Epidemiological modelling of type 2 diabetes in Saudi Arabia: predicted trends and public health implications

Abdulkareem J. Al Quwaidhi

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Abstract

Background: The Kingdom of Saudi Arabia faces one of the highest prevalence rates of type 2 diabetes mellitus (T2DM) in the world. However, there are no credible local data on the trends and future projections of the disease, and the relevant international studies underestimated the true prevalence rates. This thesis used epidemiological modelling to study the trends in T2DM prevalence in Saudi Arabia, predicted its future levels, and quantified the impact of reducing some risk factors on the disease prevalence trends.

Methods: This thesis developed and validated the "Saudi IMPACT Diabetes Forecast Model", which integrates data on the population, obesity and smoking prevalence trends in Saudis aged ≥25 years to estimate the trends in T2DM prevalence (1992-2022) using a Markov modelling approach. The model considers different reasonable scenarios of future trends in obesity prevalence, and incorporates a number of parameters to model the disease epidemiology. These parameters include the estimated diabetes incidence, case-fatality, total mortality, relative risk of diabetes if obese, and relative risk of diabetes if a smoker. The model data inputs and parameters were obtained from different sources, including local departments, medical literature and assumptions. The model results were validated against local data from the STEPwise survey in 2005, and against the model of the Global Burden of Disease study, where the model produced reasonably close results to both of these studies.

Results: The prevalence of T2DM among the Saudi population aged ≥25 years was estimated to rise substantially during the 30-year period of 1992-2022 from 8.5% to 39.5%, assuming some levelling off of obesity trends (capping), or to 44.1%, assuming uncapped increasing obesity trends. In men, T2DM prevalence was estimated to increase from 8.7% to 39.2% with capped obesity trends, or to 41.3% with continuing linear increase in obesity trends. In women, T2DM prevalence was estimated to increase from 8.2% to 39.8% with capping of obesity trends, or to 47.7% without such a capping. The model showed that if the trends in obesity start to decline by 10% in 12 years (2010-2022), a relative reduction of 13% in diabetes prevalence could be achieved. If the prevalence of obesity was halted at the 2010 levels, a 10% relative reduction in diabetes prevalence could be attained by 2022.

Conclusion: T2DM is currently a major public health challenge in Saudi Arabia, and this thesis predicted that its burden will increase substantially in the next decade. Intensive and aggressive preventive measures directed to reduce the levels of risk factors, particularly obesity and smoking, can result in reasonable reduction of the disease prevalence, and therefore should be an urgent action.

Dedication

This piece of work is dedicated to:

my father, my mother,
my wife (Nora), my daughter (Dalia), and my son (Mohammed).

With my sincere thanks for your love, patience and support.

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List of abbreviations

ADA	American Diabetes Association
APHO	Association of Public Health Observatories
BMI	Body mass index
CDC	Centres for Disease Control and Prevention
CDSI	Central Department of Statistics and Information
CHD	Coronary heart disease
DALY	Disability Adjusted Life Year
DM	Diabetes Mellitus
DPPs	Deaths, prevented or postponed
EMR	Eastern Mediterranean Region
FAO	Food and Agriculture Organisation
FBG	Fasting blood glucose
FPG	Fasting plasma glucose
GBD	Global Burden of Disease
GCC	Gulf Cooperation Council
GDP	Gross domestic product
GHO	Global Health Observatory
GNP	Gross national product
HbA_{1c}	Glycated haemoglobin
HP	Healthy People
HSE	Health Survey for England
IDF	International Diabetes Federation
IFG	Impaired fasting glucose
IGT	Impaired glucose tolerance
IPM	Incidence-prevalence-mortality
ISPOR	International Society for Pharmacoeconomics and Outcomes Research
kg/m^2	Kilograms per square metre
LYG	Life years gained
MEDCHAMPS	MEDiterranean studies of Cardiovascular disease and Hyperglycaemia: analytical Modelling of Population Socio-economic transitions
MENA	Middle East and North Africa

mg/dl	Milligrams per decilitre
mmol/l	Millimoles per litre
MODY	Maturity onset diabetes of the young
MOH	Ministry of Health
NCDs	Non-communicable diseases
NDP	National Diabetes Programme
NGOs	Non-governmental organisations
NHANES	National Health and Nutrition Examination Survey
NOO	National Obesity Observatory
OGTT	Oral Glucose Tolerance Test
ONS	Office for National Statistics
OR	Odds ratio
PAR	Population attributable risk
PHC	Primary health care
PHCC	Primary health care centre
QALY	Quality Adjusted Life Year
RR	Relative risk
RTA	Road traffic accident
SES	Socioeconomic status
STEPS	Stepwise surveillance
TP	Transition probability
T2DM	Type 2 diabetes mellitus
UAE	United Arab Emirates
UI	Uncertainty interval
UK	United Kingdom
UKPDS	United Kingdom Prospective Diabetes Study
UN	United Nations
UN-ESA	United Nations; Department of Economic and Social Affairs
US	United States
US$	United States dollar
WC	Waist circumference
WHO	World Health Organisation
WHR	Waist-to-hip circumference ratio
95% CI	95% confidence interval

Chapter 1. Introduction

1.1. Background

Diabetes mellitus (DM) as a disease was first recognised around 3000 years ago by the ancient Egyptians and Indians who described some clinical features very similar to what is now known as DM. The Greek word *"diabetes"* means "a siphon" referring to excessive urination, while the word *"mellitus"* means "honey sweet" referring to a sweet taste of urine. In 1776, excess sugar in blood and urine was first confirmed in Great Britain.[1, 2]

With passage of time, an extensive understanding of DM aetiology and pathogenesis has been achieved. Currently, DM is defined as "a group of metabolic diseases characterised by hyperglycaemia resulting from defects in insulin secretion, insulin action or both. The chronic hyperglycaemia is associated with disturbances in carbohydrate, fat, and protein metabolism and can lead to long-term damage, dysfunction and failure of various organs, especially the eyes, kidney, nerves, heart and blood vessels".[3]

DM is classified into four major types based on aetiology and clinical picture: type 1 DM, type 2 DM (T2DM), gestational DM, and other specific types. Type 1 DM usually results from absolute insulin deficiency and is caused by destruction of β cells in the pancreas mostly due to a cellular mediated autoimmune process. T2DM is characterised by insulin resistance and relative insulin deficiency. Gestational DM is a glucose intolerance of varying degrees of severity which starts or is first recognised during pregnancy. There are also many other specific types of DM which can result from specific genetic syndromes, surgery, drugs, malnutrition, infections, and other illnesses.[4, 5]

T2DM is the most common type of the disease, accounting for around 85-95% of all diagnosed cases of DM.[4, 6] The diagnosis of T2DM usually occurs after the age of 40 years,[5] but can occur in younger adults and even children. People with T2DM can remain asymptomatic for many years and the diagnosis is often made incidentally or when complications occur.[5, 7] In contrast to type 1 DM, T2DM patients are not dependent on insulin therapy and are not prone to

ketosis, but may require insulin for control of their hyperglycaemia if this is not achieved with diet alone or with oral hypoglycaemic agents.[5, 6]

The aetiology of T2DM is complex, and is known to be multifactorial. T2DM is associated with several risk factors which influence the disease occurrence, but are not necessarily causal factors. These risk factors can be demographic (e.g. age), genetic, or behavioural (e.g. obesity, physical inactivity, diet, smoking).[8] Behavioural risk factors are often known as 'modifiable risk factors', as changes to these factors have been found to change the disease occurrence in high-risk individuals.[8]

T2DM is now one of the most common non-communicable diseases (NCDs) globally, and its levels are progressively increasing. It has been estimated that around 366 million people worldwide, or 8.3% in the age group 20-79 years had T2DM in 2011.[9] This number has been projected to rise to 552 million (9.9%) by 2030.[9] The disease is associated with severe complications which affect health and productivity. More than 50% of people with diabetes die of cardiovascular disease (primarily heart disease and stroke). T2DM is the single most common cause of end stage renal disease which requires either dialysis or kidney transplantation.[6] People with T2DM carry a risk of lower limb amputation that may be more than 25 times greater than that seen in those without the disease. T2DM is also a major cause of adult blindness due to retinal damage.[6] The disease (in 2011) caused around 4.6 million deaths in the 20-79 age group, and at least US$ 465 billion in healthcare expenditures, which was equivalent to 11% of total healthcare expenditures in adults.[10]

1.2. What is this thesis about?

This thesis used 'epidemiological modelling' as a tool to examine the trends in prevalence of T2DM in the Kingdom of Saudi Arabia during the 30-year period of 1992-2022. The thesis developed the 'Saudi IMPACT Diabetes Forecast Model' which integrates information on trends in the structure of the Saudi population with trends in the prevalence of two risk factors for T2DM: obesity and smoking. Also, this thesis estimated the impact of reducing the levels of obesity and smoking in Saudi Arabia on the future projections of T2DM prevalence.

1.3. Why is this thesis important?

It is now well recognised that it is the low and middle income countries that face the greatest burden of T2DM.[11] This has been attributed mainly to the rapid and progressive urbanisation and socioeconomic development in these countries, which has resulted in great changes in the lifestyle of their populations toward sedentary life and consuming 'Westernised' diets.[11] Among all low and middle income countries, the World Health Organisation (WHO)'s Eastern Mediterranean Region (EMR) has been recognised as a major hot-spot for T2DM, where the estimates and projections of its burden exceed those of other world regions. The International Diabetes Federation (IDF) has ranked the region of Middle East and North Africa (MENA), which comprises the largest part of EMR, to have the highest global prevalence of diabetes in 2011 (12.5%) and 2030 (14.3%).[9] However, the health care systems in these countries are generally not yet ready to deal with such an increasingly worrisome health problem. Public health planners and decision makers in these countries need to be more aware of the current high burden posed by T2DM and its complications and, crucially, prepare for its most likely increase during the coming decades.[10, 12]

The Kingdom of Saudi Arabia is one of the largest and richest countries in the EMR. It has witnessed substantial socioeconomic development in recent decades, as it is a leading oil-producing country. The levels of T2DM in Saudi Arabia have been estimated to be among the highest in the world. The IDF has ranked Saudi Arabia to be among the top 10 countries globally with the highest projected prevalence of diabetes in 2011 (19.6%) and 2030 (22.3%).[9] Furthermore, the prevalence of some risk factors for T2DM in Saudi Arabia (e.g. obesity) has also been estimated to be among the highest globally.[13] Although there are currently efforts undertaken by the Saudi Ministry of Health (MOH) toward creating T2DM prevention strategies, it appears that these strategies require further developments and more aggressive implementation. The lack of a structured national risk factors and morbidity surveillance systems in the Kingdom makes understanding past trends and making future projections of the diabetes burden a very urgent and difficult task.

Nevertheless, there are some studies that provided useful estimates and projections of the prevalence of T2DM in Saudi Arabia.[9, 14-17] These studies based their estimates and projections solely on the demographic changes (urbanisation and ageing), and did not directly take into account major determinants of T2DM, such as obesity. Therefore, it is most likely that such studies underestimated the actual trends and future projections of T2DM prevalence in Saudi Arabia, and their estimates have been well surpassed by the 'observed' data from national surveys.[18, 19] On the other hand, there is only one international study[20] that attempted to incorporate the trends in body mass index (BMI) to inform the estimates of T2DM in Saudi Arabia. However, that study only provided estimates to 2008, with no future projections. Furthermore, all these available studies did not provide 'what if' policy analyses to examine the likely impact of reducing the levels of some risk factors on the disease future projections (which is an essential feature in order to engage with policy makers).

Thus, this thesis uses 'epidemiological modelling' as a logical analytical framework to make inferences about past trends and future projections in T2DM prevalence in Saudi Arabia. These inferences are based primarily on integrating demographic trends, as well as the trends in two risk factors for T2DM (obesity and smoking). In addition, this thesis uses this framework to explore health care policy strategies to reduce T2DM prevalence, by providing different 'what if' analyses to estimate the likely impact of reducing obesity and smoking on the T2DM prevalence projections in Saudi Arabia.

1.4. Why does this thesis use modelling?

Modelling is being increasingly used in the fields of epidemiology and public health. Models are used mainly to guide policy decisions in many areas that affect human life and health. Since models combine data from various local sources with trial based effectiveness evidence, they can form a helpful tool for decision making process.[21] Models permit policy makers to examine and compare between various future policy options and intervention scenarios within a population; hence they provide a helpful tool for appropriate planning and resource allocation.[22, 23]

There is a large number of published diabetes modelling studies.[24-29] Most of these models have been related to the 'clinical' and 'health economics' aspects of T2DM (e.g. modelling the disease clinical progression and complications, modelling the health care costs of diabetes, and modelling the cost-effectiveness of some drug treatments and interventions).[24, 25] These modelling studies have utilised a large variety of data on the disease complications and health care costs from several developed countries.[26, 27] There are fewer published diabetes models that attempted to study the trends in the prevalence of T2DM and forecast its future burden in specific populations.[30-32] However, most of these models are proprietary, and all of them have been used in developed countries and require different types of data inputs that might not be available in less developed settings.

