD simulation in mental health related problems is marginally higher than the application of DES. This is the opposite compared to their application in general healthcare related problems (such as found in Katsaliaki and Mustafee (2011)).

The growth in the number of papers on mental health care using OR methods is sluggish prior 2005. Thereafter, there was a relatively steady slope in growth up to around 2018. Figure 3.2 presents the cumulative number of papers and the counts for each year group.

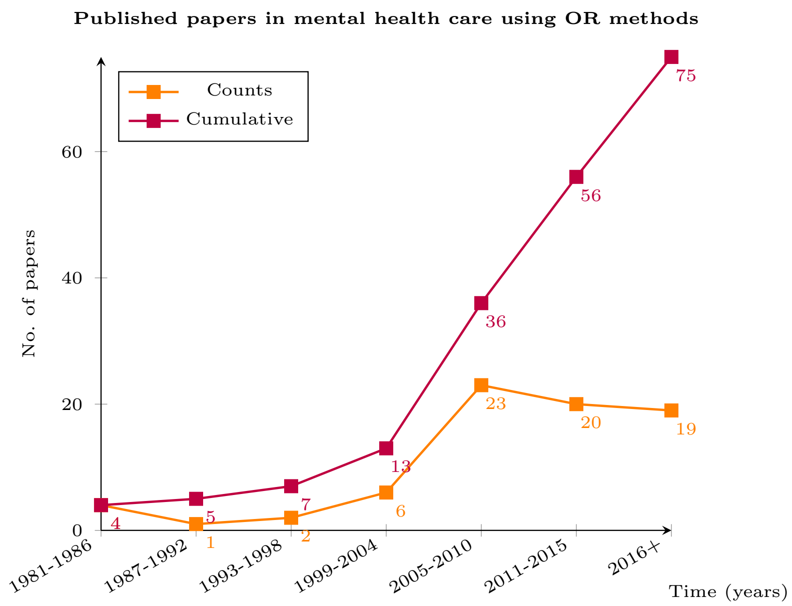


FIGURE 3.2: Cumulative and counts of published papers

The results indicate that Markov models have been used mainly for cost benefit analysis of treatment such as drugs or therapies, epidemiology, and healthcare system operation to estimate the service use. The method was used to model the health status of an individual, system network such as a community mental health service, being in treatment and whether in contact with the justice system.

In order to give us a convenient method for classification of the area of study for each included article, we employed the four classifications discussed in Long and Meadows (2018). These include: medical decision making and treatment evaluation; epidemiology, prevention and screening; healthcare system operations; and healthcare design and planning. Table 3.1 summarises the included literature based on the method used and the area of study.

Table 3.1: Literature classification based on methods and areas of study

Methods	N (%)	Area of studies	N (%)
Markov	29 (37.7%)	Medical decision making and	
DES	12 (15.6%)	treatment evaluation	33 (41.8%)
SD	13 (16.9%)		
ABM	5 (6.5%)	Epidemiology	16 (20.3%)
Queueing Theory	2 (2.6%)		
Mathematical Programming	3 (3.9%)	Prevention and screening	6 (7.6%)
Microsimulation	2 (2.6%)	Healthcare design and planning	10 (12.7%)
Decision Tree	2 (2.6%)		
Mathematical model	1 (1.3%)	Healthcare system operation	14 (17.7%)
Other Simulation	8 (10.4%)		
Total	77 (100%)	Total	79 (100%)

The results in Table 3.1 highlight that the majority of studies addressed issues around medical decision and treatment evaluation. This area was addressed using Markov models and DES. The treatment evaluation includes pharmachological studies which assess the efficacy of treatment such as drugs with respect to cost benefit. Some studies have covered more than one area of study, hence the total is more than the number of studies included in the final phase.

Studies categorised under the healthcare system operation include those which claimed to support the decision making and policy, clinical knowledge, and patient flow. Whereas those studies included in healthcare design and planning have been done for system analysis, evidence based practice and organisational performance.

3.4 Simulation modelling in healthcare systems from single to mixed paradigms

The literature search yielded classification of simulation methods used in mental health care, see Table 3.1 from the previous subsection. For the purpose of the study, this section will highlight and summarise those studies using methods DES, SD, or ABM. Table 3.2 gives a list of the main references used in the subsequent discussion which is the result from the literature search.

Table 3.2: Literature classification based on simulation methods

Method	References
DES	Najafzadeh et al. (2017); La et al. (2016); Kim et al. (2013); Klok et al. (2007); Kuno et al. (2005); Koizumi et al. (2005); Heeg et al. (2005); Laux et al. (2005); Vasiliadis et al. (2017); Patten and Meadows (2009); Heeg et al. (2008); Chepenik and Pinker (2017)
SD	Zimmerman et al. (2016); Wolstenholme et al. (2010); Smits (2010); Wang et al. (2013); Lane and Husemann (2008); Hovmand and Gillespie (2010); Bliss et al. (2010); Tanaka (2010); Wittenborn et al. (2016); Ghaffarzadegan et al. (2016); Sheldrick et al. (2016); Lyon et al. (2016); Page et al. (2017)
ABM	Cerdá et al. (2015); Silverman et al. (2015); Kalton et al. (2016); Mooney and El-Sayed (2016); Cohen et al. (2017)

3.4.1 Discrete Event Simulation

The application of Discrete Event Simulation (DES) in healthcare has been reviewed in several studies (examples in Fone et al. (2003), Jun et al. (1999), and Günal and Pidd (2010)). Jun et al. (1999) summarised that many healthcare related studies focused on patient flow modelling, where they addressed issues such as patient scheduling and admissions; or problems related to the availability of resources. They asserted that DES has been used to help improving patient flow in the system, while ensuring quality and efficient healthcare delivery.

Günal and Pidd (2010) reviewed literature that used DES for evaluating healthcare performance. They concluded that the use of DES are mainly to address problems related to specific units in healthcare systems such as: evaluating staff requirement, patient's waiting time, and utilisation of hospital beds. They argued that although the reviewed studies captured the detailed healthcare processes, there is only a small number of models that represented the whole system.

Our literature search on DES application in mental health care highlighted that most of the studies using the method were in the area of medical decision making and treatment evaluation (6 studies). This includes the cost benefit analysis of treatment either using medication or non medication. The second area of application is related to healthcare system operation which includes decision support and policy, and patient flow (5 studies). One study in particular is categorised under epidemiology since it used epidemiology data to estimate the population size and recurrence cases in major depression.

In the cost benefit analysis, a study by Najafzadeh et al. (2017) investigated the efficacy of two different treatment methods. The first one was the usual treatment where the decision on the course taken was solely dependent on the clinician's judgment. The second method used the information on a patient's individual characteristics such as genomic factor, patient's lifestyle and the environment which may contribute to the response in taking the medication. Using a prediction tool, this information was used to choose the best medication which was considered safe and beneficial for the patient.

The developed model in Najafzadeh et al. (2017) had two separate treatment pathways capturing the choice either using the prediction tool or a clinician's best judgment. Each course of treatment captured the necessary states which may arise as a consequence of the treatment taken. This includes response, relapse, suicide attempt, remission, or even death from other cause. The study aimed to analyse the cost benefit of the two decision making processes. Based on their results, the authors concluded that using the prediction tool to help in choosing the medication improved the quality of life of an individual affected by depression and potentially reduced the cost of treatment.

The benefit of using DES to compare different medication treatments has been demonstrated in a study done by Laux et al. (2005). The authors take advantage of the DES method by including the patient's characteristics as well as the interrelation of dynamic variables concerning the patient's course of medication during the treatment. Although the characteristics of patients were modelled as fixed, the assignment to the individual patient was random. The model was designed to take account of the duration of taking the medication and the number of visits to mental health specialists such as a psychiatrist, as well as the location of treatment (inpatient and outpatient). The model also included only two health states of individuals which either being in-between relapses or in relapse. This study aimed to examine the cost and benefit of each medication assessed, and concluded that the expensive medication has potential to save cost in the long run and is shown to be more effective.

A more comprehensive model for a disease course of schizophrenia, which takes into account social and environmental factors as well as a patient's characteristics and episode history, was also modelled using DES by Heeg et al. (2005). The authors asserted that the model was built on literature to inform the structure, the epidemiology, and the treatment course. Due to the scarcity of comprehensive data, the modellers relied on expert judgment on three aspects: the required parameters; the validation of the model structure; and the assumptions of the model. The authors also described that they only model patients whose condition has progressed to a more severe condition as their treatment patterns were arguably more dynamic and possibly covered a longer duration.

The model developed by Heeg et al. (2005) was based on the treatment offered in two community settings (for intensive and less intensive treatment at home), in a hostel where staff were provided and in a hospital. The authors focused their model on the relationship between a patient's compliance and treatment cost. They argued that DES is suitable for modelling their complex problem due to the flexibility in incorporating interrelated dynamic variables influencing the health status. The results suggested that an increase in a patient's compliance significantly reduced the annual cost per patient suffering from schizophrenia.

Pharmacotherapy for people affected by mental health conditions comes with many different medications. Cost benefit analysis studies of certain medications have been done using DES technique, such as Heeg et al. (2008) which compares the costs between two types of drugs for people with schizophrenia. A more comprehensive cost comparison study between different drugs for people with bipolar (a combined condition of depression and mania) was done by Klok et al. (2007). Their study examined the different effects of single drug therapies and combined drugs treatments to the cost. Similar in argument to Heeg et al. (2005), their use of DES enables them to capture an individual patient's characteristics with different possible choice of drug treatments. One highlight from their results is that using the combined drugs (especially between quetiapine/lithium) was concluded as more effective compared to any monotherapy or even placebo. The detailed explanation of drugs involved is not in the scope of this review. In fact, the authors also suggested that the overall cost for any single drug therapy was more costly than any combined drug therapy. This study not only examined the cost benefit of pharmacotherapy for patient suffering from bipolar, but also showed that medication treatment helps improve mental health conditions in this case.

Other types of treatment for people with mental health problems are based on therapy. Our literature search filtered one study that assessed the usefulness of a cognitive therapy in preventing a relapse in depression (Patten and Meadows (2009)). The study used a simulation method and epidemiology data to estimate the recurrence cases in the population.

In the area of patient flow, DES has been applied to examine various policies relating to service capacity in various healthcare settings. La et al. (2016) combined community based and residential settings with state specialist hospitals in their model for the adult population of North Carolina. Their aim was to examine the relationship between the waiting time to admission and the acute beds capacity in the psychiatric hospital. The results highlighted the need for increasing the beds in the acute hospital in order to reduce the waiting time. The authors suggested that the reduction in waiting time can also be done by increasing the beds in community based services. This suggestion is intuitive as community based services were set-up to act as receiving services from the acute services. However, they argued that these community based services were not equipped to cater for people with severe mental health problems. Hence the additional capacity may not lead to cost savings in general.

Another study, which is based on queueing theory and simulated using DES, captured the link between hospital, residential services, and supported housing facilities. Koizumi et al. (2005) evaluated the effect of bed blocking to the number of patients waiting and associated waiting time to enter mental health services. They argued that their model can be used to identify the relationship between the availability of beds and a patient's waiting time to receive treatment at the downstream services. They found that in order to reduce the number of patients blocking the beds, it is not necessary to increase the number of beds in all facilities. In fact, they suggested that an increase in capacity in supported housing will reduce the number of patients waiting in the upstream services (i.e. in the extended acute hospitals and residential facilities).

Also based on the study done by Koizumi et al. (2005), Kuno et al. (2005) developed a model using DES, which examined the waiting time and the capacity (beds in this case) needed in the two services. Their simulation study highlighted the importance of the efficiency in transferring patients from the sub acute units to residential settings. How the patient flow was managed from the sub acute to residential affected the congestion in the downstream facility (i.e. the acute hospital).

Similar to the technique used in Kuno et al. (2005), Chepenik and Pinker (2017) modelled a psychiatric emergency service in order to understand problems related to bottlenecks in the system. The service was modelled as a series of activities consisting of, among others, triage, observation, and delays for admission and discharge. This service was linked to the inpatient service. The psychiatric emergency service was a bedded service where patients with behavioural problems were treated, medically, prior to being transferred to the inpatient unit or discharged. The authors found that changing efficiency in clinician service time, i.e. by reducing the length of consultancy, the crowding in emergency services can be reduced. They suggested that making a small change in the length of working hours for the psychiatrist, can also improve the flow from the emergency service to either inpatient or discharge.

In a small scale problem, DES can be applied to study the possible changes in a service operation such as finding the best staff configuration and service hours that can benefit both the patients and the organisation. A study by Kim et al. (2013) utilised DES for this purpose. Their study aimed to improve the service of mental health clinics by reducing the number of patients seen out of hours. The simulation model was used to run several different scenarios relating to the service capacity. The results indicated that an improvement of service can be made by combining additional hours of service and additional psychiatrists. This simulation study provides an example of implementing DES in system operation by modelling patient flow.

Expanding the coverage of psychological treatment has also been studied by Vasiliadis et al. (2017) using DES. The developed model incorporated the use of GP, psychiatrist, and other mental health specialists such as psychologists, psychotherapists and nurses. The outcome measures, generated from the model, included: recovery, response, recurrence or relapse, admission, suicide attempt, and death. The authors found that although treating more people with depression generates cost to the healthcare, nonetheless in the long run it will benefit the population and the health services. This is one example of a study where the cost benefit analysis was conducted in relation to the access to the service rather than to the use of medication alone, such as in the area of pharmacology.

It appears that either in the area of healthcare system operation or healthcare system design and planning, patient flow modelling using DES has been shown to be a significant aid for the decision makers to find the best possible service structure. The problems related to the process flow being modelled shared a similarity, i.e patient's waiting time in conjunction with limited available resources. DES has been implemented to inform evidence based structural change in providing an efficient mental health care service.

3.4.2 System Dynamics for modelling a complex system

3.4.2.1 Characteristics and concepts of System Dynamics

System Dynamics (SD) modelling is characterised by certain concepts that make it suitable for modelling a dynamic complex system such as the healthcare system (Homer and Hirsch (2006)). These concepts include the feedback loops and delays which together with the structure of the elements incorporated in the system will determine the behaviour of the system (Sterman (2000)). Modelling a system will require setting up the boundaries; either the whole system's boundaries or each element's boundaries. Often, in complex system modelling, these boundaries overlap. Brailsford (2008) outlines some reasons why SD is suitable for healthcare modelling, one of which is that SD can accommodate modelling a system where its elements have overlapping boundaries. Furthermore, SD can accommodate boundaries which encompass all the dynamic influences necessary to comprehend the totality of the system being modelled (Dangerfield (1999)).

A complex system such as healthcare often deals with large populations. Modelling this system, with very detailed characteristic for each individual in the population, would be computationally costly especially if coupled with a long period for running the simulation. SD does not need highly precise data. The entities being modelled, such as individuals in a population, can be aggregated. This is another characteristic of SD as a tool for policy or strategic level modelling (Brailsford (2008), Wolstenholme (1993)).

The process of producing the model involves the activity where stakeholders interact and communicate to elicit their views of the problems and issues in the system. Many existing SD studies have reported that this process alone enables the stakeholders to gain insights into their system (see example in Wong et al. (2012)). Conversely, the engagement with the stakeholders also assists the modeller in gaining an understanding of the system being modelled. Hence the group modelling activity facilitates learning about the system and the model building process itself for both the stakeholders and the modeller.

This engagement activity will produce a causal loop diagram of the system which provides a description of the factors influencing the system behaviour. This approach is used to address the behavioural, structural, communication and relationship issues which together determine the quality of service delivered (Cavana et al. (1999)). It is crucial to have as accurate a representation as possible of the system by capturing the factors and their relationships. The feedback loops will be generated by the interconnections of the influencing factors which are important elements in generating the system behaviour. However, Sterman (2000) emphasised that capturing feedback is more important than detailing the components in the system with a high level of precision.

It is argued that a causal loop diagram has limitations, one of which relates to its ability in capturing the stock and flow in the system. The development of a causal loop diagram should go hand in hand with the development of a quantitative model which is characterised by a stock and flow diagram. This ensures the two approaches reflect one another. The stock variables are those considered important and represent the states in the system which can generate information of the system behaviour. In most cases, other SD characteristics (such as delays) can be created by states which display the discrepancies between the incoming flow rates and the outflow rates (Sterman (2000)). The ability of System Dynamics in incorporating delays in its formulation makes it a more suitable tool for problems involving long-term forecasting strategy.

3.4.2.2 Overview of the application of System Dynamics in healthcare

The applications of System Dynamics modelling in healthcare have been recorded in literature (see for example Gönül-Sezer and Ocak (2016)). However the number of studies is significantly fewer than other approaches such as discrete event simulations (see for example Brailsford et al. (2009)). Studies that implemented System Dynamics in healthcare come under topics such as policy evaluation, analysis of systems and infrastructure, communicable disease, and resources (Katsaliaki and Mustafee (2011)).

In unscheduled care service, studies have focused on improving the service in the emergency departments. For example a study on emergency and urgent care systems by Lattimer et al. (2004) used System Dynamics modelling to investigate patient flows through the system and the system capacity. The qualitative model illustrates the patient pathway from the entry point to discharge. The modelling showed the potential consequences of continued growth in demand for emergency care and suggested that increasing the capacity of care management in the community can prevent the worst case scenario. It also found that raising demand for emergency admission reinforces the utilization of the acute facility. Consequently the high level utilization of acute beds influences the high queue in patient pathways through the system. However the result may not be generalized due to the high dependence of the model on the available routine collection of data from a range of providers.

An additional feature of patient boarding in emergency department (ED) has been addressed by Wong et al. (2012) whose model shows how a System Dynamics approach can be used to describe public funded hospitals. The study examines the issue of boarding, i.e. patients who have been admitted to the inpatient unit but stay in the ED. The resultant conceptual model highlights three main issues that relate to the healthcare system, namely the changing of population, the resource allocation and work environment, and Ministry of Health accountability. The model building process has engaged the clinician practitioners and hospital managers alike to elicit their views on the issues around the problem. The model suggests that controls applied upstream and downstream to the ED level may reduce the boarding problem in ED.

The above studies have mainly used hospital settings where the ED is located. A wide emergency system modelling of patient flow, using the System Dynamics approach, has been attempted by Brailsford et al. (2004). As with the previously mentioned studies, the qualitative model was developed, based on interviews with the key individuals, to show the patient pathway through the system. This qualitative conceptual model was used to develop a quantitative model where various experiments were run. This is one example of large scale system modelling using SD covering all emergency type patients.

The emergency service is not the only service in healthcare that has been studied using the System Dynamics approach. Lane and Husemann (2008) has developed a map to describe general acute patient pathways, which aims to assess the usefulness of System Dynamics in healthcare and to provide a suggestion as to how to improve a patient's experience with the service. The map uses a combination of stock and flow diagrams and the causal loop diagram. Its purpose is to explore and represent the experts' view on a patient's journey through the system and the factors influencing the pathways. The elements incorporated in the model are the journey through ED, hospital wards, as well as the waiting lists for operations.

A recent development in healthcare modelling using a qualitative System Dynamics approach describes the whole-system perspective. The study, by Esensoy and Carter (2015), was done for the Ontario Ministry of Health and long-term care. Although the underlying concept is patient flow through the system, the scale and the complexity of the model makes it one of the largest qualitative models of System Dynamics modelling. The broad scope of the study incorporates five sectors in the system, namely acute hospital care, home and community care, rehabilitation and complex continuing care, long-term care home, and informal care. The focus of the model is the transfer of care between these sectors. The authors define the transfer as a movement of volume and acuity. Volume represents the physical transfer of patients, such as the number of patients utilizing the resource. While acuity represents the transfer of acuity or care need associated with the flow. As the population being modelled is an elderly cohort, the movement between sectors may change the requirement in the facility. The study highlights the need for a healthcare system to be dynamic, as the population changes to adapt to the increasing demand for chronic care and old aged people care.

3.4.2.3 Application of System Dynamics in mental health care

The literature search identifies 13 studies, using System Dynamics in mental health care, eligible to be included in the discussion. Since the number is low, we add conference papers done by Wolstenholme et al. (2007) and Smith et al. (2004) in our discussion.

It appears that the healthcare system operations constitute the most applied area for System Dynamics. The second most applied area comes under epidemiology, disease prevention and planning. Only one study comes under system design and planning. Although there is an increase in the number of studies found since the review by Long and Meadows (2018) (who found 10 studies) the result suggests that the application of System Dynamics in mental health care is still very small. In fact, Bliss et al. (2010) claims that the application of System Dynamics in mental health care is not found prior 2010.

Studies under healthcare system operations include those studies describing patient flow, decision support and healthcare policy, system performance, and examination on technological support. While studies under the classification of epidemiology, disease prevention and screening include: modelling disease progression, clinical decision making, prevalence, service demand, and influencing social and risk factors in mental health.

System Dynamics modelling processes may start with the exploration of an unknown problem where the end result is the development of a causal loop diagram (CLD). This CLD captures the interrelation in the healthcare system. To produce such a diagram, engagement with experts is required. Areas such as system redesign and implementation planning can benefit from such an approach. Zimmerman et al. (2016) has demonstrated the engagement with experts in their modelling process. Their study involves modelling an outpatient mental health facility in order to support the redesign and implementation of psychotherapy treatment. The model is used to examine the feasibility of redesigning the intake and treatment policy. The result suggests that by reducing the examination duration, the system serves more patients who need the treatment. The authors conclude that a System Dynamics modelling approach, with its participatory element, is shown to be a feasible approach for engaging stakeholders and supporting the implementation planning effectively.

Within the area of healthcare system operations, studies have used patient flow to model a mental health care system with various focus. Wolstenholme et al. (2010) developed a System Dynamics model which evaluated cost benefit analysis.Their model comprises three sub-models: the treatment and recovery sector, the therapist sector, and the labour market sector. The treatment and recovery sector sub-model captures elements related to treatment delivery and its outcomes such as duration of treatment, recovery state, and relapse cases. The therapist sector sub-model incorporates service capacity based on the dynamic of human resources and the case load. Whereas the labour market sub-model captures patients with mental health problems who are in employment. The authors argued that their model is one of a kind, which combined the cost benefit analysis and System Dynamics approach, to be a dynamic cost benefit analysis model which takes into account dynamic variables characterising the system behaviour.

From the operational perspective, a study by Smits (2010) was developed to investigate how the performance of intake and treatment processes are affected by the changing of policy and service processes. The developed simulation model was used to run several experiments which reflect different intake and treatment processes of mental health patients. It evaluated the effect of assigning different levels of personnel resources to different care services. The process was redesigned by implementing brief therapy and stepped care. The result indicates that, by limiting the duration of therapy for each individual patient and only moving to more intensive care if the least restrictive treatment does not yield a better outcome, the service will perform better. This study demonstrated both the use of the causal loop diagram to show the main relations and feedback loops in the system, and the quantitative model to run the experiments. However, this study was focused on a site specific case.

A patient flow through the system with focus on the hospital in relation to residential and rehabilitation sectors has been formulated by Wolstenholme et al. (2007). The study examines the introduction of a new ward called 'triage' and a new delivery model called 'Admission Avoidance' which aims to reduce the admission rate into the inpatient unit. The triage ward provides a service as a filter for patients who are going to the inpatient unit or going home. Whereas admission avoidance serves the purpose as an active approach which puts the decision into the hands of the patients and their carer. Why is this so? In admission avoidance, the care is either provided as intensive care in the outpatient unit or as home treatment. It is not clear from the description of the study as to what type of patients go down this path or what kind of mechanisms are put in place to direct patients taking this pathway. One thing that we can learn from this model is that the population is divided into two sections, those who are known to the system and those who are not. People who are not known to the system can become known at some point. However, there is no return flow from the known to the unknown to the system.

What this means is not clear. Does it mean once people are known to the system they will stay on the record? Or is it related to the fact that a mental health condition is a long term condition?

Mental health issues in prison and forensic sectors have been addressed by Smith et al. (2004) which captures patients pathways in relation to delayed discharge. The authors stated that the initial aim of the model was to respond to questions around capacity but the result provided more interest on policy, operational management and service development. They admitted that their model is not a whole system model for describing the mental healthcare system since many more elements of the system such as primary care and community based treatment are not included.

Mapping a system using System Dynamics which captures people flow in the system has been demonstrated outside the healthcare system. Wang et al. (2013) developed a conceptual military system mapping which captures the flow of military personnel from recruitment to deployment and treatment. The authors built their model in three parts which influenced each other. The first part describes the individual level factors which influence the military personnels' mental health condition and their need to seek help. The second part of the model depicts the unit level factors which comprise unit support and leadership. These factors influence the military members' social support and their stigma. The last component of the model describes the enterprise level factors which represent the largest loop in the model. This level includes the recruitment, deployment, and treatment service. The authors concluded that the challenges in initiating change due to the complexity of their model. The challenges come in three points which can contribute to the complexity in decision making. These are the complex pathways in the military psychological system, the inherent time delay in their model, and the complexity of the model posed by the challenge in data acquisition to inform the parameters needed in the model.

The benefit of mapping a system of care using System Dynamics has also been demonstrated by Lane and Husemann (2008). Their work not only produced a map for the acute mental health patient pathway in the system, but also used the mapping process as a means to elicit experts' knowledge for describing the flow and suggesting any intervention. The resultant map conceptualises the interrelation of a healthcare system offering mental health services. This starts from the activity with the GP and onto hospital inpatient or outpatient units including Accident and Emergency (A&E). The authors conceptualised the number of admissions controlled by the available resources which are influenced by the number of patients currently occupying the wards and the available beds.

A higher level abstraction of modelling a mental health service organisation can be seen in a study done by Hovmand and Gillespie (2010). Their study offers a framework for implementing evidence based practice in organisational change. They argue that mental health services can benefit using this framework to produce a valued service and with efficiency. The developed model comprises three feedback loops representing: the reorientation, support from the community, and quality improvement which ultimately influences the whole organisation performance. The reorientation relates to the involvement of the staff to keep up with change. The support for the community feedback relates to the improvement in resources in the community which leads to an increase in the referrals and hence the provision of a valued service. The last feedback refers to the organisation learning process, in order to keep the quality of service, by providing their own implementation feedback. The study demonstrated an application of the System Dynamics model in a strategic level of the healthcare service.

Another application of System Dynamics was applied in a mental health community centre, which explored the relation between the caseworkers' clinical knowledge and their tenure (Bliss et al. (2010)). The model comprises two balancing loops: one capturing the caseworkers' employment, including hiring and leaving the job; the other describing the knowledge about mental health care and the learning process. The model was used to run experiments highlighting the management's decision on hiring caseworkers. The authors suggested that the development of clinical knowledge in caseworkers is pretty much influenced by the employment turnover. They argued that the longer the caseworkers stay in employment, the higher the level of their knowledge in mental health care and mental health organisation.

The areas of epidemiology, disease prevention and screening in mental health have been modelled using System Dynamics since 2010. Falling under this category is modelling disease progression which may be done by modelling human biological systems such as brain functioning. Modelling disease progression in a biological perspective is probably the most difficult modelling process. Not only does it involve observing changes in parts of the human body which is not always easy to do, but it also involves a data collection process informing the parameters used in the model.

Published in 2010, Tanaka's study in particular has applied System Dynamics to model prefrontial cortex activity in patients with schizophrenia compared to normal healthy people. The model describes the relationship between parts of the brain which are responsible for cognitive behaviour or decision making and chemical release. The author concluded that people with schizophrenia showed lower activity in cerebral cortex and antipsychotic medication can reduce their symptoms.

A more recent study describing the complex nature of depression and its influencing factors also employed a System Dynamics approach. Wittenborn et al. (2016) developed the first causal loop diagram of depression dynamics which captured the broad feedback mechanism of factors influencing depression. The model was built based on existing literature and can be seen as a comprehensive model of depression incorporating different dimensions: cognitive, social environment, and biological. The authors explained that depression is regarded as a condition that is produced by the underlying reinforcing factors both internally and externally. The external factors act as a trigger to cause the individual to experience negative conditions. Since all feedback loops in the model are reinforcing, this will lead to a deteriorating condition. The authors also suggested that building resilience of an individual can be done by addressing the external factors that stimulate stress.

Furthermore the variation in depression between individuals is uniquely influenced by any reinforcing loops or their combination. The consequence of this is that the treatment for people suffering from depression should be tailored according to each individual's needs. The lack of balancing loops in the model highlights how sensitive and fragile the mental health condition is.

Compared to the model developed by Tanaka (2010), the model developed by Wittenborn et al. (2016) is far more inclusive in capturing the influencing factors affecting depression. However, the complex model comes with challenges in turning it into a quantitative one. As stated by its authors, the qualitative model of depression in Wittenborn et al.'s study has not yet been developed into a quantitative model.

The challenges faced when developing a quantitative model based on the result in Wittenborn et al. (2016) may include several reasons. The authors stated that the model is the first of its kind which addresses three different dimensions: biological, social and environment, and cognitive. Each dimension has its own feedback loops and drivers which interact not only within each dimension but also across dimensions. In order to develop a quantitative model, it requires not only the feedback loops that characterise the depression, but also the drivers and the rate of change of each driver (as mentioned by the authors). The endogenous variables created as a result of the interaction between drivers are a qualitative description. Turning these variables into quantitative variables, which is the key to the quantitative model, is not an easy task. Furthermore, the model was developed from the literature which indicates the use of a certain number of studies. Variation must exist between each study and this may contribute to the quality of the developed model. The quantitative model may face issues related to overall model validation, as it is a comprehensive description of depression which will be difficult to validate against reality.

Another approach in modelling a disease progression is using a health state based model. This approach has been done largely in the area of the economic evaluation of disease. Most of these studies employ Markov models. However, this is not to say that a model based on health state cannot be done using other approaches such as System Dynamics. One of the most recent studies was conducted by Ghaffarzadegan et al. (2016) who claimed that their study using System Dynamics to model military personnel and veterans who experienced post-traumatic stress disorder (PSTD) was a novel approach. Their model represents two different types of people: those in the military and those who are veterans. The two sub-models are linked with the transitions representing the progression of health status. People in the military can have a good health condition all the way to their post-military, or develop a mental health condition during the military post but their illness is unrecognised and hence progresses to veterans where they will eventually receive treatment. Another transition depicts people in the military with diagnosed illness who then receive treatment when they have finished their service. This type of person will eventually go to healthy status after receiving successful treatment. The model has been used to estimate the diagnostic rate and annual cost involved in treatment.

One advantage of System Dynamics modelling is its ability to model a complex abstract system such as behaviour. In a healthcare system, human behaviour plays an important role in many decision making processes such as medical decision making on referring patients to have treatment, or when patients should be discharged. In mental health care, the diagnosis of a patient's disease also involves such decisions. Our literature search found one particular study done by Sheldrick et al. (2016) that modelled physician decision making on referring children with developmental-behavioural problems. The developed model captures the past knowledge about the patient's illness and the outcomes of physician decision which influence the future physician decision making. The sensitivity issue around making correct diagnosis was explicitly modelled by presenting four different types of decision outcomes (False Positive, False Negative, True Positive, and True Negative). The authors argued that their model suggested that clinical decision making is not a simple process depending only on the screening tools, but rather, it is a complex system involving the physician's own behaviour which itself changes over time.

A recent model capturing screening for mental health among high school students was developed by Lyon et al. (2016). The developed model also includes the sensitivity issue on diagnosis as done by Sheldrick et al. (2016) albeit with only two terms, false positive and true positive diagnosis. One particular feature of the model developed by Lyon et al. (2016) is the incorporation of universal screening where all students initially will undergo a mental health check. The author stated the aim is to identify which element of the system will impact the community mental health service and its outcomes by the implementation of universal screening, which arguably increases the initial service demand. They argued that their model not only serves as a tool to overcome access barriers in the mental health service but also as a tool to estimate the capacity needed in providing a mental health service in schools.

Still within the context of screening and prevention, Page et al. (2017) developed an SD model which captures the sequence of suicide states for population in Australia. Using the administrative data, the study aimed to investigate the best intervention strategy in preventing suicide for those effected by mental health problems. The intervention strategies include: GP training, coordinated care after suicide attempt, improve mental health literacy in the school setting, hospital care intervention, and provision of psychosocial therapy for those affected by suicidal ideation. Their model is a high level population model which focuses on analysing which services in the system give benefit in reducing the suicide cases in a school setting. Based on their finding, the authors argued that training for GPs, and the provision of coordinated aftercare give a promising result in reducing suicide rates. This study expanded the notion of modelling the mental health services beyond the screening as has been modelled in Lyon et al. (2016).

3.4.3 Agent-Based simulation for modelling a system with behaviour

3.4.3.1 Agent-Based Modelling for complex adaptive systems

The advancement of computer simulation has allowed the modelling of a more complex system which not only describes the interrelation of components in the system but also captures their behaviours when interactions occur and adjust their behaviours as a result of the interactions. The system is described in a more complex form as a collection of agents which have their own decision making processes (Bonabeau (2002)). The approach that allows the incorporation of agents' decisions and their behaviour is Agent-Based Modelling (ABM). This flat form involves three main concepts namely the agents, the interaction between agents and their environment, and the environment where the agents live.

Much academic literature has documented the benefit of ABM approach over other methods (see for example Bonabeau (2002) and Macal and North (2010)). One of the benefits is that ABM is able to capture the characteristics and behaviour of the systems which are often over simplified in other traditional modelling approaches due to various reasons. It is also argued that ABM can be used to address problems relating to systems' emergence behaviour.

The suitability of ABM to model such emergence behaviour is due to its capability in capturing many level modellings, namely the system and the agents at the same time. ABM is argued able to model the effect of agents' interaction to the system and the effect of the system behaviour to the agents (Railsback and Grimm (2012)). In fact ABM can accommodate more complex behaviour such as behaviour of agents that can learn and adapt to their environment (Bonabeau (2002)).