Recently, the IMPACT Diabetes Forecast Modelling methodology was originally developed for use in settings with limited data, and was initially piloted in four developing countries of the EMR (Tunisia, Syria, Turkey, and Palestinian areas).[33] An appealing aspect of the methodology is its focus on validation of the model exploring recent past trends in diabetes; a feature not often explored in other modelling approaches.[33] This important aspect helps in creating models that are relevant to specific populations, each one with different demographic and epidemiologic characteristics. Therefore, a "Saudi version" of the IMPACT Diabetes Forecast Model has been created (with assistance of my supervisor; Dr Martin O'Flaherty, University of Liverpool) specifically for this thesis. The model integrates data on trends in population structure, obesity prevalence and smoking prevalence in order to estimate the trends in T2DM prevalence and predict the likely future levels of the disease in Saudi Arabia.

In this thesis, a number of substantial improvements/ developments were undertaken to the original IMPACT model. First, the section of "sensitivity analyses" was significantly developed to involve further rigorous types of analyses. In the original IMPACT model, the uncertainties around the modelling parameters were examined by applying only the 'analysis of extremes' method (discussed in detail in chapter 4) to produce uncertainty intervals. In comparison, the Saudi IMPACT Diabetes Forecast Model used, in addition, the method of 'scenario analysis' to explore uncertainty in the future trends of key model inputs. So, all the model results were presented in different scenarios

and with uncertainty intervals. Second, the section of 'what if policy analyses' in the original IMPACT model was extensively developed and expanded in this thesis. In the original IMPACT model, there were only two policy reduction targets (one for obesity prevalence and another for smoking prevalence), and both of them were 'theoretical' targets. On the other hand, the Saudi IMPACT Diabetes Forecast Model used local policy targets, in addition to other international targets set by leading authorities. Hence, several policy scenarios/ options were analysed in this thesis, which should offer more comprehensive and 'realistic' intervention options for policy makers. The approach which I created and used in my thesis for the 'what if' policy analyses is currently being considered as a framework for use in the four EMR countries, in which the original IMPACT model is being used *(personal communication, Julia Critchley and Martin O'Flaherty, March 2013)*. Third, the original IMPACT model was validated only by comparing its estimates to the observed national data. In comparison, this thesis undertook, in addition, a substantially detailed 'concurrent validation' comparing the model estimates to other existing models of the same purpose, such as that of the most recent IDF Diabetes Atlas,[9] a recent Global Burden of Disease (GBD) project,[20] and other studies.[14-17]

1.5. Why does this thesis use only obesity and smoking as risk factors for T2DM?

As indicated earlier, this thesis used the trends in prevalence of obesity and smoking in Saudi Arabia to inform the estimates and future projections of T2DM prevalence. However, other important 'modifiable' risk factors, such as physical inactivity and diet, were not included in this thesis. Reliable nationwide data on the prevalence of obesity and smoking in Saudi Arabia at different points in time are available[19, 34-39], and could be used to estimate the likely trends and future projections of these two risk factors. On the contrary, prevalence data on physical inactivity and dietary patterns in the Saudi population are scarce, with only one published national study[19] measuring these two conditions. In general, even in more developed countries, the assessment of physical activity and dietary patterns in population studies is difficult, as there are variations in the methods of measurement of these two conditions, and most of such methods are of highly 'subjective' nature.[40]

Nevertheless, this thesis captured well the most important determinant of T2DM (i.e. obesity), considering different reasonable scenarios of the future obesity trends in Saudi Arabia, and the model was validated against both local data and other models.

1.6. The overall aim of this thesis

This thesis aims to support the Saudi Ministry of Health by providing robust estimates and future projections of T2DM prevalence, and providing quantified policy options, likely to be the most effective in reducing the disease burden in the Kingdom.

1.7. Specific objectives

1. To identify and evaluate the existing local data on prevalence of T2DM, obesity and smoking, as well as population and demography in Saudi Arabia.
2. To develop and use the Saudi IMPACT Diabetes Forecast Model to estimate the trends and likely future projections of T2DM in Saudi Arabia.
3. To conduct extensive sensitivity analyses of the modelling results to examine the uncertainties around the model parameters.
4. To validate the Saudi IMPACT Diabetes Forecast Model against local observed data, and carry out detailed comparisons of the model estimates and projections against previous existing modelling studies.
5. To conduct a series of 'what if' analyses to quantify the estimated reduction in the projected T2DM prevalence, that can be attributed to specific targeted reductions in the prevalence of obesity and smoking in the Kingdom.
6. To make recommendations regarding the appropriate preventive interventions for Saudi Arabia in order to reduce the prevalence of T2DM.

1.8. Overview of the chapters

This thesis contains 10 chapters, including this introduction chapter (chapter 1).

Chapter 2 summarises the criteria used to diagnose T2DM, and provides definitions of the relevant terms. It also presents a detailed discussion of the several risk factors associated with T2DM. Also, it discusses the available evidence regarding the role of 'modifying' the two risk factors studied in this thesis (obesity and smoking) in the prevention of T2DM.

Chapter 3 presents a literature review regarding the size of the problem of T2DM in different settings. Firstly, the chapter starts with presenting the different global estimates and projections of T2DM in the total world population. Secondly, it discusses the disease prevalence estimates in the developing countries, with a particular focus on the EMR. Thirdly, the chapter also presents a comprehensive review of the national prevalence studies of T2DM, obesity and smoking in the countries of Gulf Cooperation Council (GCC), which are neighbouring to Saudi Arabia and share similar social, cultural and economic characteristics. Finally, chapter 3 ends with an extensive discussion of the Saudi context, in terms of demography, health care system, levels of NCDs, diabetes care, and the national studies on the prevalence of T2DM, obesity and smoking.

Chapter 4 offers a theoretical discussion on modelling in terms of definition, uses, types, structure, and limitations. This chapter also discusses the steps involved in developing a model, and the existing diabetes models in the literature.

Chapter 5 provides an extensive description and discussion of the model developed for this thesis (the Saudi IMPACT Diabetes Forecast Model), data inputs used to construct the model, data sources with their strengths and limitations, assumptions, and methods of estimating and projecting T2DM prevalence in Saudi Arabia.

Chapter 6 presents the past and current trends in T2DM prevalence in Saudi Arabia (for the period 1992-2013), as estimated by the Saudi IMPACT Diabetes

Forecast Model. All results are presented with uncertainty intervals and in different modelling scenarios as methods of extensive sensitivity analyses.

Chapter 7 presents the future projections of T2DM prevalence in Saudi Arabia (for the period 2014-2022), as estimated by the Saudi IMPACT Diabetes Forecast Model. Again, all results are presented with uncertainty intervals and in different modelling scenarios as methods of extensive sensitivity analyses.

Chapter 8 discusses the available local and international policy targets to reduce the prevalence of adult obesity and smoking. Also, this chapter presents the likely impact of applying such targets on the future projections of T2DM prevalence in Saudi Arabia, as predicted by the model.

Chapter 9 provides detailed comparisons of the results of the Saudi IMPACT Diabetes Forecast Model against previous modelling studies of diabetes prevalence estimates for Saudi Arabia.

Chapter 10 presents the overall discussion and conclusions. It presents a summary of the main findings, strengths and limitations of the thesis, implications of the results, recommendations for policy action and further research, and conclusion.

Chapter 2. Type 2 diabetes: diagnosis and risk factors

In this chapter, two main topics are discussed: a) the criteria used to diagnose T2DM with defining some relevant terms, and b) the risk factors associated with the occurrence of T2DM, and the role of modifying the two risk factors studied in this thesis (obesity and smoking) in prevention of the disease.

2.1. Diagnosis of type 2 diabetes (brief overview)

Diagnosis of T2DM requires an appropriate and uniform system of classification to identify and differentiate the various forms and stages of glucose abnormalities. Such a classification is a major requirement for epidemiological and clinical research as well as for the clinical management of the disease.[3] However, the knowledge regarding diabetes aetiology and pathogenesis is still growing progressively. As a result, the criteria used to diagnose/ define T2DM have been repeatedly revised by leading organisations, such as the WHO and the American Diabetes Association (ADA), as more information relevant to the diagnosis has become available.[3]

2.1.1. Relevant definitions

2.1.1.1 Oral Glucose Tolerance Test (OGTT)

OGTT refers to the measurement of blood glucose values while fasting and at two hours (2 h) after a 75-grams oral glucose load. For children, the oral glucose load is related to body weight (1.75 g/kg).[6]

2.1.1.2. Impaired Glucose Tolerance (IGT) and Impaired Fasting Glucose (IFG)

Both of these terms refer to a metabolic stage intermediate between normal glucose homeostasis and diabetes. This metabolic stage is often referred to as *pre-diabetes* or *intermediate hyperglycaemia*.[3] IGT and IFG are not clinical entities, but rather risk factors for future diabetes and adverse outcomes.[41] IGT is associated with muscle insulin resistance and defective insulin secretion, while IFG is associated with impaired insulin secretion and impaired suppression of hepatic glucose output.[42]

2.1.2. Diagnostic criteria

Table **2.1** summarises the different criteria used at different time points to diagnose diabetes. In 1965, the WHO first published criteria for the diagnosis and classification of diabetes. These criteria were based on specific defined values for fasting blood glucose and/or OGTT, and were revised several times by the WHO, in 1980, 1985 and 1999.[41]

In 1997, the ADA revised the available diagnostic criteria. While the threshold of OGTT remained unchanged (11.1 mmol/l), the ADA recommended lowering the threshold of fasting glucose for diagnosis of diabetes from 7.8 mmol/l (140 mg/dl) to 7.0 mmol/l (126 mg/dl) (Table **2.1**).[3] Moreover, the ADA recommended that for epidemiological studies, estimates of diabetes prevalence and incidence should be based only on fasting plasma glucose (FPG) of ≥126 mg/dl. This recommendation was justified by the interest of standardisation and facilitating the field work, particularly where the OGTT may be difficult to perform and where the cost and demands on participants' time may be excessive.[3] In 1999, the WHO accepted the ADA's recommendations of using the revised threshold of fasting glucose to diagnose diabetes and using such a threshold alone for epidemiological purposes.[41]

The use of OGTT for clinical purposes is an issue of continuing debate. Although the ADA acknowledges the OGTT as a valid method to diagnose diabetes, the use of the test in clinical practice is discouraged in favour of FPG. This is due to inconvenience, greater cost and less reproducibility. On the other hand, the WHO recommends that OGTT should be retained as a diagnostic test for diabetes in clinical practice because it has been found by various studies that FPG alone fails to diagnose approximately 30% of undiagnosed diabetes cases.[41] In addition, OGTT is the only means of identifying people with IGT. Thus, the WHO recommended that OGTT should be used in individuals with an FPG of 6.1–6.9 mmol/l (110–125 mg/dl) to determine glucose tolerance status.[41]

More recently, a WHO consultation report (published in 2011) recommended that glycated haemoglobin (HbA_{1c}) can be used as a diagnostic test for diabetes.[43] Normally, A certain amount of haemoglobin is glycated (to form HbA_{1c}) as a result of exposure to plasma glucose. As the average amount of

plasma glucose increases, the fraction of HbA_{1c} also increases, so that it serves as a marker for average blood glucose levels over the previous period (8-12 weeks) prior to the measurement.[43] HbA_{1c} was introduced into clinical practice in the 1980s, and recently, there has been substantial interest in using it as a diagnostic test for diabetes and as a screening test for persons at high risk of the disease.[43]

The recent WHO consultation report has recommended HbA_{1c} as a diagnostic test "providing that stringent quality assurance tests are in place and assays are standardised to criteria aligned to the international reference values, and there are no conditions present which preclude its accurate measurement. An HbA_{1c} of 6.5% is recommended as the cut point for diagnosing diabetes. A value of less than 6.5% does not exclude diabetes diagnosed using glucose tests".[43] This report recommended that the previous 1999 diagnostic criteria should not be changed. In addition, "the diagnosis of diabetes in an asymptomatic person should not be made on the basis of a single abnormal plasma glucose or HbA_{1c} value. At least one additional HbA_{1c} or plasma glucose test result with a value in the diabetic range is required, either fasting or from the OGTT".[43]

In some laboratories, the precision of HbA_{1c} measurement is similar to that of plasma glucose. In addition, evidence reviewed by the WHO consultation suggests that HbA_{1c} gives equal or almost equal sensitivity and specificity to a fasting or OGTT measurement as a predictor of prevalent microvascular complications of diabetes (e.g. retinopathy).[43] Furthermore, compared to plasma glucose and OGTT, HbA_{1c} is more convenient, performed at any time of the day, does not require any special preparation such as fasting, and has no day-to-day variability in glucose. These advantages have made HbA_{1c} a preferred test for diagnosing diabetes and for assessing glycaemic control in diabetic individuals in some countries. Also, these properties have implications for early identification and treatment which have been strongly advocated in recent years.[43]

However, HbA_{1c} has some limitations. First, the cost of the test is much higher than measuring plasma glucose. Second, there are many genetic, haematologic and other factors that influence the measurement of HbA_{1c}. For instance, some genetic haemoglobinopathies, in addition to iron and vitamin B12 deficiency

may increase or decrease HbA_{1c} levels. Third, for many countries, the test is unavailable, the HbA_{1c} assay is not currently well enough standardised, or there are high prevalences of conditions such as haemoglobinopathies, which affect HbA_{1c} measurement.[43] Therefore, the WHO consultation has indicated that these limitations make it difficult to recommend using HbA_{1c} as a diagnostic test universally at this time. It has been concluded that the choice of diabetes diagnostic method will depend on local considerations such as cost, availability of equipment, population characteristics, presence of a national quality assurance system, etc.[43]

Table 2.1. The WHO and ADA diagnostic criteria for diabetes and intermediate hyperglycaemia at different points in time[41, 43]

	WHO 1965	WHO 1980	WHO 1985	ADA 1997	WHO 1999	WHO 2011
Normal						
Fasting glucose	Not specified	Not defined	Not defined	---	< 6.1 mmol/l	The WHO 1999 criteria retained
2 h glucose	*< 6.1 mmol/l*			---	*Not specified but <7.8 mmol/l implied*	
Diabetes						(HbA_{1c}) can be used as a diagnostic test for diabetes with a recommended value of **6.5%** as the cut point for diagnosing diabetes
Fasting glucose	Not specified	≥ 8.0 mmol/l **and / or**	≥ 7.8 mmol/l **or**	≥ 7.0 mmol/l **or**	≥ 7.0 mmol/l **or**	
2 h glucose	*≥ 7.2 mmol/l*	*≥ 11.0 mmol/l*	*≥ 11.1 mmol/l* **or** ***Random blood glucose:*** *Plasma (venous)≥11.1 mmol/l Plasma (capillary) ≥12.2 mmol/l Whole blood (venous) ≥10.0 ;(capillary) ≥11.1 mmol/l*	*≥ 11.1 mmol/l*	*≥ 11.1 mmol/l*	
IGT						
Fasting glucose		< 8.0 mmol/l **and**	<7.8 mmol/l **and**	Not required	< 7.0 mmol/l **and**	
2 h glucose	*6.1 – 7.1 mmol/l*	*≥ 8.0 and < 11.0 mmol/l*	*≥ 7.8 and < 11.1 mmol/l*	*≥ 7.8 and < 11.1 mmol/l*	*≥ 7.8 and < 11.1 mmol/l*	
IFG						
Fasting glucose	Not defined	Not defined	Not defined	5.6 to 6.9 mmol/l	≥ 6.1 and <7.0 mmol/l **and**	
2 h glucose				*Measurement not recommended (but if measured should be < 11.1 mmol/l)*	*< 7.8 mmol/l (if measured)*	

It is important to mention that in this chapter and others, a distinction was made between “developed” and “developing” countries. This distinction was based on the classification of countries by the World Economic Situation and Prospects (WESP), United Nations.[44] WESP has classified countries as developed economies, economies in transition and developing countries, based on a combination of different criteria that reflect the living standards, industrial base, and other indicators. According to this classification, European countries, US, Canada, Japan, Australia, and New Zealand have been classified as developed countries, and the remaining countries (including Saudi Arabia) as developing. However, for some countries, the dichotomy of developed versus developing might be too restrictive to capture the diversity in development outcomes. Therefore, WESP and other organisations (e.g. the World Bank) have developed an additional classification of the level of development of countries, as measured by per capita gross national income (GNI).[44] Accordingly, countries have been grouped as high-income (GNI per capita >$12,276), upper middle income (GNI per capita between $3,976 and $12,275), lower middle income (GNI per capita between $1,006 and $3,975) and low-income (GNI per capita <$1,005). According to that classification, Saudi Arabia has been classified among the high-income countries.[44]

In this thesis, for the purpose of simplicity, the first classification of WESP (developed and developing countries) is used.

2.2. Risk factors for type 2 diabetes

T2DM is a disease with a multifactorial aetiology, and is associated with a variety of risk factors which influence the disease occurrence. Modifications of some risk factors, particularly behavioural factors (e.g. obesity, physical activity, diet, smoking), have been found to change the disease occurrence in high-risk individuals.[8] However, evaluation of risk factors requires careful attention, since the aetiology of T2DM is complex and involves interaction between various risk factors. In addition, the disease is heterogeneous in different families and populations.

The following sections summarise the major known risk factors for T2DM.

2.2.1. Demographic risk factors

2.2.1.1. Age

The incidence and prevalence of T2DM are generally low before age of 30 years.[6, 45-48] It has been well documented that the prevalence of T2DM rapidly increases with increasing age in a large number of studies conducted in different populations and ethnic groups.[5, 49-54] However, this increase in T2DM levels by age has been noticed to vary between ethnic strata of a population. For example, in the United States (US), prevalence of diabetes in Pima Indians aged 25-29 years (13%) is as high as that for non-Hispanic whites aged 60-64 years.[8] Ethnicity, as a risk factor, is discussed in detail in section 2.2.1.3.

Increasing global life expectancy, which has resulted in ageing populations, has been suggested as one of the most important reasons for the epidemic levels of T2DM in the world.[5, 55] This might be more evident in developing countries during the last few decades. These countries have witnessed 'demographic transition'[56], which has taken place due to several factors. First, there has been a massive reduction in infant and childhood mortality due to infectious diseases, which has been achieved through many effective control programmes of communicable diseases (e.g. vaccination) that have allowed for survival during the early years of childhood and adolescence. Second, the extensive improvements in sanitation and drinking water supplies have resulted in marked decrease in death at all ages. Third, the socioeconomic advances in developing countries have led to considerable progress in health care, including preventive and curative services. Consequently, life expectancy has increased in most developing countries and placed larger proportions of population in the ≥60-year age group, in which chronic degenerative diseases (e.g. T2DM) become the major determinants of health status.[56]

King et al.[16] and Wild et al.[15] reported marked differences in the age structure of the diabetic populations of developed and developing countries. For developed countries, the largest number of people with diabetes was in the age group of ≥65 years in 1995 and 2000, and this age group was estimated to experience the greatest increase in number of cases by the year 2025 and 2030. On the other hand, for the developing countries, the age group of 45-64 years contained the largest number of people with diabetes in 1995 and 2000, and

this tendency is predicted to be further accentuated by the year 2025 and 2030 (Figure **2.1**).[15] These differences in prevalence by age structure might be explained by the shorter life expectancy of individuals with diabetes in developing countries.[16] In addition, the disease incidence has been noticed to be higher at younger ages in developing compared to developed countries.[57] Moreover, ethnicity might be another explanation of these differences in age of onset of the disease across populations as discussed in section 2.2.1.3.

It has been suggested that people tend to exercise less, lose muscle mass and gain weight as they age.[58] As a result, they are likely to have concomitant increases in insulin resistance related to obesity and physical inactivity.[58] Then, as time passes, β-cells in the pancreas fatigue from the increased insulin secretion needed to compensate for increasing levels of insulin resistance. However, the onset of diabetes at younger ages in many developing (e.g. Asian) countries may be attributed to an earlier decline in metabolic homeostasis and/or a shorter latency to the development of diabetes.[58]

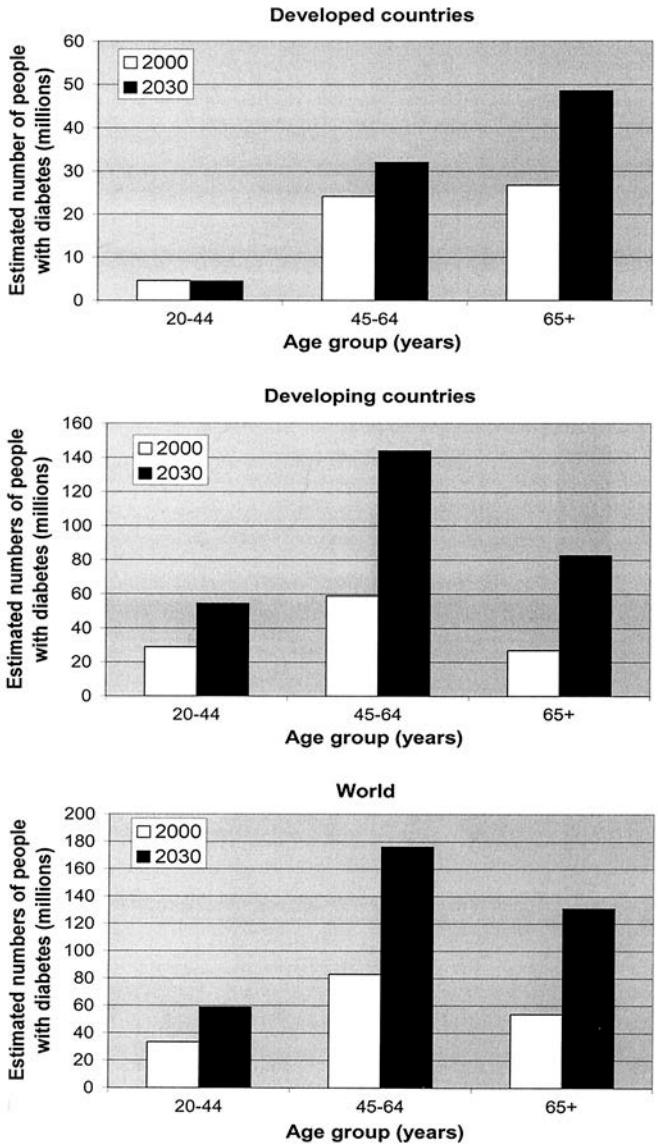


Figure 2.1. Estimated number of adults with diabetes by age group and year for the developed and developing countries and for the world (*Wild et al.*[15])

2.2.1.2. Sex

There is now good evidence on sex differences in susceptibility to a number of adverse health outcomes, particularly autoimmune disorders, such as rheumatoid arthritis, systemic lupus erythematosus and multiple sclerosis.[59] However, there is no similar considerable evidence on sex differences in diabetes. This lack of evidence has been based mainly on the observation that the overall sex balance in diabetes is almost equal.

Gale and Gillespie[60] carried out a comprehensive review of more than 100 studies on sex differences in diabetes. They have pointed out a pronounced excess of T2DM in women in the first half of the 20th century, but the disease has now an almost equal prevalence in both sexes, although there is still some

little excess in women. However, men seem more susceptible than women to the consequences of obesity and physical inactivity, which has been attributed to possible differences in insulin sensitivity and regional deposition of fat.[60]

An example of old studies, included in the review by Gale and Gillespie,[60] is the United States National Health Survey in 1935-1936.[61] In that study, the sample was 2.5 million people from 83 cities, and it was found that prevalence of T2DM was higher by 20% in women than men of the age group 25-34 years. This excess in women increased by 60% for the age group 35-44 years and almost by 100% in the age group of 45-64 years.

King et al.[16] suggested that the likely explanation for such a 'female bias' in developed countries is the greater longevity of women than men. However, as mentioned earlier, diabetes in developing countries is more common in the middle-aged individuals than elderly, which makes the previous explanation less likely. In this case, it has been suggested that differential distribution of risk factors (especially diet, physical inactivity, and central obesity) in men and women may explain such sex differences.[16] This explanation is supported by results of several studies from developing countries. For instance, the Turkish Diabetes Epidemiology Study (TURDEP)[62] showed that the adult Turkish women have a significantly higher BMI (mean 27.45 ± 5.76 kg/m^2) than men (mean 25.47 ± 4.58 kg/m^2). Prevalence of diabetes was also significantly higher in women (8%) compared to men (6.2%). Authors suggested that 'lack of employment outside the home' might contribute to the higher prevalence of obesity in Turkish women. According to that study, physical activity of women in Turkey, like most of countries in the EMR, is confined to house-work and they have no tradition for sporting activities due to social and cultural restrictions.

Some data currently showed that the male/female ratio started to increase considerably by the second half of the last century.[60] For instance, in the United Kingdom (UK), the ratio in the age group of 35-49 years increased from 0.65 during 1945-1949 to 1.78 during 1960-1963.[60, 63] Moreover, although African Americans showed a clear female excess in diabetes prevalence over the period 1963-1985, the prevalence in black males increased more rapidly relative to their female counterparts over the same period.[60, 64] More recently, the estimates of IDF for both 2011 and 2030 showed little sex difference in the

predicted number of people with diabetes. For 2011, it has been estimated that there were about four million more men than women with diabetes (185 million men versus 181 million women). However, this difference is expected to decrease to two million (277 million men versus 275 million women) by 2030.[10]

2.2.1.3. Ethnicity

As mentioned earlier in chapter 1, modernisation and adopting 'western' lifestyles have been suggested to be the major reasons for the epidemic levels of T2DM in the world, particularly in developing countries. Such lifestyles are associated with low physical activity, consuming high-caloric foods and increasing levels of obesity. This has been supported by many studies that compared the prevalence of T2DM in ethnic groups living in different environments/societies. For example, in South Korea, the prevalence of T2DM in rural and small town areas was 2% and 4% respectively, compared with 13% and 16% found in Seoul.[65] In addition, African Americans have a prevalence of diabetes (12%) at least 12 times higher than that observed in Native African Black people (1%).[65] Furthermore, Schulz et al. reported a substantially higher prevalence of T2DM among Pima Indians living in Arizona (38%), compared to those living in a 'primitive' rural mountain region in Mexico (6.9%) although they were genetically related.[66]

Nevertheless, a large number of studies in multi-ethnic populations revealed that some ethnic groups have a higher prevalence of T2DM than other ethnicities living in the same environment and sharing similar lifestyles and dietary habits.[65] These observations suggest that some ethnic groups have a higher predisposition/ susceptibility to develop T2DM compared with others, when exposed to similar adverse environmental conditions.[65] In the US, for example, T2DM is approximately twice as common in blacks and Hispanics as in non-Hispanic whites.[8] Another study reported a high prevalence of diabetes (20.1% in males and 15.5% in females) and IGT (29.7% in males and 16.8% in females) among the minority of Arab Americans.[67] According to the authors, these rates were considerably higher than those reported for the white, African-American, and Hispanic populations in the US and for rural Arab populations. However, they are consistent with rates reported in urban Arab populations.[67] In South Africa, Indian immigrants were found to have higher prevalence of DM