The agents in ABM have two characteristics, namely being unique and autonomous. Being unique implies that each agent is different in its characteristics and autonomous means that each agent has its own decision making process in order to achieve its goals. Moreover, agents can learn from the situation and adjust their behaviour accordingly. This adapted behaviour is not only a result from learning their own condition, but also from acknowledging other agents' states and the state of the environment (Railsback and Grimm (2012)).

Human beings can be classified as complex systems which consist of different elements with their own functions and behaviours. Modelling human behaviour which describe their characters is not easily done. It is not surprising that many models only capture certain elements of the characteristics. Other systems such as healthcare can benefit from ABM in particular if they have to include human behaviour.

3.4.3.2 Agent-Based Modelling in healthcare

Agent-Based Models have been applied in many areas of study such as social sciences, where the varieties of models depend on the type of system being studied, the goals of the modelling and the details of the system being modelled (Klein et al. (2018)). In general, it has been applied in problems related to process flow, organization, market, and diffusion (Bonabeau (2002)). Healthcare has just recently started to take advantage of this modelling technique.

Kay Kanagarajah et al. (2008) explored the potential use of ABM in healthcare to model a complex adaptive system. Their study used a case study of an Emergency Department to improve the service quality on patient safety, economics, and workloads. Agents represent the patients and service providers, in this case, doctors and nurses. Their behaviours are depicted as a function of what happens within the environment and will depends on the available options. Patients' movement in the environment depend on the availability of resources which is described using a stochastic function. The behaviour of agents is formulated by some determined rules. For example, when a patient is attended by a nurse or doctor based on the severity condition of the patient, and doctors' and nurses' decision to work defined by whenever they are needed.

This study went further than just modelling the complex system, it modelled a complex adaptive system. It employed the adaptive behaviour of agents based on the other agents' state. The emergence of a long waiting time due to rising demand of services will trigger the behaviour of doctors to work faster. Though the model only represents one ED, it managed to capture some complex behaviours in ED.

Another application of ABM in modelling an ED was done by Taboada et al. (2011). The developed model was used as a tool to help in a Decision Support System to assist the manager in making better operational decisions. Unlike the study done by Kay Kanagarajah et al. (2008), the ED in this study was depicted as a complex system which means that agents' behaviour was not designed to be able to adapt to the situation in the environment beyond the first level. The agents moved based on the predefined rules which were constant. The emergence behaviour of the system did not have any effect on the next movement of the agents. Another highlight of the study is that the model managed to model the mixed skill workforce applied in the ED. This is due to the ability of ABM to capture the heterogeneity of agents. However the developed model was not validated and tested against the real data due to lack of availability of empirical data.

The most recent study, by Kaushal et al. (2015), also applied ABM in an Emergency Department to help reduce the patients' waiting time. It could be argued that the approach was not purely ABM as it involved the development of DES which captured the processes in the ED. However, it showed how the complex ED service could be evaluated using ABM. The model was used to evaluate the Fast Track Treatment (FTT) strategy applied in the ED and demonstrated that the Waiting Time Before Seen (WTBS) reduced significantly. Moreover the reduced waiting time was achieved without additional resources and without compromising the quality performance in the ED. One thing one can learn from this study is the method of validating the model. The validation was done by comparing the results from the simulation and the empirical data. This process was implemented by evaluating each agent as well as aggregated agents.

In health related issues, ABM has been applied to capture the complexity of the spread of cholera in a refugee camp (see the study done by Crooks and Hailegiorgis (2014)). The developed model was designed to represent the interrelation between the agents and between agents and their environment. The spread of disease through water was modelled in two scenarios, namely the contaminated water and the runoff rain water. The scenarios highlighted that both contaminated and running rain water passing the contaminated water, play a significant role in spreading cholera. The model showed that in order to confine and limit the spread of cholera, the agents' movement needs to be restricted. This is one study that has demonstrated the use of an Overview, Design concept, and Details (ODD) framework in constructing an Agent-Based model, as developed in Railsback and Grimm (2012).

The above studies focused on the system modelling which included all types of patients accessing the system. This leads to a question: has mental health care benefited from the ABM tool? Analysing a mental health care system which encompasses all elements in the real system is a tremendously challenging process. What elements of the system need to be incorporated and how should the system be approached in order to generate a representative model requires a thorough study of the system. This, however, is not to say that it is impossible to utilize ABM for studying the mental health care system.

3.4.3.3 Application of Agent-Based Modelling in mental health care

The number of studies in the area of mental health care that employed ABM is very limited, indeed our literature search only found 5 studies. Here we describe those studies and how they have used AB as a modelling tool. One of such studies, done by Silverman et al. (2015), has described a system approach to healthcare which included three levels of approach: individual, organizations, and society. This study focused on finding the effective and economical interventions which, if implemented, could help improve the population health status including their mental well being as well as assuring the quality of care service relative to low costs. The study came up with four recommendations for interventions, two of which relate to the potential roles of nurses. It recommended that the system should reduce the number of patients assigned to advanced practice nurses and allow the nurses to make decisions on admitting patients without case manager approval. The other two recommendations are to increase the volume of contact of patients in out-patients mode per month and to increase the required hospitalization days.

The first two recommendations focused on the empowerment of nurses to take a more advanced role in determining the course of treatment for patients. This, it is argued, can speed up the decision making process. The two last recommendations refer to the use of hospital resources, in this case the beds. The more frequently that patients have contact with the service, while maintaining the patients in their families or other facilities outside the hospital, consequently will reduce the use of the hospital beds. However, patients who are deemed to need hospitalization will be treated until they are assured fit for discharge.

Within the same year, Cerdá et al. (2015) published a study which modelled urban adult population involved in violence and experienced post traumatic stress disorders related to the crime. The aim of the study was stated as to examine the resource allocation for violence prevention and medication treatment interventions for those experiencing post-traumatic stress disorder (PTSD). The authors stated that the Agent-Based Modelling technique was employed as the study focused on individual experience, and so was well suited for tackling their complex problem related to violence and PTSD.

The intricacy of the characteristics of individuals in Cerdá et al. (2015) was modelled based on socio-demographics, the neighbourhood where the individual resided, and the experience of traumatic events. These elements were linked to one another to describe their interrelation which also linked to the experience of PTSD. The treatment received by the affected individuals was Cognitive Behavioural Therapy (CBT). The authors suggested that the PTSD prevention strategy combined with treatment intervention, i.e allocating the police force to the high crime area and focusing on the social determinants of violence together with the provision of CBT, would reduce the prevalence of PTSD symptom. Furthermore they concluded collaboration between the public health and criminal justice systems to address violence and its related mental health problems was necessary.

The versatile method of Agent-Based Modelling technique enables the creation of multi agents in a complex mental health care system. A study by Kalton et al. (2016) demonstrated how a complex care system, interlinked with social and criminal justice, can be modelled to investigate the benefit of the introduction of care coordination for people with severe mental health conditions. The authors argued that the Agent-Based Modelling allows the modelling of the dynamic of each person affected by the illness in both ways, the internal response to the treatment received and the response due to the interaction with the environment.

The developed model in Kalton et al. (2016) therefore has two main compound state charts; one for describing the mental health condition and the other for describing the physical locations of the patients. The model captures four health conditions: healthy, mild, moderate, and severe. The physical locations comprise home, hospital, jail, and homeless. On top of these two state charts, another state chart describes the possibility that a patient ends up involved with substance abuse or not.

The aim of the study, in Kalton et al. (2016), was to investigate the effect of care coordination to the overall system performance, such as improvement in patient compliance to the care appointment and the coordination of transfer between service providers. The authors concluded that the inefficiencies in the system were due to the fragmentation of care. The main feature of the model is the patient's compliance in taking medication. Other aspects such as physical health conditions or any negative social interaction have not been included.

A particular study using the Agent Based Modelling approach, done by Mooney and El-Sayed (2016), investigated the influence of stigma and social exclusion to the development of depression in patients with obesity. This is one study which links the mental health condition with the social norm and hence the interaction between individuals in the population is the main feature. The study is purely examining social networks and there is no impact evaluation on the health service use.

The prevalence rate among the obese was investigated. The results highlighted that in low obesity cases, the rate of depression is higher compared to where the prevalence of obesity is high.The authors argued that their study suggests that intervention for preventing depression should address both the individual and social behaviour.

The area of comparing treatment models after natural disasters to reduce the burden of chronic post traumatic stress disorder has benefited from the use of ABM. Cohen et al. (2017) compared the effectiveness of two intervention models, stepped care and usual care. The stepped care treatment was given by offering Cognitive Behavioural Therapy for those individuals detected with PTSD. The usual care was offered for individuals without PTSD, which aims to improve the coping and functioning of individuals experiencing the disaster. The authors concluded that the stepped care design treatment was shown to be more effective compared to the usual treatment. This study utilised a large population based data and has included issues such as relapse and natural recovery.

3.4.4 Hybrid simulation in healthcare

In the previous subsections we have seen some applications of individual simulation methods (DES, ABS and SD) in healthcare and in particular in problems related to mental health and its care system. In the current subsection we look at the application of hybrid simulation in healthcare. By hybrid simulation we mean a mixed or combination of any two or more simulation methods of DES, ABM, and SD.

A recent literature review on the application of simulation modelling to Emergency Department, by Salmon et al. (2018), highlighted that out of the 254 studies included in the review, 209 (82.3%) used DES as their sole method. Only a small number of studies used ABM (9.9%), SD (7.1%), or a hybrid between simulation methods (either DES-SD or DES-ABM) (5.1%). The author also found that the hybrid simulation studies were used to address mainly operational and strategic issues. The report did not offer a complete list of the literature found, hence it is difficult to check and reference on the hybrid simulation studies.

In the area of clinical medicine, a study done by Caudill and Lawson (2013) used a combination of a differential equation and an agent based simulation. The study developed a simulation model to capture the spread of infections in hospital wards as a result of the interaction between patients and health workers. The antibiotic resistance was modelled as an intra-host dynamics where bacteria-level in each individual person was monitored. Another model was referred to as the inter-host dynamics where the interaction between individuals was modelled. The authors argued that their hybrid model offered a more realistic description of the complex healthcare system.

Health technology assessment is one area where hybrid simulation method can be applied. Djanatliev et al. (2012) demonstrated the use of a hybrid simulation between an ABM and SD to assess the efficacy of healthcare technology in their case Mobile Stroke Units to prevent more severe conditions such as severe brain damage. They offered a concept with the core model as an the Agent-Based model where complex patients' behaviour is incorporated. Sitting at the environment level are three different sub models consisting of a model for a disease progression, a model of capturing the population dynamics and a model dedicated for healthcare financing.

A hybrid simulation between SD and DES also has been applied to model a complex healthcare problem. The feature of SD simulation as a continuous approach has benefited studies in the area of forecasting population growth where detailed characteristics of individuals in the population can be ignored. This approach has been used in Mielczarek and Zabawa (2016) to model healthcare demands which captures the population dynamics and the different characteristics of patients according to their disease. SD was used to model the population according to their age and sex groups. DES was used to model the healthcare demand according to different age groups. This is an example of how an SD model is used as a feed for the DES model. The study looked at the healthcare demand in general, however the model can be used to forecast demand for a specific disease group.

We have presented examples of studies which have used a combination of two simulation approaches. In practice, a model could be developed using a combination of the three simulation approaches discussed above. An example of such a study was found in a conference proceeding by Viana et al. (2012), which used DES to model the health clinic for eye treatment, ABM to model individuals in the population and SD to model the progression of disease, in this case is age-related macular degeneration. The authors argued that the use of each approach for its related problem was a natural choice and best fit for the purpose.

Djanatliev and German (2013) also made use of the combination of the three simulation approaches to extend their model in Djanatliev et al. (2012) where they used ABM and SD. ABM was used to model individuals with behaviours and SD was used to model population dynamics at a high level. In their latest model, the addition of the DES model was used to model treatment processes in a hospital. Their model started with an SD model which generated affected individuals in population.

A similar approach, where SD is used to model population at a high level, is demonstrated in the study done by Gao et al. (2014). Their study employed a combination of three simulation approaches; SD, ABM, and DES to model a population affected with diabetic mellitus and diabetic end stage renal disease. Their SD model described the population with different categories according to the ages, gender, ethnicity, body weights, and diabetic diagnosis. The ABM was used to model the individuals with diabetic problem and the DES to model the healthcare process. This is a complex model where detailed characteristics of individuals affected by the disease are incorporated. The developed model was used for health economics evaluation to estimate the cost related to the prevalence of diseases under investigation.

3.5 Conclusions

Findings from the literature review highlight three main points related to the questions posed in the introduction section. These are the use of OR methods in problems related to mental healthcare, the areas of application that have been explored, and the gaps that can be identified from the existing studies.

The literature around mental health care modelling has used various OR methods. The number of studies that utilised Markov modelling technique is still far more than any other methods. With respect to specific simulation methods (i.e. SD, ABM, DES), the number is not large either.

The areas of study, explored in the existing literature, cover the strategic and operational level. Furthermore, the included literature highlighted that the service systems under study have covered GP, hospital, psychiatric emergency, outpatient clinic, residential, as well as community mental health. The community services can include intensive and intensive home treatment. The network of the services can include other services outside the health system such as the justice system.

In mental healthcare, DES has been used in costs benefit analysis to address issues related to different treatments (medications and therapies), or in system operations to address waiting time and service capacity. SD has been used to address issues related to epidemiology, disease prevention and system design and planning. ABM has been applied to address issues related to resource utilisation, disease prevention, and different treatment models.

Although hybrid simulation has been applied in health care in general, however, we have not found from this literature search any study in the area of mental health, in particular depression, that has used a hybrid method combining simulation techniques (DES, ABM, and SD). Based on the findings, we propose to develop a simulation model which makes use of System Dynamics and Agent Based to model the progression of depression and its related health service need. The next chapter will describe the development of the hybrid model.

Chapter 4

Modelling Disease Progression and Treatment Pathways

4.1 Introduction

Conceptual modelling is defined as an abstraction of the simulation model of the real system. It is regarded as an important phase in model development, and that good conceptual modelling will enhance the confidence in the resulting simulation model (Robinson (2014)).

Developing a simulation model which reflects a real problem is not a straight forward activity, especially when the issues dealt with are complex such as in healthcare. In order to understand the complex issues related to mental health, we developed a qualitative model Causal Loop Diagram. This diagram helps choosing the boundary to be addressed in the simulation model. The development of the simulation model itself was divided into three stages. The first stage was dedicated to developing an Agent-Based model. The second stage was to develop an SD model and the third stage was to combine the AB and SD models into a hybrid model.

This chapter serves to describe the conceptualisation and development of the hybrid model. To start with, we outline the framework for developing hybrid model.

This will give us the foundation on which approach to use and how we can develop a model with the purpose outlined in the introduction chapter. Thereafter the discussion will follow the points as provided by Monks et al. (2019) with the structure adapted to suit the current study.

4.2 Framework for developing a hybrid simulation

An individual simulation paradigm has a certain framework that guides a modeller to develop a model. One may refer to a comprehensive work in Sterman (2000) for developing an SD model, Pidd (2009) for DES and SD, Railsback and Grimm (2012) for ABM, or Robinson (2014) and Law (2015) for general simulation covering ABM as well as SD and DES.

In Robinson (2014), the basic concepts of the three simulation methods (DES, SD, and ABM) are discussed. DES is a discrete simulation method for modelling a system with queues. In DES, system is represented as entities flowing through activities; activities are separated by queues; heterogeneity is represented in the variation of the duration entities undergo each activity. SD is a continuous simulation method for modelling a system with network. In SD, the focus is information and feedback; a system is represented as a network of stocks and flows; stock changes continuously; stocks are accumulations representing the state of the system (Sterman (2000)). ABM is a discrete simulation to model a system from an individual perspective. In ABM, individuals or agents can be designed having characteristics and behaviour; having network; live in environment; and interact with other agents or their environment (Macal and North (2010)).

In the literature review chapter, we discussed studies that have used the three approaches one way or another. We also highlighted studies which have used a combination of DES, SD, and ABM. This leads us to a question on whether hybrid simulations have a certain framework with which a modeller can be guided in developing a model.

- Framework for developing a hybrid simulation using System Dynamics and Discrete Event.

  The development of a framework for a hybrid simulation model has been done in line with the need to conceptualize the method. One such framework in healthcare was developed by Chahal and Eldabi (2008), and this proposed three different formats depending on the nature of the problem. The first format is hierarchical, which is designed for describing a problem where the management of the system is a top to bottom type. In this case SD is used to model at the strategic level and DES is used at the process level. The process is run by the governing rules defined at the strategic level. A study by Viana (2014) employed this approach.

  The second format is called the process-environment, this is designed for systems that represent the network. In this model, each element of the systems is interconnected to form a network and described using DES. The environment in which the network lives is then described by SD.The third format is called the integrated framework. In this case SD and DES are applied where appropriate in the system. The whole system consists of elements where some are described by DES and some by SD. In the third format, there is no description of the environment. The whole system behaviour will emerge as the two approaches are run together.

  A more elaborate reference containing a framework for combining DES and SD is offered by Morgan et al. (2017). The framework was drawn from literature not only based on healthcare modelling, but also other areas of application within Operational Research or Management Science. The authors outlined five different designs of mixing SD and DES. These include parallel, sequential, enrichment, interaction, and integration. Brailsford et al. (2019) commented that the enrichment and interaction are similar to process environment and hierarchical design in Chahal and Eldabi (2008) respectively.

In parallel design, although a system is modelled using different methods at different parts, each method runs separately. For this reason, parallel design is not regarded as a framework for a hybrid simulation by Brailsford et al. (2019).

- Framework for developing a hybrid simulation using Discrete Event and Agent-Based Modelling.

  A specific framework for developing a simulation model using DES and ABM has not been found yet. However one can develop such model using framework offered in either Chahal and Eldabi (2008) and Morgan et al. (2017). This type of hybrid modelling framework will naturally have some element of behaviour, be it of human or other types of agent, which is represented by ABM. The DES model will describe the process of the system. It has been applied in healthcare to study Emergency Medical Services, e.g. study by Fakhimi et al. (2014), which incorporated three factors namely social, economic, and environment. The agents in this model are ambulances. The result from running the ABM is forwarded to the DES model.

  In any pure DES model, individuals or patients are modelled without any character such as decision making or other type behaviour. The combination of ABM and DES allows one to model any healthcare service more realistically. Patients, as entities undergoing a process in the system, are modelled with certain characteristics such as their health and social status (Viana (2014). Their characteristics and interactions with other entities and the environment may influence the service they received or the service received by others.

- Framework for developing a hybrid simulation using Agent-Based Modelling and System Dynamics.

  To find a framework for developing a hybrid model which combines ABM and SD is not easy. However one can always learn from existing studies that have employed such a combination in order to derive a concept to follow.

In fact, studies that have used a hybrid model between ABM and SD have referred to the framework offered by Chahal and Eldabi (2008). In general, the framework offered in Morgan et al. (2017) can be applied to this type of hybrid modelling. This is possible, since ABM is regarded as a variation of DES in Law (2015).

A framework to combine ABM and SD techniques has been proposed by Liu et al. (2018), which captures the intervention at the aggregated level and the dynamics of linguistic variables that characterised the individual agents. The framework offers a mathematical formulation for defining the decisions made by individual agents. The interaction between individual agents affects the clustering of agents into groups, and they then receive interventions specified for the cluster. The framework basically offers to model individuals with ABM and to model the system, be it social or healthcare, using SD.

An example of the application of a hybrid model between ABM and SD, by Djanatliev et al. (2012), was discussed in the previous chapter. Their work referred to the framework developed by Chahal and Eldabi (2008) as the Process Environment Format.

4.2.1 What can be learned from the existing framework?

A formal framework which outlines the different possibilities of forming a hybrid simulation model which combines ABM and SD has not been found, at least at the time the simulation model was developed for the purpose of this study. However, such a model can be developed from existing frameworks by combining two simulation methods, such as in Chahal and Eldabi (2008) or Morgan et al. (2017). Indeed, a recent literature review, done by Brailsford et al. (2019) which proposes a framework for developing a hybrid simulation model, has referenced the two works for defining the type of hybridisation.

The literature review section explored studies which utilised ABM and SD. We can see that it is natural to use ABM to model agents which can be characterised using health status or other social demographic status, particularly if the agents' network in life is a key factor to be investigated.

The SD method on the other hand has been applied to address problems which are more high level and where the individual's characteristics are not considered important enough to be detailed. It is deemed suitable to use SD where a network of services such as in a health service is important to be displayed.

Considering the advantages of both methods, ABM and SD, we propose to use ABM for describing the agents in a population and SD for describing the healthcare services. We explore in detail the development of the two modelling techniques in the subsequent sections.

4.3 Phase 1: Agent-Based model for disease progression

Disease progression has been modelled using SD or ABM techniques. Depending on the complexity and purpose, the model can be developed using either method. Wakeland et al. (2004) compared the feasibility of SD and ABM in simulating the dynamic of cellular receptors. They concluded that ABM is suitable for providing insights into the receptor binding that are difficult to achieve from using SD model. ABM capability in capturing the network or interaction between agents (in this case cells), is essential when studying disease progression in biomedical perspective. SD, on the other hand, captures effectively the structure of the interconnection between variables (in this case stocks). With SD the interrelation cannot be evaluated at individual cell level but only at aggregated level.

Another example study that compares SD and ABM was done by Figueredo and Aickelin (2011), its purpose being to look at the dynamic between the tumor cells and immune effector cells. They concluded that there are cases where ABM cannot be used instead of SD or vice versa, even if the underlying mathematical model is the same. If the number of the cells is large, SD is more efficient in simulating the cells due to computational issues. However, the results cannot be compared easily due to the fact that SD is a continuous simulation and ABM is a discrete simulation. Furthermore, ABM captures stochastic element and behaviour of the agents at individual level. While in SD, the change of states happens instantaneously in an aggregated and homogeneous way.

From the two examples above, it seems that the choice whether to use SD or ABM depends mainly on what level of interaction the model will address, or whether there is an element of heterogeneity in the model. If ABM is used then there are other aspects to consider such as the size of the agent population. Wakeland et al. (2004) concluded that ABM is suitable for dealing with problems related to the movement, state changes of individual agents, and interaction between agents.

Modelling the course of depression can be done using various simulation techniques. A recent systematic review done by Kolovos et al. (2017) found four different techniques used in model-based economic studies with Quality Adjusted Life Years (QALYs) or Disability Adjusted Life Years (DALYs) as their outcome measures. The authors found that the majority of studies used decision trees models (DT) or cohort-based state-transition Markov models (CMMs), and only a small number of studies used individual-based state-transition models (ISMs) or discrete-event simulation (DES) models. Similar findings were found in the previous review by Afzali et al. (2012) with an absence of DES models in their included studies.

The suitability of ISMs and DES models to model the progression of depression was argued due to the characteristics of depression. These characteristics include the fact that the population suffering from depression is heterogeneous, the continuous symptom severity of depression, the time element in the depression progression, and the depressive episode is recurrent (Kolovos et al. (2017)).

The application of ABM in modelling non-communicable diseases has been reviewed by Nianogo and Arah (2015). The authors argued that the use of ABM was around problems relating to the physical activity of the agents. ABM can also be argued as giving more freedom to designing a system where agent behaviour can influence an outcome such as treatment efficacy. Its bottom up approach gives detailed attention on each individual agent being modelled. Depending on the purpose of the model, it mainly assumes that individuals will have their own characteristics. Furthermore it allows the individuals to learn from what happens to other individuals and the environment they live in, and make a decision based on learning (Railsback and Grimm (2012)). This offers a suitable method when it comes to modelling patients where individual characteristics such as the demographic profile and the illness experienced play important roles in the main analysis of the system.

Studies captured in the reviews by Kolovos et al. (2017) and Afzali et al. (2012) used states to represent different health status. We can argue that this representation can also be modelled using the ABM technique. In fact when the characteristic, such as the disease, gets complicated, the ABM is probably more suitable than other techniques such as Markov or DES. The disease, in our case depression, can be categorised as mild, moderate or severe. Each category can even further be divided into either in treatment or not etc.

Unlike in analytic methods, where a system can be described mathematically, the ABM approach employs symbols and words to formulate a model. Railsback and Grimm (2012) provide a framework for the development and the formulation of an AB model. The framework consists of Overview, Design concepts, and Details (ODD). In the subsequent section we utilise the framework to describe our Agent-Based model.

4.3.1 Overview

The development of an Agent-Based model is based upon the epidemiology of depression which focuses on the prevalence of depression in the population. It is concerned with the rate of depression episodes or instances in a population. This could be the ratio of the number of people registered in primary care who are affected or have been affected by depression at any point in time. By population we mean the population of a certain geographical area covered by a certain local health board. This could be any geographical area but to simplify the matter we refer to one of Wales's local health boards.

- Purpose
  - The purpose of the model is to describe the progression of depression in response to seeking or receiving treatment. Individuals who are affected by depression will generate a demand on the health service. How the service is provided will have an impact on the condition of the individuals. We seek to answer questions pertaining to: the size of demand in the health service; the dynamic of the population who suffer from depression; and the relationship between health service coverage and burden of depression.
- Entities, state variables, and scales
  - Entities in the model represent people in the population who are affected by depression; aged 18 and above. For the purpose of the model, the population will not vary by age or sex. Although capturing variability is one of the advantages of ABM, for each different category, it also requires a different set of parameters. The difficulty in getting parameters, which are required for the model, makes is impossible to separate the population by gender and age. However, it is possible to extend the properties of the agents later on, if the data is available.

    Another point to mention is that each entity does not have any connection with other entities. The connection of individuals is essential when modelling a communicable disease. Since depression is a non-communicable disease, the connection or communication between agents is not seen as essential for inclusion in the model. However, this is not to say that the agents do not interact. The interaction of agents is performed with the treatment model which is developed in SD.

- State variables represent the behaviour of an agent. They describe the agent's health condition and are modelled by using a statechart. This statechart contains: a state where a population does not have depression or when depression is not detected; three states which represent three different severities of depression (mild, moderate, and severe). Furthermore, for each condition (mild, moderate or severe) there are three other related states: in treatment, untreated, and out of care. At any point in time, a person can only be in one state. The transition from a lower severity state to a more severe state represents the deterioration of depression. The model also incorporates the absorbing state where individuals can die from any one of the states. Once they have died they will be taken off the population.

- Scales in the model are of two kinds: time scale and population scale. The simulation runs for 2 years and the time unit used is one week. All corresponding rates used to govern the transition from one state to another will be adjusted as weekly rates. The population will be scaled to 5000 individuals. The use of a small number of population is deemed necessary because the Agent Based Modelling uses large computational resources which slow down the simulation run.

• Process overview and scheduling

  - At the beginning of the simulation, all entities are in the population and at some point they will be affected by depression. Depression is a long term condition which takes time for the symptoms to be detected. We use the prevalence rate to generate the number of people with depression. A certain proportion of affected individuals will fall into one of three categories: mild, moderate or severe. At this point, their number will generate a demand for the service. The model for the health services will be explained in subsequent sections.

    Individuals with depression will adapt to the decision, as a result of accessing the service, whether they will be in the treatment or not. A proportion of people with depression will access the service and will change their state to be 'in treatment' where they stay for the duration of treatment. Those who do not access the service will either remit naturally, recur to the same condition and may or may not eventually access the service, or experience deterioration in their condition. For those whose condition deteriorates, they will progress to a more severe condition. People wherever they are in their current state will not be immune from dying from all causes. Dead individuals will be removed from the population.

4.3.2 Design concepts and details

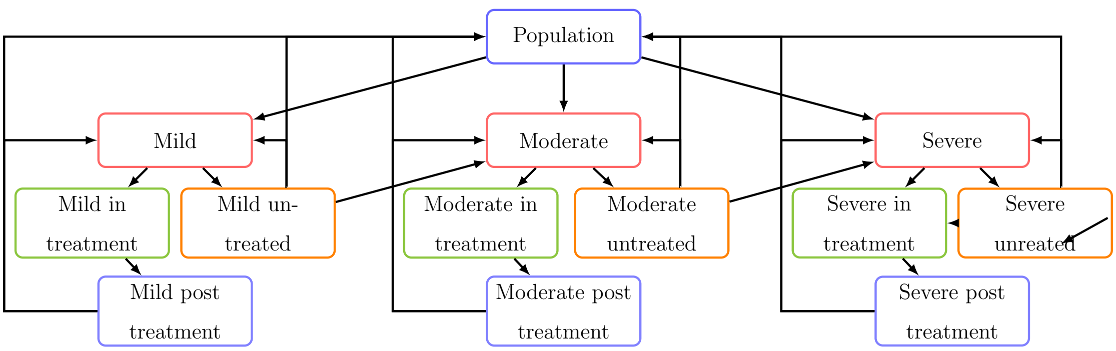
- Basic principles: The agents described in this model represent the individuals in the population. Their characteristics describe their health conditions, which, in this case, is depression. People with depression will eventually interact with the system model which influences their health status.
- Emergence: The progression of depression as a result of the decision made whether to access the healthcare or not is the emergence of the model.
- Adaptation: Individuals detected with depression will adapt to the decision made regarding service coverage. They will decide whether or not to enter the treatment. The number of individuals entering the treatment depends on the service coverage.
- Objectives: Each individual in the population with depression has an objective to eventually minimise the risk of their disease progressing to a more severe state.
- Interaction: The interaction captured in the model is hierarchical, where individuals interact with the system of care outside the AB model.
- Stochasticity: Some transitions, from one state to another, are governed by a stochastic decision. For example is the duration for being in treatment,

the value of which is generated from a probability distribution, and different for each person in treatment. The idea is to represent the real situation where the change of health state takes a different duration from one person to another. This stochastic element is also one of the reasons why we use the Agent-Based to model an individual's health conditions. It will be difficult to incorporate this variability at the individual level if we were to use System Dynamics method.

- Collectives: Individuals with the same health condition at each time unit will together generate a demand of the relevant service.
- Initialisation: The model has a population size of 5000. The parameters for the baseline scenario will be presented in the discussion about data and parameters.
- Input data: Parameters used in the AB model will be described in Chapter 5.

Figure E.1 presents the conceptual model for depression progression. It captures the three main conditions: mild, moderate and severe depression. Each condition is expanded to: being in treatment, untreated and post treatment. The arrows represent the transition between the conditions. A more elaborate description on the transition is in Chapter 5, and a more comprehensive diagram as developed in AnyLogic software is provided in Appendix E

FIGURE 4.1: Model for depression progression.



4.4 Phase 2: System Dynamics model for treatment pathways

System Dynamics has two approaches namely the qualitative approach and the quantitative approach. The qualitative method requires the modeller to engage with the stakeholders or anyone who has knowledge of the problem being addressed. This method generates a Causal Loop Diagram (CLD) which describes the interrelationship between variables. The purpose for the development of this qualitative model is for the stakeholders to come up with an agreed formulation of the complex issues pertaining to their organisation and some potential solutions (Powell and Mustafee (2017)). This is how the CLD should be built. As outlined in Chapter 1, we spent a year in South Australia where we developed the CLD as a means to engage with the stakeholders and as an exploration tool for the problem in-hand. However, the method of developing the CLD as described in the theory was not implemented in practice due to several challenges.

First, how a group of stakeholders is identified will depend on who, in the system, is interested to join in and share their expertise. The process of identifying stakeholders is not easy, especially if we embark on the project with almost no knowledge of the system and we are not part of the system itself. We will rely on a key influential individual to identify the experts in the system. This does not guarantee that the experts will share all the information about their system. The issue faced on studying any human system is how to gain trust so that the key experts will share their knowledge. We spent a significantly long time before finally being able to find the experts who were interested in our project.

Second, another issue around the group modelling exercise is that it is not always possible for all the stakeholders to sit at one table due to time constraint or other personal reasons. We overcame this barrier by visiting the stakeholders one by one at different times and places. It can be argued that this method generates a more in-depth discussion with each stakeholder. Moreover, stakeholders may posses more up to date information about their system than any published literature. However, the trade off is that the modelling exercise takes a long time to accomplish.

Due to the challenges above, we were left with no choice but to start developing the CLD model with summarizing the literature. The key variables are identified from text books on mental health. We then searched the literature to support the connection between variables. The purpose of this exercise is two fold; first as a facilitator for learning and second to generate the initial diagram to be used in discussion with the experts. The first draft of the diagram was presented to the stakeholders to be evaluated. This diagram represents the general issues around the mental health status of individuals in relation to help seeking behaviour and hence the patients flow in the system. Some key factors influencing the mental health condition are also identified. These factors are classified as social economics, physical health, and health behaviour.

The conversations with the stakeholders and the identification of variables from the literature lead to development of a second part causal loop diagram. This second diagram represents the key issues around system performance. What factors are considered as influencing the performance without reducing the quality of service. The developed diagram may not be representative of the whole system, as one expert stated that his view was only based on what happens in the system he works in and he has limited knowledge on other parts of the system. As a result, the developed CLD is very context specific.

The second method in System Dynamics is the quantitative approach. This approach is characterised with a stock and flow diagram which accommodates feedback and delays. The development of this diagram depends on the variables, identified from the causal loop diagram, which will be used to represent the system.

However, the final diagram received very little feedback from the experts in South Australia. It is not clear as to why. Perhaps the experts were still not familiar with the method, i.e. CLD, and were unable to give rigorous comments. Experts on System Dynamics, CLD method in particular, may find that some links and polarities are contrary to the common knowledge. It follows that we did not develop the quantitative care pathways model based on the CLD. Nonetheless, the CLD provides a summary of the literature around mental health mixed with experts opinions on related health care services based on the context of South Australia.

The purpose of developing the stock and flow diagram is to model the treatment pathways for people affected by depression. Since we were unable to draw the treatment pathways from the CLD model, and as, the available data from the local Health Board did not yield treatment pathways as intended, we consulted published recommendations for treatment pathways for depression. Drawing on the recommendations for treatment, the model was developed for each level of severity of depression. These separate pathways not only made it clear for each treatment pathway for each category of depression, but also provided a convenient way to estimate service use based on the separate levels of depression. The developed model is intended to give an estimation of the service use based on the severity which can then be used to evaluate the related health costs.