(7.6% in males and 13.5% in females) and IGT (7.1% in males and 4.8% in females) than the original native population.[68] In Singapore, DM prevalence was higher among citizens of Indian origin (13.3% in males and 12.3% in females) than their counterparts of Chinese (8.5% in males and 7.7% in females) and Malay origins (8.6% in males and 10.1% in females).[69]

However, the previous studies did not adjust their results for some important potential confounders such as age, sex, obesity, etc. So, although they were carried out among ethnic groups within the same environments, the differences in diabetes prevalence can still be explained by variations in prevalence of obesity and other behavioural risk factors among these ethnicities.[8] On the other hand, there are several studies that undertook adjustments for known demographic and behavioural risk factors, and still found a significant part of ethnic differences unexplained.[70, 71] For instance, Haffner et al. determined prospectively the eight-year incidence of T2DM in 617 Mexican Americans and 306 non-Hispanic whites. Results of this study showed that 40 Mexican Americans (6.5%) and 6 non-Hispanic whites (2%) developed T2DM. The age-adjusted ethnic odds ratio (OR) [Mexican Americans/non-Hispanic whites] for diabetes incidence was 8.13 in men (95% confidence interval (CI): 1.10–59.9) and 3.62 in women (95% CI: 1.37–9.55). The authors adjusted for age, sex, ethnicity, BMI, and level of educational attainment with multiple logistic regression analyses. Again, it was found that Mexican Americans continued to show a statistically significant increase in diabetes incidence (OR: 2.72; 95% CI: 1.02–7.28).[70] These findings were supported by Marshall et al. who conducted a case-control study in Colorado among 279 cases (diabetics) and 488 controls (normal glucose tolerance) with almost equal ethnic distribution (183 non-Hispanic white vs. 157 Hispanic males; and 208 non-Hispanic white vs. 219 Hispanic females). In this study, Hispanics were found to be twice as likely as non-Hispanic whites to have T2DM, after adjusting for age, sex, obesity, family history of diabetes, education, and income.[71] These observations might indicate existence of some genetic (discussed in the next section) or other unknown risk factors which differ by ethnicity.[8] However, these two studies might be constrained by the relatively small sample sizes.

2.2.2. Genetic risk factors

T2DM is a heterogeneous syndrome that appears to be composed of subtypes where genetic susceptibility is strongly associated with environmental factors at one end of the spectrum, and highly genetic forms at the other end.[72] The hereditary basis of diabetes has been suspected for more than 2000 years, and since the middle of the last century, extensive research has been conducted to investigate the genetics of this disorder.[73] The evidence of a genetic component in the aetiology of T2DM comes primarily from the observations of its familial clustering and ethnic differences.[74]

Although some monogenic forms of diabetes have been identified such as Maturity Onset Diabetes of the Young (MODY), T2DM seems to be a polygenic disorder in the majority of cases.[72] The disease shows a clear and reproducible familial aggregation, with a complex interaction between genetic defects and environmental factors such as obesity. Such interaction complicates the task of identifying any single genetic susceptibility factor to T2DM.[72]

Recently, several twin studies have suggested that T2DM is highly concordant among monozygous (MZ) twins (who are genetically identical) and less so among dizygous (DZ) twins (who share on average only half their genes).[8, 75] In their extensive literature review on the risk factors for T2DM, Rewers and Hamman[8] have reported many twin studies that revealed such a concordance. In these studies, the concordance ranged between 34–100% in MZ twins, and 16–40% in DZ twins.[8] However, according to the reviewers, most studies had potential ascertainment biases. For example, twins in these studies were found because they were diabetics; not because they were twins, i.e. there were no systematic surveys of all twins in study areas because ‘twin registers’ were not available.[76] Twins were referred for investigation from hospitals, other collaborated organisations and as self-referral after programmes in radio or television. This method of twin ascertainment led to a bias towards discovery of concordant as against discordant twin pairs as they had a double chance of recognition.[76] In the only study which had no ascertainment bias, as indicated by the reviewers, concordance rate was the lowest among all reviewed studies (34% in MZ twins and 16% in DZ twins).[8]

In addition to the role of twin studies in identifying a possible genetic component in T2DM aetiology, there are also many studies of various candidate genes.[8] Candidate genes are those genes selected as having a plausible role in the control of glucose homeostasis.[72] Reasons for candidacy are numerous: (1) known or presumed biological function in glucose homeostasis or energy balance in human; (2) gene implicated in subtypes of diabetes, such as MODY; (3) gene associated with diabetes or associated traits in animal models; (4) gene responsible for an inherited disease which includes diabetes; (5) product differentially expressed in diabetic and normal tissues.[72] Study of candidate genes is the most commonly used approach to tackle the genetic determinants of T2DM. However, almost all identified candidate genes have only small effect on the polygenic forms of diabetes. No genes with major effects/ associations have been identified.[8, 72] Possible explanations for failure to identify such genes include the possibility that they do not exist. Moreover, it is also possible that the incomplete understanding of pathophysiological mechanisms of T2DM (and the genes that control them) has misled the choice of candidate genes.[72]

Rewers and Hamman[8] reviewed more than 40 studies of 13 candidate genes in different populations. The majority of these studies have not resulted in positive association for candidate genes and T2DM. Although there were some isolated positive findings, most of these were not replicated on repeated analysis in other or larger populations. Examples of the most commonly studied candidate genes are the insulin gene and glucokinase (GCK) gene - (GCK is an enzyme that catalyses the formation of glucose-6-phosphate from glucose, and is the major rate limiting step in glycolysis).[8] Mutations in various regions of candidate genes have been reported by some studies. These mutations result in defects in glucose homeostasis (e.g. hypoinsulinaemia due to mutations in the insulin gene,[72] and GCK dysfunction which impairs the process of glycolysis as a result of mutations in the GCK gene[8]).

In conclusion, it appears unlikely that candidate genes are associated with a substantial proportion of T2DM in the general population.[8] According to Velho and Froguel,[72] all the described genetic defects account for not more than a few percent of all cases of T2DM. The majority of susceptibility genes to T2DM still require investigation and detail description in order to improve the understanding of molecular mechanisms that maintain glucose homeostasis

and of the precise molecular defects leading to chronic hyperglycaemia. A nosological classification of T2DM based on primary pathophysiological mechanisms will then be possible. Also, this could lead to the development of more specifically targeted anti-diabetic drugs or even gene-based therapies.[72]

2.2.3. Behavioural and environmental risk factors

2.2.3.1. Background

Historically, the first evidence for an environmental factor in the aetiology of T2DM was described by Indians in the sixth century. Three Hindu physicians wrote of diabetes: *"It is the disease of the rich and one that is brought about by the gluttonous overindulgence in oil, flour and sugar"*.[77] Diabetes and its relationship to overnutrition were also described in Chinese medicine in about 400 BC.[77] One thousand years after that date, diet was implicated as an important risk factor for T2DM by Thomas Willis.[77]

Migration studies and studies of secular trends indicate that a western lifestyle is associated with a higher prevalence of T2DM.[78] For example, a surge in the prevalence of T2DM concomitant to the adoption of a western lifestyle occurred when Japanese people emigrated to the US during the second half of the 20th century. At the same period, there was a shift from traditional agriculture to a modern American lifestyle characterised by lack of physical activity, a western diet and high rates of obesity.[78] Thus, it was suggested that environmental factors played an important role in the aetiology of T2DM and the sharp increase in its prevalence among this group, because genetic characteristics of populations are unlikely to change in such a short period of time.[78]

The role of environmental/ behavioural factors in the aetiology of T2DM may be more obvious in populations living in transition. In the past, the disease was more prevalent in the industrialised countries, which were far more affluent than other countries. Later, when the developing countries started to witness progressive and rapid socio-economic developments, the levels of T2DM in such countries started to increase dramatically. However, this might be a complex issue which requires further investigations. Although early studies in the white US and UK populations showed that people with greater affluence, education and social standing had a higher risk of diabetes, recent studies

showed the highest rates of disease in the most deprived sections of the community[79] (discussed in section 2.2.3.6). Some researchers now postulate that T2DM appears to be a disease of *'newly'* affluent more than *'established'* affluent populations.[80]

Behavioural/ environmental risk factors for T2DM are often known as 'modifiable' risk factors. There is now increasing evidence supporting that some lifestyle changes (e.g. weight loss, increased physical activity, dietary restrictions) are associated with changes in the occurrence of T2DM.[8, 81-83] Section 2.2.4 discusses in more detail the role of modifying the two risk factors studied in this thesis (obesity and smoking) in preventing T2DM.

In the following sections, the major behavioural/ environmental risk factors for T2DM (obesity, physical inactivity, diet, smoking, and socioeconomic status) are discussed.

2.2.3.2. Obesity

A. Background and definitions

Fat, stored in the adipose tissue, forms a normal physiological part of the body, and has several functions.[84] It acts as storage of energy in periods of lower energy intake compared with energy expenditure (negative energy balance) and has also a function as a thermal insulator. Furthermore, adipose tissue around certain organs protects them against mechanical damage. The amount of body fat is extremely variable in different individuals. The physiologically normal amount of body fat depends primarily on age and sex. Newborns have 10–15% body fat, which increases to 25% during the first year of life. However, body fat starts to slowly decrease again to 15% of body weight at the age of 10 years, when differences between the sexes become more apparent. During sexual maturation, girls experience an increase in their body fat again, up to about 25%, whereas boys keep about the same body fat. During adulthood, body fat increases slowly with age in both men and women.[84]

Obesity results when the amount of body fat exceeds normal physiological values. The WHO defines obesity as the accumulation of adipose tissue to excess and to an extent that impairs both physical and psychosocial health and well-being.[85, 86] There are various laboratory and imaging techniques that can

accurately measure the amount of body fat. For example, the use of computed tomography (CT) or magnetic resonance imaging (MRI) allows for three-dimensional views of body composition, and are used to obtain information on body fat distribution.[84] However, these methods are expensive and time-consuming. Hence, they are not suitable for field work, epidemiological studies and most clinical work.[86] Instead, the WHO recommends the body mass index (BMI) as a measure of obesity. BMI is a simple index of weight-for-height and is defined as the weight in kilograms divided by the square of the height in metres (kg/m^2). It is the most widely accepted measure of obesity in populations and in clinical practice.[86] In adult populations, it has been found that the relationship between morbidity/mortality and BMI is U-shaped, and the risk for adverse health effects increases beyond a BMI of 25 kg/m^2.[84] Based on this relationship, the WHO recommends its cut-off points for overweight and obesity in adults. Overweight in adults is defined as a BMI greater than or equal to 25 kg/m^2, while obesity is defined as a BMI greater than or equal to 30 kg/m^2.[87] BMI provides the most useful population-level measure of overweight and obesity as it is the same for both sexes and for all ages of adults, and has been widely used in most studies worldwide.[87]

However, BMI should be considered as a rough guide because its reliability is prone to some limitations in persons with extremes of age, very muscular builds (overestimates obesity), and extreme height.[85, 87, 88] In addition, it has been found that in some ethnic groups, particularly Asians, the above-mentioned cut-off values of BMI are not suitable for classification of overweight and obesity. The mean or median BMI in Asians is lower than that observed for non-Asian populations; so the BMI distribution is shifted to the left. This trend leads to the concern that application of the standard WHO's BMI cut-off points will underestimate obesity-related risks in these populations.[89] In 2002, the WHO has recommended different BMI cut-off points for Asian populations. An expert WHO consultation[89] indicated that there were three specific factors which led to development of new cut-off points in Asians. First, there was increasing evidence of the emerging high prevalence of T2DM and increased cardiovascular risk factors in parts of Asia where the average BMI is below the cut-off point of 25 kg/m^2. Second, there was increasing evidence that the associations between BMI, percentage of body fat, and body fat distribution

differ across populations. In particular, in some Asian populations a specific BMI reflects a higher percentage of body fat than in white or European populations. Some Pacific populations also have a lower percentage of body fat at a given BMI than do white or European populations. Third, there had been two previous attempts to interpret the WHO BMI cut-offs in Asian and Pacific populations, which contributed to the growing debates on whether there are possible needs for developing different BMI cut-off points for different ethnic groups.[89] The WHO recommended a BMI cut-off value of 23-27.5 kg/m^2 for overweight and ≥27.5 kg/m^2 for obesity in Asians.[89]

Another limitation of BMI is that it only estimates the 'total' adiposity of the body. Thus, it may miss many cases of 'central / abdominal' obesity, in which the body fat accumulates mainly around the waist. Some studies revealed that central obesity is associated with a greater prevalence of metabolic diseases, including T2DM and dyslipidaemia.[86] The simple clinical measure of central obesity is the waist circumference (WC). The WHO recommends a cut-off point of WC ≥102 cm in men and ≥88 cm in women for definition of central obesity.[90] Again, Asian populations, particularly people of South Asian origin (Indians, Pakistanis, Bangladeshis), seem more prone to carrying excess fat centrally than the White populations and show raised obesity-related risk although they may not be considered obese by conventional WC criteria. Therefore, the WHO thresholds for central obesity in Asians are a WC ≥90 cm in men and ≥80 cm in women.[90] In addition to WC, the waist-to-hip circumference Ratio (WHR) is another measure of central obesity. A WHR >1.0 in men and WHR >0.85 in women are used as cut-offs for identifying individuals with central obesity. However, WC is more commonly used than WHR for measuring the abdominal obesity.[90]

B. Obesity and type 2 diabetes

According to the WHO,[87] the worldwide obesity has more than doubled since 1980. In 2008, for example, 1.5 billion adults, aged ≥20 years, were overweight. Of these, over 200 million men and nearly 300 million women were obese, which means that more than one in ten of the world's adult population was obese in 2008. It has now been estimated that around 65% of the world's population live in countries where overweight and obesity are associated with more deaths than underweight. In 2010, around 43 million children under five

were overweight. The vast majority of these overweight children (35 million) live in developing countries, compared to 8 million in industrialised countries.[87] The estimated economic burden of obesity in developed countries ranges between 2% and 7% of health care costs, and is higher in developing countries. However, these figures are likely to underestimate the true burden because of the difficulties of attributing specific costs to associated obesity and the exclusion of indirect costs from most studies.[91]

The association between obesity and T2DM has been reproducibly observed in both cross-sectional[71, 92] and prospective studies,[93, 94] and has been consistent across various populations even when using different measures of fatness and different diagnostic criteria for T2DM.[95] The current parallel global epidemics of obesity and diabetes seem to be related.[95] Such a relation is obviously evident in children, who are increasingly affected by obesity and in whom the prevalence of T2DM is currently approaching that of type 1 diabetes.[96]

Guh et al.[97] have conducted a relatively recent systematic review and meta-analysis, which included a total of 89 large prospective cohort studies reporting risk estimates of any of 18 comorbidities related to overweight and obesity. The first reviewed comorbidity was, of course, T2DM. The systematic review covered studies that used BMI and/or WC to define overweight and obesity (by the conventional definitions stated in section A above). The reported relative risks (RRs) in studies were synthesised, and pooled RRs were estimated, comparing the risk of the comorbidity in overweight (BMI ≥25-29.9 kg/m^2) and in obese (BMI ≥30 kg/m^2) to the individuals with 'normal weight'. Among the total 89 studies, there were nine studies reporting incident T2DM in overweight and obese individuals. The estimated pooled relative T2DM risks related to being overweight or obese are summarised in Table **2.2**. In general, elevated BMI and WC were significantly associated with T2DM in both men and women. The association between increased WC and T2DM was similar but weaker in comparison with BMI.