The subsequent sections describe more on the Causal Loop Diagram and the Stock and Flow.

4.4.1 Causal Loop Diagram for mental health and help seeking behaviour

The CLD in figure 4.2 highlights the complexity of the issues around mental health care. A certain number of key elements and their relations are used to inform the direction of the formulation of the quantitative model.

The mental health state of an individual is influenced by many factors. We can categorise the factors into two, those that are related to the other states of the individual and those that are related to the system the individual lives in. The factors related to the individual can be further divided into the individual's physical health and their social economic condition. Those related to the system can include health care system, justice, and other social care.

We have discussed some aspects that influence the mental health status from the point of other physical conditions in the background chapter. Here, we explore in more detail according to what is stated in the Causal Loop Diagram.

One possible feedback loop that is highlighted from the diagram includes the comorbidity of other physical illnesses and depression. Mental health affects and is affected by the comorbidity with other physical illnesses, and this comorbidity influences the depression condition.

Depression due to comorbidity with other physical illnesses has been found to increase the risk of developing a heart attack and possibly leading to death. This depression could also influence the adherence to comply with the treatment offered which in turn could influence diet. Apart from depression, alcohol and substance use disorders and cognitive impairment can also influence the adherence to treatment.

Comorbidity of depression with other physical illnesses also influences the onset for either communicable or non-communicable diseases; the outcome of treatment for physical conditions; and help seeking behaviour. The comorbidity with physical illnesses influences the need for GP's awareness of any mental health condition which may not be apparent.

Stigma is a big issue in mental health discourse. It is influenced by several factors such as public awareness and knowledge of mental health conditions, hospital care, dependency, resilience as well as the mental health condition itself. Stigma also influences discrimination which in turn influences disadvantages in life and structural discrimination.

Structural discrimination is a form of discrimination displayed in an institution such as a hospital. This is influenced by the availability of resources such as the availability of housing support as part of the social support system, availability

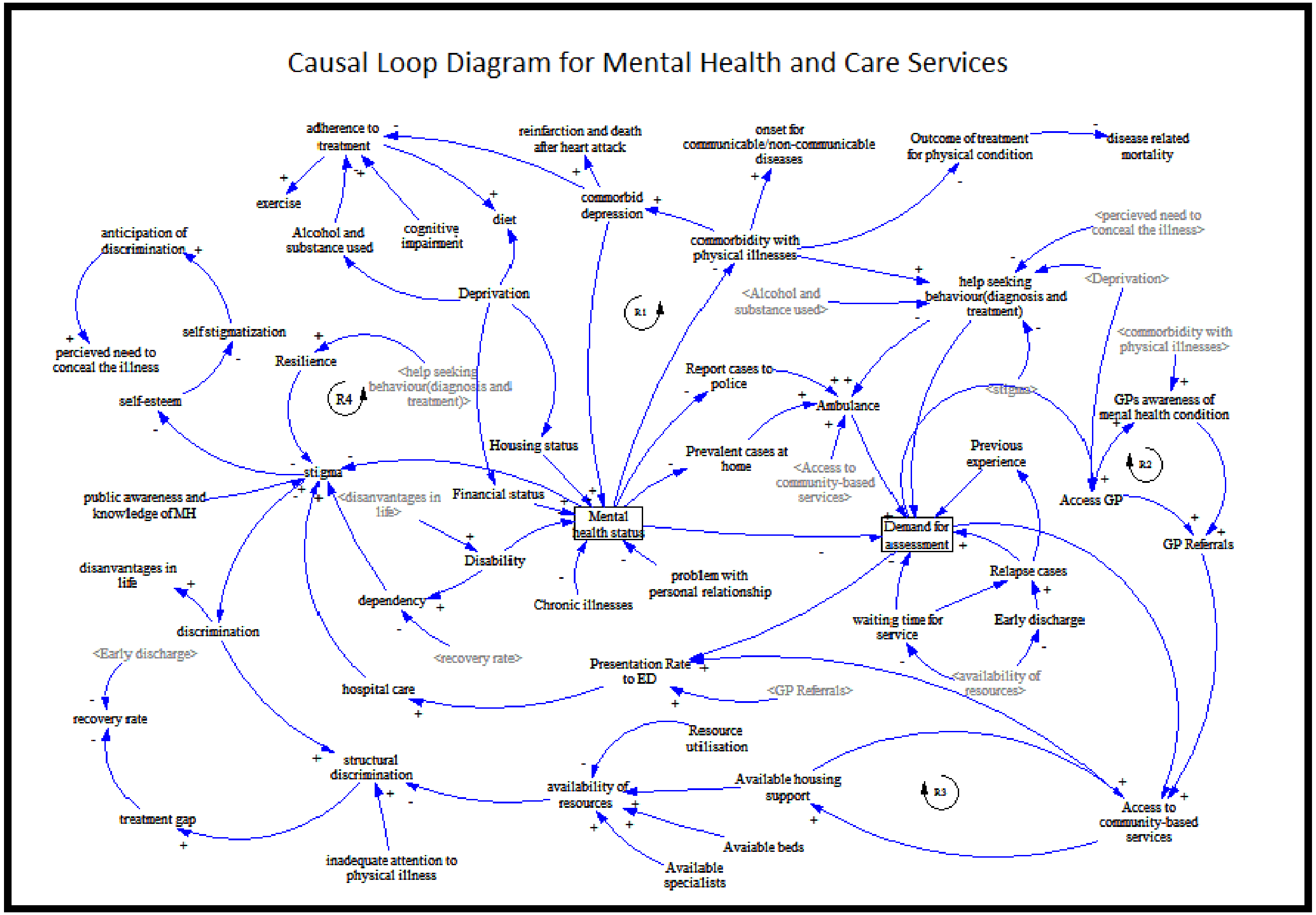


FIGURE 4.2: Influence diagram capturing mental health, help seeking and access to health care services (built in Vensim PLE).

of beds in the inpatient units, or even availability of human resources such as specialists. In some cases inadequate attention to physical illnesses may influence discrimination. If structural discrimination occurs, it may indicate a problem with a treatment gap which may in turn affect the recovery rate of the individual.

Stigma affects not only discrimination but also the self-esteem of an individual. Self-esteem affects self stigmatisation which may internalise anticipation of discrimination and lead to a perceived need to conceal the illness.

The CLD also captures the services which are affected by mental health conditions. Services system such as the Ambulance services play an important role in providing emergency response to people affected by mental health conditions. This may happen at home, at the police station or in other community based services. In cases where incidents occur for the first time, this response might trigger the need for assessment.

The demand for assessment mainly affects the community services, such as the GP, whose role is seen as the main gate keeper to more specialist health services. Although in some cases the Emergency Department or the Accident and Emergency department in the hospital can be accessed for the initial assessment. This demand for services is not only affected by the first time incidents, but also by any relapse cases and the waiting time for the service. Relapse cases may be influenced by early discharge due to the lack of availability of resources.

For those individuals accessing the GP, their conditions may suggest the need for further referrals to other mental health services such as community-based services. Community-based services provide more specialist services and can be both inpatient or outpatient services.

Community based services do not act independently in providing service for people with mental health conditions. People experiencing disadvantages in social economic areas may need to have other support services available to them such as housing services or disability services. The need for other support requires the community based services to collaborate with other service systems.

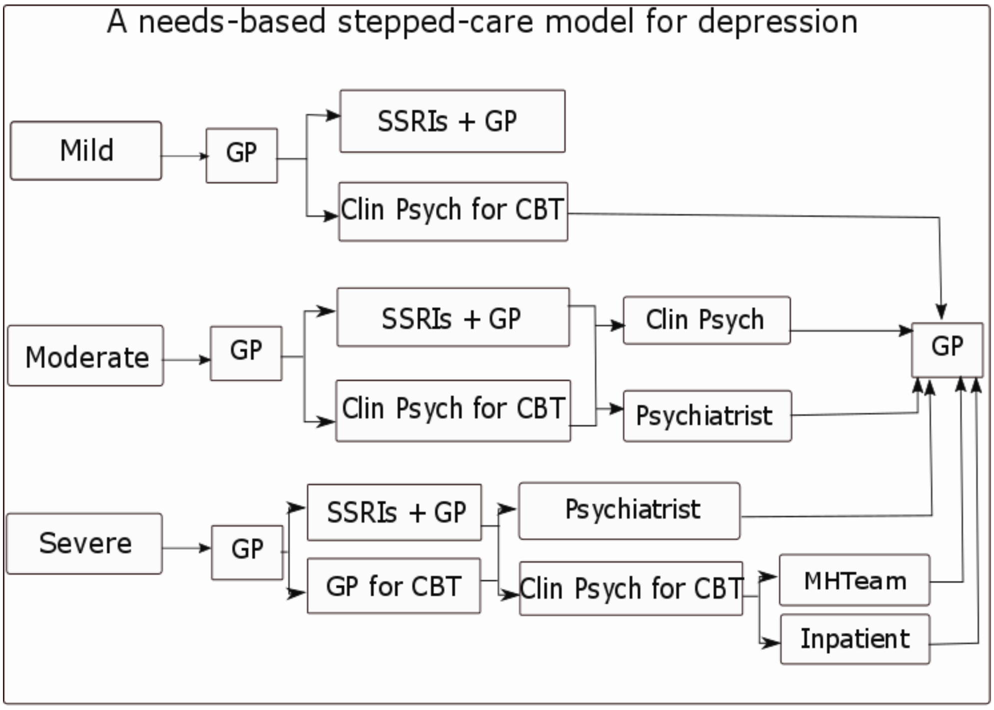
4.4.2 Stock and flow diagram

The stock and flow diagram was developed based on the treatment pathways recommended in Andrews, G. and the TOLKIEN II Team (2006). Although the NICE recommendation, outlined in Chapter 2, provides up to date and extensive description, to our knowledge, the TOLKIEN II provides clear outlined pathways for all mental health conditions, which describe the patient flow during the treatment. Whether both recommendations, by the National Collaborating Centre for Mental Health (2010) and Andrews, G. and the TOLKIEN II Team (2006), are widely implemented in practice today, is not the scope of this study.

4.4.2.1 Tolkien II model for depression.

The discussion in this section is entirely based on TOLKIEN II produced by Andrews, G. and the TOLKIEN II Team (2006). It is a report generated by Australian mental health experts on recommendations for clinical pathways and costing for treating mental health conditions. The authors state that their work was based on collected data of people suffering mental health conditions, evidence on best treatment for each mental health condition, and extensive expert opinions on the best treatment structure. The treatment structure covers the required staff and the facilities needed. The resulting model also incorporates the direct costing based on the recommended treatment. Figure 4.3 describes the treatment pathways for managing depression for adults as one of the recommendations produced in the report.

Figure 4.3: Recommended treatment pathways for depression simplified from Andrews, G. and the TOLKIEN II Team (2006).



TOLKIEN II covers 15 different mental health conditions and their recommendations are based on a stepped care model. The stepped care model is a treatment model which assumes that any treatment of a mental health condition should start with the low intensity and cost treatment regardless of the severity, unless there is a risk of fatal consequence involved. Hence, in general, the management of treatment starts with a GP. At this point, other than initial diagnosis, the treatment only involves GP advice with other additional resources such as books or web sites containing information on self management for coping with the conditions. For patients whose conditions are not improving, then treatment will involve more intensive care such as drugs or therapies which are administered in either primary care services or inpatient care.

The report conveniently separates the treatment pathways for depression based on the severity. The recommendations recognise the individual patient characteristics and differences in responding to the received treatment. The treatment for people suffering from depression is divided into four possible pathways. Three of the treatment pathways refer to the treatment for each level of major depression (mild, moderate, and severe). A separate treatment pathway is dedicated for those with persistent depression. The last treatment pathway will not be used in this project.

4.4.3 Model assumptions

The treatment pathways for depression developed in Andrews, G. and the TOLKIEN II Team (2006) are based on an Australian system and the reader might argue that it is not necessarily suitable for a different context such as the UK. However, the basic ideas on using the stepped care model are also applied in the UK health-care system. This can be seen from the NICE guideline discussed in Chapter 2. Both recommendations, i.e the NICE guideline and TOLKIEN II, produce similar pathways. In order to give a clear pathway model, we used the recommendation pathways built by TOLKIEN II. However, we also acknowledge and refer to the recommendations given by the NICE guideline whenever information is not available in the TOLKIEN II.

The recommendation model assumes that the treatment for mild depression is largely managed by a GP. This is particularly so at the initial stage (step 1) where all patients should consult their GP where they will receive 4 times consultations along with other resources to help them manage their own conditions. The majority of those with mild depression might remit within 6 weeks. For those whose condition persists after 6 weeks, they will be offered a choice of either taking medication (which again will be under the supervision of a GP) or having therapy (in this context Cognitive Behaviour Therapy) managed by a clinical psychologist.

Medication should start with a generic one (NICE recommendation) with a duration of 46 weeks (TOLKIEN II). The number of GP visits for administering medication is 6 times and the number of clinical psychologist visits is 6 visits. All patients receiving clinical psychologist treatment should visit their GP at the end of the treatment. This ensures that the GP gets updated with the patient's progress.

Up to this point, the care pathways are similar for mild and moderate depression. Some additional treatment for people with moderate depression after this point is made to either continue the treatment with a clinical psychologist for more intensive therapy or to visit a psychologist for more intensive treatment with medication. At the end of the treatment people will visit their GP for a final evaluation.

Mild and moderate depression, according to this treatment recommendation, will not need any inpatient care or management from a Mental Health team. Their care is managed entirely by the outpatient services.

It is a different case for individuals with severe depression. Their treatment pathways are more complex, involving inpatient care as well as a Mental Health team. People with severe depression share similar care pathways to those with moderate depression for the majority of their treatment. However, in the case where inpatient care is needed due to high risk of suicide or difficulty in managing the patient in more open facilities, inpatient care and Mental Health team services are then needed.

The treatment pathway for severe depression also admits the possibility that some people might need to be admitted to the inpatient facility at the initial stage. This creates additional need for inpatient facilities.

Our assumption is that the developed model was intended for adult patients only, which tallies with the recommendation proposed by the NICE. Hence the element of aggregation in the model still apparent. Aggregation provides a convenient way where it is difficult to acquire detailed data.

4.4.4 Conceptual model

The purpose of developing a System Dynamics model is to represent the treatment pathways for depression. From the literature review in Chapter 3, we have found studies that have used SD for patient flow modelling in order to estimate the service utilisation or to represent the health system network. Parragh and Einzinger

(2012) compared the use of SD and ABM in healthcare utilisation and summarised that SD offered a more standardised practice in modelling a healthcare system. The network of the system can be captured from the structure which can give insights into the system qualitative properties. They also added that it is easier to parameterise the model in SD since, in many healthcare situations, it is not possible to acquire detailed data.

The treatment pathways model in this study will represent the situation when an individual agent in AB model is in the treatment state. Since there are many different health services that an individual can go to during the treatment, it will be difficult if we were to expand the 'in treatment state' from the AB model to accommodate each person's utilisation. Moreover, the network of the services will be more difficult to detect and to be modelled in the AB model. Overall, adding the treatment pathways to the AB model will be more computationally costly, because the computation of the utilisation of the services is done at each individual level. Since one of the purposes of developing the treatment model is to estimate the overall utilisation, it is sufficient to aggregate all the individuals who uses the same service.

The SD model will depend on the AB model, i.e. the number of people needing the treatment will come from the AB model. Our AB model is designed to use a small number of population for the computational reasons. As a result, the SD model will deal with a small number of the population.

System Dynamics is a continuous simulation where, in this case, individuals flowing in the system are aggregated. However, the individuals' characteristics are lost once they are in the system. This makes it difficult to track which particular individuals are receiving treatment in a particular facility.

The developed simulation model can be made to accommodate the variety in the system by breaking down the aggregated variable to several variables where each of them represents a special characteristic of an individual. This ultimately will make the model more complicated visually and computationally, not to mention that this process will require extensive data as each characteristic represented in the model will require a different set of parameters.

Taking into consideration the assumptions made in the previous subsection, where depression has three different levels, and without making the model over complicated, we developed the model for depression care pathways by separating the pathways based on the severity level. This process not only ensures clear pathways for each severity level, but also provides an easy way to monitor the need for each facility by different levels of severity.

Each treatment service was modelled as a stock. In System Dynamics, the stock represents an accumulation. Hence the purpose of representing the service as stock is to measure the dynamic of the service use over time and to get an estimation on the total service use or need at the end of the simulation model run.

The stock is influenced by the inflow and outflow connected to the stock. Depending on which service, the inflow to that service may depend on the output from another service. As an example, the inflow to a stock representing the number of people who use medication will depend on the outflow from a stock representing initial GP visits. To compute the number of people who will need further treatment such as medication, we also need a parameter representing the proportion of people who choose to have medication. An endogenous variable is then created to hold the number of people needing medication at every time step.

The variables created in the System Dynamics model are not all of endogenous type. For example, the inflow for the initial GP consultation will depend on the number of people who need the service. This number is generated by the Agent Based model, which is outside the System Dynamics model environment. Hence any variable representing this number is regarded as an exogenous variable.

The outflow from each stock also depends on the value of the stock and the time taken to stay in the stock. The time parameter represents the delay in the stock. The interpretation of this delay is that people entering the stock will spend some time in treatment. The constant time parameter indicates the average time taken for completing treatment. At each time step the proportion of people finishing treatment, or going through the outflow, will then depend on the number of the people in treatment divided by the time taken on average for treatment.

The stocks representing the service use will not all be modelled as having both inflows and outflows. Some stocks were modelled only having inflows as their determinant. The intended use of this type of stock is to record the total accumulation in service use over time. This type of stock can be used for counting purposes such as measuring the total cost benefit of the service use. This can be achieved by weighting the inflow with some constant parameter representing the cost of the service or some quality measure per individual.

The recommendation for treating depression from NICE guidelines gives details of the types of possible different treatments. For example the types of therapies include CBT, CCBT, ECT, etc. However, the SD model only incorporates the therapy as CBT. The reason to only use one type of therapy for modelling the service is due to the difficulty in obtaining information on the different types of the therapy used in detail. Another reason is that the model developed in TOLKIEN II only includes CBT for the type of therapy. The developed model serves as a foundation model for this type of service. The model can be expanded should more services need to be included.

The following pages consist of descriptions of the System Dynamics model in detail. Tables 4.1, 4.2, 4.3, 4.4, 4.5, 4.6 list all the stocks and flows, variables and parameters needed for the model. Figures 4.4, 4.5, and 4.6 display the developed SD model for mild, moderate, and severe depression respectively.

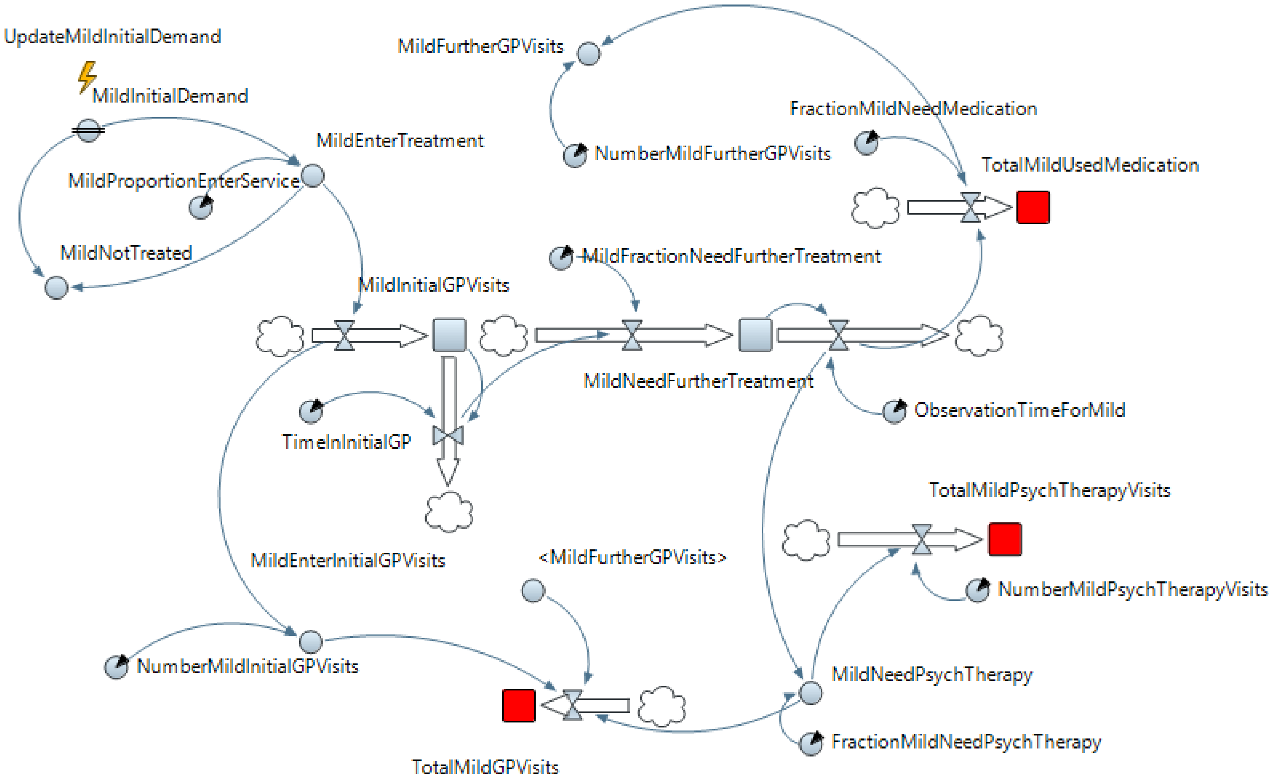


FIGURE 4.4: SD Model for Mild Depression

Table 4.1: Variable description for mild depression SD model

Type of Variables	Description	Equation
Stocks		
Initial GP visits (X_1)	Stock representing the number of individuals having consultation with GP at the initial stage.	$\frac{\partial X_1}{\partial t} = I_1 - O_1$
Need further treatment (X_2)	Transition stock for those who need further treatment after the initial GP visits.	$\frac{\partial X_2}{\partial t} = I_2 - O_2$
Total used medication (X_3)	To count the total number of patients who used medication.	$\frac{\partial X_3}{\partial t} = I_3$
Total GP visits (X_4)	To count the total number of GP visits generated by the patients.	$\frac{\partial X_4}{\partial t} = I_4$
Total Psychological Therapy visits (X_5)	To count the total number of Psychological Therapy visits generated by the patients.	$\frac{\partial X_5}{\partial t} = I_5$
Flows		
Inflow to initial GP visits (I_1)	The rate of individuals who enter the GP consultations.	$I_1 = a_1$
Outflow from Initial GP visits (O_1)	The rate of individuals who finish with their GP consultation.	$O_1 = X_1/T_1$
Inflow to further treatment (I_2)	The rate of individuals who need further treatment after their first GP consultation.	$I_2 = O_1 * p_2$

Table 4.1 continued

Type of Variables	Description	Equation
Outflow from Need further treatment (O_2)	The rate of individuals who will go to have further treatment.	$O_2 = X_2/T_2$
Inflow to total used medication (I_3)	The rate of individuals who used medication.	$I_3 = O_2 * p_4$
Inflow to Total GP visits (I_4)	The rate represents the number of GP visits needed by the individuals. The rate from a_5 represents the end of treatment GP visits.	$I_4 = a_3 + a_4 + a_5$
Inflow to Psychological Therapy visits (I_5)	The rate representing the number of therapy visits needed.	$I_5 = a_5 * p_5$
Auxiliary variables		
Initial demand (a_0)	Exogenous variable generated from the Agent Based model to update the number of individuals affected by mild depression every time step.	
Enter treatment (a_1)	Endogenous variable representing the rate of individuals entering the health service.	$a_1 = a_0 * p_0$

Table 4.1 continued

Type of Variables	Description	Equation
Not treated (a_2)	Endogenous variable representing the rate of individuals not entering the health service.	$a_2 = a_0 - a_1$
Further GP visits (a_3)	Endogenous variable to account for the rate of additional GP visits due to the use of medication.	$a_3 = I_3 * p_3$
Enter initial GP visits (a_4)	Endogenous variable to account for the total number of GP visits at the initial stage.	$a_4 = a_1 * p_1$
Need Psychological Therapy (a_5)	Endogenous variable to account for the rate of individuals with depression who need psychological therapy.	$a_5 = O_2 * p_6$

Table 4.2: Parameter description for mild depression SD model

Parameter[1]	Description
Time in initial GP (T_1)	Time spent for the initial consultation.
Observation time (T_2)	Time representing observation duration if the affected individuals responded to the initial GP consultation.
Proportion enter service (p_0)	A constant representing the proportion of individuals who enter the service.
Number initial GP visits (p_1)	a constant representing the number of GP visits needed at the initial stage.
Fraction need further treatment (p_2)	A constant representing the proportion of individuals who need further treatment after the initial GP consultation.
Number further GP visits (p_3)	A constant representing the number of GP visits needed as a result of further treatment.
Fraction need medication (p_4)	A constant representing the fraction of individuals who need medication.
Number Psychological Therapy visits (p_5)	A constant representing the number of visits needed to have Psychological Therapy.
Fraction need Psychological Therapy (p_6)	A constant representing the proportion of individuals who need Psychological Therapy.

[1] The parameters needed for the SD model will be described in the Chapter 5.

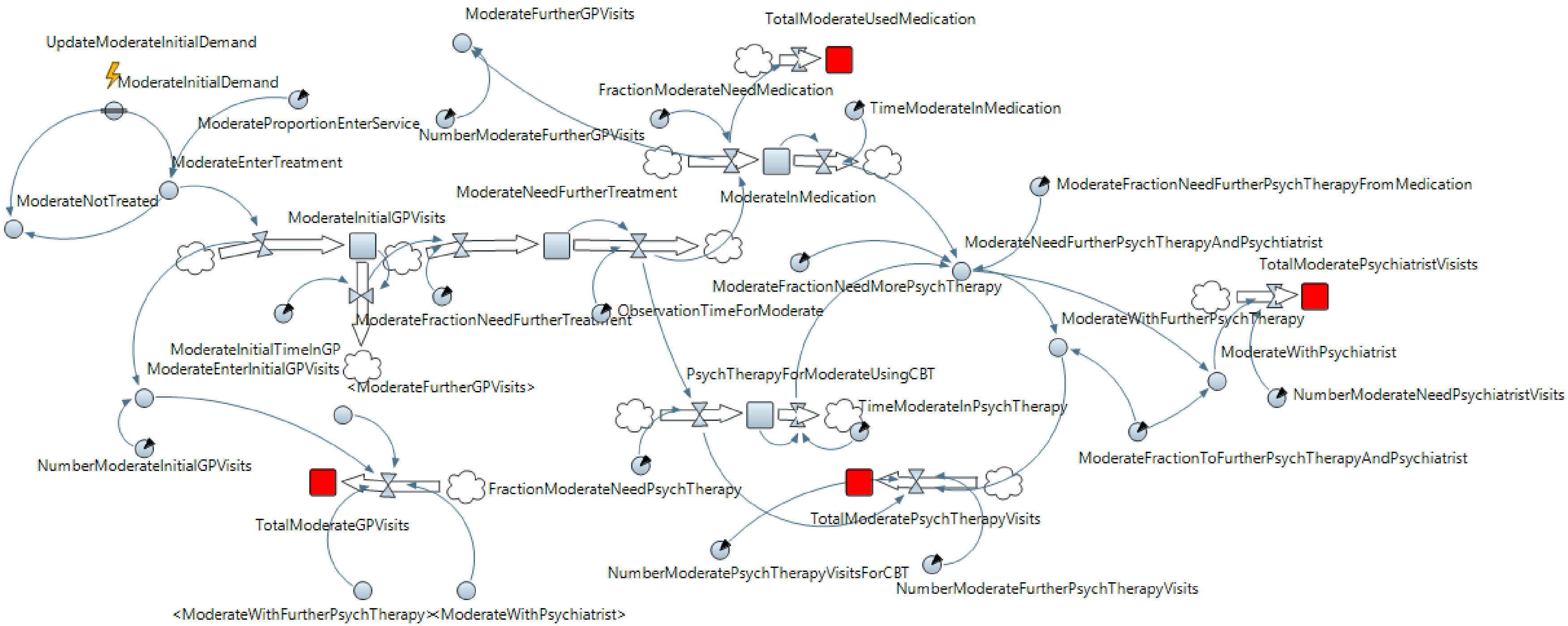


FIGURE 4.5: SD Model for Moderate Depression

Table 4.3: Variable description for moderate depression SD model

Type of Variables	Description	Equation
Stocks		
Initial GP visits (X_1)	Stock representing the number of individuals having consultation with GP at the initial stage.	$\frac{\partial X_1}{\partial t} = I_1 - O_1$
Need further treatment (X_2)	Transition stock for those who need further treatment after the initial GP visits.	$\frac{\partial X_2}{\partial t} = I_2 - O_2$
In medication (X_3)	Stock representing the number of patients who used medication.	$\frac{\partial X_3}{\partial t} = I_3 - O_3$
Psychological Therapy after CBT (X_4)	Stock representing the number of patients who have psychological therapy after having CBT.	$\frac{\partial X_4}{\partial t} = I_4 - O_4$
Total used medication (X_5)	To count the total number of patients who used medication.	$\frac{\partial X_5}{\partial t} = I_5$
Total Psychological Therapy visits (X_6)	To count the total number of Psychological Therapy visits generated by the patients.	$\frac{\partial X_6}{\partial t} = I_6$
Total Psychiatrist visits (X_7)	To count the total number of Psychiatrist visits generated by the patients.	$\frac{\partial X_7}{\partial t} = I_7$

Table 4.3 continued

Type of Variables	Description	Equation
Total GP visits (X_8)	To count the total number of GP visits generated by the patients.	$\frac{\partial X_8}{\partial t} = I_8$
Flows		
Inflow to initial GP visits (I_1)	The rate of individuals who enter the GP consultations.	$I_1 = a_1$
Outflow from Initial GP visits (O_1)	The rate of individuals who finish with their GP consultation.	$O_1 = X_1/T_1$
Inflow to further treatment (I_2)	The rate of individuals need further treatment after their first GP consultation.	$I_2 = O_1 * p_2$
Outflow from Need further treatment (O_2)	The rate of individuals who will go to have further treatment.	$O_2 = X_2/T_2$
Inflow in medication (I_3)	The rate of individuals who use medication.	$I_3 = O_2 * p_3$
Outflow from using medication (O_3)	The rate of individuals who finish using medication.	$O_3 = X_3/T_3$
Inflow to Psychological Therapy (I_4)	The rate of individuals who need Psychological Therapy with using CBT.	$I_4 = O_2 * p_6$
Outflow from Psychological Therapy with CBT (O_4)	The rate of individuals who finish Psychological Therapy with CBT.	$O_4 = X_4/T_4$

Table 4.3 continued

Type of Variables	Description	Equation
Inflow to total use medication (I_5)	The rate to count total individuals who used medication	$I_5 = I_3$
Inflow to total psychological Therapy visits (I_6)	The rate to count the total number of psychological Therapy visits	$I_6 = (I_4 * p_7) + (a_6 * p_8)$
Inflow to total Psychologist visits (I_7)	The rate to count the total number of Psychologist visits	$I_7 = a_7 * p_9$
Inflow to total GP visits (I_8)	The rate to count the total number of GP visits	$I_8 = a_3 + a_4 + a_6 + a_7$
Auxiliary variables		
Initial demand (a_0)	Exogenous variable generated from the Agent Based model to update the number of individuals affected by moderate depression every time step.	
Enter treatment (a_1)	Endogenous variable representing the rate of individuals entering the health service.	$a_1 = a_0 * p_0$
Not treated (a_2)	Endogenous variable representing the rate of individuals not entering the health service.	$a_2 = a_0 - a_1$
Enter initial GP visits (a_3)	Endogenous variable to account for the total number of GP visits at the initial stage.	$a_3 = I_1 * p_1$

Table 4.3 continued

Type of Variables	Description	Equation
Further GP visits (a_4)	Endogenous variable to account for additional number of GP visits due to further treatment	$a_4 = I_3 * p_4$
Need further Psychological Therapy and Psychiatrist (a_5)	Endogenous variable to count the number of individuals who need further treatment from Psychological Therapy and Psychiatrist	$a_5 = (O_3 * p_{11}) + (O_4 * p_5)$
Further Psychological Therapy (a_6)	Endogenous variable to count the number of individuals who need additional Psychological Therapy	$a_6 = a_5 * p_{10}$
With Psychiatrist (a_7)	Endogenous variable to count the number of individuals who need Psychiatrist	$a_7 = a_5 * p_{10}$

Table 4.4: Parameter description for moderate depression SD model

Parameter[1]	Description
Time in initial GP (T_1)	Time spent for the initial consultation.
Observation time (T_2)	Time representing observation duration if the affected individuals responded to the initial GP consultation.
Time in medication (T_3)	Time spent in medication treatment.
Time in Psychological Therapy (T_4)	Time spent for having Psychological Therapy.
Proportion enter service (p_0)	A constant representing the proportion of individuals who enter the service.
Number initial GP visits (p_1)	A constant representing the number of GP visits needed at the initial stage.
Fraction need further treatment (p_2)	A constant representing the proportion of individuals who need further treatment after initial GP consultation.
Fraction need medication (p_3)	A constant representing the fraction of individuals who need medication.
Number further GP visits (p_4)	A constant representing the number of GP visits needed as a result from further treatment.
Fraction need more Psychological Therapy (p_5)	A constant representing the proportion of individuals who need additional Psychological Therapy

Table 4.4 continued

Parameter[1]	Description
Fraction need Psychological Therapy (p_6)	A constant representing the proportion of individuals who need Psychological Therapy.
Number Psychological Therapy visits for CBT (p_7)	A constant representing the number of visits needed for having Psychological Therapy.
Number further Psychological Therapy visits (p_8)	A constant representing the number of visits needed for having additional Psychological Therapy.
Number need Psychiatrist visits (p_9)	A constant representing the number of Psychiatrist visits needed.
Fraction to further Psychiatrist and Psychological Therapy visits (p_{10})	A constant representing the proportion of individuals who need additional visits to Psychiatrist and Psychological Therapy.
Fraction need further Psychological Therapy from medication (p_{11})	A constant representing the proportion of individuals who need additional Psychological Therapy from having medication.

[1] The parameters needed for the SD model will be described in the Chapter 5.

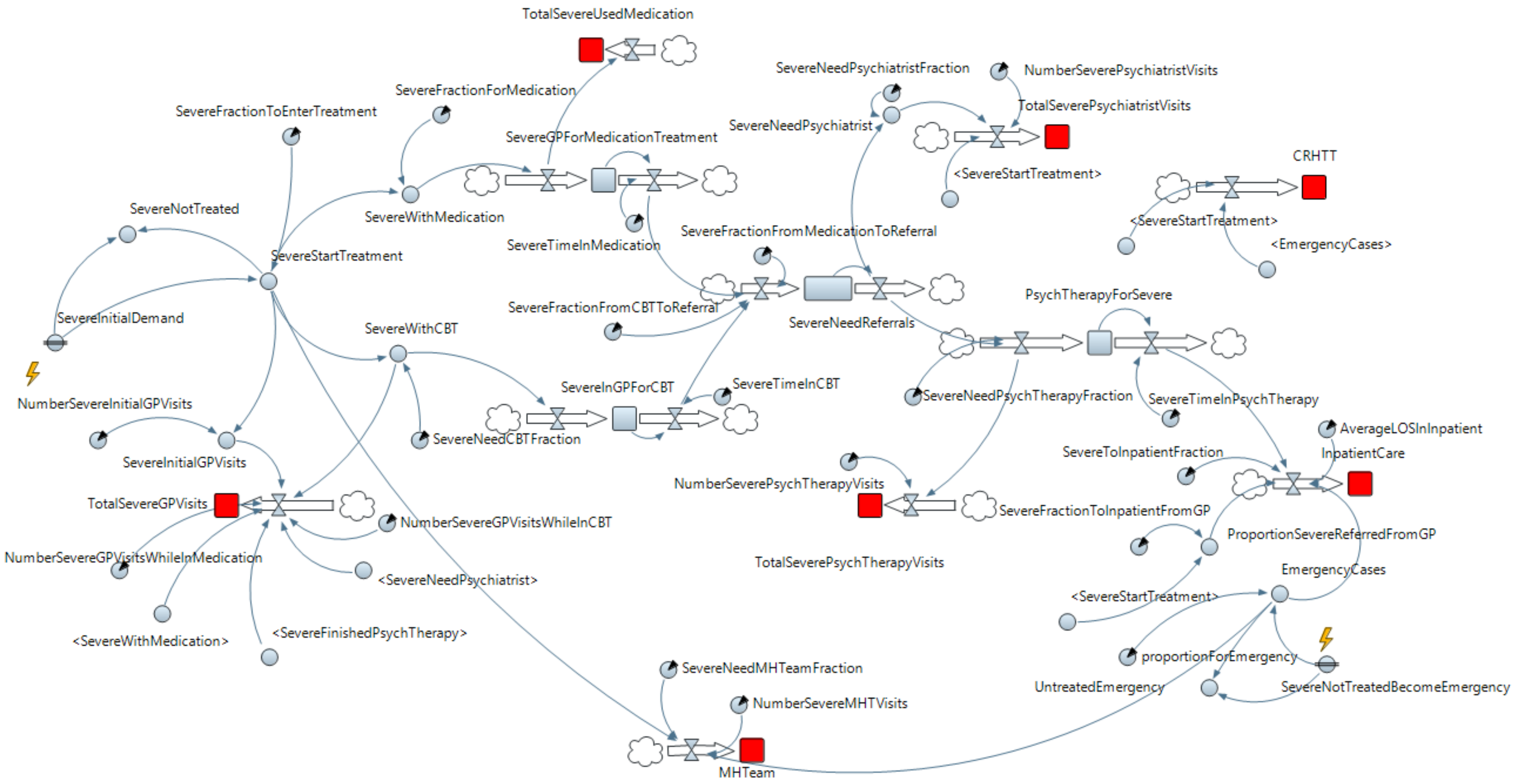


FIGURE 4.6: SD Model for Severe Depression

Table 4.5: Variable description for severe depression SD model

Type of Variables	Description	Equation
Stocks		
GP for CBT (X_1)	Stock representing the number of individuals having consultation with GP for having CBT.	$\frac{\partial X_1}{\partial t} = I_1 - O_1$
GP for medication treatment (X_2)	Stock representing the number of individuals having consultation with GP for having medication.	$\frac{\partial X_2}{\partial t} = I_2 - O_2$
Need referrals (X_3)	Transition stock representing the number of patients who need referrals for further treatment.	$\frac{\partial X_3}{\partial t} = I_3 - O_3$
Psychological Therapy (X_4)	Stock representing the number of patients having Psychological Therapy.	$\frac{\partial X_4}{\partial t} = I_4 - O_4$
Total GP visits (X_5)	To count the total number of GP visits.	$\frac{\partial X_5}{\partial t} = I_5$
Total used medication (X_6)	To count the total number of individuals having medication.	$\frac{\partial X_6}{\partial t} = I_6$
Total Psychological Therapy visits (X_7)	To count the total number of Psychological Therapy visits generated by the patients.	$\frac{\partial X_7}{\partial t} = I_7$
Total Psychiatrist visits (X_8)	To count the total number of Psychiatrist visits generated by the patients.	$\frac{\partial X_8}{\partial t} = I_8$

Table 4.5 continued

Type of Variables	Description	Equation
Inpatient care (X_9)	To count the total number of inpatient care in weeks.	$\frac{\partial X_8}{\partial t} = I_9$
CRHTT (X_{10})	To count the total number of patients served by the Crisis Resolution Home Treatment Team.	$\frac{\partial X_{10}}{\partial t} = I_{10}$
MHTeam (X_{11})	To count the total number of MHTeam visits.	$\frac{\partial X_{11}}{\partial t} = I_{11}$
Flows		
Inflow to GP for CBT (I_1)	The rate of individuals who enter the GP consultations for having CBT.	$I_1 = a_3$
Outflow from GP for CBT (O_1)	The rate of individuals who finish with GP consultation for having CBT.	$O_1 = X_1/T_1$
Inflow to GP for medication treatment (I_2)	The rate to count individuals who need GP visits for having medication.	$I_2 = a_4$
Outflow from GP for medication treatment (O_2)	The rate of individuals finishing GP visits due to having medication.	$O_2 = X_2/T_2$
Inflow to referrals (I_3)	The rate of individuals who need referrals for more treatment.	$I_3 = (O_1 * p_6) + (O_2 * p_7)$
Outflow from referrals(O_3)	The rate of individuals referred to further treatment.	$O_3 = X_3$

Table 4.5 continued

Type of Variables	Description	Equation
Inflow to Psychological Therapy (I_4)	The rate of individuals who need Psychological Therapy.	$I_4 = O_3 * p_8$
Outflow from Psychological Therapy (O_4)	The rate of individuals who finished Psychological Therapy.	$O_4 = X_4/T_3$
Inflow to total GP visits (I_5)	The rate to count total number of GP visits	$I_5 = a_5 + (a_3 * p_5) + (a_3 * p_5) + a_{10} + a_4 + O_4$
Inflow to total used medication (I_6)	The rate to count total number of individuals who used medication	$I_6 = I_2$
Inflow to total Psychological Therapy visits (I_7)	The rate to count the total number of Psychological Therapy visits	$I_7 = I_4 * p_9$
Inflow to total Psychiatrist visits (I_8)	The rate to count the total number of Psychiatrist visits	$I_8 = a_{10} * p_{11}$
Inflow to total inpatient care (I_9)	The rate to count the total number of inpatient use in weeks	$I_9 = ((O_4 * p_{12}) + a_9 + a_7) * T_4$
Inflow to CRHTT (I_{10})	The rate to count the total number of individuals who have in contact with CRHTT	$I_{10} = a_1 + a_7$
Inflow to total MHteam visits (I_{11})	The rate to count the total number of MH team visits	$I_{11} = a_1 * p_{10} * p_{16} * p_{15}$

Table 4.5 continued

Type of Variables	Description	Equation
Auxiliary variables		
Initial demand (a_0)	Exogenous variable generated from the Agent Based model to update the number of individuals affected by severe depression every time step.	
Enter treatment (a_1)	Endogenous variable representing the rate of individuals entering the health service.	$a_1 = a_0 * p_0$
Not treated (a_2)	Endogenous variable representing the rate of individuals not entering the health service.	$a_2 = a_0 - a_1$
With CBT (a_3)	Endogenous variable to account for the number of individuals having CBT.	$a_3 = a_1 * p_1$
With medication (a_4)	Endogenous variable to account for the number of individuals having medication.	$a_4 = a_1 * p_2$
Number initial GP visits (a_5)	Endogenous variable to count the number of individuals having initial consultation with GP.	$a_5 = a_1 * p_3$

Table 4.5 continued

Type of Variables	Description	Equation
Not treated become emergency (a_6)	Exogenous variable generated from the Agent Based model to count for the number of individuals who need emergency treatment.	
Emergency cases (a_7)	Endogenous variable to count the number of individuals who need emergency service	$a_7 = a_6 * p_{14}$
Untreated emergency (a_8)	Endogenous variable to count the number of individuals who cannot be treated in emergency service .	$a_8 = a_6 - a_7$
proportion referred from GP (a_9)	Endogenous variable to count the number of individuals who need emergency service referred from GP.	$a_9 = a_1 * p_{13}$
Need psychiatrist (a_{10})	Endogenous variable to count the number of individuals who need Psychiatrist	$a_{10} = O_3 * p_{10}$

Table 4.6: Parameter description for severe depression SD model

Parameter[1]	Description
Time in CBT (T_1)	Time spent for having CBT.
Time in medication (T_2)	Time spent when using medication.
Time in Psychological Therapy (T_3)	Time spent having Psychological Therapy.
Time in inpatient stay (T_4)	Average time spent in the inpatient service.
Fraction to enter treatment (p_0)	A constant representing the proportion of individuals who enter the service.
Need CBT fraction (p_1)	A constant representing the proportion of individuals who need CBT treatment.
Fraction for medication (p_2)	A constant representing the proportion of individuals who use medication.
Number initial GP visits (p_3)	A constant representing the number of GP visits at initial stage.
Number GP visits while in medication (p_4)	A constant representing the number of GP visits needed as a result of using medication.
Number GP visits while in CBT (p_5)	A constant representing the number of GP visits needed while having CBT.
Fraction from CBT to referral (p_6)	A constant representing the proportion of individuals who need referral after having CBT.
Fraction from medication to referral (p_7)	A constant representing the proportion of individuals who need referral after having medication.

Table 4.6 continued	
Parameter[1]	Description
Need Psychological Therapy fraction (p_8)	A constant representing the proportion of individuals who need Psychological Therapy.
Number Psychological Therapy visits (p_9)	A constant representing the number of Psychological Therapy visits needed.
Need Psychiatrist fraction (p_{10})	A constant representing the proportion of individuals who need Psychiatrist.
Number Psychiatrist visits (p_{11})	A constant representing the number of visits needed for Psychiatrist.
To inpatient fraction (p_{12})	A constant representing the proportion of individuals who need inpatient care.
Fraction to inpatient from GP (p_{13})	A constant representing the proportion of individuals who need inpatient care directly from GP.
Proportion for emergency (p_{14})	A constant representing the proportion of individuals having emergency service.
Need MH Team fraction (p_{15})	A constant representing the proportion of individuals who need Mental Health Team service.
Number MH visits (p_{16})	A constant representing the number of visits when receiving service from the MH Team.

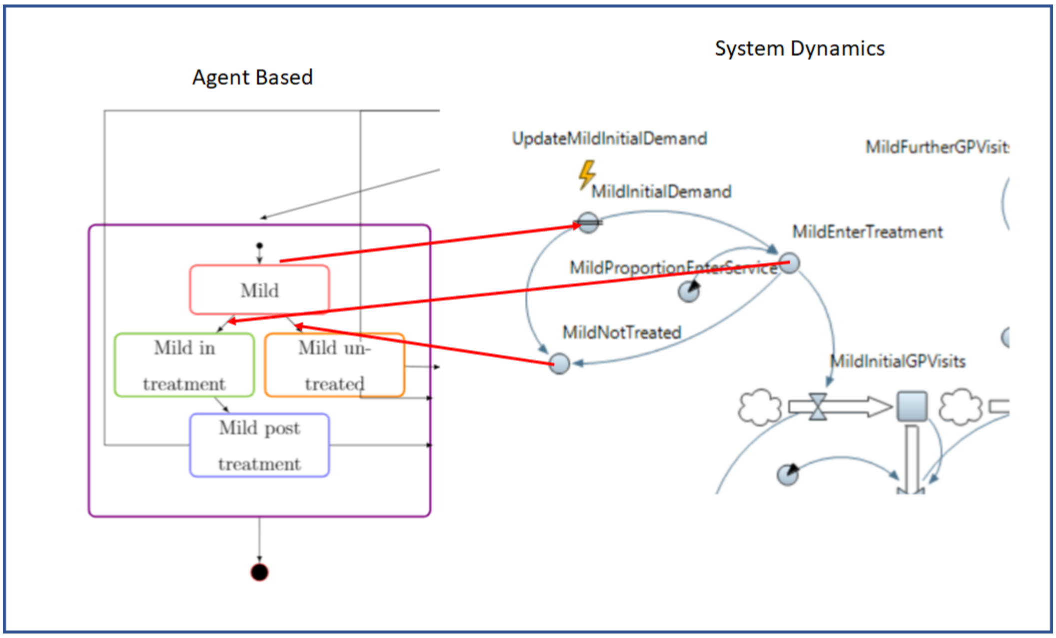
[1] The parameters needed for the SD model will be described in the Chapter 5.

4.5 Phase 3: Connecting the AB and SD models

The previous two sections explained the development of the Agent Based model and the System Dynamics model. This section will describe the connection of the two models. This includes the purpose and the technical development of connecting the models.

The purpose of connecting the models lies in the overall aim of the study i.e. to build a mixed method simulation model comprising of an Agent Based model and a System Dynamics model. These two submodels are intended to run synchronously where the dynamic of one submodel will affect the other. In our case, we want to investigate, among others, the effect of the provision of service to the progression of depression and vice versa.

Figure 4.7: Illustration for connecting AB and SD



Since the Agent Based model consists of three different levels of depression (mild, moderate, and severe), the connection between AB model and SD model is designed in four different locations. Each location has three connection points. The first three locations, each corresponds to the level of severity and its corresponding treatment pathways. One particular location of connections is designed to respond to crisis intervention. This happens when people with severe depression have to be admitted to respond to their crisis need. Figure 4.7 illustrates the intended connections (in red arrows) between the two submodels for mild condition.

The overall model will start with the Agent Based model, which is used to represent the progression of depression. The AB model can give an estimation of the number of people falling into one of the three conditions (mild, moderate, and severe). We assume that when individuals reach this state, their condition is known to them but they have not yet made a decision to contact the service.

The number of individuals falling into these states will be recorded and forwarded to the System Dynamics model. A dynamic variable is created in the System Dynamics to hold the value from the AB model. This variable represents the number of individuals who need treatment and will be updated at each time step.

The number of individuals who need treatment becomes a subject to service limitation. We incorporated a limiting function for computing the number of people with depression who can enter the service. The form of the function depends on the conditions being included in the model. For example, when the capacity of a service is known, the limiting function can incorporate this capacity. The function can use the capacity as a control for allowing individuals to enter the service.

However, due to the complexity of the model and the difficulty in getting the data, we used a constant parameter as a proportion of individuals who can start the treatment. The limitation of this design is that, regardless of the size of the number of people who need treatment, the proportion who enter the service is always a constant proportion of its size. This disregards the available capacity of the service. In other words the service will always be able to accept individuals with depression regardless of the actual number of individuals already in the system.

The results from using the limiting function are the number of people entering the service and the number of people who cannot enter the service. This reflects the reality that individuals with depression may not be able to contact the service due to various reasons (as mentioned in the background chapter). Likewise, those individuals who enter the service can also do so due to various reasons. For example, mental health literacy, where people are aware of their conditions and the available health care services for treating their conditions.

The two results, i.e. the number of people entering and the number of people not entering the service, will be used in the Agent Based model to govern the transition from the ill states to either the state of being in treatment or the state of not being in treatment respectively. Considering that the two simulation methods are different in nature (by this we mean that AB is a discrete modelling technique while SD is a continuous modelling technique) this transfer of information from SD to AB has to be treated cautiously.

There are two possible ways to design the connection from SD to AB model. The first one is to use the variable value generated by SD model as a rate of transition in the AB model. The assumption: by 'rate' we mean that the underlying distribution is exponential, with the average parameter the value generated from SD. The exponential distribution is the setting available from the simulation software AnyLogic for using the 'rate' as the type of transition.

Arguably, we can model the underlying distribution to reflect any real data. The result from this design is a stochastic transition from one state to another in the AB model. This design is perfectly fine when we do not have any part of the SD model which needs exact corresponding results from the performance in the AB model as a result of this transition.

The design of our model requires precise corresponding results generated by both SD and AB models. By this we mean that the number of people entering the service in SD has to correspond with the number of people making transition from ill state to being in treatment state in the AB model. Similarly to the number of people not entering the service. The use of stochastic transition in this case does not guarantee matching values resulting from the two models. Clearly this design is not suitable for the type of problem defined in this study.

The second possible way to form the connection is to use deterministic transition, where the number of individuals making transition is governed by the exact value acquired from the SD model. To achieve this, we designed the rule governing the transition using 'message'. The value acquired from the SD model is used to generate the number of messages needed to be sent for people in an ill state. This type of transition rule controls the number of people entering the treatment in AB to equal the number of people entering the health system in SD model.

The use of the second design, in connecting the models from SD to AB, requires further consideration of treating the values from the SD as an integer value to be used in the AB model. This will not pose any problem since the total of two variables, i.e. the ones representing people who enter and people who do not enter the service, preserves the value generated from the AB model in the first place. This conclusion was derived from the evaluation process of the two models which will be mentioned in chapter 5.

4.6 Conclusions

The developed hybrid model has been designed using a combination of an Agent Based and a System Dynamics simulation. The Agent Based was utilised to model the disease progression and the System Dynamics was used to model the treatment pathways.

The Agent Based is seen as natural to be used for modelling individual patients. Its flexibility in including characteristics such as different health states, in our case, and accommodating different transition rules between states has been seen in the current study.

The System Dynamics on the other hand is deemed natural to be used for modelling health care pathways where detailed characteristics are not of concern. In order to give an estimation of the service use based on the different severities of depression, we developed separate pathways for each level of severity.

The two simulation models were designed to run interactively. The connection between the AB and SD models required special care as the two modelling techniques are different in nature. In the current study, the connection represents the exchange of information on the number of individuals demanding the service on the one hand and hence the change in their health state on the other.

Chapter 5

Model Parameterisation and Model Testing

5.1 Introduction

Detailed data which contains individual patients' health history is very difficult, if not impossible, to acquire. This is due to the fact that the health system is fragmented and often each subsystem has its own data collection system which is not necessarily linked to any other system. What is deemed important to collect in one healthcare service might not be in another service. Data collection might also be driven by key indicators underlying the legal framework of the service. Hence, comprehensive data which captures all the necessary information for a simulation study (from the movement of patients in the service, to how their condition developed as a result of receiving the service) will have to come from different sources.

The current study requires data to populate the two sub models, i.e. the Agent Based and the System Dynamics models. One big challenge faced is the acquisition of data to inform all the parameters needed for running the developed model coming from one geographical context.

Another point to highlight is that in the current study we assume that the population being modelled consists of adults and is mixed in gender. The differentiation of parameters by gender is not possible in the current state. This is due to the fact that literature (used for the current study) in the area of epidemiology of depression, which are population based studies, did not make a distinction between gender. Not to mention that the population based studies which can inform the parameters needed in this project are scarce. The variation may exist in treatment, but the rate of recovery was not significant with the gender differentiation as found by Whiteford et al. (2013).

In this chapter, we describe the necessary parameters and the sources of the parameters. We divide the discussion into three sections where the first one will detail the population demographic profile for Wales. This is necessary as one of the purposes of developing the simulation model is to generate an estimation for one of Wales' local health boards which is our collaborator in the current study.

The second section will describe the parameters used for the Agent Based model and the third section will describe the parameters used in the System Dynamics model.

5.2 Wales's population profiles

The overall population estimate for Wales at mid-year 2016 is 3,113,150. Table 5.1 presents the estimate for Wales' population compared to the United Kingdom broken down into age groups and gender. The proportion of adults in Wales (82.11%) is quite similar to the proportion of adults for the UK (81.13%). In fact the comparison by each group (gender and age groups) is very similar. In addition, there are about 21.79 under 16 years per 100 adults population in Wales. While in the whole UK, there are about 23.26 under 16 per 100 adults UK population. The composition of males and females for both Wales and the UK is almost balanced and fairly similar in figure. In Wales there are about 97.12 males for every

100 females, compared to 97.32 males for every 100 females for the whole UK population.

Investigating the estimate for Wales' population further, we find that the composition of group (by gender) for each local health board is very similar. Table 5.2 highlights the comparison. The male population was estimated in the range of 49.05% and 49.63% compared to female population's range of 50.37% and 50.95% across all the age group (both groups have a difference of 0.58% in range).

The adult only population group, in Wales, has a similar result. The male population's range is given by 48.58% and 49.29%, compared with the female population's range of 50.83% and 51.42%. This gives a slight difference in range being 0.71% for male and 0.59% for female respectively.

The adult group in each local health board has a proportion range between 81.30% and 83.93%. The adult proportion for the whole of Wales (82.11%) falls close to the median for the adult group from all the local health boards (82.21%). Among the adult population in Wales, the proportion between male and female is relatively balanced across local health boards, which ranges between 94.47 and 96.89 males per 100 females population.

The life expectancy for all population groups in Wales, based on estimates for 2010-2014, is 78.3 years for the males and 82.28 years for the females (StatsWales (2018c)). Breaking this down, based on local health boards, there is little variation between each local health board. This estimate gives us: Betsi Cadwadadr University Health board (78.73 and 82.44), Hywel Dda Univesity Health Board (79.18 and 82.90), Abertawe Bro Morgannwg University Health Board (77.40 and 81.71), Cardiff and Vale University Health Board (78.60 and 82.93), Cwm Taf University Health Board (76.63 and 80.89), Aneurin Bevan University Health Board (78.09 and 82.02), and Powys Teaching Health Board (80.21 and 83.60).

Figure 5.1 displays the number of deaths recorded due to mental & behavioural disorders and suicide in Wales up to 2011 extracted from StatsWales (2018b). The mental and behavioural disorders recorded only those deaths due to psychoactive

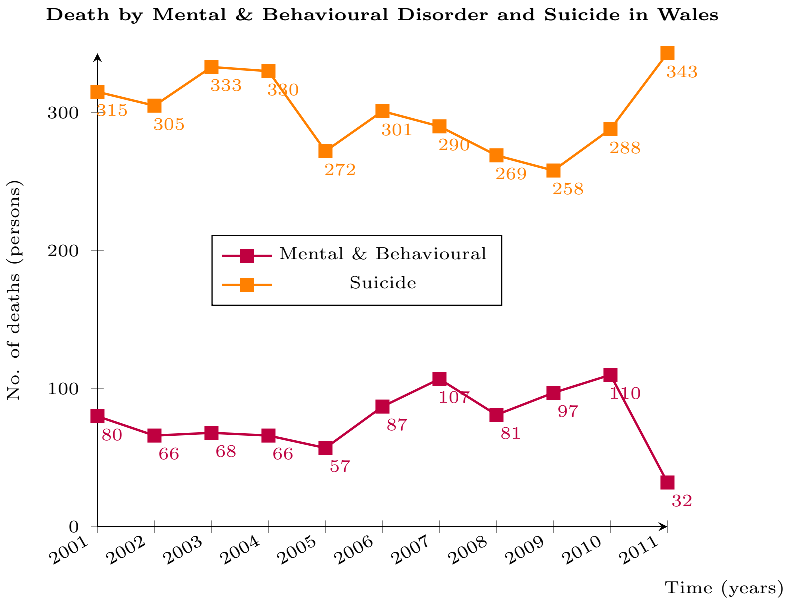


FIGURE 5.1: Number of deaths by mental and behavioural disorders in Wales.

substance use. Suicide records include those falling under the headings of event of undetermined intent and intentional self-harm. Suicide is not registered under cause of death by mental health & behavioural disorders, rather it comes under the external causes of morbidity and mortality. This general classification of cause of death adds to the difficulty in filtering those deaths due to specific mental health disorders such as depression.

Table 5.1: Wales vs UK population estimate for mid 2016

Age groups	Male	Female	Total (Wales)	UK Male	UK Female	Total (UK)
All ages	1,534,038 (49.28%)	1,579,112 (50.72%)	3,113,150 (100.00%)	32,377,674 (49.32%)	33,270,380 (50.68%)	65,648,054 (100.00%)
Age 0 - 15	285,669 (51.28%)	271,410 (48.72%)	557,079 (17.89%)	6,346,343 (51.22%)	6,043,754 (48.78%)	12,390,097 (18.87%)
Age 16 - 64	957,581 (49.84%)	963,853 (50.16%)	1,921,434 (61.72%)	20,671,336 (49.88%)	20,772,536 (50.12%)	41,443,872 (63.13%)
Age 65 & over	290,788 (45.82%)	343,849 (54.18%)	634,637 (20.39%)	5,359,995 (45.37%)	6,454,090 (54.63%)	11,814,085 (18.00%)
Total adults (16 +)	1,248,369 (48.84%)	1,307,702 (51.16%)	2,556,071 (82.11%)	26,031,331 (48.88%)	27,226,626 (51.12%)	53,257,957 (81.13%)

Data source: StatsWales (2018d).

Table 5.2: Wales population estimate for mid 2016 by local health boards

Local Health Board	Male	Female	Total (% of Wales)	Adult Male	Adult Female	Total (% of Wales' adults)	(% of each LHB)
Betsi Cadwaladr UHB	342,794 (49.34%)	352,032 (50.66%)	694,826 (22.32%)	279,409 (48.91%)	291,835 (51.09%)	571,244 (22.35%)	(82.21%)
Powys Teaching HB	65,500 49.49%)	66,837 (50.51%)	132,337 (4.25%)	54,614 (49.17%)	56,456 (50.83%)	111,070 (4.35%)	(83.93%)
Hywel Dda UHB	188,808 (49.21%)	194,848 (50.79%)	383,656 (12.32%)	155,423 (48.78%)	163,170 (51.22%)	318,593 (12.46%)	(83.04%)
Abertawe Bro Morgannwg UHB	262,817 (49.63%)	266,731 (50.37%)	529,548 (17.01%)	215,076 (49.21%)	221,978 (50.79%)	437,054 (17.10%)	(82.59%)
Cwm Taf University HB	146,121 49.05%)	151,772 (50.95%)	297,893 (9.57%)	117,655 48.58%)	124,544(51.42%)	242,199 (9.48%)	(81.30%)
Aneurin Bevan UHB	287,051 (49.08%)	297,780 (50.92%)	584,831 (18.79%)	231,346 (48.59%)	244,793 (51.41%)	476,139 (18.63%)	(81.41%)
Cardiff and Vale UHB	240,947 (49.17%)	249,112 (50.83%)	490,059 (15.74%)	194,846 (48.74%)	204,926 (51.26%)	399,772 (15.64%)	(81.57%)
Total population	1,534,038 (49.28%)	1,579,112 (50.72%)	3,113,150 (100.00%)	1,248,369 (48.84%)	1,307,702 (51.16%)	2,556,071 (100.01%)	(82.11%)

Data source: StatsWales (2018e). Total population of adults adds up to over 100% is due to rounding up effect.

5.3 Parameter estimation for the Agent Based model

The parameters needed for the Agent Based model are intended to be used in the decision rules governing the transition between states in the state chart. The transition is represented by an arrow indicating the direction of the transition. In some cases, the simplified version of figure E.1 is used to help visualising the described transition.

It is worth mentioning that all the given parameters represent the adult population suffering from depression. The derivation of these parameters was not always straight forward. This is due to the fact that there is no single health record that contains all necessary information needed for the developed model. In order to overcome this, parameters were obtained from different sources including the existing population based studies.

5.3.1 Prevalence rate of depression

The table 5.3 gives the average prevalence for the 7 health boards of 7.94% for the year 2016-17. This figure is much lower than the population survey reported in Mental Health Foundation (2016) which stated that, during 2015, 13% of people aged 16 and over in Wales received mental health treatment. The difference might be due to the fact that the reported figure by Mental Health Foundation (2016) was estimated for all kinds of mental health problems including depression. Whereas the estimation presented in table 5.3 only accounted for depression.

The report from 'Understanding Society, the UK Household Longitudinal Study' stated that as many as 19.3% (CI: 17.6%, 21.1%) of people in Wales experienced some kind of depression or anxiety during 2015-16 (Office for National Statistics (2018)). This is again a much higher figure than recorded in table 5.3. A possible reason is that the population survey did not cover the population of Wales in their entirety but was based on representative samples. Another point is that the measurement did not clearly differentiate between anxiety and depression, and not all people reported with experience of depression and anxiety were known to the system i.e. have accessed the care service. Whereas the reported figure in table 5.3 was taken from GP registers for those patients whose reviews had been conducted.

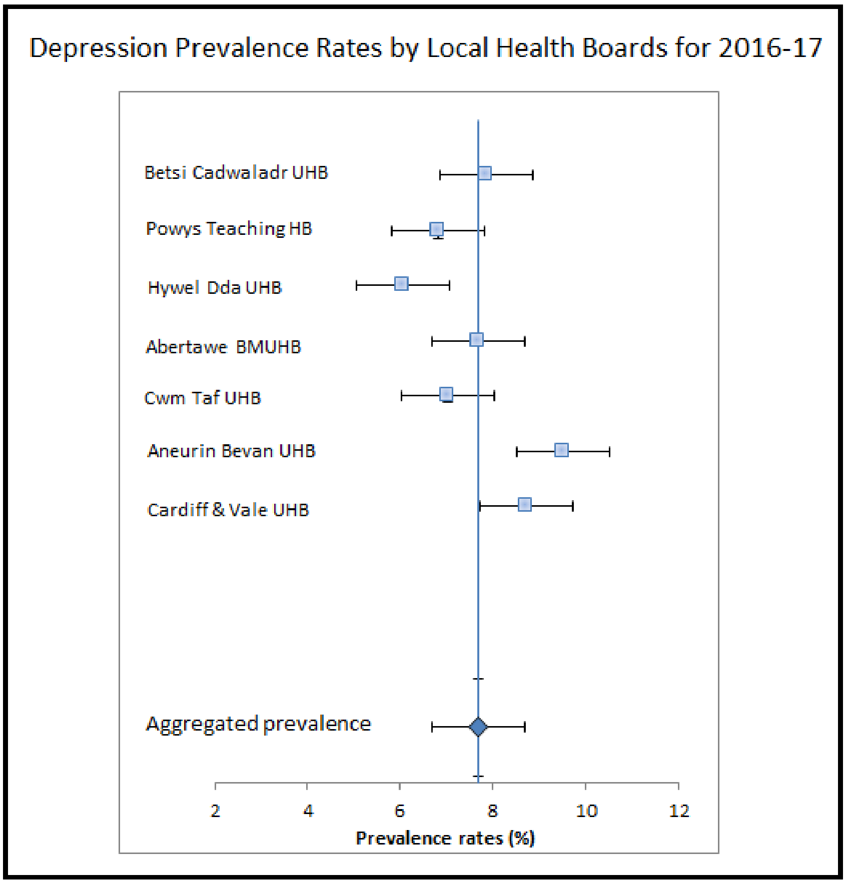
Table 5.3: Depression registers by local health boards

Local Health Board	**2015-16**[a] (New diagnoses)[b]	**2016-17**[a] (New diagnoses)[c]	**% Increase in registers** (New diagnoses)	**Prevalence est** 2016-17[d]
Betsi Cadwaladr UHB[1]	48,454 (5582)	54,636 (5189)	12.76% (-7.04%)	7.86%
Powys Teaching HB[2]	8,411 (652)	9,017 (596)	7.20% (-8.59%)	6.81%
Hywel Dda UHB	19,180 (1732)	23,280 (1847)	21.38% (6.64%)	6.07%
Abertawe Bro Morgannwg UHB	34,021 (2973)	40,752 (3215)	16.52% (8.20%)	7.70%
Cwm Taf University HB	17,418 (1282)	20,936 (1213)	20.20% (-5.38%)	7.03%
Aneurin Bevan UHB	45,987 (4167)	55,721 (4328)	21.17% (3.86%)	9.53%
Cardiff and Vale UHB	37,489 (3907)	42,747 (4071)	14.03% (4.20%)	8.72%
Wales	210,960 (20295)	247,089 (20459)	17.13% (0.82%)	7.94%

[a] Data source: StatsWales (2018g) for all patients with depression registered in GP.
[b] Data source: GP Contract (2018a) for adults aged 18 and above with new diagnoses of depression.
[c] Data source: GP Contract (2018b) for adults aged 18 and above with new diagnoses of depression.
[d] Estimated as: 2016-17 registers (numerator) / mid 2016 population estimate for local health board (denominator).
[1] UHB: University Health Board.
[2] HB: Health Board.