Table 2.2. Pooled relative T2DM risks (with 95% CIs) related to being overweight or obese, as estimated by Guh et al.[97]

Measure of overweight/ obesity	Overweight		Obesity	
	Men	Women	Men	Women
BMI	2.40 (2.12–2.72)	3.92 (3.10–4.97)	6.74 (5.55–8.19)	12.41 (9.03–17.06)
WC	2.27 (1.67–3.10)	3.40 (2.42–4.78)	5.13 (3.81–6.90)	11.10 (8.23–14.96)

However, Guh et al.[97] included studies from only western populations (countries in Europe or North America, Australia or New Zealand). In addition, the number of reviewed studies for T2DM was relatively small, and the pooled RRs were reported as sex-specific only (no age-specific RRs). Moreover, as with all systematic reviews, the reported results might be affected by potential publication bias.

The biological link between obesity and T2DM relates primarily to the adipose tissue in the body.[96] Adipose tissue is not only a passive fuel storage, but has been also recognised as an endocrine organ which secretes hormones and communicates with the central nervous system in order to regulate appetite and metabolism.[96] The main biological/pathological pathways which link obesity and T2DM are briefly summarised in the following points:

- ***Elevated leptin levels.*** Leptin is a protein produced by adipocytes. The main role of leptin is to regulate food intake and energy expenditure by reducing food intake and increasing sympathetic nervous system outflow, therefore inducing weight loss.[91] Leptin levels are elevated in obesity and this has been found to positively correlate with insulin resistance. Leptin can impair the production of insulin and reduce the effects of insulin on the liver.[91]
- ***Elevated levels of adipocyte-derived free fatty acids.*** In adipose tissues, glucose is involved in lipogenesis via its conversion to glycerol-3-phosphate, which is then combined with 'non-esterified fatty acids (NEFAs)' to form triglycerides. An important role of insulin is to prevent the breakdown of triglycerides (lipolysis), which liberates NEFAs.[91] In obese individuals, the levels of these fatty acids are raised, which results in impairment of glucose

metabolism by reducing insulin-stimulated glucose uptake in skeletal muscle, and increasing the hepatic glucose output.[91, 96]

- ***Elevated levels of proteins secreted by adipose tissue.*** In addition to leptin, adipose tissue secretes many other proteins that modulate glucose metabolism and insulin action. Examples of these proteins include adiponectin, adipsin and resistin. Again, studies have generally suggested that circulating levels of these proteins are elevated in individuals with T2DM.[96]
- ***Elevated levels of adipocyte-nonspecific proteins.*** There are some proteins which are secreted by adipocytes as well as other cells and tissues. For instance, Cytokines such as tumour necrosis factor α (TNF α) and interleukin-6 are produced by macrophages and also by adipocytes.[96] These proteins are involved in innate immunity and contribute to the process of inflammation, either directly through acting on inflammatory cells or indirectly by acting on the liver to produce acute phase proteins.[91, 96] Cytokines have been found to induce 'suppressor of cytokine signaling-3 (SOCS-3)', which is an intracellular signalling molecule that impairs the signalling of both leptin and insulin. In obesity, SOCS-3 levels are elevated and thus may result in obesity-associated resistance to the actions of both leptin and insulin.[96]

Nonetheless, not every obese individual develops diabetes and, therefore, obesity alone is not sufficient to cause T2DM. The relationship between obesity and T2DM is complicated by the effects of several modifying factors. These factors include duration of obesity, distribution of body fat, physical activity, ethnicity and genetics. The following sections concisely discuss these factors and their possible modifying effects.

(i) Duration of obesity

There is little evidence that quantifies the relationship between duration of obesity and risk of T2DM. Reasons for this paucity of information include the difficulty to measure the actual onset of obesity, which can only be obtained by recall or by detailed longitudinal follow up studies. Furthermore, it is also difficult to differentiate between the effects of degree and duration of obesity in case the weight is changing.[95]

Examples of studies which have reported an association include one study among Pima Indians, who have one of the highest levels of T2DM in the world. In that study, Everhart et al.[98] prospectively investigated 1057 individuals for a total of 5975 person-years of follow up. The association of duration of obesity with incidence of T2DM adjusted for age, sex, and current BMI was highly significant. This adjusted incidence of T2DM in cases/1000 person-years of obesity was 24.8 for people with less than 5 years of obesity, 35.2 for people with 5-10 years of obesity, and 59.8 for people with at least 10 years of obesity. In addition, another prospective study, conducted in Japan,[99] observed 1598 men aged ≥30 years for a period of 10 years or more, and these participants were free from serious disease conditions with initial BMI <25.0 kg/m^2. Obesity in this study was classified as 'ordinary obesity' if BMI >25.0 kg/m^2 and 'extreme obesity' if BMI ≥27.8 kg/m^2. Results showed that the age-adjusted ORs for T2DM were significantly increased among individuals who were obese for 10-19.9 years and ≥20 years (ORs 2.10 and 2.84 for ordinary obesity and 6.14 and 4.15 for extreme obesity, respectively). Additional adjustments for physical activity, smoking, alcohol consumption, family history, and observation period did not change the findings remarkably.

(ii) Body fat distribution

There is considerable evidence which suggests that both overall adiposity and fat distribution are independently important risk factors for T2DM in both men and women.[100] However, both cross-sectional and longitudinal data are not consistent as whether the total adiposity (measured by BMI) or abdominal adiposity (measured by WC, WHR, etc) is a stronger predictor of T2DM. For example, a meta-analysis[100] was conducted based on 32 published studies from 1966–2004, and demonstrated that the three major obesity indicators (BMI, WC, WHR) have similar associations with incident diabetes. The pooled RRs for incident diabetes in this study were 1.87 (95% CI: 1.67, 2.10), 1.87 (95% CI: 1.58, 2.20), and 1.88 (95% CI: 1.61, 2.19) per standard deviation of BMI, WC, and WHR respectively.

Nevertheless, as indicated earlier, the effect of body fat distribution in predicting T2DM is more evident in some particular populations, such as people of South Asian origin. South Asians are more prone to abdominal obesity and low muscle

mass with increased insulin resistance compared with white western individuals.[57] The risk of T2DM starts at a lower BMI for Asians, and they have lower rates of overweight and obesity than their European counterparts, using conventional definitions with the previously mentioned BMI cut-offs.[57] These observations have been supported by using the imaging technology of CT scan, which showed that healthy Chinese and South Asian individuals have a greater amount of visceral adipose tissue than Europeans with the same BMI or WC.[57]

McKeigue et al.[101] carried out a population survey of around 3760 men and women aged 40-69 years in London. The study showed that the prevalence of diabetes was 4.3 times higher in the South Asian than European participants (19% vs. 4% respectively). However, mean BMI was almost equal in European and South Asian men (25.9 vs. 25.7 kg/m^2 respectively), and slightly higher in South Asian women (27.0 kg/m^2) than their European counterparts (25.2 kg/m^2). On the other hand, WHR was clearly higher in South Asians (0.98 in men and 0.85 in women) than Europeans (0.94 in men and 0.76 in women). Within each ethnic group, WHR was positively correlated with glucose intolerance, which may confirm the existence of an insulin resistance syndrome, prevalent in South Asian populations and associated with a pronounced tendency to central obesity in this group.

(iii) Physical activity

Physical activity is generally defined as "bodily movement produced by the contraction of skeletal muscle that requires energy expenditure in excess of resting energy expenditure".[102] There is considerable evidence supporting that physical activity is an important component on long-term weight control.[102-105] Physical activity generally affects body composition and weight favourably by promoting fat loss. However, the rate of weight loss is positively related, in a dose-response manner, to the frequency and duration of the physical activity session/ programme.[102] It has been observed by a large number of studies that a minimum of 150 minutes/ week of moderate-intensity physical activity (e.g. 30 minutes of brisk walking daily) is associated with health-related benefits.[103, 104] However, higher levels of physical activity may be necessary to improve long-term weight loss outcomes. For example, an additional 200–300 minutes/ week of physical activity has been reported to improve weight loss in overweight and

obese individuals. This is approximately equivalent to 65 minutes of moderate-intensity physical activity per day.[104] Moreover, studies have demonstrated that exercise alone can have a significant impact on body weight when maintained for ≥12 months, and that individuals who reduce their level of leisure-time physical activity can have weight regain after a specific period of time. Thus, for exercise to be effective long term, it should be maintained long term in overweight and previously overweight individuals.[104] Another important observation is that weight loss resulting from increased physical activity without caloric restriction is relatively slow, while the combination of increased physical activity and dieting appears to be more effective for long-term weight regulation than is dieting alone[102] (discussed in the next section).

(iv) Diet

Obesity generally results from an imbalance between energy intake and energy expenditure.[106] Relative excessive energy intake can of course result from excess dietary intake of fat, carbohydrates, proteins, etc. However, progress in understanding the role of diet in the aetiology of obesity has been seriously confounded by the profound under-reporting, which is now widely recognised as a feature of obesity. Several studies have reported that obese individuals might under-report their self-reported intake by an average of 30% due to many reasons, such as forgetfulness, underestimation of portion size, inadequate knowledge of food composition, or even self-deception.[107] The evidence is inconsistent regarding the relation between intake of individual macronutrients (fat, carbohydrate and protein) and obesity, with fat overconsumption being the most commonly suggested dietary factor to have a role in the aetiology.[107, 108] Many studies have found that each individual macronutrient exerts different effects on eating behaviour, predominantly due to their effects on satiety. It has been suggested that, in contrast to carbohydrate and protein, fat appears to have a weak satiating capacity, and subjects readily overeat in response to high fat foods. As fat has twice as much energy per gram as protein or carbohydrate, this may eventually result in energy density.[107] On the other hand, carbohydrates are converted to fat only after several days' consumption of considerably large amounts (more than 500 grams of carbohydrates per day). Thus, it has been postulated that the lipogenesis from carbohydrates does not represent a major metabolic route in the development of obesity.[108] According

to the review of Vögele, several large field studies have shown a positive linear relationship between body weight and fat consumption, but a negative correlation with carbohydrate intake.[108] However, the results of prospective studies of dietary fat intake and weight gain are clearly inconsistent, although most cross-sectional studies do suggest an association. For instance, Seidell reviewed many studies with different findings. While some studies found no relation between percentage of energy from fat and weight gain prospectively, others observed a positive association which was specific only to one sex.[106]

Nevertheless, some researchers now suggest that the current epidemiologic methods are likely to be inadequate for performing valid studies of the relation between dietary intake of 'individual' macronutrients and obesity.[106] This is mainly due to inaccurate estimates of energy intake and energy expenditure as well as of dietary fat intake measurements, in addition to biases as a result of under-reporting[77, 106] (as previously mentioned). Rather, it is believed that the 'total' energy intake is the factor which has a more obvious association in most studies. The strongest evidence for that might come from several intervention studies that compared the effects of exercise and that of reducing energy intake on changes in body weight.[104] These interventions have reported that reductions in energy intake (e.g. diet) have a greater impact on body weight than changes in energy expenditure (e.g. exercise), although the combination of diet plus exercise has the greatest impact on weight loss. For example, one intervention study reported reductions in body weight of 11.4, 8.4, and 0.3% in male participants with 12 weeks of diet plus exercise, diet alone, or exercise alone, respectively. A similar pattern of weight losses of 7.5, 5.5, and 0.6% was observed in women engaging in the same study.[104]

(v) Genetics and ethnicity

Evidence from some studies suggests that obesity interacts with family history of diabetes in promoting T2DM risk. For example, Haffner et al.[109] examined 549 non-diabetic persons with a parental history of diabetes and 1167 non-diabetic persons without such a history. It has been found that, compared to persons without a parental history of diabetes, those with such a history had a more atherogenic pattern of cardiovascular risk factors, including higher BMI and serum insulin concentrations. However, after adjustment for serum insulin

concentration, BMI and WHR between the two parental history groups were no longer statistically significant, which might suggest that the association was mediated through hyperinsulinaemia.