We performed a meta analysis on the prevalence rates in table 5.3 using the guidelines in Neyeloff et al. (2012). The Forest plot in figure 5.2 shows the prevalence rates analysis which gives us an overall rate of 7.7%. We assumed that the population is different from one local health board to another, and utilised the random effect model to perform the computation. The heterogeneity test gives a value of 5.98 which is lower than the value in χ^2 table (12.59) for 6 degree of freedom with 95% confidence. This indicates that the prevalence rates across the seven health boards are similar. The random effect value gives a small negative value which interpreted as 0% of the heterogeneity is due to random chance.

Figure 5.2: Forest plot for depression prevalence rates in Wales year 2016-17



Based on the result generated from the meta analysis, we will use the prevalence rate of 7.7% per year for depression. This rate is used in the transition from state 'Population' to each composite state of 'Mild', 'Moderate', and 'Severe'.

5.3.2 Proportion, recovery and progression rates of depression

Figure 5.3: Model for depression progression with prevalence, progression and recovery transitions.

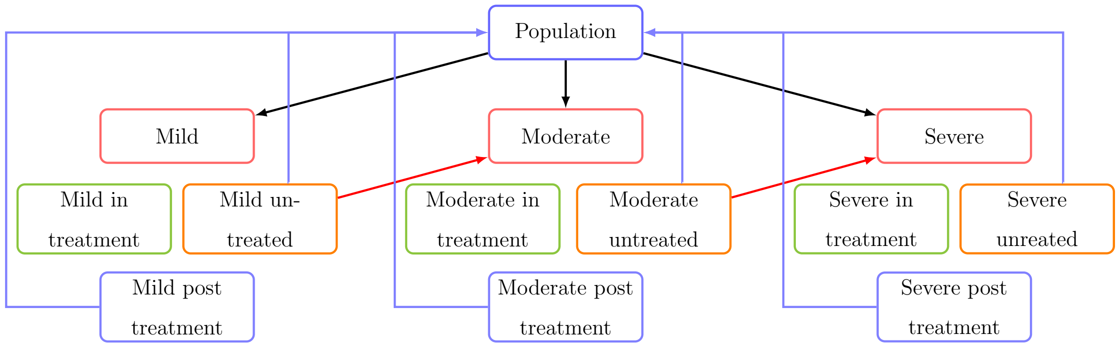


Figure 5.3 highlights the intended proportion, recovery and progression transitions. The proportion for each severity of depression is included in the black arrows coming from the population. Hence it is used along with the prevalence rate for depression. The recovery transitions are represented by those blue arrows from 'untreated' and 'post treatment' states to the 'Population'. The progression transitions are represented by the red arrows; one from untreated mild to moderate condition and the other from untreated moderate to severe condition.

Studies that investigated the rate of depression progression using population based longitudinal data are not many in number. This is perhaps due to the fact that to conduct such a study will be very costly. We endeavored to used, if possible, as many parameters as we can get from a single study. This is intended to reduce variation and biases. Although, biases will always have to be acknowledged since the parameters used in the current study came from several literature sources.

A particular study investigating the progression of depression was based on a longitudinal population study conducted by Simon et al. (1999). The study sought to examine the relationship between recognition and outcomes of individuals suffering from depression. The term 'Recognised' was defined as the recognition of the symptoms by the GP who then made a correct diagnosis.

The authors used the division of severity levels as mild, moderate, and severe. They followed individuals who were diagnosed by the primary GP for 12 months and the change in their conditions from the baseline was recorded. Table 5.4 summarises the findings from the study.

Table 5.4 provides rich information on three points: the progression of depression from each severity level at the baseline, the proportion of individuals suffering from each condition at the baseline, and the recovery rates from each severity level.

Table 5.4: Depression progression reproduced from Table 2 in Simon et al. (1999).

	Baseline mild n = 296		Baseline moderate n = 391		Baseline severe n = 321	
	Recog	Unrecog	Recog	Unrecog	Recog	Unrecog
12-mo recovered	79.3%	81.7%	64.5%	74.7%	54.9%	57.8%
12-mo mild	6.9%	5.6%	3.2%	7.2%	7.8%	4.4%
12-mo moderate	6.9%	7.0%	19.4%	12.0%	9.8%	20.0%
12-mo severe	6.9%	5.6%	12.9%	6.0%	27.5%	17.8%

For the purpose of our study, we used the progression rates of 7.0% and 6.0% from mild to moderate and from moderate to severe respectively, for those individuals who did not get treatment in our model. We did not use the progression rates for improving conditions, such as from the moderate to mild and from severe to moderate. The reason is based on our assumption that, for individuals who receive treatment, the recovery indicates the improvement of the condition. Moreover, if we consider the movement from the worst condition to the better one explicitly, then by the design of our ABM, it will trigger the need for the treatment. This will generate false demand on the treatment.

Rates for recovery can be split into two kinds. For those individuals who enter the treatment, it is assumed their conditions were recognised in the first place. Accordingly, the rates for the recovery from treatment are 79.3%, 64.5% and 54.9%, for individuals with mild, moderate, and severe respectively.

As for those individuals who did not access the treatment, their recovery rates will follow the rate of recovery from the unrecognised depression. We assume that the missed diagnoses were followed by missing the chance for their depression being treated. Although the study in Simon et al. (1999) did not imply that being unrecognised means that the individuals did not get treated later on. Being unrecognised simply means the GP missed recognising the symptoms at the baseline. The rates of recovery from the untreated condition are 81.7%, 74.7%, and 57.8% for mild, moderate, and severe respectively.

A meta analyses study done by Whiteford et al. (2013) found aggregated recovery rates for individuals with major depression. The results stated that natural recovery, i.e. recovery rate from the untreated conditions, are given by 23% within 3 months, 32% within 6 months and 53% within 12 months. These rates are for the adult population and are not separated by level of severity.

We can see that the natural recovery rates, provided by Simon et al. (1999), for being unrecognised are slightly higher than the recovery rates for being recognised. Logically this implies that it is better for individuals for their depression to be unrecognised, as they will have a better chance to recover. Again, we cannot assume that the individuals whose depression conditions were not recognised at the baseline did not get treated between the survey at the baseline and the follow up survey after 12 months. Despite this issue, and since there is no other population based studies provide better parameters, we use the results for our baseline scenario which will be explained in the subsequent chapter.

The last point that we can take from the results in Table 5.4 is the proportion of individuals who suffered from each level of severity at the baseline. For this purpose, we simply use the stated number of the individuals included in the survey divided by the sum of all individuals in the three levels. This gives us the proportions of 29.36%, 38.79% and 31.85% for mild, moderate and severe respectively. These rates may not represent the current rates in Wales. However, in the absence of estimates for the Wales population, it is feasible to use the rates for the baseline scenario as they came from the same study as the rates of recovery and progression.

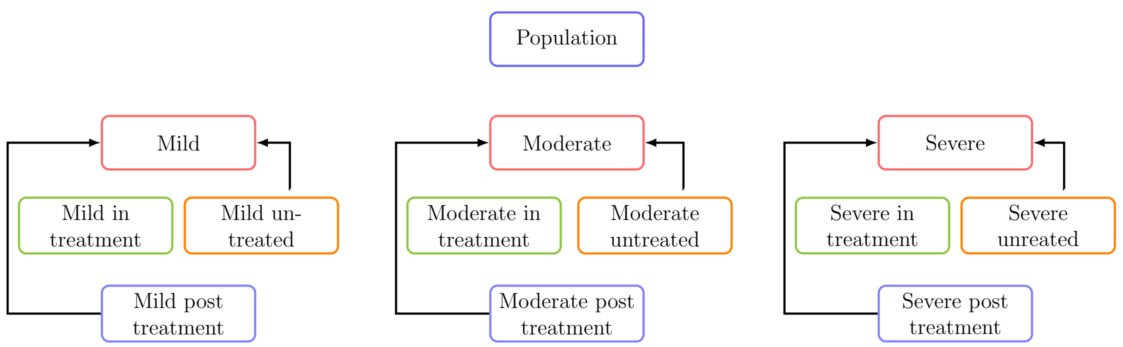
5.3.3 Recurrence and mortality rates of depression

The term ‘recurrence’ in mental health terminology is defined as the emergence of symptoms that meet the diagnoses criteria after a recovery. This is different from the term ‘relapse’ which is defined as the occurrence of the symptoms during the recovery. The definition of relapse and recurrence used in the current study follow the definitions and durations explained in Nierenberg et al. (2003).

Studies investigating the relapse and recurrence vary in their use of the two terms, hence, for the purpose of the current study, we will not differentiate between relapse and recurrence. We will refer to the re-emergence of depressive symptoms simply as recurrence, and it can happen when the affected individuals have completed the treatment or when they are untreated. The important point to note here is that the developed model in the current study assumes that when recurrence happens, it will potentially generate demand for the service.

Figure 5.4 highlights the recurrence transitions. The model allows recurrence to be captured for affected individuals who have been treated and those who have not. Death can be assumed to happen from any of the conditions in the model.

FIGURE 5.4: Model for depression progression with recurrence transitions.



Longitudinal population-based studies on the course of depression recording recurrence have been done with different focus and duration of observation. A study by Gonzales et al. (1985) for example, observed people with unipolar depression who completed treatment for a duration of 3 years. The authors found that 31% of people with major depression who recovered, relapsed within 1 year. The rate was found to be much lower in the study done by Limosin et al. (2004), which estimated that around 10.7% people with major depression treated by a GP would experience relapse during a 4 to 6 month period. The duration of the observation is much shorter in the later study which perhaps explains the variation.

More recent population-based study on first onset and chronicity in major depression done by Eaton et al. (2008) found a similar figure to Gonzales et al. (1985) for recurrence of depressive episode. The study followed individuals with major depression for 23 years after their first onset. The authors concluded that only about 50% recovered and never had recurrence. Whereas for as many as 15% their conditions persisted and around 35% experienced recurrence.

The above studies did not mention the recurrence rate for individuals who did not get treatment. One particular longitudinal population-based study which investigated treated and untreated major depression was conducted by Wang (2004). The study observed individuals in the population for a duration of 6 years. Those individuals with depressive symptoms at the baseline were categorised into whether they accessed the service or not. Their conditions were recorded at each survey time which took place every 2 years.

Table 5.5 is reproduced from Table 2. in Wang (2004) (with χ^2 values not included). Each time frame was conducted 2 years apart, so Time 1 in the table means the survey was conducted 2 years after the baseline survey. The table reports that the proportion of individuals accessing the service at the baseline was 48% compared to the proportion of untreated at the baseline of 52%.

The current study used the result reported at Time 1, i.e. 2 years after the baseline survey. The reason for this is that the time frame is the closest to the first survey. This gives the rate for recurrence for treated and untreated depression of 33% and 14% respectively. The authors also stated that the recurrence rate for affected individuals who accessed the service is higher than those who did not receive

Table 5.5: The proportion of recurrence reproduced from Table 2 in Wang (2004).

	Reported MDE at			
At Baseline Participants with MDE	At Any Time N (%)	Time 1 N (%)	Time 2 N(%)	Time 3 N(%)
Treated MDE (n = 292)	146(50%)	95(33%)	71(26%)	64(21%)
Untreated MDE (n = 317)	94(29%)	47(14%)	35(12%)	43(13%)
P values	<0.001	<0.001	<0.001	0.01

The percentage were weighted.

MDE is major depressive episode.

treatment. The recurrence proportion value for the treated cases is close to the recurrence rate found in Eaton et al. (2008). The results presented in Table 5.5 did not differentiate between the severity levels. Therefore, we used these values for all cases in our model.

The last point to be discussed in this subsection is the parameter for the mortality transitions. The mortality rate was derived from the population data in Wales. Table 5.6 summarises the mortality and suicide rates in Wales for 2016. The population mortality rate for all causes of death was estimated as 1045.7 per 100,000 population, with the confidence interval given between 1034.4 and 1057 per 100,000 population. The mortality rate for the male population in Wales is higher than the female mortality rate.

Table 5.6: Wales's mortality[a] and suicide[b] rates for 2016

Gender	**Deaths**	**Death Rate (CI)**	**Suicide**	**Suicide Rate (CI)**
Males	16382	1227.3 (1208, 1246.5)	265	20.0 (17.5, 22.4)
Females	16684	898.8 (885.1, 912.6)	57	4.0 (3.1, 5.2)
Persons	33066	1045.7 (1034.4, 1057)	322	11.8 (10.5, 13.1)

[a] Data source: Office for National Statistics (2017a). Age-standardised mortality rates per 100,000 population. Counts are from all underlying causes.

[b] Data source: table 4 in Office for National Statistics (2017b). Age-standardised suicide rate per 100,000 population.

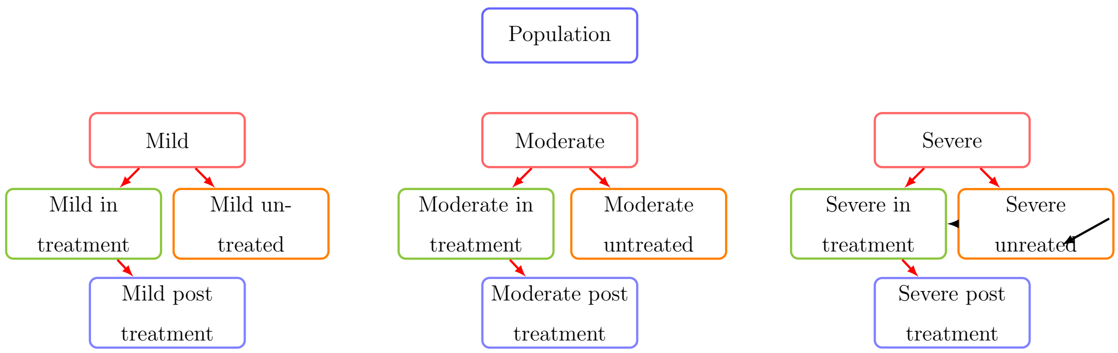
A high contrast between the male and female death rates due to suicide can also be seen from Table 5.6. The estimate for the male suicide rate in Wales was even higher than the overall suicide rate (20.0 and 11.8 per 100,000 respectively). Unfortunately, the records did not specify in detail the cause of suicide in particular, whether it was due to depression.

Although existing studies on depression may have found a correlation between suicide and depression, it is not easy to determine the impact of depression on overall mortality from the data. Notwithstanding, due to the small rate of suicide, for the purpose of the current study, we only used the mortality rate for all causes of death as the death rate.

5.3.4 The rates for entering the service and duration of treatment

The subsequent paragraphs describe the rates used to govern the transition to enter the service, i.e. being in treatment and untreated, and the transition exiting treatment for each level of severity. Figure 5.5 highlights the transitions in red arrows.

FIGURE 5.5: Model for depression progression with transitions for accessing the service and duration of treatment.



The transition rates for each condition to being in treatment and not being treated come from the values generated as results from the interaction with the System

Dynamics model. These values change at each time step depending on the number of individuals entering and not entering the service.

Similarly for the rates of transition of remaining in the severe state and from the condition of not being treated to be in treatment for the severe case. These two rates correspond to the values generated in the System Dynamics model for severe depression. Figure 5.5 highlights the two transitions in black arrows. The discussion on the variable for these transitions can be found in the next subsection.

The duration of treatment for depression varies depending on several factors, one of which is the severity level. The guidelines in Andrews, G. and the TOLKIEN II Team (2006) prescribe that the duration for the initial consultation with a GP, for all types of severity, is about 4 weeks. During this stage, and for an additional 2 weeks, some people with depression will remit and others will need to be referred for more treatment. This is particularly so for the mild and moderate conditions, but not quite so for the severe cases.

Furthermore, the guidelines estimate that around 70% of people with mild condition remit during the first 6 weeks and 30% of people with moderate condition. If we comply with the prescribed guidelines and ignore any delay issues in treatment (such as the waiting time for treatment) the maximum duration of treatment is approximately 52 weeks for mild condition.

For the moderate condition it will take longer as individuals may need far longer therapy treatment. The guidelines suggest the duration for using medication of 46 weeks for both mild and moderate conditions. However, it did not suggest any length of time for the therapy treatment, and only prescribes the number of visits the patients should have. If we assume the therapy treatment is scheduled weekly then, for moderate conditions the total duration could take as long as 56 weeks or even more.

The NICE guidelines for depression treatment suggest that CBT should be given at the second step, i.e. for those whose condition is mild or moderate that do not respond to first step treatment, treatment should take place between 9 and

12 weeks. As for the high-intensity psychological interventions which fall within the third step, and for individuals with severe condition or a condition which persists, treatment should be given over a period of 3 to 4 months. Furthermore, for all people with depression, the follow up therapy sessions should be given for a duration of 3 to 6 months (National Collaborating Centre for Mental Health (2010)).

The suggested treatment for severe condition is different from those for mild and moderate condition. Thirty percent of people suffering from severe depression remitted only after taking some drugs and/or therapy. If this is the case, treatment duration may take up to a year. The remaining 70% will need longer treatment. The guidelines only prescribe the number of visits needed for psychiatrist, psychological therapist or mental health team visits. The exception is for the average duration of inpatient stay needed, which is 10 days. These guidelines suggest that the inpatient stay is only accessed by about 5% of severe cases. This is due to the design of the recommendation that the majority of people suffering from severe depression should be treated in community outpatient services.

Summarising the explanation above, we set the transition from being in treatment to finishing the treatment as follows. The duration of treatment will follow the triangular distribution with minimum, mean and maximum as 4 weeks, 26 weeks and 52 weeks for mild depression. The duration of treatment for moderate takes values of 4 weeks, 26 weeks and 56 weeks. The duration of treatment for severe is set for 26 weeks, 52 weeks, and 76 weeks. The choice of triangular distribution is due to the absence of real data for the duration of treatment if the step care model is implemented. The mean duration of roughly 26 weeks is taken for the mean duration of depression found in Üstün et al. (2004) and Posternak and Miller (2001). For severe depression we used 26 weeks for the minimum value and used 52 weeks as the mean. Fifty two weeks is the duration of treatment when the possibility of 30% of people with severe depression appear to respond to any treatment in Andrews, G. and the TOLKIEN II Team (2006).

The set up of the above durations does not assume that the depression will be cured at the end of treatment. This set up is estimated for the recommended treatment duration. In reality, the condition may persist for years, which is especially so for persistent cases which are not modelled in the current study.

5.4 Estimating parameters for the System Dynamics model

The treatment pathways for depression were built based on the recommended pathways developed in Andrews, G. and the TOLKIEN II Team (2006). The recommendation comes with suggestions on the duration of treatment and the number of visits needed for each service. However, not all the suggested services will have both treatment duration and the number of treatments needed. When difficulties have arisen from estimating the duration for treatment, we consulted the treatment recommendations suggested by The National Collaborating Centre for Mental Health (2010).

The types of parameters needed in the SD model, apart from the endogenous and exogenous variables (see Table 4.1, Table 4.3 and Table 4.5), can be divided into three categories. The first one relates to any fraction which can be regarded as probability. For example, the fraction entering the service represents the probability of individuals entering the service. The second category is related to the duration of the treatment for each service providing that duration is needed. Some services may not need the duration if the intended stock, presenting a service, acts as a means to count the total accumulation for the service. The third type referred to as a multiplier of a service. For example the number of GP visits needed at the initial stage of treatment. We assume that throughout the model the values of the parameters are constant for all individuals receiving treatment.

The recommendation for treatment for severe cases assumes that around 10% of affected people would choose the CBT treatment. The recommendation states the number of additional GP visits to go alongside the CBT. However, it is not clear how long the duration of CBT is needed. The recommendation from National Collaborating Centre for Mental Health (2010) states that for low-intensity psychotherapy the duration of treatment should be between 9 to 12 weeks. As for the high intensity therapy, it suggests to offer treatment for 4 months duration.

The time in CBT, where the affected individuals are still in the initial stage of treatment, will take about 16 weeks. This is due to the total duration of 4 weeks with the GP at the initial stage followed by CBT for 12 weeks. The 12 weeks is taken from the maximum duration for the high intensity psychotherapy provided in National Collaborating Centre for Mental Health (2010). This value is also used for the duration of service in the Psychological Therapy at the follow up stage.

A high proportion of people affected by severe depression (90% in the recommended model), would use medication. The duration for having medication is prescribed as 12 months. However, a 4 weeks initial GP consultation occurred for this group too. Hence, the total duration (56 weeks) of using medication is assumed to include the total time with the GP (4 weeks) and the time prescribed for medication (52 weeks).

The Table 5.7 provides a summary of the statistics from the ABUHB inpatient data for 2014-2017 financial years. It indicates that the maximum duration of stay could reach as high as 435 days in one of the wards. However, the average proportion of the outliers is under 10%. The average mean duration of stay is given as 10.25 days, and the values for the median indicate that the mean could be affected by the outlier values.

If we compare the length of stay to the one estimated in Andrews, G. and the TOLKIEN II Team (2006), it gave us 10 days. This length of stay is close to the average mean duration of patient stay in the five inpatient services belonging to the Aneurin Bevan University Health Board. We use the value 10.25 days (equivalent to 1.5 weeks) as the parameter for the inpatient length of stay in the SD model.

Table 5.8 presents the summary for the parameters.

Table 5.7: Statistics for patient LOS in each ward belongs to ABUHB

Wards/LOS Stats	**Min**	**1st Q**	**Median**	Mean	**3rd Q**	**Max**	**Outlier > value**	**proportion of Outliers**
Talygarns OOH	0.5	0.5	0.5	0.79	1.00	12.00	1.75	5/173(2.9%)
Talygarn	0.5	0.5	1.00	9.01	8.00	300	19.25	304/2592(11.7%)
Carn-y-Cefn	0.5	1.00	4.00	11.70	9.00	276.00	21.00	125/953(13.1%)
Ty Cyfannol	0.5	3.00	7.00	19.49	21.00	435.00	48.00	137/1380(9.9%)
Adferiad	0.5	1.00	4.00	10.27	10.00	295.00	23.50	213/2085(10.2%)

[1] Data consists of inpatient records from 01/04/2014 to 31/03/2017.

[2] The LOS of 0.5 is assigned for those patients who were recorded as admitted and discharged on the same day.

[3] The outliers were computed based on 3rdQ + 1.5*IQR and rounded up where necessary.

[4] Talygarn OOH is an inpatient facility provided for out of hours service. The duration is short as patients arriving at out of hours service will be transferred to any of the other inpatient wards on the following day.

[5] The analyses were done in R.

Table 5.8: List of parameters for System Dynamics model

Description	**est. value**	**Source**
SD Model (Mild)		
Time in initial GP	4 weeks	[1]
Observation time	2 weeks	[1]
Proportion enter service	varies	scenario for treatment coverage
Number initial GP visits	4 visits	[1]
Fraction need further treatment	30%	[1]
Number further GP	6 visits	[1]
Fraction need medication	0.67 (20% of 30%)	[1]
Number Psychological Therapy visits	6 visits	[1]
Fraction need Psychological Therapy	0.33 (10% of 30%)	[1]
SD Model (Moderate)		
Time in initial GP	4 weeks	[1]
Observation time	1 week	adapted from [1]
Time in medication	46 weeks	[1]
Time in Psychological Therapy	6 weeks	[1]

Table 5.8 continue

Description	est. value	Source
Proportion enter service	varies	scenario for treatment coverage
Number initial GP visits	4 visits	[1]
Fraction need further treatment	70%	[1]
Fraction need medication	0.57 (40% of 70%)	[1]
Number further GP visits	8 visits	[1]
Fraction need more Psychological Therapy	0.33 (10% of 30%)	[1]
Fraction need Psychological Therapy	0.43 (30% of 70%)	[1]
Number Psychological Therapy visits for CBT	6 visits	[1]
Number Further Psychological Therapy visits	6 visits	[1]
Number need Psychiatrist visits	6 visits	[1]
Fraction on further Psychiatrist and Psychological Therapy visits	0.5	adapted from [1]
Fraction need further Psychological Therapy from medication	0.25 (10% of 40%)	[1]
SD Model (Severe)		
Time in CBT	16 weeks	[1, 2]
Time in medication	56 weeks	[1, 2]
Time in Psychological Therapy	16 weeks	[2]

Table 5.8 continue

Description	est. value	Source
Fraction to enter treatment	varies	[1]
Need CBT fraction	10%	[1]
Fraction for medication	90%	[1]
Number initial GP visits	4 visits	[1]
Number GP visits while in medication	12 visits	[1]
Number GP visits while in CBT	6 visits	[1]
Fraction from CBT to referrals	70%	[1]
Fraction from medication to referrals	70%	[1]
Fraction need Psychological Therapy	0.43 (30% of 70%)	[1]
Number Psychological Therapy visits	10 visits	[1]
Need Psychiatrist fraction	0.57 (40% of 70%)	[1]
Number Psychiatrist visits	10 visits	[1]
To inpatient fraction	0.17 (5% of 30%)	[1]
Fraction to inpatient from GP	0.05	[1]

Table 5.8 continue

Description	est. value	Source
Proportion for emergency	0.5	scenario for treatment coverage
Need MH Team fraction	1	adapted from [1]
Number MT Team visits	10 visits	[1]
Time in inpatient stay	10.25 days (1.5 weeks)	[3]

[1] Andrews, G. and the TOLKIEN II Team (2006),

[2] National Collaborating Centre for Mental Health (2010),

[3] The average mean value from Anuerin Bevan University Health Board data in Table 5.7.

5.5 Model testing

Model validation and verification are another important step in simulation model building. The importance of model validation, as explained in Pidd (1998), encompasses the practical and theoretical points of view. The practical point includes the fact that a simulation model can be used to explore and explain real system behaviour; to explore the possible best solutions to the problem in-hand faced by the real system; or to propose new system design that can be better used than the current system design. Whereas the theoretical view looks at how the developed model is close to representing reality. The closer the model is to the reality, the better the use of the model to help the organisation solve its problems.

Validation is not the same as verification. The validation process involves comparison of the outputs from the model with the observation from the real system (Pidd (1998)), or the relation between the input-output from the model with the relation in the real system within the specified context (Pidd (2009)). Verification, on the other hand, involves the process of ensuring that the input-output relation resultant from the model developed in the computer is the same as the one used to develop the model (Pidd (2009)). In other words, ensuring that the code developed for the model is correct and representative of the conceptual model (Robinson (2014), Brailsford et al. (2019)).

Both validation and verification of a simulation model are very difficult to achieve (Sterman (2000)). While the procedure for comparison can be done using statistical methods, it is the observation data from the real system that renders the difficulty in conducting the validation, as the real data may not always be available (Pidd (1998)). However, *"Testing, verification and validation may be viewed as processes that allow boundaries to be defined in terms of model performance"* (Murray-Smith, 2015, p.19).

In the previous subsections we explained that the parameters used to run the model came from many different sources, some with questionable quality. The lack of real data which come from a single context makes it difficult to perform the validation. Therefore, the procedures conducted in this study are mainly for testing or verifying the model concept. The exact result from the model output that matches the reality will be very difficult to get. In our case, we used the parameter values as our guideline for approximation to test the model construction.

Although model verification was done at each stage of model development, by iterating through the modelling cycle (Robinson (2014), Railsback and Grimm (2012)), model testing was also conducted when the model was completed to help increase the confidence level about the overall model. The confidence about the model will depend on the confidence of the whole model as well as the sub-models (Murray-Smith (2015)). In our case, the sub models were the Agent Based model and the System Dynamics model. Whereas the whole model is the Agent Based and the System Dynamics combined together.

In order to ensure that the model built for this project was convincing and fit for purpose, we conducted the model testing in three parts. The first test related to the Agent Based model. The aim of the testing was to verify that the model outputed similar proportion to the rates governing the model.

The second part related to the System Dynamics model. Similar to the test done for the Agent Based model, in the System Dynamics model, we check the accumulation of patients in each service (stock variable in SD). Certain outputs of the SD model can be compared to the ones generated by the AB model.

The third part or the testing procedure was to check the construction of the hybrid model (i.e. checking the connection points between the SD and the AB models). The aim of the third test was to verify that the two models (AB and SD) are responding to each other during the simulation run.

The subsequent sections describe the three testing procedures. For the purpose of the testing, we ran the model for 2 years, with an initial population size of 5000. The seed was set to be 1, as we ran only one experimentation and to ensure the result can be replicated.

The preliminary results from the model testing were presented to experts in Aneurin Bevan University Health Board in December 2018. The purpose of the presentation was to gain a critical review of the model structure, as the development of the model was based on the treatment recommendations, and to acquire information on the parameters used in the baseline model.

There were some suggestions that the structure of the model built for severe depression should be altered to reflect the current pathways and to change some terminology used in the model. It was suggested that all the severe cases would generate demand to the Crisis Resolution Home Treatment Team (CRHTT). The initial model did not include the service from the CRHTT, as it was not modelled by Andrews, G. and the TOLKIEN II Team (2006). Furthermore, it was explained that people with severe depression who access the Mental Health Team also access the Psychological Therapy and Psychologist services. Hence the model for severe depression was amended accordingly to accommodate the suggestions. This amendment will theoretically lead to an increase in the use of the Mental Health Team service and the CRHHT service, as the number of individuals with severe depression increases.

5.5.1 Testing the construction of the Agent Based model

The aim of testing the Agent Based model is to compare the prevalence rate generated by the model with the prevalence rate used from the population as explained in the previous section. The overall depression prevalence rate used in this testing is 7.7% per year (from the analysis of prevalence in Wales). The proportion of mild, moderate, and severe are 29.36%, 38.79%, and 31.85% respectively. Due to a lack of comprehensive prevalence data on depression based on severity in UK context, the previous rates were taken from a study by Simon et al. (1999). We used these proportions and the prevalence rate as transition rates from population (i.e hidden depression state in the model) to the mild, moderate, and severe depression respectively.

The first testing yielded total prevalence which is lower than the prevalence rate from the data. Hence, calibration was conducted with the purpose of adjusting the prevalence rate to gain the total prevalence as intended (i.e 7.7%). Keeping all other parameters fixed and varying the prevalence rate to be between 0.077 and 0.095, the calibration process was run for 500 iterations. The optimisation facility within Anylogic allows testing to be set so as to minimise the absolute difference between the prevalence rate resulting from the model run and a scalar. Based on the setting, the result indicated that the best value for the prevalence rate is 0.081.

The testing was repeated, using the prevalence rate of 0.081, to gain the confidence from the results generated by the Agent Based model. The results from testing the AB model are summarised in Table 5.9.

TABLE 5.9: Results from testing the Agent Based model

Severity	**Data**	**1stQu.**	**Mean**	**3rd Qu.**	**SD**	**95% CI**	**p value[a]**
Mild	0.2936	0.2813	0.2925	0.3033	0.0165	(0.2911 , 0.2940)	0.1509
Moderate	0.3879	0.3786	0.3891	0.4008	0.0176	(0.3875 , 0.3906)	0.1315
Severe	0.3185	0.3786	0.3184	0.3302	0.0166	(0.3169 , 0.3198)	0.8621
Total	0.0770	0.0745	0.0765	0.0783	0.0028	(0.0762 , 0.0767)	< 0.0001[b]

Note: The test was based on population size 5000, 2 years running time and 500 iterations.
[a] The p values were calculated using one sample t-test against the data values.
[b] Testing against 0.0768 with 95% CI yields p-value of 0.0079.
All statistical tests were conducted using R.

5.5.2 Testing the construction of the System Dynamics model

The structure of System Dynamics model was tested iteratively as the model was being built. Since the model comprises of three sub systems, one for each severity, we test each sub model separately. The purpose of the SD model is to represent the treatment pathways, hence the points of interest were the accumulation points where the patients received treatment. This necessitated us to check the accumulation at each point of service against the expected value, if the prevalence were to occur.

Figure 5.6, Figure 5.7 and Figure 5.8 display testing results from 100% of service coverage for the severe, the moderate, and the mild model respectively. The points of interest include the dynamic variables representing the number of people with severe depression starting their treatment and those not entering the treatment.

The three figures highlight that the interface between the SD and AB model worked as intended. The number of people starting treatment corresponded to the number of people with severe depression in the initial demand which came from the AB model. As expected with 100% coverage, no one should enter the state of not being treated. During the model run, the number of people not being treated remained zero for all the severity levels.

The total prevalence for severe depression accounted for around 282 people. It was assumed that 90% of people were given medicine and the result from the model indicated that the total number of people using medicine was about 265.5 ($\tilde{9}4\%$). The exact percentage is not likely to be achieved due to the rounding effect in computing the proportion of people receiving a particular service.

Figure 5.6: Testing Result for 100% Coverage from Severe Model

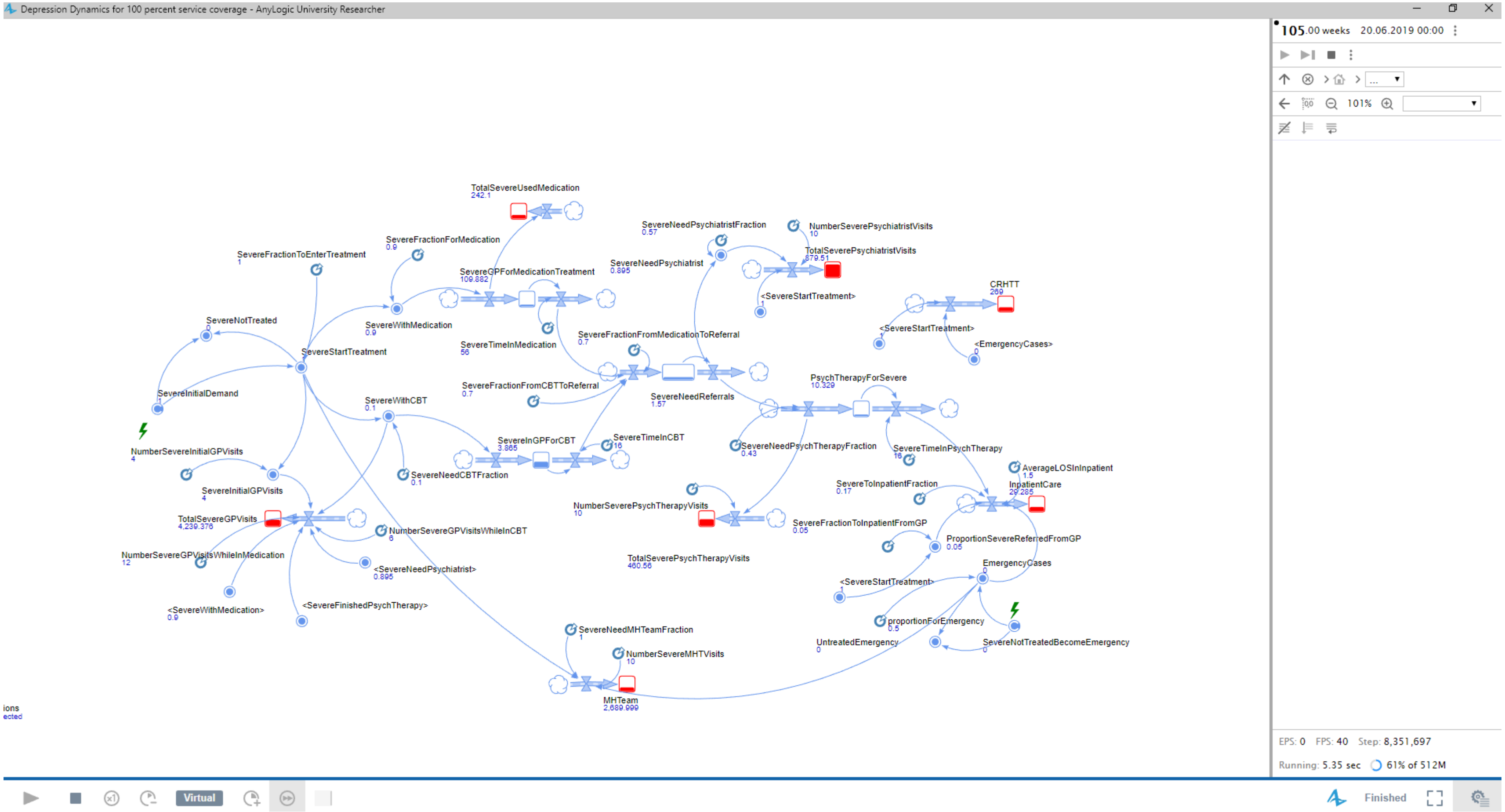


Figure 5.7: Testing Result for 100% Coverage from Moderate Model

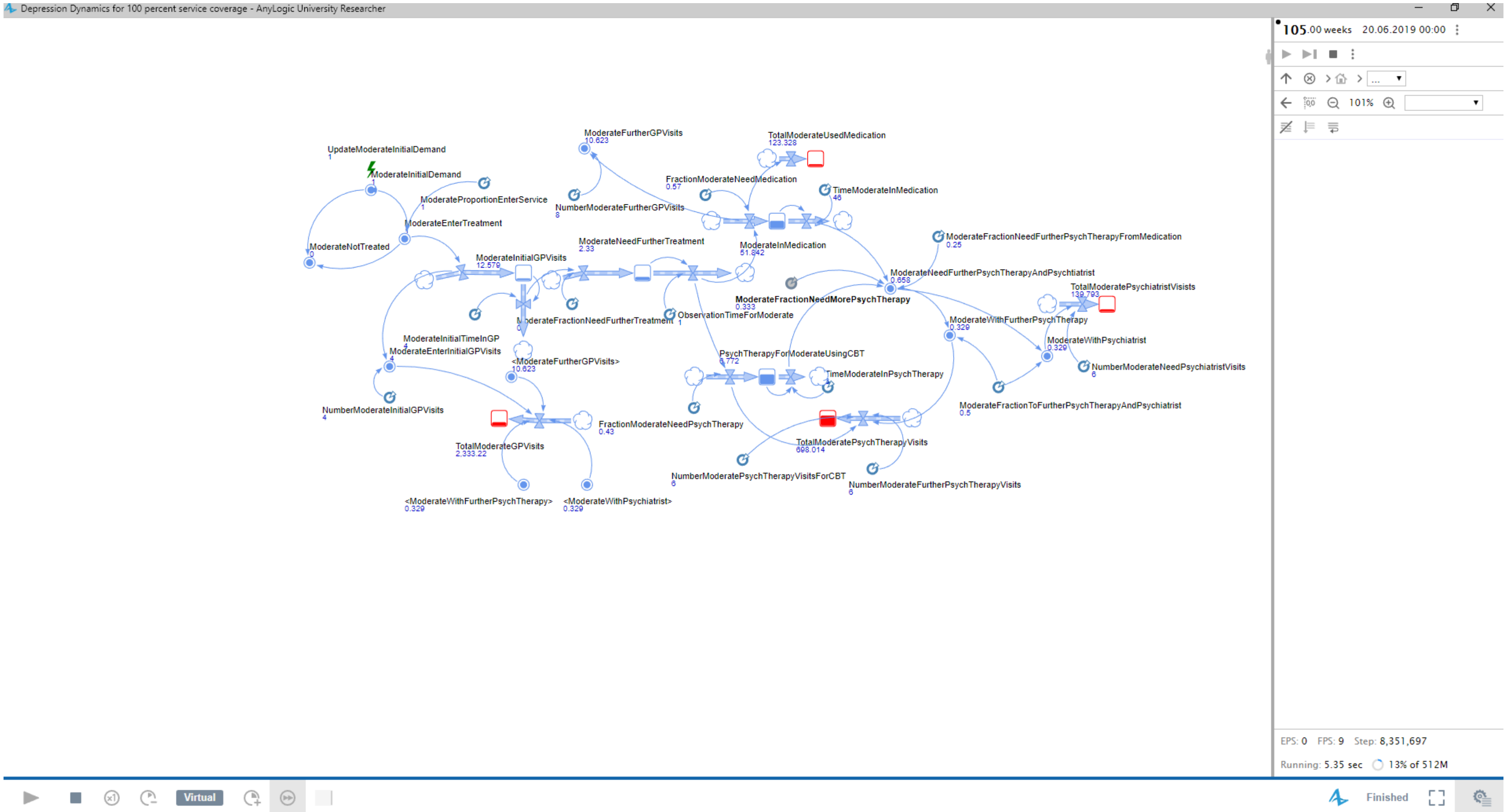
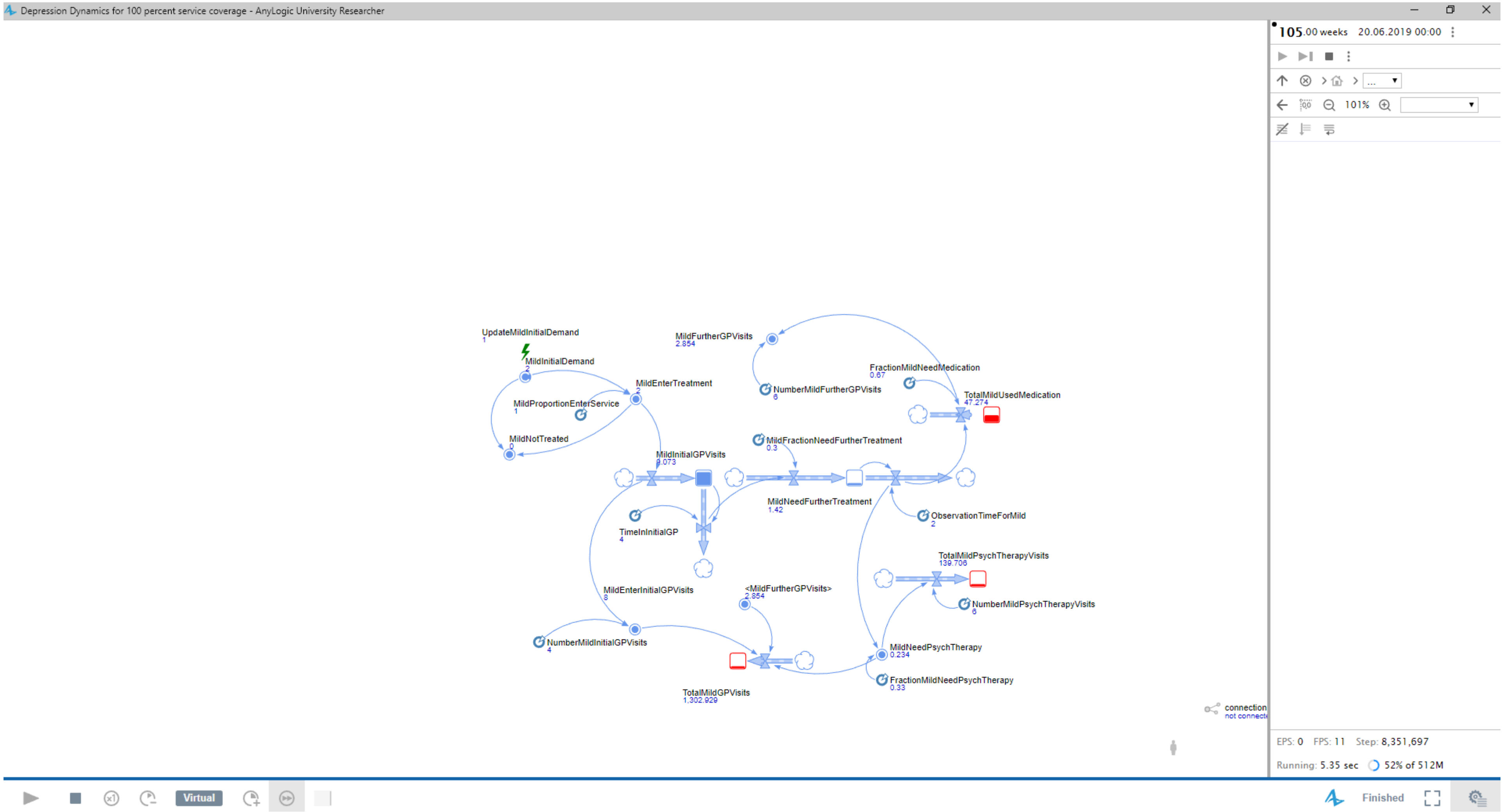


Figure 5.8: Testing Result for 100% Coverage from Mild Model



In order to give a simple description of the estimation procedure, take for example the results from the model for mild condition. One important accumulation point is the total number of GP visits. The simulation run estimated around 231 people suffered from mild depression. At the initial stage they would need 4 GP visits which gives a total of 924 GP visits. Then 30% of people will need further treatment, 70% of which were given medication (around 48 people) with 6 more GP visits each, and 30% had therapy which at the end only need 1 more GP visit. The estimate gives a total of around 1,236 GP visits compared to the model result of 1,275 visits. Again the model result will not be as precise as the estimation, due to the rounding effect in the process. Figure 5.8 displays the testing results for the mild model.

The testing for the moderate model was similar. Another extreme value testing was conducted for 0% service coverage. The expectation from running the model with 0% coverage is that no one will enter the SD model for the whole duration of the testing. This was confirmed by the observations during the model run for all the three sub models.

5.5.3 Testing the construction of the hybrid model

The aim of this testing is to investigate the appropriate construction of the hybrid model. The combined model has several points of connections between the Agent Based and the System Dynamics models. The nature of the connections between the two models captures the dependency between the models. These connection points facilitate the testing procedure whether the two models indeed communicate during the simulation run by exchanging information.

The prevalence of depression (for each category of severity) in the AB model is used to generate demand for the SD model. This demand is updated each week and sequentially the SD model computes the rate of people entering the service. Since the rate is defined to be the key element in determining the size of demand entering the service, this process yields two rates; one for entering the system of care and the other for not entering the system.

The two rates will then be fed back to the AB model to be used as the transition rates from being recognised states (mild, moderate, or severe) to the state whether being in treatment or not treated. This construction necessitates testing the model which gives intuitive results, hence it requires setting up scenarios with extreme values. We used two values which represent the service coverage in the SD model. The first value is 0% coverage of service. This means that, if the construction of the model is correct and whatever the size of the demand from AB model is, we expect no one will enter the service. As a consequence, the transition rates (in AB model) for entering and not treated will be 0% and 100% respectively. The vice inverse should work with the 100% treatment coverage.

The transitions which were set to follow the exponential distribution with the rates from the SD model worked well with the AB part. However, when we compared the result from the AB to the SD part, we did not get the equivalent number of people. Our investigation identified that the construction using 'rate transition' on the AB part did not give the correct number of people who needed the service in the next time step. This stochastic transition seems to be the cause of the problem. The number of people entering the system or not entering the system, generated by SD part, was used as a mean for the exponential distribution. As a consequence, the actual number of people moved to being in treatment or not treatment could be higher or lower than the actual number generated by the SD model.

To remedy this issue, we changed the transition type in the AB part. Rather than using the 'rate transition', we used transition triggered by message instead. The number of people generated by SD was used to generate the number of messages received by people in AB. The messages are of two types, 'being treated' and 'not treated'. This set up ensures the number of people moving to being in treatment in the AB part is equal to the number of people entering the system in the SD part. Analogously, the number of people entering the state of not in treatment in the AB model will be equal to the number of people not entering the system generated in the SD model.

The transition triggered by message requires additional control at each time unit. This control is set up using an event which is updated at each time unit. Within this event, it is required to write a simple loop control for sending the message to the statechart. The message is set up in random to reflect that anyone with the condition can receive the message. Although the transition using message controls the number of people discretely, the randomness of the result is reflected by the random delivery of the message.

This type of transition improved the performance of the simulation, i.e. the comparison number of people entering or not entering the treatment in the AB model is close to the number of people entering or not entering the system in the SD. It reduces the discrepancy of the total counts from each sub model. The discrepancy of the counts due to the time in running the model and the fact that, at the end of simulation time, there are some transitions which have not been made or the information of number of people from the AB to the SD part has not been calculated in the flow for entering the service.

In order to check the values, we created datasets for each category in each model. The datasets were intended to store the value at each time step. The observations were conducted during the experimentation run as well as at the end of the simulation run, to capture any unexpected values stored in each dataset.

Table 5.10 summarises the results from testing the connection of the Agent Based and the System Dynamics models using the set up explained in the previous paragraphs. As expected with 0% service coverage, the proportion of people getting treated in the AB model is 0% across the severity levels. These results also similar to the one generated by the SD model. Similarly, for the service coverage of 100%, as expected, all people with mild and moderate depression finally made transition to being in the treatment state.

Table 5.10: Results from testing the connection between AB and SD model

Treatment Coverage	Model	Treated Mild	Treated Moderate	Treated Severe	Untreated Mild	Untreated Moderate	Untreated Severe
0%	AB	0%	0%	0%	237(100%)	310(100%)	259(100%)
0%	SD	0%	0%	0%	237(100%)	310(100%)	259(100%)
100%	AB	244(100%)	347(100%)	264(100%)	0%	0%	0%
100%	SD	244(100%)	347(100%)	264(100%)	0%	0%	0%

The percentages were computed against the prevalence of each category.
The difference between the prevalence for each category in 0% and 100% coverage due to the random effect of the experiment run.

Corresponding values from the AB model displayed in table 5.10 include the values from a lagged week which were produced in the SD model. In other words, the SD model will have values a week ahead of AB for the values related to whether being in treatment or not. This also confirmed the scheduling process in the design of the interface between the two models.

5.6 Conclusions

We have described two main points in this chapter: the parameters and the model testing. The developed model has two types of parameters: the parameters related to the Agent Based model, and the parameters related to System Dynamics model. Since it is not possible to obtain all the parameters from a single dataset, we utilised different resources.

We consulted websites such as official government websites (StatsWales and the Office for National Statistics), and other personal websites belonging to medical experts such as QOF database. In general, data from these websites are classified by individuals' characteristics and disease types. The data are also broken down to different Local Health Boards.

The limitation of the data obtained from a website is not comprehensive enough to generate more detailed information, such as the disease progression. Whilst the parameters needed for the Agent Based model, are mostly related to how depression progresses in relation to receiving treatment. This necessitates us to consult existing literature, either on epidemiology or treatment recommendation.

In the absent of detailed medical data, longitudinal population based studies are an ideal source of information for disease progression. However, to our knowledge, there is no such study produced in the context of population in the UK let alone in Wales. For this reason, we used results from existing population based studies done in other context.

As for the model testing, we conducted in three phases. The testing for the Agent-Based model, System Dynamics model, and the combination of the two models. The combined model necessitates us to test the connection points between AB and SD models. As part of the model testing, we also presented the model and the preliminary results to the experts. The presentation also aimed to gain validation for the structure of the model.

Chapter 6

Results from the Simulation Study

6.1 Introduction

We run the experimentation using the parameter settings as outlined in Chapter 5 and have a model run-time as summarised in Table D.1 in Appendix D. This experimentation has three scenarios representing different service coverage which, in the analysis, are discussed together. The different percentages of service coverage used in the experimentation were 47%, 65% and 80%, which were adapted from the statement by NICE (2015). Although the study in NICE (2015) only mentioned mild and moderate types of depression, for the purpose of our study, we also used the percentages for severe cases. We set 47% service coverage as the baseline scenario in this regard.

The model was run with different service coverage for four main purposes. The first purpose is to get the prevalence of depression at different severity levels. Although the setting of the experimentation was random, i.e. each simulation run was stochastic, we expected that the model should yield relatively consistent results across the different service settings. This is due to the fact that prevalence results, which were generated by the Agent Based model, were recorded at the starting point of the creation of the patients, and hence should not be affected by different service coverage.

The second purpose is to find out the effect of the different service coverage on the progression of depression. The model captures two different types of disease progression; the progression from mild to moderate depression and the progression from moderate to severe depression. We expect that the higher the service coverage, the slower the progression of depression, which logically means that the more people are getting treatment, the better it is for their condition.

The third purpose is to monitor the effect of different service coverage on the prevalence of relapse cases in each of the severity levels. The model was designed to allow relapse cases to occur either from the condition which is being treated or not treated. Despite this setting, we expect that the more people with depression that get treated, the less the occurrence of relapse cases from the condition would be.

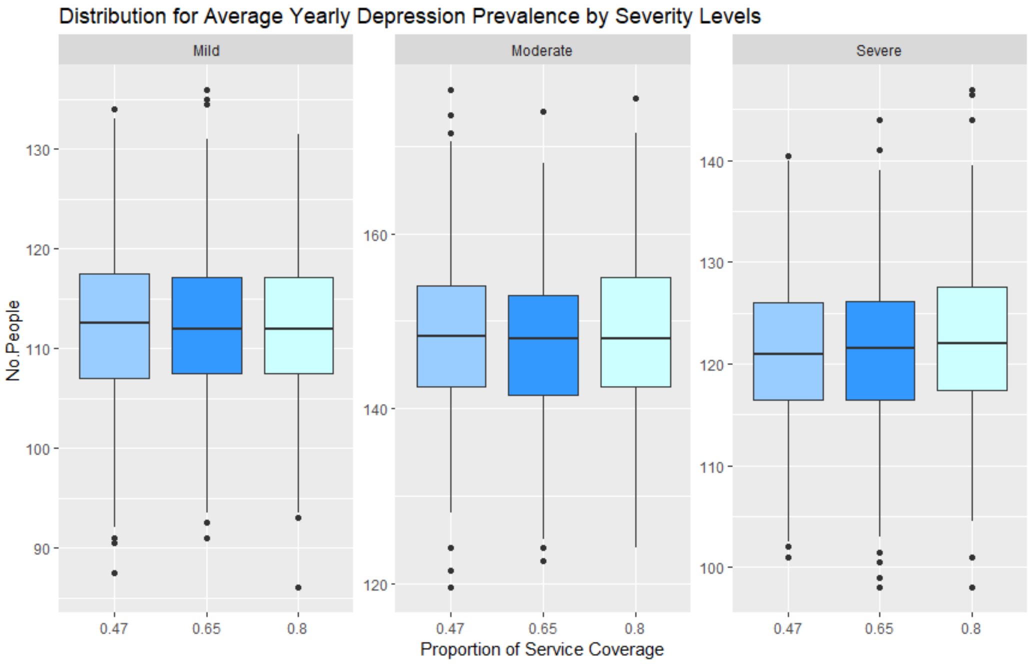
The fourth purpose is to estimate the burden of depression. We will evaluate the healthcare costs and the disability adjusted life years (DALYs) associated with the prevalence of depression and the service use generated by the model. The discussion will compare the service costs of the different levels of service coverage and find out which service is affected by the different coverage. By evaluating the associated health service costs against the different levels of service coverage, we can find the best strategy for the mental health care service.

6.2 Model performance indicators

6.2.1 Estimating the population with depression

The first purpose is concerned with estimating the depression prevalence by severity level. Figure 6.1 summarises the prevalence of depression by different service coverage and severity levels. The figure highlights that the medians for each severity are relatively consistent across the different service coverages. The results were also analysed using 95% confidence intervals which are displayed in Table 6.1.

FIGURE 6.1: Distribution of depression prevalence by service coverage



In order to find out whether there is any difference between the service coverage across different severities, we conducted Levene's test for equal variance and Shapiro-Wilk for the normality test. The assumption for normal distribution and equal variance which are required for conducting the ANOVA test are provided in Table A.1 in Appendix A. The results indicate that normality and equal variance tests are not significant. Based on these results, we performed ANOVA to test whether the means in each different service coverage are different for each level of depression severity. The results indicate that there is not enough evidence to conclude that the mean prevalence for each severity are different. This confirms the stability of the results generated by the model despite using random setting.

Table 6.1 presents the model output for the average yearly mean prevalence for mild, moderate and severe depression.

Table 6.1: Average depression prevalence by severity and service coverage

	Prevalence		
Service Coverage	Mild Mean (95% CI)	Moderate Mean (95% CI)	Severe Mean (95% CI)
45%	112.34 (111.65 , 113.02)	148.36 (147.60 , 149.12)	121.03 (120.38 , 121.67)
65%	112.34 (111.68 , 113.00)	147.85 (147.12 , 148.58)	121.41 (120.75 , 122.08)
80%	112.36 (111.74 , 112.98)	148.75 (147.98 , 149.53)	122.24 (121.57 , 122.91)

Projecting the prevalence rate generated by the model to the population of Wales gives an indication of the number of people in Wales affected by depression. Table 6.2 provides tabulation of prevalence by Wales Local Health Boards. The minimum estimate is the typical minimum value generated from the simulation runs, and analogously with the maximum value.

The projection shows that Betsi Cadwaladr health board has the highest estimate for the number of people with depression. The statistical data from multiple health boards, shown in Table 5.3, reveal that Aneurin Bevan health board has the highest number of patients suffering from depression. Cardiff and Vale health board has the next highest number of patients with depression, followed by Betsi Cadwaladr. This is not surprising as we just scaled the simulation results based on the population size of the health board. The higher the population size, the higher the estimate for the number of people with depression.

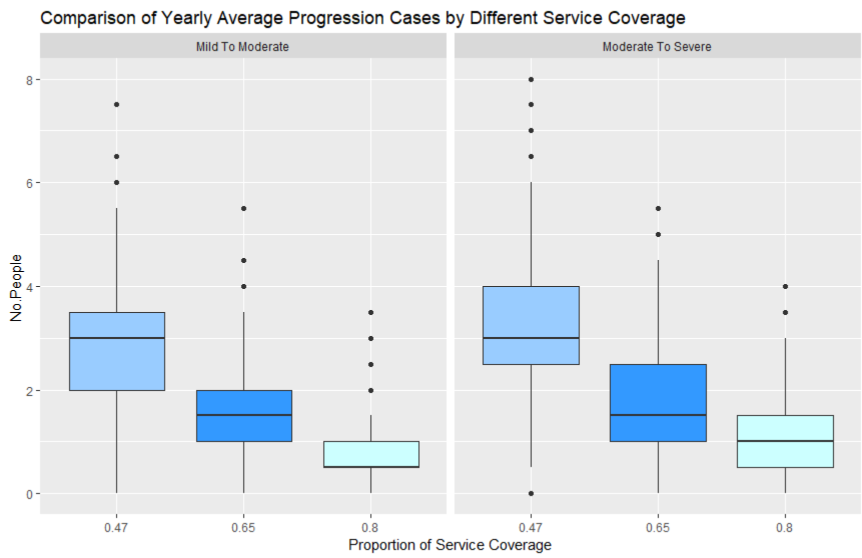
TABLE 6.2: Depression prevalence projected to population in Wales by LHB

Context	Population size	min	median	max
Model	5,000	304	393	500
Aneurin Bevan	476,139	28,902	37,377	47,614
Betsi Cadwaladr	571,244	34,675	44,843	57,124
Powys	111,070	6,742	8,719	11,107
Hywel Dda	318,593	19,339	25,010	31,859
Abertawe Bro Morgannwg	437,054	26,529	34,309	43,705
Cwm Taf	242,199	14,701	19,013	24,220
Cardiff and Vale	399,772	24,266	31,382	39,977

Results are typical 1 year prevalence.

The developed model also gives prevalence on the progression from mild to moderate and from moderate to severe. Figure 6.2 provides the distribution of the progression by different service coverage. The trend shows that the higher the service coverage the better the outcome. In other words for people with depression who receive treatment the possibility of their condition progressing to a worse condition is reduced.

FIGURE 6.2: Distribution of depression progression by service coverage



The interquartile range for the number of occurrences of the progression from mild to moderate has less spread compared to the interquartile range from moderate to severe, for a service coverage of 65% and 80%. Although the median occurrences for 47% service coverage shows similar values in both types of progression, the first quartile and third quartile of moderate to severe progression shows higher values compared to mild to moderate progression.

TABLE 6.3: Average progression cases by severity and service coverage

	Progression	
Service Coverage	Mild to Moderate Mean (95% CI)	Moderate to Severe Mean (95% CI)
47%	2.81 (2.70 , 2.92)	3.32 (3.21 , 3.44)
65%	1.53 (1.45 , 1.61)	1.79 (1.71 , 1.87)
80%	0.89 (0.76 , 0.87)	1.07 (1.00 , 1.23)

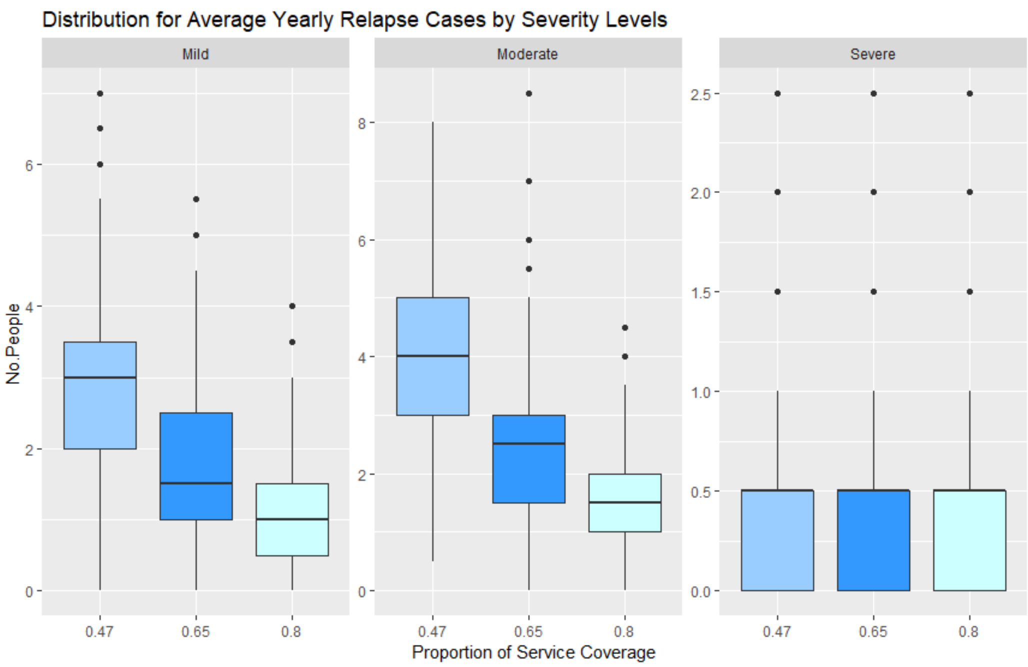
We conducted tests to find out if there is any difference between the service coverage with respect to depression progression. The assumptions on normality and equal variance, on progression data, were tested and the results can be seen in Table A.3 and Table A.4 in Appendix A. Both normality and equal variance tests indicate significant p-values which implies that the means are different across different service coverage.

Since the assumptions for conducting a parametric test are violated, we performed a non-parametric test, the Kruskal-Wallis sum rank test. This test does not require an assumption that the data comes from a normal distribution. The results indicate that the progression from mild to moderate and from moderate to severe are significant with p-values < 0.0001 in both cases. This implies that at least one of the medians for depression progression, across the different service coverage, is not equal. The test results are summarised in Table A.5 in Appendix A. It is suggested that the level of service coverage may affect the frequency of progression of depression.

Based on the results from the Kruskal-Wallis test, we performed a posthoc multiple comparison of means to find out which of the service coverage is different at 99% confidence level. The results can be found in Table A.6 in Appendix A. All pairwise comparisons show true values confirming the difference between tested groups. This indicates that the median occurrences for depression progression, in both types of progression, are different across all three different service coverages.

Moving on to the third purpose, we investigated the effect of different service coverage to the number of relapse cases. Figure 6.3 presents the distribution of relapse cases from three different service coverages by different levels of depression severity. Across the different service coverage, mild and moderate depression have a similar trend which indicates a relationship between the service coverage and the number of people experiencing a relapse. It seems that the higher the service coverage the less the frequency of occurrence of a relapse. This implication does not seem to apply to the severe cases where the boxplot shows similar figures across the three different service levels.

FIGURE 6.3: Distribution of relapse cases by service coverage



The results were analysed further and Table 6.4 summarises the mean relapse cases for each different service coverage by severity levels with their corresponding 95%

confidence interval.

Table 6.4: Average relapse cases by severity and service coverage

	Relapse Cases		
Service Coverage	Mild Mean (95% CI)	Moderate Mean (95% CI)	Severe Mean (95% CI)
45%	2.90 (2.79 , 3.01)	3.92 (3.79 , 4.05)	0.44 (0.40 , 0.49)
65%	1.71 (1.62 , 1.79)	2.47 (2.37 , 2.57)	0.42 (0.38 , 0.46)
80%	1.15 (1.08 , 1.22)	1.63 (1.55 , 1.71)	0.40 (0.36 , 0.44)

The normality and equal variance assumption for conducting ANOVA are somehow violated. The Levene's test for equal variance only suggests that in severe cases the variances are equal across the service coverage (p-value 0.6367). The mild and moderate cases both have p-values less than 0.001, which indicates some violation in the homogeneity of variance assumption.

For the above reasons, a non-parametric test was also conducted for the different severities of depression. The Kruskal-Wallis rank sum test gave a p-value for mild and moderate at less than 0.001, and for severe at 0.2148. Again, only on severe cases we can say that there is not enough evidence to suggest that the medians of relapse cases are different across different service coverage. A summary for the tests is provided in Table A.7 and Table A.8 in AppendixA.

In order to find out which pair of service coverages has different means on relapse cases, we conducted a posthoc multiple comparison of means with 99% confidence level. The results showed that the medians are different for all possible pair combinations of service coverage in mild and moderate cases. However, this is not so for severe cases. All possible pairwise comparisons in severe cases revealed no difference. The results from this test can be seen in Table A.9 in Appendix A.

6.2.2 Estimating the service needs

The mental health services captured in the simulation model comprises GP, Psychological Therapy, Medication, Psychiatrist, Community Mental Health Team, Crisis Resolution Home Treatment Team, and Inpatient facility. Medication and CRHTT have the number of people affected by depression as their unit of measure. The inpatient facility has the number of weeks as the unit of measure. Whilst other services have the total number of visits as their unit of measure.

A typical simulation result on service use is described in Table 6.5 and Table 6.6. All results are presented as yearly average with their 95% confidence intervals. Across the seven different services, apart from the inpatient service, there is a tendency for a higher service coverage to be associated with a higher service use to some degree.

Table 6.5: Typical simulation results for mental health service use with different service coverage.

Service Coverage	Average prevalence Mean (95%CI)	GP (visits) Mean (95%CI)	Psych. Therapy (visits) Mean (95%CI)	Medication (people) Mean (95%CI)
47%	381.72 (380.51 , 382.93)	1031.11 (1026.02 , 1036.20)	180.09 (179.28 , 180.97)	58.45 (58.16 , 58.74)
65%	381.60 (380.44 , 382.75)	1746.90 (1740.51 , 1753.29)	301.80 (300.73 , 302.87)	99.21 (98.84 , 99.58)
80%	383.35 (382.22 , 384.48)	2105.07 (2097.72 , 2112.41)	363.55 (362.32 , 364.77)	119.58 (119.16 , 120.00)

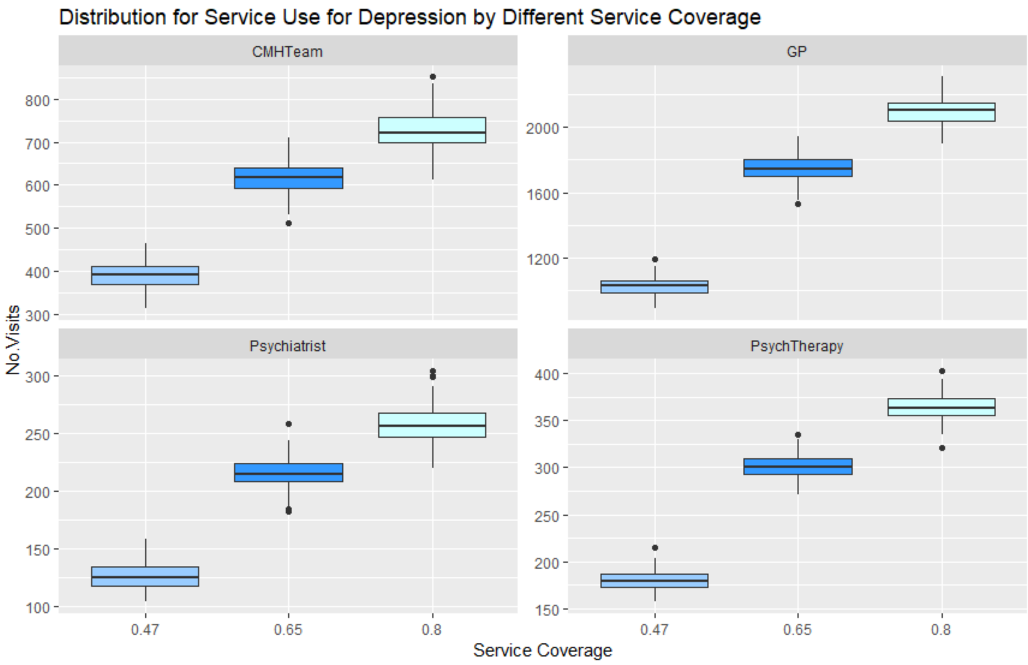
Table 6.6: Typical simulation results for mental health service use with different service coverage.