On the other hand, several other studies have observed that the association between T2DM and obesity was more apparent in individuals without a family history of diabetes. For instance, in a study among Japanese Americans,[110] a total of 79 non-diabetic and 78 type 2 diabetic men were investigated. Family history of diabetes in a sibling or parent was found in 24 normal men and 45 type 2 diabetic men. Both general adiposity and body fat distribution were significantly associated with T2DM. The relationships between diabetes and both general adiposity and body fat distribution were more apparent in those men without a family history of diabetes than in those with a family history. This study and others[111] might suggest that a higher level of obesity is required for the development of T2DM in individuals without a genetic predisposition to the disease.[95]

Also, as described in detail in section 2.2.1.3, a large number of studies have revealed that some ethnic groups have an elevated risk of T2DM compared to other ethnicities.[8, 65-69] In all these studies, which have not adjusted for some confounding variables (e.g. BMI), obesity might be a modifying factor for increased levels of the disease. However, it has also been discussed that some ethnic groups, particularly Asian Indians, appear to have an elevated risk of T2DM compared to other ethnic groups at similar or lower levels of BMI.[101] Asian Indians are more likely to have abdominal obesity than other ethnicities, and this difference in body fat distribution has been proposed to have an association with the risk of T2DM when adjusting for many other potential confounding factors.[101]

2.2.3.3. Physical inactivity

As previously indicated, early suggestions of a relationship between physical inactivity and diabetes emerged from the observation that societies that had shifted their lifestyles from traditional (which included large amounts of regular physical activity) to westernised sedentary habits experienced major increases in the prevalence of T2DM.[102] The epidemiological transition (chapter 3) in developing countries, during the last decades, is an obvious example which

suggests such an association.[112] Moreover, several ecologic studies have suggested that T2DM prevalence is consistently lower in populations with higher levels of habitual physical activity.[8]

Also, a large number of cross-sectional as well as prospective and retrospective observational studies have found a significant association between physical inactivity and T2DM.[8, 102] For example, a prospective study was carried out among 1728 non-diabetic individuals from the high risk population of Pima Indians. During an average follow-up period of 6 years, it was found that total activity was related to diabetes incidence in women and men after adjusting for age. After additional adjustment for BMI, the relation between activity and diabetes incidence was weakened in both men and women. When the age-adjusted diabetes incidence rates were examined by levels of activity stratified by tertile of BMI, the diabetes incidence rate remained lower in more active than in less active men and women from all BMI groups.[105]

The available evidence suggests a number of possible biological pathways for the protective effect of physical activity on development of T2DM. First, it has been suggested that physical activity increases sensitivity to insulin. In a comprehensive report of "Physical Activity and Health" by the US Department of Health and Human Services,[102] an extensive literature review has indicated that physical activity is more likely to improve abnormal glucose tolerance when the abnormality is primarily caused by insulin resistance than when it is caused by deficient amounts of circulating insulin. Therefore, physical activity is likely to be most beneficial in preventing the progression of T2DM during the earlier stages of the disease process, before insulin therapy is required. The second suggested protective mechanism of physical activity is that exercise appears to have a synergistic effect with insulin. During a single prolonged session of physical activity, contracting skeletal muscle has been suggested to enhance glucose uptake into the cells. This effect appears to be related to both increased blood flow in the muscle and enhanced glucose transport into the muscle cell.[102] Third, physical activity has also been found to reduce intra-abdominal fat, which is a known risk factor for insulin resistance. In many studies, physical activity has been inversely associated with intra-abdominal fat distribution, and can reduce those body fat stores.[102]

2.2.3.4. Diet

The role of diet in the aetiology of T2DM was proposed by early Indians who, as mentioned earlier, observed that the disease was almost confined to rich people who consumed oil, flour and sugar in excessive amounts.[77] During the First and Second World Wars, declines in the diabetes mortality rates were documented due to food shortage and famines in the involved countries such as Germany and other European countries. For example, in Berlin, diabetes mortality rate declined from 23.1/100,000 in 1914 to 10.9 in 1919.[113] In contrast, no change in diabetes mortality were described in other countries which had no shortage in food at the same time period such as Japan and North American countries.[113] Importantly, however, these observations only indicate a probable dietary component in the aetiology of T2DM, and do not provide absolute evidence. The reason is the existence of many potential confounding factors and competing risks such as ethnicity, genetics and others.

Again, the epidemiological transition in developing countries has always been attributed to adopting a western lifestyle and high-calorie dietary habits.[112] This has been supported by studies (previously discussed in section 2.2.1.3) that compared T2DM prevalence among urban societies and those societies that remain to adopt a traditional physical activity and dietary habits.[65, 66] In the EMR, for example, unhealthy diet has been reported among the main causes of the alarming high rates of NCDs, including T2DM, in the region. The mean daily caloric intake among countries of EMR in 2000 was 3000 kilocalories per capita, and it seems there was no improvement between 1994 and 2000.[114]

However, evidence on the role of diet in the aetiology of T2DM remains controversial. While some studies have found an association between T2DM and high intake of carbohydrates[115] and fats[116], other studies have not reported such an association.[117, 118] For over 40 studies, reviewed by Mann and Toeller,[77] half of them have been found to report a positive association between high intake of sugars and development of T2DM, and a comparable number of studies suggesting no association. An example of studies with a positive association is the study of Ludwig et al.[115] which investigated 548 ethnically diverse schoolchildren for 19 months. It has been found that for each additional serving of sugar sweetened drink consumed, both BMI (mean 0.24 kg/m^2) and

frequency of obesity (OR 1.60) increased after adjustment for anthropometric, demographic, dietary, and lifestyle variables. On the other hand, Peterson et al.[117] studied 23 diabetic patients: 12 with type 1 and 11 with T2DM, with differing degrees of glycaemic control. Two diets, each lasting 6 weeks, were compared. Both diets were high in fibre and low in fat. In one diet 45 grams of complex carbohydrate was replaced by 45 grams of sucrose taken at mealtimes. There were no significant biochemical differences between the two diets in either type 1 or type 2 patients. In type 2 patients, the mean fasting plasma glucose was 9.1 mmol/l on the control diet, and 8.9 mmol/l on sucrose. Glycosylated haemoglobin for the type 2 patients was 9.3% on control and 9.0% on sucrose. Moreover, there were no differences in mean daily plasma glucose levels or diurnal glucose profiles.

As with carbohydrates, the relationship between dietary fats and T2DM is also inconsistent. Several prospective studies have found associations between fat intake and subsequent risk of developing T2DM. For example, in the San Luis Valley Diabetes Study,[119] a total of 1,317 subjects without a prior diagnosis of diabetes were prospectively investigated for a period of 4 years. In that study, 24-hour diet recalls were reported prior to an oral glucose tolerance test. Persons with previously undiagnosed diabetes (n= 70) and impaired glucose tolerance (n= 171) were each compared with confirmed normal controls (n= 1076). The adjusted ORs relating a 40 grams/day increase in fat intake to T2DM and impaired glucose tolerance were 1.51 (95% CI: 0.85–2.67) and 1.62 (95% CI: 1.09–2.41) respectively. Restricting cases to diabetic persons with fasting glucose >140 mg/dl and persons with impaired glucose tolerance confirmed on follow-up, the ORs increased to 3.03 (95% CI: 1.07–8.62) and 2.67 (95% CI: 1.33–5.36) respectively. In contrast, Colditz et al.[120] prospectively followed up a large cohort of 84,360 US women for 6 years. They examined the relations of the various diet components, including fat, fibre and sucrose and the risk of T2DM among two groups of women (those with BMI of <29 kg/m^2 and others with BMI ≥29 kg/m^2). After controlling for BMI, previous weight change and alcohol intake, no associations were found between intakes of fat, sucrose, carbohydrate or fibre and risk of diabetes in both groups. However, as mentioned earlier, these association studies might suffer from different constraints, such as poor assessment of actual dietary intake, inability to

disentangle dietary and other confounding factors, in addition to over-interpretation of data derived from observational studies.[77]

2.2.3.5. Smoking

Studying the effect of smoking on T2DM might be difficult, as those people who smoke are more likely to be less active (sedentary), which is a risk factor for T2DM. However, several studies have assessed the association between smoking and incidence of glucose abnormalities, suggesting that active smoking could be independently associated with IGT, IFG, and T2DM.[121-126] According to these studies, smoking may be a modifiable risk factor for T2DM. Some reviews[127-129] of such studies revealed that they are generally large, prospective and population-based, with a follow-up period greater than 10 years in most studies. The results generally were presented after adjustments for possible confounders such as age, BMI, WC, physical activity, blood pressure, etc.

For instance, Perry et al.[121] conducted a large prospective cohort study among a sample of 7735 British men, aged 40-59 years from 24 towns in Britain. All subjects were non-diabetic at baseline and followed up for a mean period of 12.8 years. Baseline values (adjusted for age and BMI) showed that current smoking was significantly higher among men who developed T2DM during the follow up period, compared to those who did not develop the disease. However, in the multivariable analysis, the relative risk for diabetes was higher among smokers (adjusted RR: 1.2; 95% CI: 0.8-1.8), but the association lost its significance and was not independent of other risk factors (obesity and low physical activity were the strongest). In the Osaka Health Survey in Japan,[122] a total of 6250 middle-aged men were followed up for a period of 4-16 years (60,904 person-years). Participants were free of T2DM, IFG and hypertension at entry. The RR of T2DM among current smokers compared to non-smokers was 1.47 (95% CI: 1.14–1.92) after adjustment for many covariates, including age, BMI, alcohol consumption, physical activity, parental history of diabetes and the level of fasting plasma glucose, total cholesterol, triglycerides, high-density lipoprotein cholesterol and haematocrit. Importantly, a ‘dose-response’ relationship was found for this association; the number of cigarettes smoked daily was significantly related to the development of T2DM.

There are many other examples of prospective studies which reported a positive association between smoking and T2DM among men. Rimm et al.[123] reported a RR of 1.94 in smokers compared to non-smokers of a large cohort of male health professionals across the US. Moreover, another study[124] analysed glycaemic status and smoking habits in 3718 Chinese men, and found that smoking is independently associated with diabetes after adjustment for age, BMI, alcohol, and family history of diabetes (OR: 1.7).

In women, not as many studies have been performed as in men. However, most studies in women have also produced similar results.[128] One of the largest prospective studies is the Nurses' Health Study in the US.[125] In this cohort study, a total of 114,247 female nurses, who were free of diabetes at baseline, were followed up for 12 years (1,277,589 person-years). Current smokers were found to have an increased risk of diabetes, and a significant dose-response trend for higher risk among heavier smokers was observed. The RR of diabetes, adjusted for several covariates (e.g. age, BMI, alcohol consumption), was 1.42 among women who smoked 25 or more cigarettes per day compared with non-smokers. In another study, Hu et al.[126] carried out a new analysis of results from the same cohort after 16 years of follow up. They followed 84,941 female nurses, who were confirmed non-diabetic at baseline, from 1980 to 1996. Overweight or obesity was the single most important predictor of diabetes in this study. However, other risk factors, including current smoking, were associated with a significantly increased risk of diabetes, even after adjustment for BMI. The adjusted RR for diabetes in the smokers was around 1.4 when compared with non-smokers.

Willi et al.[130] have carried out a relatively recent systematic review and meta-analysis of studies of association between active smoking (in contrast to passive or second-hand smoking) and T2DM. They have identified 25 large prospective cohort studies (n= 1.2 million participants) which reported risk of IFG, IGT, or T2DM in relationship to smoking status and excluded persons with T2DM at baseline. The reported incident cases of diabetes were 45,844 during a study follow-up period ranging from 5 to 30 years. They found that 24 studies reported adjusted RRs greater than 1 (range for all studies: 0.82-3.74). The pooled adjusted RR of incident diabetes in smokers compared with non-smokers was 1.44 (95% CI: 1.31-1.58). RRs in the involved studies were

adjusted for a number of potential confounding factors, such as age, BMI, WC, physical activity, alcohol consumption, heredity, education, and others. Results were consistent with a “dose-response phenomenon”, where the risk of T2DM was greater for heavy smokers (≥20 cigarettes/ day; RR: 1.61) than for lighter smokers (RR: 1.29) and lower for former smokers (RR: 1.23) compared with active smokers. However, Willi et al. have not reported sex- or age-specific RRs, and they have estimated only one adjusted pooled RR for both men and women. In addition, potential publication bias could occur and affect the reported results.