Service Coverage	Psychiatrist (visits) Mean (95%CI)	CMHTeam (visits) Mean (95%CI)	CRHTT (people) Mean (95%CI)	Inpatient (weeks) Mean (95%CI)
47%	126.97 (126.02 , 127.91)	387.06 (384.27 , 389.85)	82.63 (82.18 , 83.09)	75.90 (76.42 , 77.38)
65%	216.23 (215.06 , 217.40)	615.66 (612.12 , 619.20)	92.94 (92.44 , 93.43)	58.61 (58.15 , 59.08)
80%	260.04 (258.62 , 261.45)	722.81 (718.60 , 727.02)	93.54 (92.99 , 94.10)	43.05 (42.58 , 43.51)

Figure 6.4, Figure 6.5 and Figure 6.6 present the distribution of service use for different services where the trend is captured visually based on the service coverage.

The Levene's test for equal variance and the Shapiro-Wilk test for normality reveals that across different service coverage, for each service type, are very significant. This implies that the groups in the data across the different services have a different variance and do not come from normal distribution. The results from the test can be found in Table B.1 in Appendix B.

FIGURE 6.4: Distribution of the service use based on baseline parameters



Based on normality and equal variance tests, we conducted a non parametric test to find out whether there is any difference in the medians between the groups in the service use data. The results indicated that the medians across the different levels of service coverage are different in each service type. Table B.2 in Appendix B summarises the non-parametric tests.

FIGURE 6.5: Distribution of the service use based on baseline parameters

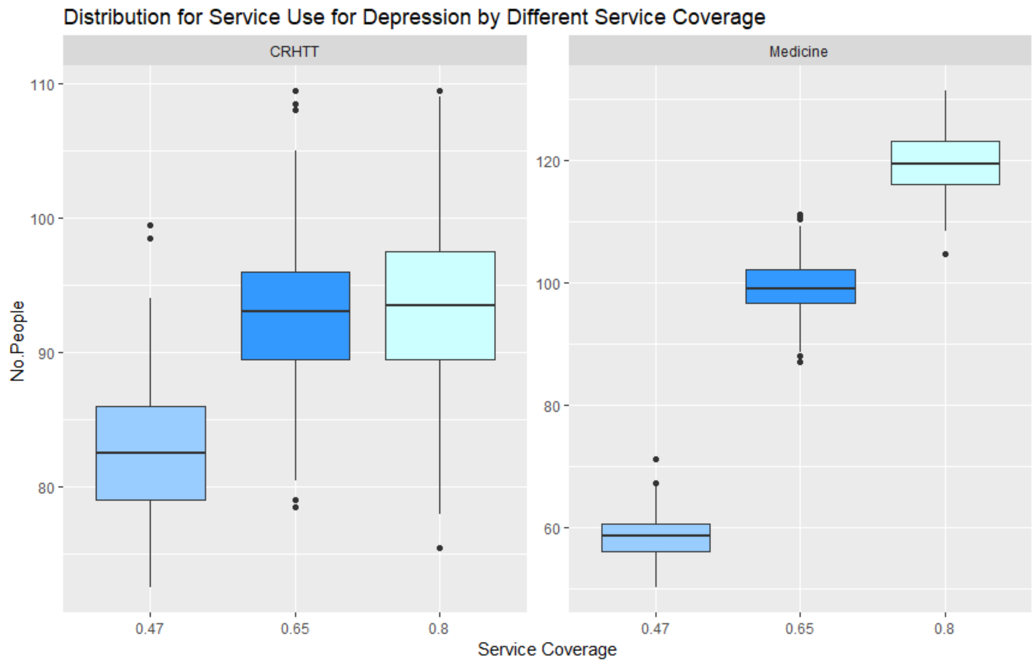
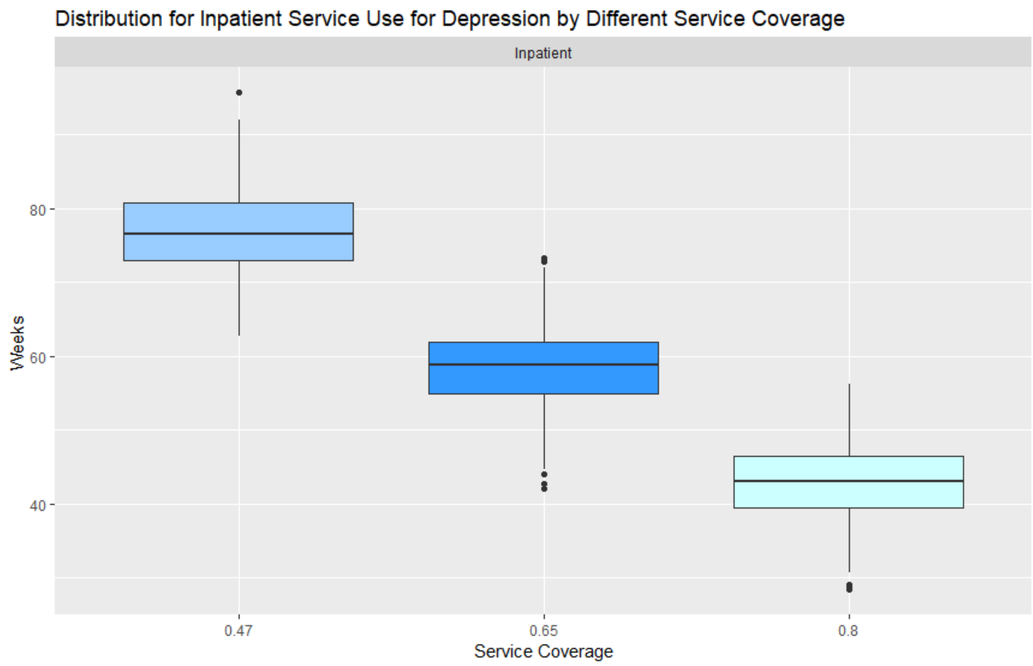


FIGURE 6.6: Distribution of the service use based on baseline parameters



The comparison test for service use was conducted on every service type to investigate which level of service coverage had different medians. The results revealed that all but one pair of service coverage (65% and 80%) in the Community Resolution Home Treatment Team (CRHTT) show a difference in medians. This implies that the level of service coverage may lead to different volumes of service use.

The pattern we see from the boxplots in Figure 6.4 and Figure 6.5 indicates that an increase in the service use relates to an increase in the service coverage. The reverse trend is observed in Figure 6.6 where inpatient care reduces with an increase in service coverage. The next subsection investigates the impact of the different service coverage on healthcare costs related to depression.

6.2.3 Estimating the costs of mental health services

The total Welsh government expenditure for health and social care during 2017-18 was estimated at £6,534,940,000 of which 11.4% was contributed to mental health illnesses (StatsWales (2018f)). The cost related to mental health problems has increased from year to year (4.77% from 2016-17 to 2017-18) and it was estimated as the biggest proportion in health and social care expenditure.

The total cost per head for mental health problems varied from one local health board to another. However, StatsWales (2018f) estimated the cost per head during 2017-18 as £238.8. The cost was divided into the cost per head for the primary service (£22.02), the cost for the secondary service (£215.83), and other costs (£0.93).

Table 6.7 summarises the NHS expenditure for mental health care in Wales local health boards. The expenditure includes costs incurred in both primary and secondary services. The data source categorises the expenditure into general mental illness, mental illness affected by the elderly population, mental illness affected by children and adolescents, and other mental illnesses. There is no specific category for depression. However, since depression is a common mental health condition, we can assume that it comes under the general mental illness category.

Studies that have attempted to estimate the cost associated with mental health care have measured the cost using different measurements. An example is a study

Table 6.7: NHS expenditure for mental health care in Wales 2017-2018 (£000).

Wales Local Health Board	General Mental illness	Elderly Mental illness	C&A[1] MH service	Other Mental illness	Total costs
Aneurin Bevan	54,194	41,123	8,417	19,805	123,539
Betsi Cadwaladr	76,102	55,988	19,569	19,215	170,873
Powys	7,072	11,298	1,091	23,024	42,485
Hywel Dda	39,974	24,174	6,574	13,033	83,754
Abertawe Bro Morgannwg	56,350	44,868	5,472	23,862	130,552
Cwm Taf	47,240	21,391	4,901	6,070	79,602
Cardiff and Vale	57,554	32,852	6,273	18,764	115,444
Average costs per LHB	48,355.14	33,099.14	7471	17681.86	106,607

[1] Child and Adolescent
Data source (StatsWales (2018f)

done by King's Fund (2008) which estimated the cost into two separate estimates: the service cost, and the total cost. The authors explained that the service cost included all costs related to the service use, such as the direct healthcare cost, the social service, and the justice system. Whereas the total cost comprised the service cost and the cost associated with loss of employment. The authors used the prevalence of mental health as their estimate for the service need.

During 2007, the King's Fund (2008) study estimated that for those affected by depression, the average service cost was £2,085.00; the cost associated with loss of employment was estimated as £7,226.00; the total average cost was £9,311.00. The report stated that the cost associated with a medication course for a year was £56.34 per individual affected by depression. We use this estimate for our cost estimation related to medication.

The National Institute for Health and Care Excellent has produced a report statement for quality of framework related to the implication of depression and anxiety in the health services. The report from NICE (2015) states that the estimate used the incident cases for those affected in England during 2013/14. Of the total eligible population affected by depression and anxiety, only 47% were offered referrals for mental health services. However, only 67% of those offered referrals proceeded to receive intervention (where 60% of those received a low-intensity psychological treatment and 40% received a high-intensity psychological intervention).

The report from NICE (2015) also detailed the costs used in the study. The

GP cost was estimated as an additional 5 minutes consultation from the usual time. The cost was £14.50 per individual assessed irrespective of whether the individual was offered the psychological intervention or not. The cost related to the psychological intervention was estimated as £45.00 and £1,125.00 per person for low-intensity and high-intensity intervention respectively.

The NICE report indicated that an increase in the coverage of the service for those affected by depression and anxiety would have an impact on the service cost. This is particularly so when high-intensity psychological intervention is offered. The authors estimated that for those affected by anxiety, the cost for cognitive behavioural therapy was as high as £2000.00 per person per year.

The result of service cost estimates from studies such as King's Fund (2008) and NICE (2015) give us overall estimates for those affected by depression and/or anxiety. These studies neither separated the mental health service used in more detail such as those associated with the professional (psychologist or psychiatrist), nor separated the depression condition into different levels of severity. In order to help us with generating an estimate of service cost, we consulted a report on the unit cost for health and social care done by Curtis and Burns (2017). This report did not separate the cost based on severity of depression, however, it gave more detail on the breakdown of the health service types.

Table 6.8 gives details of the service costs quoted from Curtis and Burns (2017). It presents general highlights on the service types involved in mental health care as well as the estimated costs. The costs listed in Curtis and Burns (2017) are more comprehensive with a variation in costs. This variation is due to whether the calculation included carbon emissions, whether the professional possessed qualifications for dealing with mental health conditions, and depends on the age classification of the affected individual.

For the purpose of our study, we used the costs associated with GP, CMHT, CBT, MH service (inpatient), Psychologist, and Psychiatrist. The cost for having the course of medication (£56.34 per individual per year) was quoted from King's

Table 6.8: List of service costs for mental health care

Service types	Costs	Description
Community services		
GP	£38.00	per contact
CMHT	£197.00	average cost per contact
CMHT	£248.00	median average per contact
Assertive Outreach Team	£132.00	average cost per team contact
Early Intervention Team	£184.00	average cost per team contact
Behavioural Activation	£17.00	per session per person
CBT	£100.00	per session (CAMHT)
Mental Health services		
MH care cluster	£407.00	per bed day
MH care cluster (initial assessment)	£319.00	per bed day
Secure MH service	£545.00	per bed day
Low-level secure service	£443.00	per bed day
Medium-level secure service	£515.00	per bed day
Psychiatrist	£108.00	per hour
Clinical Psychologist	£55.00	per hour

Source Curtis and Burns (2017)

Fund (2008). This cost is inflated to reflect the 2018 value to be £73.84 (see Appendix C for details).

Table 6.9 provides an estimate on the impact of depression on the cost of health services. The results were computed from the average yearly use of services generated from the model based on a population size of 5000. In order to reflect the population size of ABUHB, we used the adult population in the health board (476,139) and factorised the calculation accordingly.

The model gave estimates for the prevalence and the service use for each type of service. The service coverage was varied to cover 47%, 65% and 80% and the estimated costs were evaluated for each service as well as for the Aneurin Bevan University Health Board. The values for different service coverage were quoted from the report done by NICE (2015). The report estimated that around 47.2% of people suffering with mild or moderate depression were offered further psychological intervention, but only 67% took up the referral. The study also ran the scenario for increasing the service coverage to 65% and 80%, hence the two values were also used in this study.

Table 6.9 summarises the results from running the model using the baseline parameters set-up and the different scenarios for the service coverage. The three scenarios yielded a similar average yearly depression prevalence. This makes the comparison of different service coverage comprehensible.

The increase in service coverage generated an increase in costs for each service except the inpatient service (highlighted in red). The increase in costs is due to the fact that an increase in service coverage means that the number of individuals accessing the service, and accordingly the number of visits to the service, are also increased.

The recommendation in Andrews, G. and the TOLKIEN II Team (2006) suggested providing care in the outpatient service and reducing the use of inpatient care. This is reflected in the results for inpatient service use. An increase in the service coverage reduced the use of inpatient care. The model suggested that the majority of people with depression were cared for outside the inpatient unit. Considering that inpatient care is the most expensive type of care, the results show one potential saving for the health system.

Looking at the grand total of the costs, it seems that there is not much difference between 65% and 80% service coverage. Although the overall trend shows that an increase in the service coverage could increase the total care costs, it seems that 80% service coverage offers better value. This is understandable, since the increase in service means a reduction of the inpatient use by severe cases.

The results from the model were also used to estimate costs for all other local health boards in Wales. Table 6.10, Table 6.11 and Table 6.12 summarise the estimated care costs for all local health boards in Wales. The biggest care costs for mental health related to depression, suggested by the model, related to the health board with the largest population. Aneurin Bevan Health Board comes the second highest spender. Whereas Powys Teaching University Health Board, which caters for the smallest number population, spent the smallest costs.

Table 6.9: Estimation for service costs for depression

Service Coverage (%)	Description	N	GP	Medication	Psychological Therapy	Psychiatrist	Inpatient	CMHTeam	Grand Total (£)
	Total prevalence	382							
	Cost (Average £)		38.00	73.84	55.00	108.00	407.00	197.00	
47%	Service use		1,031	58	180	127	531	387	
	Costs(£; pop size 5000)		39,182.18	4,315.95	9,904.95	13,712.76	216,239.10	76,250.82	359,605.76
	Costs(£; ABUHB adults 476,139)		3,731,319.00	411,007.73	943,248.39	1,305,866.13	20,592,449.49	7,261,365.59	34,245,256.33
	Total prevalence	382							
	Cost (Average in £)		38.00	73.84	55.00	108.00	407.00	197.00	
65%	Service use		1,747	99	302	216	410	616	
	Costs(in £; pop size 5000)		66,382.20	7,325.67	16,599.00	23,352.84	166,979.89	121,285.02	401,924.62
	Costs(in £; ABUHB adults 476,139)		6,321,576.91	697,623.21	1,580,722.77	2,223,890.95	15,901,494.92	11,549,972.45	38,275,281.22
	Total prevalence	383							
	Cost (Average in £)		38.00	73.84	55.00	108.00	407.00	197.00	
80%	Service use		2,105	120	364	260	301	723	
	Costs(in £; pop size 5000)		79,992.66	8,829.79	19,995.25	28,084.32	122,649.45	142,393.57	401,945.04
	Costs(in £; ABUHB adults 476,139)		7,617,701.01	840,860.64	1,904,147.66	2,674,469.79	11,679,907.12	13,560,139.67	38,277,225.89

The model was run with a population size of 5000; time frame 2 years; random seed.
The results are averaged for yearly costs.
The CRHTT was not included in the evaluation due to difficulty of getting the reference for the yearly costs of individuals having contact with the CRHTT.

Table 6.10: Estimated health service costs for depression with 47% service coverage by Wales local health board

Service Coverage (%)	Wales Local Health Board	Population size (adults)	GP (£)	Medication (£)	Psychological Therapy (£)	Psychiatrist (£)	Inpatient (£)	CMHTeam (£)	Grand total per HB (£)
	Model	5,000	39,182.18	4,315.95	9,904.95	13,712.76	216,239.10	76,250.82	359,605.76
	Aneurin Bevan	476,139	3,731,232.80	410,998.23	943,226.60	1,305,835.97	20,591,973.77	7,261,197.84	34,244,465.20
	Betsi Cadwaladr	571,244	4,476,517.05	493,091.88	1,131,628.65	1,566,666.37	24,705,057.69	8,711,564.68	41,084,526.32
	Powys	111,070	870,392.95	95,874.47	220,028.56	304,615.25	4,803,535.37	1,693,835.72	7,988,282.31
47%	Hywel Dda	318,593	2,496,633.65	275,006.16	631,129.55	873,757.87	13,778,452.72	4,858,595.50	22,913,575.45
	Abertawe Bro Morgannwg	437,054	3,424,945.70	377,260.47	865,799.60	1,198,643.32	18,901,632.72	6,665,145.18	31,433,426.99
	Cwm Taf	242,199	1,897,976.96	209,063.66	479,793.80	664,243.35	10,474,578.76	3,693,574.47	17,419,231.00
	Cardiff and Vale	399,772	3,132,787.69	345,079.03	791,944.33	1,096,395.50	17,289,267.50	6,096,588.56	28,752,062.62
	Grand total per service (£)		20,030,486.80	2,206,373.90	5,063,551.09	7,010,157.63	110,544,498.52	38,980,501.95	183,835,569.89

Table 6.11: Estimated health service costs for depression with 65% service coverage by Wales local health board

Service Coverage (%)	Wales Local Health Board	Population size (adults)	GP (£)	Medication (£)	Psychological Therapy (£)	Psychiatrist (£)	Inpatient (£)	CMHTeam (£)	Grand total per HB (£)
	Model	5,000	66,382.20	7,325.67	16,599.00	23,352.84	166,979.89	121,285.02	401,924.62
	Aneurin Bevan	476,139	6,321,430.87	697,607.09	1,580,686.25	2,223,839.58	15,901,127.57	11,549,705.63	38,274,396.99
	Betsi Cadwaladr	571,244	7,584,086.69	836,948.60	1,896,415.83	2,668,033.95	19,077,252.06	13,856,667.99	45,919,405.11
	Powys	111,070	1,474,614.19	162,732.35	368,730.19	518,759.99	3,709,291.28	2,694,225.43	8,928,353.43
65%	Hywel Dda	318,593	4,229,780.85	466,781.21	1,057,665.04	1,488,010.27	10,639,724.82	7,728,111.68	25,610,073.86
	Abertawe Bro Morgannwg	437,054	5,802,521.21	640,342.36	1,450,931.87	2,041,290.43	14,595,845.77	10,601,620.63	35,132,552.26
	Cwm taf	242,199	3,215,540.49	354,853.82	804,052.24	1,131,206.90	8,088,472.48	5,875,022.11	19,469,148.03
	Cardiff and Vale	399,772	5,307,548.97	585,719.26	1,327,163.09	1,867,162.31	13,350,776.92	9,697,271.00	32,135,641.55
	Grand total per service (£)		33,935,523.27	3,744,984.69	8,485,644.51	11,938,303.42	85,362,490.88	62,002,624.47	205,469,571.23

Table 6.12: Estimated health service costs for depression with 80% service coverage by Wales local health board

Service Coverage (%)	Wales Local Health Board	Population size (adults)	GP (£)	Medication (£)	Psychological Therapy (£)	Psychiatrist (£)	Inpatient (£)	CMHTeam (£)	Grand total per HB (£)
	Model	5,000	79,992.66	8,829.79	19,995.25	28,084.32	122,649.45	142,393.57	401,945.04
	Aneurin Bevan	476,139	7,617,525.03	840,841.21	1,904,103.67	2,674,408.01	11,679,637.29	13,559,826.41	38,276,341.61
	Betsi Cadwaladr	571,244	9,139,065.41	1,008,792.59	2,284,433.32	3,208,599.86	14,012,552.48	16,268,294.50	45,921,738.17
	Powys	111,070	1,776,956.95	196,144.89	444,174.48	623,865.08	2,724,534.88	3,163,130.76	8,928,807.06
80%	Hywel Dda	318,593	5,097,020.31	562,621.68	1,274,069.34	1,789,493.55	7,815,051.24	9,073,118.93	25,611,375.05
	Abertawe Bro Morgannwg	437,054	6,992,222.40	771,818.76	1,747,800.80	2,454,872.88	10,720,886.54	12,446,735.87	35,134,337.26
	Cwm taf	242,199	3,874,828.45	427,713.13	968,565.91	1,360,398.84	5,941,114.83	6,897,516.05	19,470,137.21
	Cardiff and Vale	399,772	6,395,765.13	705,980.34	1,598,708.22	2,245,464.96	9,806,363.19	11,384,992.45	32,137,274.28
	Grand total per service (£)		40,893,383.69	4,513,912.60	10,221,855.73	14,357,103.18	62,700,140.46	72,793,614.97	205,480,010.64

6.2.4 Estimating the burden of depression using DALYs

Disability Adjusted Life Years (DALYs) has been used as a metric to measure the burden of disease. Essentially the current study uses the prevalence cases for every severity of depression and the disability weights associated to each severity, see more description in Appendix C. The disability weights used are based on the finding in Salomon et al. (2015). The study estimated the disability weight for mild, moderate, and severe depressive disorders as 0.145, 0.396 and 0.658 respectively.

Table 6.13 presents the number of untreated depression categorised by the level of severity and different service coverage. The results generated by the model are projected to the population under Aneurin Bevan Local Health Board. The results indicate that for 1 year prevalence, the typical number of depression prevalence tends to decrease as the service coverage increases.

TABLE 6.13: Number of untreated depression by different service coverage

Severity	Population size	Service coverage		
		47%	65%	80%
Mild		70	37	20
Moderate		90	51	29
Severe		75	41	22
Total model	5,000	235	129	71
ABUHB	476,139	22,371	12,253	6,729

Results are typical 1 year prevalence.

Table 6.14 presents the burden of depression by different severity levels and projected to the population in Aneurin Bevan University Health Board. The results indicate that as depression severity increases, so does the number of years lived with disability. However, with an increase in service coverage the burden of years lived with disability tends to reduce.

Table 6.14: DALYs counts

Severity	Population size	Disability weight	Service coverage		
			47%	65%	80%
Mild		0.145	10	5	3
Moderate		0.396	36	20	11
Severe		0.658	49	27	15
Total model	5,000		95	52	29
ABUHB	476,139		9,060	4,969	2,740

Results are typical 1 year prevalence.

Finally, Table 6.15 presents DALYs averted if the service coverage is increased from one level to another using the current settings of parameters. It shows the benefit of offering a healthcare service to cover more people with depression.

Table 6.15: DALYs averted

Severity	Population size	Service coverage		
		47% to 65%	65% to 80%	47% to 80%
Mild		5	3	7
Moderate		16	9	24
Severe		23	12	35
Total model	5,000	43	23	66
ABUHB	476,139	4,091	2,229	6,320

Results are typical 1 year prevalence.

6.3 Conclusions

We have seen from this chapter how the developed hybrid model of System Dynamics and Agent Based was used. The Agent Based model has been shown capable of capturing the disease progression which characterised an individual's health condition. Whilst System Dynamics has offered, in a high aggregated level, the possibility of estimating the health service use related to different health conditions.

The prevalence of depression generated from the model was used to estimate the service use and its related burden of disease. The results showed different service coverage related to the progression of depression and the number of relapse cases. The higher the service coverage, the smaller the number of individuals whose condition deteriorated or relapsed.

The costs related to the health service have also been estimated. The results suggested that, in general, an increase in service coverage related to an increase in healthcare costs. However in some cases, the increase could offer benefit to the individuals as well as to the health economy. This can be seen from the utilisation of inpatient care which showed that the increase in the service coverage reduced the use of inpatient services.

The prevalence of depression, resultant from the simulation experimentation, can be used to estimate the burden of disease using DALYs. The results indicated that the increase in service coverage reduced the years lived with disability. This suggests that in order to reduce the burden of depression, the increase in service coverage is inevitable.

Chapter 7

Discussion and Conclusions

7.1 Introduction

The literature review highlights a gap in applying hybrid simulation methods in mental health related problems. Based on this finding, we formulate four research questions and two classifications of objectives. The first research question and the first classification of objectives concern the development of a hybrid simulation model. The purpose is to represent disease progression and related treatment pathways in a single model. We answer the question and fulfil the objectives in Chapter 4.

The research questions 2, 3, and 4, and the second classification of objectives concern the use of the developed hybrid simulation model. The purpose is to investigate the relationship between different levels of service coverage and depression progression as well as the burden of disease. The answers to these questions and accomplishment of the objectives are provided in Chapter 6.

The following sections provide: a discussion on the findings which answers each research question; and conclusions to the study which outlines some contributions, limitations, and recommendations.

7.2 Discussion

7.2.1 How can we build a hybrid simulation model which addresses depression progression and its related treatment pathways?

The research employs two simulation modelling methods: the Agent Based Modelling and the System Dynamics. The Agent Based Modelling is used to describe the progression of depression, whereas the System Dynamics is used to describe the health service related to treatment pathways. The two models are connected to run synchronously to investigate the impact of depression progression on the health services and vice versa.

The use of the Agent Based Modelling approach for describing depression progression is similar to the model developed by Kalton et al. (2016). The difference is that the model in Kalton et al. (2016) only captures four different health conditions: healthy, mild, moderate, and severe. Whereas our model expands each condition (mild, moderate, and severe) to include states: being in treatment, untreated, and out of care.

The developed Agent Based model also captures other states as a feedback from receiving or not receiving treatment. These states include: relapse, response to treatment (i.e recovery), and death. These states are considered necessary and have been modelled in Najafzadeh et al. (2017) using Discrete Event Simulation. In fact, we include progression from mild to moderate and from moderate to severe state explicitly in the model.

We use the Agent Based model to generate demand for the healthcare services. The output measures generally relate to the number of individuals being in a particular state in the model. These include the number of prevalence in each severity level, the relapse cases and the progression cases. This design is different from the model the purpose of which is to evaluate the healthcare resource utilisation, such as in Cerdá et al. (2015) or in Silverman et al. (2015).

Considering the purpose of developing an Agent Based model is to represent depression progression, we can argue that Agent Based Modelling is not only suitable for the purpose, but also relevant. This is due to the fact that Agent Based Modelling offers greater flexibility than has been displayed in the current model. The individual agent can have its own unique characteristic, independent decision making rules, connections to other agents, and be responsive to its environment (Railsback and Grimm (2012)).

However, we are not able to use the AB model in its fullest capacity. The biggest challenge we faced is in getting quality data from a single context, with detailed characteristics of individuals and at the same time capturing their disease progression. Moreover, data on how the patients make decisions regarding their treatment and how patients' interaction with other individuals (involved in their care) influences their decision on receiving treatment, will not readily be available in any health records. The lack of such detailed data means we are unable to dis-aggregate the population by its characteristics such as sex and age. Despite this challenge, we are able to capture the characteristics in the different severity levels of depression, and the stochastic element in the transition from one state to another. We can argue that these two elements, i.e severity levels and stochastic transitions, warrant us to use an Agent Based Modelling approach and construct the basic model for individuals in the population.

The treatment pathways related to depression, on the other hand, are modelled using a System Dynamics approach. The model captures the complex networks of health services ranging from primary to inpatient care. The structure of the SD model is based on the stepped care model for depression developed in Andrews, G. and the TOLKIEN II Team (2006). This stepped care concept is also recommended in National Collaborating Centre for Mental Health (2010). The NICE guideline is mentioned in Welsh Government (2012) as one of the treatment guides to be followed for best practice in delivering treatment for people with mental health in Wales.

The developed model captures the resources of services needed and their links within the clinical perspective. The recommended stepped care treatment model also has been applied in the study by Smits (2010). The current model includes several health services, while Smits (2010)'s model focuses on one clinic. The use of System Dynamics for analysing the health service use by capturing patient pathways is similar to the model designed in Lane and Husemann (2008). The main difference from the current model is that the complex model in Lane and Husemann (2008) has never been quantified.

We use the SD model not only to represent the network of services for treating depression, but also to estimate the service use. One feature of SD is feedback, which depends on the states of the system (stocks). Feedback can be either a reinforcing or a balancing one. The feedback depends on the state of the system or the stock. For example, in a system with only one stock with inflow and outflow, for a reinforcing feedback to be formed, the state of the system has to positively influence the net increase rate in the inflow. On the other hand, for a balancing feedback to be formed, a system or stock has to positively influence the outflow rate, which ultimately reduces the stock (Sterman, 2000, p.263-277).

The current structure of the SD model does not have reinforcing feedback. However, at some stocks, the balancing feedback is apparent. Take for example the stock which represents the number of individuals needing to visit a GP for the initial contact in Figure 4.4. If the number of individuals needing initial GP contact increases, this will increase the outflow from the GP. As a consequence, the increase in outflow from the GP will reduce the number of individuals at the GP. However, the overall behaviour of the stock (in this case the number of people at the GP) will depend on both the inflow and outflow rates.

Although from the SD model we can see the network between services as patient flow in the system, the use of the model is relatively simple in this study. One might pose a question as to why the system of care has to be modelled separately using System Dynamics? Would not it be sufficient to use the Agent-Based Modelling? To answer these questions, we need to look at the initial purpose of the use of the Agent-Based Modelling. The AB model is designed to capture the disease progression. The complexity of the disease is reflected by the use of separate states to describe different levels of depression and other related conditions. One such state is used to reflect the condition of the patient receiving treatment. Because the treatment pathways for depression are complex, and if we were to incorporate the treatment pathways in the AB model, then we need to break down the state representing the patient being in the treatment to accommodate the pathways. This will further complicate the structure of the Agent-Based model. This might have an impact on running the simulation model. The computation will be very slow, especially if we use large numbers of the population, as evaluation of the service use is taken at each individual level.

Suppose we do not incorporate the SD model into the AB model. Considering that the population is assumed to be homogeneous (adult population), why do we construct AB model for disease progression? Is it not enough to model the disease progression and the treatment pathways in a single model with System Dynamics? Initially, we would like to capture the variability in the disease progression model. This variability can be found in the individual's demographic profile, different severity of depression, and different duration of disease progression between one individual to another. Although the current AB model does not incorporate an individual patient's demographic profile, it can still be expanded, providing the data is available. This can be done without changing the model structure (as has been investigated by Parragh and Einzinger (2012). Moreover, the stochastic element captured in the different duration of state transition cannot be easily modelled in SD.

It seems the separation of a disease model from a treatment model is necessary in this case. The combination of Agent Based Modelling and System Dynamics not only offers greater flexibility in modelling two different levels (disease progression and treatment pathways), but also seems more natural. On an individual level, the model can be used to generate an insight into the progression of the disease inherent in the individuals in the population. At a service level, the model can be used to estimate the service utilisation.

The design of the current hybrid model uses a format similar to that offered by Liu et al. (2018), where individuals are modelled using ABM and the health system is modelled using SD. This also refers to the "Process - Environment" form of framework in Chahal and Eldabi (2008), where each element in the model is modelled separately but all elements run synchronously. It is asserted by Brailsford (2016) that this type of hybrid modelling is applied in many healthcare simulation models.

7.2.2 Using a recommended treatment model, how can the prevalence of depression affect healthcare services?

The recommended stepped care treatment model suggests the majority of treatments for depression are administered at the community base settings (Andrews, G. and the TOLKIEN II Team (2006)). In this setting, the General Practitioners serve as gate keepers in the system and overarching the pathways from start to finish. The simulation results reflect this by the high volume of GP visits compared to other services. Although the rate of accessing the healthcare services by people with mental health conditions varies from country to country, a study by Oakley Browne et al. (2006) found similar results that GPs are accessed more than the specialist services.

The results also highlight that there is a relationship between different levels of service coverage and the health service use. The increase in the level of service coverage tends to increase the service use. The reverse is observed at the inpatient service. It is suggested that an increase in the service coverage tends to reduce the inpatient care utilisation. This is in line with the recommendation to treat mental health patients in a community setting, and an increase in community care reduces the use of inpatient care by Machado et al. (2018).

The impact of different service coverage to the healthcare costs is also highlighted in the findings. Generally, an increase in the service use will increase the costs to the health services. The reduction of inpatient use by people with severe depression does not necessarily reduce the total costs incurred by the condition. Although the use of inpatient care reduces, people suffering from severe depression will be treated elsewhere, such as in outpatient services or even in their own home environment. This ultimately increases the costs to the relevant services.