The metabolic effects of smoking have been examined mainly in non-diabetic individuals by many studies. In these studies, insulin sensitivity has been determined in order to test the effect of smoking on glucose metabolism. This is most often performed by using the ‘euglycaemic hyperinsulinaemic clamp technique’.[128] This technique is regarded as being the gold-standard method to assess and quantify insulin sensitivity in most metabolic studies, and is often used in clinics and laboratories to measure insulin action on glucose utilisation in humans and animals for clinical and basic science research.[131, 132] In brief, the concept of this technique is measuring the steady state amount of glucose metabolised per unit of body weight during a whole-body exposure to a predetermined amount of insulin, while maintaining the plasma glucose within the euglycaemic range.[132] After an overnight fast, insulin is infused intravenously at a constant rate which results in a new steady state insulin level that is above the fasting level (hyperinsulinaemic). Consequently, glucose disposal in skeletal muscle and adipose tissue is increased, whereas the endogenous hepatic glucose production is suppressed. Under these conditions, a bedside glucose analyser is used to frequently monitor blood glucose levels, while dextrose is given intravenously at a variable rate to “clamp” blood glucose concentrations in the normal range (euglycaemic).[133] The quantity of exogenous glucose infused to maintain euglycaemia is a reflection of the amount of glucose metabolised in peripheral tissues, and therefore reflects the sensitivity of target tissues to insulin. The more glucose infused per unit of time, the more sensitive the individual is to insulin.[132]

Eliasson et al.[134] examined 57 male smokers, who were middle-aged (40-60 years), non-obese and non-diabetic. The degree of insulin resistance in the

participants was quantified using the euglycaemic clamp technique. In that study, smoking was independently correlated with degree of insulin resistance, even after multivariate analysis to adjust for age, lean body mass, body fat, BMI, WHR and alcohol consumption. Furthermore, a review[128] has reported two studies that compared the insulin sensitivity in smoking and non-smoking men. It was shown that the measures of insulin sensitivity were significantly lower (10% to 40%) in the smokers.

2.2.3.6. Socioeconomic status

The observed variations in diabetes prevalence across different levels of socioeconomic status (SES) might be a complex issue, as these variations have been attributed to several factors. In addition, SES is usually defined in studies using different indicators (e.g. education level, income, occupation, area of residence, etc). Currently, the relevant evidence often makes a distinction between developing and developed countries regarding the relationship of SES and the risk and prevalence of diabetes. Generally, in developing countries, a number of studies have showed a higher prevalence of diabetes in groups of high SES.[79, 80] In contrast, in developed countries, the incidence and prevalence of diabetes have been found to be inversely related to SES, with the highest prevalence in those of lowest SES.[79] The commonest suggested contributing factor to such variations has been the differential distribution of obesity (and related factors such as diet and level of physical activity) across different strata of SES in developed and developing countries.

In developing countries, the observations of low levels of obesity among individuals with low SES versus high levels among those with higher SES have usually been explained by three main reasons. First, people with low SES usually have lack of food and higher levels of physical activity and energy expenditure. Second, people with higher SES are more likely to have a greater capacity to obtain adequate food supplies. Third, cultural values in many developing countries favour fat body shapes.[135] Monteiro et al.[135] have indicated that evidence from studies in the developing countries prior to 1989 strongly suggested that obesity in the developing world would be essentially a disease of the socioeconomic elite. However, between 1989 and 2003, a comprehensive review of relevant studies showed a different picture. The authors adopted an

income definition of developing countries used by the World Bank, and used certain defined cut-offs of the annual gross national product (GNP) per capita in order to classify such countries into three categories: low income countries, lower-middle income countries, and upper-middle income countries. Interestingly, they have found that the burden of obesity in a particular developing country tends to shift towards the groups of lower SES as that country's GNP increases. The prevalence of obesity was found to be relatively lower among groups with lower SES in most low-income and some of the lower-middle income developing countries. On the other hand, there was an inverse association between SES and obesity (especially among women), in lower-middle income and upper-middle income developing countries.[135] The reviewers have argued that the positive association between SES and levels of obesity in the 'poorer' countries is probably attributed to the same three reasons indicated above. On the other hand, the inverse association observed in the middle-income countries could be a more complicated issue. Monteiro et al.[135] have indicated several likely explanations for such an inverse association. It has been argued that food scarcity and high energy expenditure patterns are likely to be less common in a society after a certain stage of economic growth has been reached, even among its poorer social classes. Individuals with lower SES are more likely to have a lower level of education and health-related knowledge, in addition to greater difficulty in obtaining the more expensive and less energy-dense foods. Furthermore, people with lower SES are also likely to have less leisure-time and recreational exercise. In contrast, people with a high SES are more likely to have flexible choices of 'healthy' food and physical activity patterns. Hence, such people might have environments with less 'obesogenic' factors than those with a low SES.[135] These explanations have also been suggested to justify the inverse association between SES and obesity/ diabetes in the developed countries.[136, 137]

2.2.4. Role of modifying the behavioural/ environmental risk factors in prevention of type 2 diabetes

There is evidence from a number of studies showing that interventions with lifestyle changes have resulted in preventing (or at least delaying) T2DM. Randomised trials revealed that lifestyle changes were approximately twice as effective as metformin therapy in preventing the disease.[83, 138] These lifestyle

changes included modifications of different behavioural/ environmental risk factors such as obesity[81], physical activity[81, 139], diet[81, 126], and smoking[140]. Tuomilehto et al.[82] reviewed a number of intervention trials[81, 141-148] in different countries/ populations. In these trials, the incidence of T2DM was estimated in the intervention and control groups, and the difference in incidence between the two groups was quantified in each study. All these trials showed that the incidence of T2DM was significantly lower among those participants in the intervention groups, who received the lifestyle intervention (reducing weight, increasing physical activity, intake of low-fat diets, etc.) alone or combined with drugs, compared to those in the control groups.

The following two sections focus primarily on *obesity* and *smoking*, as the only two risk factors studied in this thesis.

2.2.4.1. Obesity

Among the studies reviewed by Tuomilehto et al.,[82] the Finnish Diabetes Prevention Study[81] was the only study in which the participants were recruited based on being overweight/ obese with IGT at the baseline. According to the reviewers, the Finnish Diabetes Prevention Study is the first 'proper' controlled trial on prevention of T2DM where the study participants were individually randomly allocated into intervention and control groups. The first part of this study was conducted during the period 1992-2000 in five clinics in Finland, with the aim to prevent T2DM with lifestyle modification alone. A total of 522 participants at "high risk" to develop diabetes were selected after screening for IGT in middle aged (40-64 years), overweight (BMI >25 kg/m^2) subjects. The presence of IGT before randomisation was confirmed in two successive OGTTs.[81, 82]

The participants were randomly allocated into either the "intensive intervention" group or the "control" group. Those in the intervention group had frequent consultation visits with a nutritionist, and received individual advice about how to achieve the intervention goals. Five goals were set for intervention, as follows: 1) reduction in weight of 5% or more; 2) total fat intake less than 30% of energy consumed; 3) saturated fat intake less than 10% of energy consumed; 4) fibre intake of at least 15 grams/1000 kilocalories; and 5) moderate exercise for 30 minutes/day or more. Several dietary behaviours were recommended to

participants in the intervention group (e.g. frequent ingestion of wholemeal products, fruit and vegetables, low-fat milk and meat, etc). In addition, these participants were individually guided to increase their level of physical activity, through recommending endurance exercise (e.g. walking, jogging, swimming, etc), and supervised and progressive circuit-type resistance training sessions.[81, 82] On the other hand, participants in the "control" group were only given general verbal and written advice about healthy lifestyle at the beginning of the trial.[81, 82] All participants in both groups were followed up annually by performing a fasting plasma glucose test and OGTT. If either fasting or OGTT values reached diabetic levels, a second confirmatory OGTT was performed. Diagnosis of T2DM was only recorded if the second test also reached diabetic levels. Otherwise, the participants remained in their randomly allocated group.[81, 82]

The results of the study showed that during the first year, body weight decreased on average 4.2 kg in the intervention group, compared to 0.8 kg in the control group participants (the difference was statistically significant; p= 0.0001). It has been found that most of this weight reduction was maintained during the second year of the trial. Furthermore, indicators of central adiposity and fasting glucose and insulin, 2-hour post-challenge glucose and insulin, and HbA_{1c} were also reduced significantly more in the intervention group than in the control group during both the first and second year.[81, 82]

In 2000, a total of 86 incident cases of diabetes were diagnosed among the 522 participants (27 in the intervention group + 59 in the control group). The absolute risk of diabetes was 32/1000 person-years in the intervention group, compared to 78/1000 person-years in the control group. Importantly, the effect of the intervention was found to be rapid, where the difference in incidence of diabetes between the two study groups was already statistically significant after two years (6% in the intervention group and 14% in the control group).[81, 82] The study also showed that both sexes benefited from the lifestyle intervention. The incidence of diabetes was reduced by 63% in men and by 54% in women in the intervention group compared with the control group. All participants (in the intervention and control groups) who reached all the five lifestyle targets by the 1-year visit did not develop diabetes. In contrast, around one third of those participants who did not reach a single one of the targets developed type 2 diabetes.[81, 82]

2.2.4.2. Smoking

The results have been inconsistent regarding the effect of smoking cessation on the risk of developing diabetes. Theoretically, the reversal of the risk of diabetes upon cessation of smoking supports the concept of causality. However, it has been suggested that there are some lifestyle factors which may complicate the applicability of such a concept among people who choose to quit smoking.[149] For instance, some studies have showed that smoking cessation is associated with weight gain and a subsequent increase in the risk of diabetes.[150, 151]

Most studies have observed that current smokers and ex-smokers showed a higher risk for developing diabetes than non-smokers. Nevertheless, according to Hur et al.,[140] the majority of such studies have not considered changes in smoking habits during the follow-up period, and, hence, the effects of smoking cessation on the risk of developing diabetes could not be properly assessed. In addition, the reported increased risks of ex-smokers in these studies have not been statistically significant, or have not been adjusted for some covariates such as age, BMI, family history, etc. Moreover, the definition of 'ex-smokers' was inconsistent across studies. Thus, in their prospective study, Hur et al. undertook repeated measurements of smoking status during the follow-up period to assess the relationship between smoking status and fasting glucose level changes.[140] The study was started in 1990 in South Korea, with baseline examinations in 1990 and 1992, and continued with follow-up examinations every 2 years up to 1998 and 2000. A total of 27,635 non-diabetic men (aged 35-44 years) were enrolled at the baseline. They were randomly selected from records of the Korea Medical Insurance Corporation, which provides health insurance to government and private school employees and their dependants. The participants were classified as non-smokers (those who reported not smoking consistently from 1992 to 1996), ex-smokers (those who reported smoking cessation at baseline or during the follow-up periods) and sustained smokers (those who reported current smoking consistently from 1992 to 1996), based on repeated self-reported questionnaires in 1992, 1994 and 1996.[140] To explore the effect of smoking cessation, ex-smokers were further classified as having quit smoking before 1992, during 1992–1993 or during 1994–1995. Baseline fasting serum glucose level and other risk factors were measured in

1990 and 1992. The outcome was newly developed diabetes, defined as a fasting glucose level of ≥7.0 mmol/l in 1998 and 2000 (averaged).[140]

When compared with non-smokers, the reported risk ratio was 0.98 (95% CI: 0.81–1.17) for ex-smokers and 1.62 (95% CI: 1.40–1.88) for current smokers, when the participants were categorised based on baseline smoking status only. However, when smoking status was re-defined based on the repeated assessments at 2-year intervals, the diabetes risk ratio in ex-smokers was found to vary by the length of time since smoking cessation. Compared with non-smokers, the fully adjusted risk ratio for diabetes in participants who quit smoking before 1992, during 1992–1993 and during 1994–1995 was 0.95 (95% CI: 0.72–1.25), 1.44 (95% CI: 0.96–2.15) and 2.13 (95% CI: 1.51–3.00), respectively, after adjustment for age, baseline fasting serum glucose, weight change, baseline BMI, family history of diabetes, alcohol consumption and exercise status. The authors argued that there is a gradual reduction in the risk for diabetes over time after cessation of smoking, and that 'early' smoking cessation could decrease the risk to that of non-smokers in the long term.[140]

Overall, this chapter demonstrates that T2DM is associated with several risk factors, which interact with each other, making the aetiology of the disease complex. The next chapter discusses the size of the problem of T2DM in the world, developing countries (particularly EMR), GCC countries, and Saudi Arabia.

Chapter 3. Size of the problem of type 2 diabetes in the world, developing countries, and Saudi Arabia

This chapter presents a literature review of the estimates and projections of T2DM prevalence in the world. Further discussion focuses on levels of the disease in the developing countries, the WHO's Eastern Mediterranean Region (EMR), and then, more specifically, the countries of the Gulf Cooperation Council (GCC). Lastly, this chapter presents a detailed discussion of the context of Saudi Arabia, in terms of demography, health care system, levels of NCDs, diabetes care, and the relevant studies on prevalence of T2DM and the two risk factors studied in this thesis (obesity and smoking).