Another point to highlight is that the treatment pathways considers giving medicine for treating people with depression. The results indicate that the use of medicine will increase with the increase of the service coverage. Although the model does not evaluate the efficacy of the medicine per se, studies on cost benefit analysis of medication have found that medication can help in improving mental health conditions. For example, a study by Lin et al. (2015) analyses the benefit of increasing the medication coverage in decreasing relapse cases.

7.2.3 How can different levels of service coverage affect the progression of depression?

The developed model incorporates two different types of depression progression: the progression from mild to moderate condition, and from moderate to severe condition. The progression from moderate to severe shows a slightly better response to the increase in service coverage compared to the progression from mild to moderate conditions. However, in general, the results indicate that the higher the service coverage, the less the progression of depression to more severe conditions.

The findings also indicate that people with mild and moderate depression respond better with the increase of service coverage compared to severe depression. This suggests that increasing the service coverage may help in preventing people with mild and moderate depression to relapse. In fact receiving treatment (medicine or therapy) whether short or long term prevents relapse (Montgomery (1996); Koran et al. (2001); Lin et al. (2015)).

7.2.4 What recommendations can be made to healthcare providers to reduce the burden of depression?

The mental health code of practice for Wales, the Strategy, and the Measure 2010 (Welsh Government (1983, 2012, 2010)) all focus on delivering mental health services which take into account individual patient's needs based on demographic profile, social, culture, and financial. The services must incorporate the patient's decision on choosing the treatment. The treatment and care for people with mental health, such as depression, should aim to alleviate the illness or prevent it from developing into a worse condition. The treatment should be designed so that the individual will have a better experience from the treatment they receive, while at the same time, efficiency in the system must be monitored continuously.

All of the above points suggest that the interaction between patients and the service providers is an important element in a healthcare system. Therefore, it is also an element to be considered whenever decisions are made regarding the provision of treatment and care. The question remains: how big is the demand for mental health care, or depression in particular? Do we have enough capacity to treat all people with mental health problems including depression? These two questions might not be easily answered. However, we can propose a tool which can be used to address such problems.

Our literature review suggests that various simulation methods have been used to address problems related to demand and capacity in mental health care. However, none is found that has used a combination of simulation methods. The developed hybrid simulation model, in our study, shows a great potential in modelling mental healthcare related problems. It addresses the interrelation between individuals with depression and the care service system. How depression manifests in an individual affects the healthcare system, and how in turn, the provision of healthcare affects the individual's depression progression. It serves as a tool to analyse healthcare utilisation. As suggested by Parragh and Einzinger (2012), that healthcare utilisation corresponds to interactions between patients and the healthcare providers. We will highlight some potentials our model can offer, in addressing the problems related to mental health care services.

The Welsh Government (1983) stresses the need to provide mental health care which is effective as well as efficient. The treatment should be offered with an aim to prevent the condition from deteriorating. The Agent Based model addresses this issue by describing the progression of depression for each individual patient. This enables evaluation on how the provision of service can influence the disease progression and vice versa at an individual level. Our results show that the provision of service which covers more population has the potential to reduce the risk of more people with depression developing into a more severe condition. The results support the strategy that better access to early intervention can benefit population (Welsh Government (2012)). So, with the changing demographic of population and the increased needs of people with mental health problems, it means the mental health care system has to be adaptive in order to at least maintain the current level of provision. It is suggested that the increase in treatment coverage not only improves the outcomes of public health in general, but also in economic savings (Campion et al. (2017)).

The Strategy in Welsh Government (2012) outlines the need for medical treatment to encompass nursing, psychological intervention, and other specialist mental health care. The model takes into consideration the stepped care treatment model, which encompasses different services. Although the model does not evaluate the efficacy of the stepped care model compared to other treatment models that may be implemented, the stepped care model of intervention may offer more cost benefit, as has been found by Cohen et al. (2017), due to lower cost and wider reach compared to the usual care. This is ideal if service coverage is to be increased. Moreover, the model supports the outcomes set out in the Strategy in a sense that the mental health services should be integrated services and person centred; with the care provided more at the community based to reduce the use of inpatient services.

The model evaluates the service coverage up to 80%. This is not to suggest that the healthcare providers should consider this figure. Rather, the results indicate that in order to reduce the burden of depression, increasing the service coverage is inevitable (as suggested in Ormel et al. (2019)). The increase will ultimately increase the volume of treatment given across the services, except for the inpatient services.

To evaluate the implication of increasing the service coverage in practice, further studies designed close to the local context are necessary. This requires standardised treatment pathways and a better collection of data. The standardised treatment pathways give guidelines on patient flow in receiving the treatment. This helps to reduce the variation in practice. On the other hand, the quality data can be used to run the simulation model as developed in this study. The data needed is that which can inform the history of depression progression and the health service use by people suffering depression in its entirety. Such quality data will enable better cost evaluation on investment in mental health resources. It can help in making better decision as to where and to how much should be spent in the future. This is one benefit the model can offer to support the Strategy, outlined in Welsh Government (2012), in delivering safe, efficient and effective services.

7.3 Conclusions

7.3.1 Study contributions

The literature review of the simulation model applied in mental health care suggests some gaps: that the use of simulation methods in mental health care in general is very infrequent; and none of the existing studies have used the hybrid simulation technique. The current study aims to fill these gaps by developing a hybrid simulation model capturing disease progression and treatment pathways.

Mental health and mental health care are very complex. Study of such a complex system may benefit from using different simulation methods which complement each other. The combination of Agent Based Modelling for disease progression and System Dynamics for treatment pathways demonstrates the relevance and suitability of the method in the current context. Although the technique is used specifically for depression and its related treatment pathways, it can also be applied to other similar contexts where disease progression and its related treatment pathways are two interacting elements to be addressed in the model.

The developed model and the proposed use of the model are shared with wider audiences from various backgrounds at conferences, seminars or closed group presentations. Presentations and engagement with healthcare managers and clinicians alike not only introduce the use of hybrid simulation in healthcare, but also provoke a discussion on the suitability of the method of addressing the problems related to mental healthcare. Although a precise estimate will never be achieved in the current situation, due to the fact that comprehensive data is not available from a single context, the results are expected to give some insights into the advantages of hybrid simulation applied in healthcare. Other contributions of the study will be highlighted in the section on recommendations.

7.3.2 Study limitations

The developed hybrid simulation is intended to represent the disease progression and treatment pathways as accurate to the real context as possible. Despite this attempt, the model is subject to some limitations. First, the model suffers from a lack of available detailed data providing information on depression progression. This limitation makes it impossible to calibrate the model using the local data. Although the structural validation of the model can be done by local experts, the limitation in the data may affect the accuracy and quality of the estimate generated by the model.

Second, the population characteristics are assumed to be homogeneous and aggregated. The model only concerns the adult population of mixed gender. Although the National Collaborating Centre for Mental Health (2010) recommends not to vary the treatment given to adults suffering depression, it is wise to estimate the service use based on gender to enable service delivery which is suited to individual patient's needs. Again, in order to separate the population by gender, we need a separate set of parameters for each type. This is one of the consequences of not having good quality data.

Third, the system model was developed based on the treatment pathways which mainly include the clinical settings. Studies have found that people suffering from mental health conditions may affect other services, such as social support, housing support and the justice system. For example a study by Smith et al. (2004) includes mental health in prison and forensic sectors.

Fourth, the current model did not explore the emerging behaviour as a result of the networks between agents in the system. Only one type of agent is incorporated in the model, i.e patient type. Other types of agents, such as clinicians or family members who may have an influence in the decision making process are not included in the design.

Fifth, the care pathways model was developed based on the guideline by Andrews, G. and the TOLKIEN II Team (2006) which is similar to that found in National Collaborating Centre for Mental Health (2010). The two guidelines used in this study have been developed using a sound methodology. They were both developed using evidence based practice and extensive experts' opinions. However, it is not known whether the guideline is widely implemented in practice. The wider the variation, between the treatment pathways outlined by the guideline and the actual patient pathways in practice, the more questionable the potential use of the model in real life.

7.3.3 Recommendations for future research

The limitations outlined above lead to some recommendations that can be made to improve the quality and accuracy of the model in future research. First, it is recommended to collect data from a longitudinal population based study specific to the local context. In the area of public health, study on disease progression is mainly designed using a longitudinal population base. The long time horizon in such a study design allows a follow up observation on conditions affecting the population involved in the sample. The results from the population based study give information on the history of disease, which is ideal to be used in any simulation model describing the disease progression. The availability of detailed data from the local context can facilitate the calibration of the model relevant to the local context.

However, quality data, which can give all the parameters needed in a hybrid simulation model, may be difficult, if not impossible, to get. In that case, it is recommended to look at a different approach of building the model. To address both disease progression and service use, we can use a single method, such as System Dynamics. This modelling approach not only can accommodate an aggregated level of data but can also run the model quickly. The drawback is that we cannot evaluate any interaction from an individual level, and it will be difficult to accommodate any stochastic element in the system.

Second, in order to generate more accurate results, the model can incorporate more detailed individuals' characteristics such as age and gender. Although to obtain data detailing a population's characteristics may be time consuming, the results generated by the model can be used to evaluate the best provision of care based on the individual's needs.

Third, the current model is limited to the clinical pathways. In order to capture the whole system perspective, other support systems which may be affected by people suffering from mental health conditions can be incorporated. However careful consideration is required when developing too detailed a model. This is due to the fact that many healthcare systems do not necessarily link with other support systems in their day to day data collection. A model which incorporates cross system boundaries will require not only an engagement of experts from these systems, but also the linkage data capturing the movement of people using the systems.

Fourth, the current model does not capture the network system of the agent. Future research may take advantage of the powerful feature of the Agent Based Modelling method for analysing a social network. Other types of agents, such as clinicians, medical decision makers, carers and family members who may influence the patient's decision on choosing the treatment can also be incorporated into the model. The relationships between agents can be evaluated and may give insights into a better care service.

Fifth, developing a treatment pathway model using a guideline may be quicker than exploring the treatment pathways from scratch. This may be suitable for an academic exercise, where the purpose is to examine the feasibility of a certain modelling method. However, if a modelling purpose is to help the practitioner and decision maker make better decisions, it is suggested to develop the model based on the current practice. Any future study may start by directly describing the model based on the real patient pathways, which may be described by the experts or as a result of exploring the data.

Finally, we can conclude that the combination of Agent Based Modelling and System Dynamics offers an interesting avenue in modelling a system where disease progression and treatment pathways are two interrelated factors. However, this modelling opportunity comes with its own challenges, which may relate to data collection and structure of the model. In order to overcome these challenges, future research should consider a multi disciplinary study including experts from different fields, such as Public Health, Data Science, as well as Operational Research.

Appendix A

Summary of statistical tests for prevalence, progression and relapse data

In order to test the results generated by the simulation model, we conducted tests following the steps below:

- To test the normality and homogeneity of variance in the data.
- If the normality and equal variance tests show significant, then we perform a non-parametric test; in our case we perform Kruskal-Wallis.
- If the normality and equal variance tests show non significant, we perform ANOVA test.
- Following Kruskal-Wallis test, if the result is significant, then we perform a posthoc test after Kruskal-Wallis.
- Following ANOVA test, if the result is significant, we perform Tukey HSD test.

For all the tests conducted, we assume that the observations are random independent. Analyses are done in R.

A.1 Test results for prevalence data

Table A.1 shows the normality test (Shapiro-Wilk) and the equal variance test (Levene's Test) for conducting ANOVA for the prevalence data. The results show that across the different service coverage, the data are normally distributed (p-value > 0.05) and the equal variance can be assumed (p-value 0.05).

TABLE A.1: Results from normality and equal variance test for prevalence data

Service Coverage	Levene Test (F, pr > F)	Shapiro-Wilk Test (W, p-value)
Mild	1.9898 , 0.1371	0.99894 , 0.4987
Moderate	1.0831 , 0.3388	0.99878 , 0.302
Severe	0.2974 , 0.7428	0.99932 , 0.4643

Since the normality and equal variance tests across different severity prevalence data show non significant at 0.01 or 0.05, the ANOVA test was then performed. One more assumption to be met is that all the observations are random. We can assume that the data are random due to the random nature of the simulation model.

Table A.2 summarises the results from ANOVA test for the prevalence data. All p-values show not significant at 0.01. We can conclude that the means prevalence are equal across different service coverage for all different severity levels.

TABLE A.2: Results from ANOVA test for prevalence data

	Df	Sum Sq	Mean Sq	F value	$Pr(> F)$
Mild Prevalence					
Service Coverage	2	0	0.07	0.001	0.999
Residuals	1497	83367	55.69		
Moderate Prevalence					
Service Coverage	2	206	102.95	1.387	0.25
Residuals	1497	111135	74.24		
Severe Prevalence					
Service Coverage	2	384	191.91	3.391	0.0339
Residuals	1497	84716	56.59		

Figure A.1, Figure A.2 and Figure A.3 present the diagnostic from fitting the ANOVA to the prevalence data.

FIGURE A.1: Diagnostic checking on ANOVA applied in mild prevalence data

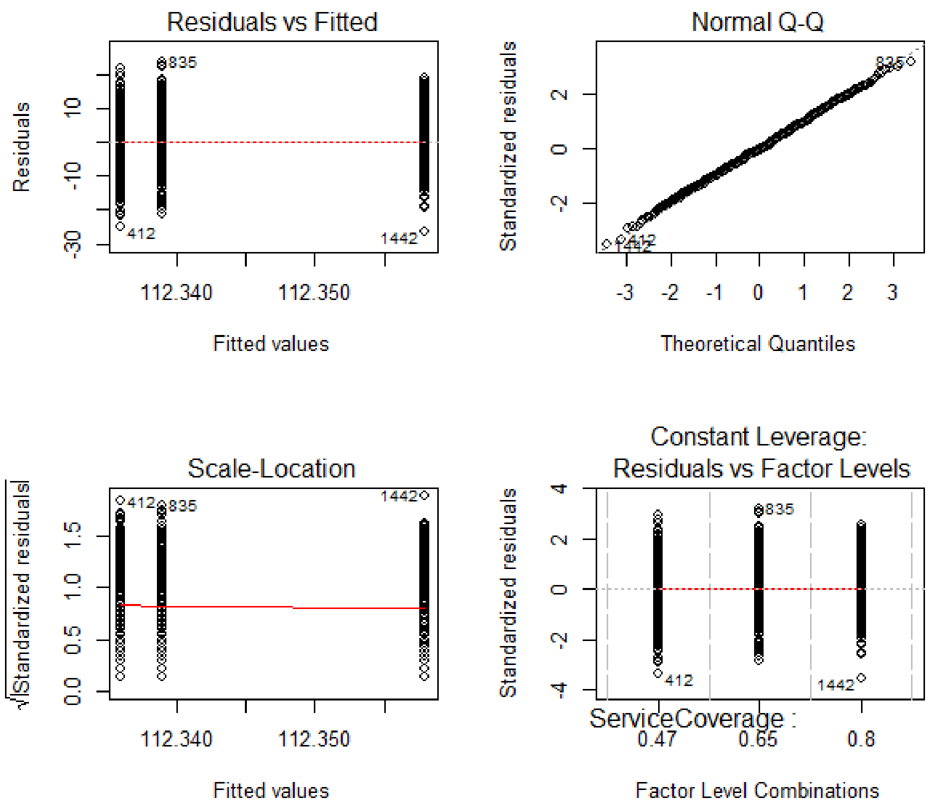


Figure A.2: Diagnostic checking on ANOVA applied in moderate prevalence data

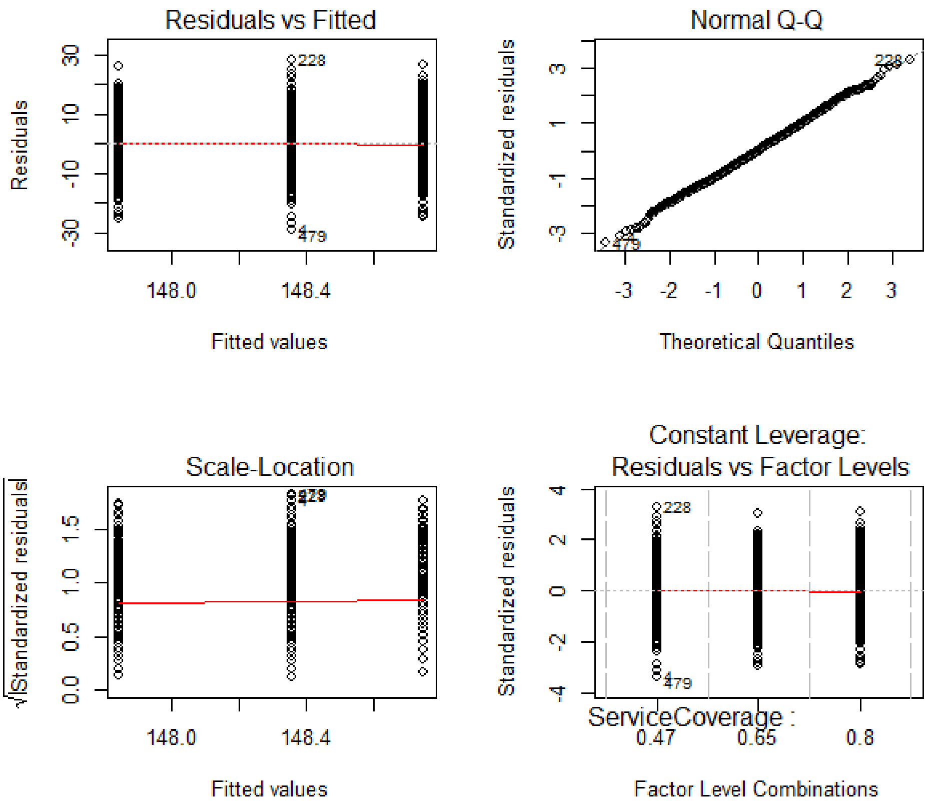
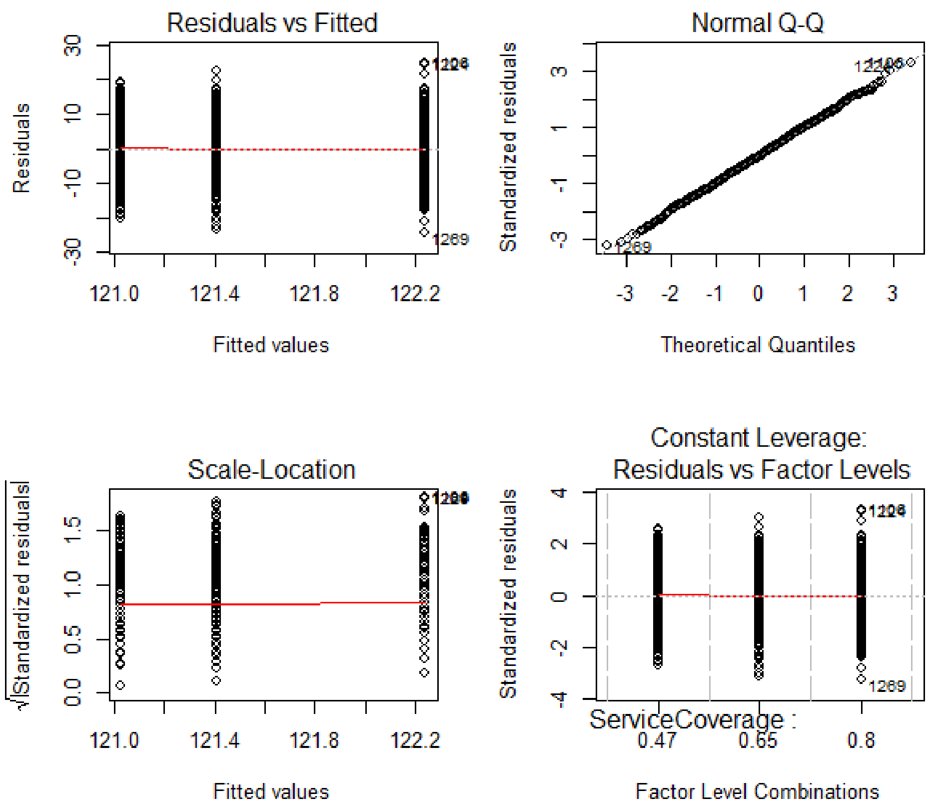


FIGURE A.3: Diagnostic checking on ANOVA applied in severe prevalence data



A.2 Test results for progression data

Table A.3 displays the results from Shapiro-Wilk test for normality. The p-value suggested that for both types of depression progression, the data are not normally distributed across the different service coverage.

TABLE A.3: Results from Shapiro-Wilk normality test on progression data

Progression	W value	p-value
Mild to moderate	0.97164	2.2e-16
Moderate to severe	0.9743	1.334e-14

Table A.4 summarises the results from Levene's test for homogeneity of variance on the progression data. The results suggest that, for the two types of depression progression, the variance is not equal across the different service coverage.

Table A.4: Results from Levene's test on progression data for homogeneity of variance (centre = median)

Progression	F value	df	Pr(>F)
Mild to moderate	73.188	2	2.2e-16
Moderate to severe	65.161	2	2.2e-16

Based on the results in Table A.3 and Table A.4, we perform non parametric tests on the progression data, i.e. Kruskal-Wallis test on progression data.

Table A.5 shows the results from running Kruskal-Wallis test on the progression data. The results indicate that, for both depression progression, the median are different across different service coverage. In order to find out which service coverage is different from other service coverages, we performed a posthoc comparison.

Table A.5: Results from Kruskal-Wallis rank sum tests for depression progression

Progression	Chi-squared	df	p-value
Mild to moderate	659.39	2	2.2e-16
Moderate to severe	712.56	2	2.2e-16

Table A.6 shows results from running a posthoc test after Kruskal-Wallis. The test aim is to find out which service coverage are different from one another. The comparison for progression from mild to moderate and from moderate to severe was set at 99% confidence interval. The results show that for all possible pair combination of service coverage, the means are different.

A.3 Test results for relapse data

Table A.7 summarises the results from Levene's test for equal variance and Shapiro-Wilk for normality test. The results suggest that the normality and equal variance are not fully met. The Levene's test for equal variance suggests that, in mild and moderate cases, the variance is not equal. While in severe cases, there is not

Table A.6: Results for multiple comparison test after Kruskal-Wallis on progression data

Service Coverage	obs.diff	critical.dif	difference
Mild to moderate			
65% - 47%	394.181	80.41054	TRUE
80% - 47%	695.008	80.41054	TRUE
80% - 65%	300.827	80.41054	TRUE
Moderate to severe			
65% - 47%	435.821	80.41054	TRUE
80% - 47%	720.703	80.41054	TRUE
80% - 65%	284.882	80.41054	TRUE

p-value = 0.01

enough evidence to suggest that the data is not normally distributed. Furthermore, the Shapiro-Wilk tests suggest that, in all cases, the data are not normally distributed. Based on these results, we performed a non parametric test on relapse data.

Table A.7: Results from normality and equal variance test for relapse data

Severity	Levene's Test (F, pr > F)	Shapiro-Wilk Test (W, p-value)
Mild	F = 37.428 , p = <2.2e-16	W = 0.94512 , p-value = <2.2e-16
Moderate	F = 54.7851 , p = <2.2e-16	W = 0.95464 , p-value = <2.2e-16
Severe	F = 0.6996 , p = 0.4969	W = 0.79965 , p-value = <2.2e-16

Table A.8 summarises the results from conducting a non parametric test, Kruskal-Wallis test on relapse data. The purpose is to find out which group has different median than the other.

Table A.8: Results from Kruskal-Wallis rank sum tests for relapse cases

Severity	Chi-squared	df	p-value
Mild	525.48	2	2.2e-16
Moderate	584.72	2	2.2e-16
Severe	3.0761	2	0.2148

The results suggest that in mild and moderate cases, there is at least a difference between groups medians. This is not quite so for the severe case. In order to find out which groups are different, we performed a posthoc multiple comparison test. Table A.9 shows the results of the comparison between service coverage. It seems that in mild and moderate cases, all combinations of service coverage have different medians, but not in severe cases.

Table A.9: Results for multiple comparison test after Kruskal-Wallis on relapse data

Service Coverage	obs.diff	critical.dif	difference
Mild			
65% - 47%	389.502	80.41054	TRUE
80% - 47%	615.330	80.41054	TRUE
80% - 65%	225.828	80.41054	TRUE
Moderate			
65% - 47%	377.476	80.41054	TRUE
80% - 47%	656.246	80.41054	TRUE
80% - 65%	278.770	80.41054	TRUE
Severe			
65% - 47%	16.393	80.41054	FALSE
80% - 47%	44.285	80.41054	FALSE
80% - 65%	27.892	80.41054	FALSE

p-value = 0.01

Appendix B

Summary statistical tests for service use data

Table B.1 summarises the results from the normality and homogeneity tests conducted on service use. The equal variance test used the the different service coverage, 47%, 65% and 80%, as factor levels. The results revealed that across the different service types, the variances are not equal. The Shapiro-Wilk tests yielded very significant results too which means all the data in the service do no come from a normal distribution. Based on these two tests, we conducted a non parametric test to find out if there is any difference in service use across the different level of service coverage.

TABLE B.1: Results from normality and equal variance test for different service use

Service Type	Levene Test (F, pr > F)	Shapiro-Wilk Test (W, p-value)
CMHTeam[1]	32.2 , 2.033e-14	0.90965 , < 2.2e-16
GP	28.135 , 1.012e-12	0.86293 , < 2.2e-16
Psychiatrist	29.882 , 1.883e-13	0.89697 , < 2.2e-16
PsychTherapy[2]	23.034 , 1.404e-10	0.86322 , < 2.2e-16
CRHHT[3]	6.1149 , 0.002265	0.99328 , 2.511e-06
Medicine	27.151 , 2.615e-12	0.86288 , < 2.2e-16
Inpatient	0.9903 , 0.3717	0.96567 , < 2.2e-16

[1] Community Mental Health Team
[2] Psychological Therapy
[3] Community Resolution Home Treatment Team

Table B.2 presents the results from conducting non parametric test on the service use data. The results reveal that across all the different services, the p-values are very significant; indicating the difference in the service use across different level service coverage.

Table B.2: Results from Kruskal-Wallis rank sum tests for service use data

Service Use	Chi-squared	df	p-value
CMHTeam	1278.3	2	$< 2.2e\text{-}16$
GP	1331	2	$< 2.2e\text{-}16$
Psychiatrist	1307.9	2	$< 2.2e\text{-}16$
PsychTherapy	1332	2	$< 2.2e\text{-}16$
CRHHT	663.45	2	$< 2.2e\text{-}16$
Medicine	1330.9	2	$< 2.2e\text{-}16$
Inpatient	1297.9	2	$< 2.2e\text{-}16$

Table B.3 presents the posthoc results after conducting Kruskal-Wallis test. The comparison tests indicates that, across different service types, the medians of service coverage are different except for the Community Home Treatment Team. It seems in CRHTT has no difference between 65% and 80% service coverage.

Table B.3: Results for multiple comparison test after Kruskal-Wallis on service use data

Service Coverage	obs.diff	critical.dif	difference
CMHTeam			
65% - 47%	521.232	80.41054	TRUE
80% - 47%	978.768	80.41054	TRUE
80% - 65%	457.536	80.41054	TRUE
GP			
65% - 47%	500.54	80.41054	TRUE
80% - 47%	999.46	80.41054	TRUE
80% - 65%	498.92	80.41054	TRUE
Psychiatrist			
65% - 47%	509.368	80.41054	TRUE
80% - 47%	990.632	80.41054	TRUE
80% - 65%	481.264	80.41054	TRUE
Psych.therapy			
65% - 47%	500.16	80.41054	TRUE
80% - 47%	999.84	80.41054	TRUE
80% - 65%	499.68	80.41054	TRUE
CRHTT			
65% - 47%	598.550	80.41054	TRUE
80% - 47%	622.918	80.41054	TRUE
80% - 65%	24.368	80.41054	FALSE
Medicine			
65% - 47%	500.576	80.41054	TRUE
80% - 47%	999.424	80.41054	TRUE
80% - 65%	498.848	80.41054	TRUE
Inpatient			
65% - 47%	502.812	80.41054	TRUE
80% - 47%	986.874	80.41054	TRUE
80% - 65%	484.062	80.41054	TRUE

p-value = 0.01

Appendix C

Technical overview for computing burden of disease

C.1 Costs of health service

The UK Consumer Price Index (CPI) for 2008 and 2018 are 847.5 and 1110.8 respectively (data source is table 49 from Office for National Statistics (2019)). In order to estimate the price in 2018 based on 2008 price we use,

$$\frac{\text{CPI in 2018}}{\text{CPI in 2008}} \times \text{2008 UK price.}$$

C.2 DALYs for depression

Disability Adjusted Life Year (DALY) is a metric used to measure burden of disease which comprises the time lost due to death related to the disease and time lived with disability condition due to experiencing the disease. Essentially DALY is computed as:

$$\text{DALY} \quad = \text{YLL} \; + \text{YLD}$$

where YLL is years of life lost due to premature death and YLD is the years individual affected lived with disability. In a very simplest form the YLL is calculated as:

$$\text{YLL} = \text{N} \times \text{L}$$

where N is the number of deaths caused by the disease and L is standard life expectancy at age of death. Whereas YLD can be computed using either incidence or prevalence cases as follow:

$$\text{YLD} = \text{I} \times \text{DW} \times \text{L}$$

here, I can be the number of incident or prevalence cases related to the disease, DW is the disability weight corresponding to the disease, and L is average duration of disability. The unit measure for L is years.

The current study uses prevalence cases instead of incident cases, in computing YLD, due to some advantages that have been argued to be associated with its use in World Health Organization (2018d). The number of prevalence is the number of people with depression who does not get treated. The average duration is 1 year, as the average length of time horizon in the simulation result. In general, DALY is computed as:

$$\text{DALY} = \sum_{i=1}^{3} (\text{N}_i \times \text{L}_i) + (\text{P}_i \times \text{DW}_i)$$

where P is the number of prevalence and i is the severity level. The formula for YLD which uses prevalence has been applied in a study by NHS Health Scotland (2017). However, the Scottish study did not incorporate the YLL based on the argument that depression is not listed as a cause of mortality in Wang et al. (2016). A more complex formula for computing DALY which accounts for the age group and discounting factor can be found in Murray (1994).

Appendix D

Simulation model run-time set up

D.1 Model run-time set up

Table D.1 summarises the model set up for running the simulation. The model was developed in AnyLogic 8 University version 8.3.3. Copyright(c) AnyLogic North America. All rights reserved. Visit https://www.anylogic.com.

Table D.1: Model run-time setting

Item description	Setting
Initial population size	5000
Length of run-time	104 weeks (2 years)
Warming up period	26 weeks (6 months)
Number of runs $\times$ replications per iteration	50×10
Random number generation	Random seed

Appendix E

Agent Based Model

Figure E.1: Model for depression progression.

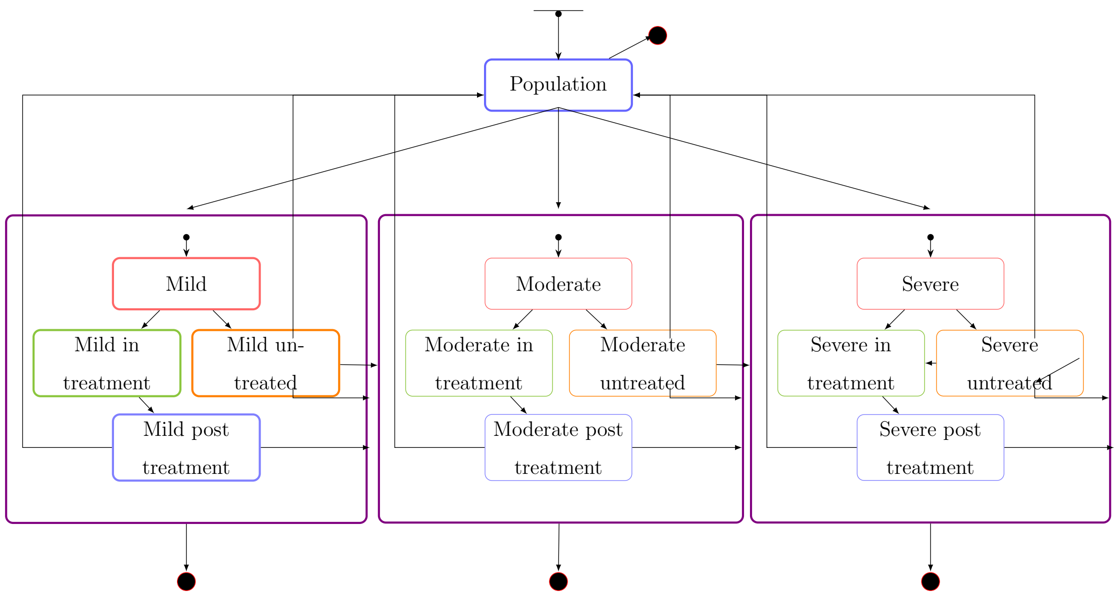


Figure E.1 illustrates the complete structure of depression progression as developed in AnyLogic. The model starts with individuals being in 'Population', where they do not have depression or at least the symptoms of depression have not been detected. The model has three composite states, and each state has four other states. To describe how the states change, take for example the composite state for mild depression. The condition of an individual will start at the state 'Mild'. Then it changes to either being 'Mild in treatment' or 'Mild untreated' depending on the decision made by the individual affected by the condition. For the individuals who enter the treatment, they will finish the treatment and move to the state 'Mild post treatment'. From this state, they either recover and go back to 'Population' or experience relapse and go to state 'Mild'. For those individuals who do not get treatment, i.e. being 'untreated', they will experience one of three conditions: they will relapse, recover, or their conditions deteriorate. For those who experience relapse, they will move to the state 'Mild' again. For those who recover, they will move to 'Population'. And for those whose conditions deteriorate, they will enter the 'Moderate' state.

The model incorporates the absorbing state represented with the black dots. It assumes that anyone can die from any condition in the statechart. Chapter 4 and Chapter 5 provide a more elaborate description for the Agent Based model.

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