3.1. Global epidemiology of type 2 diabetes

3.1.1. Background

Historically, communicable diseases used to be the major threats to health globally until the second half of the 19th century. Several devastating epidemics of these diseases occurred in the past, including cholera, typhoid, smallpox, and diphtheria, and killed huge numbers of people all over the world. While some of these diseases are still epidemic in some developing countries, a very significant drop in their levels occurred from the beginning of the 20th century as a result of extensive improvements in sanitation, housing, nutrition and cleanliness of water supplies. In addition, the discovery of antibiotics and immunisation has also played a vital role.[152] With all these improvements, the global life expectancy increased substantially. Eventually, the list of leading causes of morbidity and mortality shifted from infectious diseases to NCDs, such as cardiovascular disease, diabetes, hypertension, cancer, and stroke.[153] This phenomenon is known as the *"epidemiological transition"* which is typically defined as "the series of interrelated and complex changes in the health and disease patterns that occur in specific human populations over large periods of time".[112] In developing countries, this health transition has been attributed mainly to rapid urbanisation and changes in the population lifestyles which resulted in increased levels of various risk factors for NCDs (e.g. smoking, unhealthy diet, obesity, and physical inactivity).[4, 154]

T2DM is a global health problem. It affects a huge number of people globally and its prevalence varies by age group, ethnicity, and socioeconomic status.[6] The disease reduces both a person's quality of life and life expectancy and imposes a large social and economic burden on families as well as on health care systems.[6, 45] According to the WHO's Global Burden of Disease (GBD) Study in 2004, high blood glucose is one of the 10 leading risk factors causing death,[7] where it caused around 6% of deaths worldwide. (Table **3.1**). This is despite the fact that the true diabetes-related mortality is greatly underestimated, as diabetes is frequently underreported on death certificates.[45, 155] Diabetes results also in a great financial burden on health care departments. The direct health care costs of the disease range from 2.5% to 15% of annual health care budgets[153], and the indirect costs are more likely to be much higher. This is due to the difficult measurement of indirect cost of diabetes since it implicates not only patients but also the families and the society as a whole.[156]

Table 3.1. Ranking of the 10 leading risk factor causes of death in the world, GBD 2004[7]

Rank	Risk factor	Deaths (millions)	Percentage
1	High blood pressure	7.5	12.8
2	Tobacco use	5.1	8.7
3	High blood glucose	3.4	5.8
4	Physical inactivity	3.2	5.5
5	Overweight and obesity	2.8	4.8
6	High cholesterol	2.6	4.5
7	Unsafe sex	2.4	4.0
8	Alcohol use	2.3	3.8
9	Childhood underweight	2.2	3.8
10	Indoor smoke from solid fuels	2.0	3.3

3.1.2. Global estimates and projections of type 2 diabetes prevalence

In the last two decades, several studies of global estimates and projections of diabetes prevalence have been published. Generally, such estimates and projections are highly dependent on many factors, such as data inputs, method of estimation, assumptions, and variables used to inform the future projections. The available studies mostly tended to produce different estimates and projections of diabetes prevalence as a result of variations in those factors. In addition, the available studies were carried out in different time periods, so that they used different diagnostic criteria to define diabetes. As discussed in chapter 2, such diagnostic criteria have been revised repeatedly over time,

leading to different classification of people (as having diabetes or not). Table **3.2** summarises examples of studies of global projections of diabetes prevalence.

One of the most recent estimates is that of the IDF Diabetes Atlas 2011.[9] In this study, the IDF estimated and projected diabetes prevalence in adults aged 20-79 years for 2011 and 2030 in different world regions and countries. Detailed discussion of the methodology of this study is presented in chapter 9. In brief, diabetes prevalence data were obtained from country-level data sources (e.g. national surveys, health statistics reports, and personal communications). If no data were obtained for a country, data from neighbouring countries (with mostly similar ethnicity and socioeconomic patterns) were used. A logistic regression model was used to generate smoothed age-specific estimates which were applied to the United Nations (UN) population estimates for 2011. Estimates and projections were presented for each country separately, using changes in age, sex and urbanisation as covariates. Globally, it was estimated that there were 366 million people with diabetes in 2011, which was predicted to rise to 552 million by 2030.[9]

Another recent study is that of the WHO's GBD Study, 2011 [Global Burden of Metabolic Risk Factors of Chronic Diseases Collaborating Group (Blood Glucose)].[20] Again, the methodology used in this study is discussed in detail in chapter 9. In this study, the trends in diabetes prevalence were estimated for adults aged ≥25 years in 199 countries and territories around the world. Data on diabetes prevalence were obtained from national surveys and statistics reports, in addition to the WHO Global InfoBase. Trends in the diabetes prevalence (during 1980-2008) were modelled using a multi-level statistical approach (Bayesian hierarchical modelling). The estimates were age standardised to the WHO reference population and were informed by several country-level covariates: national income, urbanisation, age-standardised mean BMI, and national availability of multiple food types for human consumption. The global age-standardised adult diabetes prevalence was estimated at 8.3% in men and 7.5% in women in 1980, predicted to rise to 9.8% and 9.2% respectively in 2008. The number of people with diabetes was estimated to increase from153 million in 1980 to 347 million in 2008.[20]

Shaw et al.[14] used 133 population-based studies from 91 countries to estimate age- and sex-specific diabetes prevalence in adults aged 20-79 years in 216 countries. Diabetes prevalence data were obtained from published national studies and personal communications. Smoothed age- and sex-specific diabetes prevalence estimates were generated by applying logistic regression models, and then applying such estimates to each national population distribution for 2010 and 2030 (UN population estimates) to estimate national prevalence and numbers of adults with diabetes. The world prevalence of diabetes among adults in 2010 was estimated at 6.4% (285 million adults), and predicted to increase to 7.7% (439 million adults) by 2030.[14]

Wild et al.[15] estimated the global prevalence of diabetes for all age groups in 2000 (as used in the WHO GBD Study) and made projections for 2030. They obtained age- and sex-specific data on diabetes prevalence from population-based prevalence studies from a limited number of countries. The diabetes prevalence estimates were then extrapolated to all the 191 WHO member states, using a combination of criteria including geographical proximity, ethnic, and socioeconomic similarities. Smoothed age-specific estimates of diabetes prevalence were produced using DISMOD 2 software. Information on DISMOD 2 software is extensively discussed in chapter 5, as it was also used in this thesis. Concisely, DISMOD is a mathematical disease model designed to supplement data on a disease epidemiology by exploiting the causal relations between the various available variables that describe a disease process.[157] Wild et al. used as inputs into DISMOD the age- and sex-specific diabetes prevalence (from country-specific prevalence studies), remission (assumed to be zero), and estimates of relative risk of mortality among people with diabetes (from literature). DISMOD provided as outputs estimates of prevalence, incidence, and mortality that are 'internally consistent'. The prevalence estimates were then applied to the UN population estimates for individual countries for 2000 and 2030. The future projections in diabetes prevalence were informed by demographic changes alone. In addition, it was assumed that other diabetes risk factor levels (e.g. obesity and physical activity) remain constant in developed countries. In comparison, in developing countries, urbanisation was used as a proxy measure of the levels of risk factors, as urbanisation in these countries is associated with obesity, reduced physical activity, and changes in

dietary habits. The estimated worldwide prevalence of diabetes (all age groups) was 2.8% (171 million individuals) in 2000 and 4.4% (366 million individuals) in 2030 with higher rates among men than women.[15]

In a relatively older study, King et al.[16] used age-specific diabetes prevalence estimates from the WHO's diabetes database (collected from 32 countries). They applied these prevalence data to the UN demographic estimates for the world's population, in order to predict the global prevalence of diabetes in adults aged ≥20 years for three points in time (1995, 2000, and 2025). As used in the study of Wild et al.[15], for countries lacking valid prevalence estimates, data were extrapolated from neighbouring countries or those with most similar ethnic and socioeconomic characteristics. Projections in diabetes prevalence were informed by the trends in population size, age structure and levels of urbanisation. Prevalence of diabetes in adults worldwide was estimated to be 4.0% in 1995 and was projected to rise by around 35% to reach 5.4% by 2025. The number of adults with diabetes in the world was predicted to rise from 135 million in 1995 to 300 million in 2025, with the majority of this increase occurring in developing countries.[16]

Another relatively old study is that of Amos et al.[17], in which the global diabetes prevalence was estimated for 1995 and projected to 2010. Country-specific data on diabetes prevalence were obtained mainly from epidemiological studies published during the period 1980-1997, which used the WHO 1980 and 1985 diagnostic criteria with OGTT to define diabetes. As with the previously mentioned studies, when diabetes prevalence data were not available for a given country, data were obtained from another country with a similar ethnic composition and level of economic development. The country-specific diabetes prevalence data were then applied to the corresponding national age distribution, in order to estimate diabetes prevalence for 1995 and make projections to 2010. The main variables used to inform projections were the level of economic development [Gross National Product (GNP) per capita] and urbanisation. The number of people with T2DM was estimated at around 115 million in 1995 and 215 million in 2010.

However, these estimates have some limitations, such as paucity of data, particularly for many developing countries.[15] In addition, it is possible that

individual studies used for estimations and projections were not representative of the whole country in which they were performed. Moreover, some country-specific estimates were extrapolated to neighbouring countries, which might give inaccurate estimates of DM prevalence.

Table 3.2. Studies of estimates and projections of the global prevalence of diabetes

Study (year published)	Main sources of data on diabetes prevalence	Age (years)	Diagnostic criteria	Covariates used to inform projections	Global estimates and projections (of diabetes prevalence and/or number of people with diabetes)	
					year	*result*
Whiting et al. [9] (IDF Diabetes Atlas, 2011)	▪ Published prevalence studies (1980-2011) ▪ Health statistics reports ▪ Contacts with regional diabetes researchers	20-79	▪ WHO 1985 ▪ ADA 1997 ▪ HbA_{1c}	Demographic changes (changes in age, sex, and urbanisation)	2011 2030	366 million 552 million
Danaei et al. [20] (WHO, 2011)	▪ Published national surveys ▪ Health statistics reports ▪ The WHO Global Infobase	≥25	▪ ADA 1997	▪ National income ▪ Urbanisation ▪ National availability of multiple food types ▪ Age-standardised mean BMI	1980 2008	8.3% (men) 7.5% (women) 9.8% (men) 9.2 (women)
Shaw et al. [14] (2010)	▪ Published prevalence studies ▪ Contacts with regional diabetes researchers	20-79	▪ WHO 1985 ▪ ADA 1997 ▪ Self-reported	Demographic changes (changes in age, sex, and urbanisation)	2010 2030	6.4% (285 million) 7.7% (439 million)
Wild et al. [15] (2004)	Population-based prevalence studies	All age groups (both type 1 and type 2 diabetes)	▪ WHO 1985	Demographic changes (assuming constant levels of risk factors, such as obesity and physical activity, in developed countries versus using urbanisation as a proxy in developing countries)	2000 2030	2.8% (171 million) 4.4% (366 million)
King et al. [16] (1998)	The WHO's diabetes database	≥20	▪ WHO 1985	Trends in population size, age structure and levels of urbanisation	1995 2025	4.0% 5.4%
Amos et al. [17] (1997)	▪ Published epidemiological studies (1980-1997) ▪ Contacts with regional diabetes researchers	All age groups	▪ WHO 1980 ▪ WHO 1985	▪ Level of economic development [Gross National Product (GNP) per capita] ▪ Urbanisation	1995 2000 2010	115 million 147 million 215 million

3.2. Diabetes burden in developing countries

In the past, the industrialised countries were the main focus for NCDs, and these diseases were known for a long time as "diseases of affluence".[4, 158] However, in the last few decades, NCD levels (including T2DM) have increased globally with higher morbidity and mortality numbers and rates in developing countries. It has been estimated that NCDs are responsible for around 50% of the total disease burden in these countries.[11, 55] The main reason for these elevated levels is the increase in the major risk factors (e.g. obesity, physical inactivity, smoking, changes in diet) in these countries, as a consequence of rapid urbanisation and changes in the population lifestyle and nutrition. In addition, increasing life expectancy has resulted in ageing populations and elevation of the rates of chronic diseases.[46] It has been well documented by various studies that T2DM prevalence is lowest among people who still have a more active 'traditional' or 'primitive' lifestyle in developing countries, in spite of similarities in ethnicity and genetic characteristics (as discussed in chapter 2).[52, 66, 159-161]

The estimates and future projections of diabetes burden in developing countries are rising progressively. Over the 30-year period from 1995 to 2025, the increase was estimated to be around 170% in the number of adults with diabetes in developing countries, from 84 to 228 million, compared to 42% increase, from 51 to 72 million, in developed countries. Thus, by 2025, more than 75% of people with diabetes will reside in developing countries, as compared with 62% in 1995.[16] Between 2000 and 2030, the estimated percentage change in the number of people (all ages) with diabetes in developing versus developed countries was estimated to range from 104-163% and 20-54% respectively.[15] Another study estimated that between 2010 and 2030, there will be a 69% estimated increase in the numbers of adults with diabetes in developing countries and a 20% estimated increase in developed countries.[14] These great differences in the projected numbers of diabetes cases have been attributed to two main factors. First, the population demographic differences have been projected to be large between developed and developing countries. For developed countries, total population size has been projected to remain relatively stable, with an 11% increase from 1995 to 2025 of 1 billion. On the other hand, the population increase in developing countries will be around

80%, from 2.5 billion in 1995 to 4 billion in 2025.[16] Second, the levels of diabetes risk factors (particularly obesity) in developing countries have been estimated to increase substantially over time. In a recent WHO study[13], the regions of Southern Africa, North Africa and Middle East, and Central Latin America have been classified to have the highest prevalence rates of obesity (particularly in women) globally in 1980 and 2008. However, most global estimates and projections of diabetes prevalence did not directly account for the increased prevalence of risk factors (e.g. obesity) in developing countries. Instead, as mentioned in section 3.1.2, these global projections mainly relied on demographic changes and urbanisation to inform future estimates. Some of these studies (IDF[9] and Wild et al.[15]) have acknowledged that the reported projections of diabetes burden might be higher if the observed increasing levels of obesity in some countries have been modelled directly.

The age distribution of people with diabetes has also been found to be different in developing countries (discussed in chapter 2). While the majority of diabetes cases in developed countries are in the older age groups, the majority of cases in developing countries tend to be among young and middle-aged people.[16] This implies that the health, social, and economic burdens of the disease extend to even younger ages and for a longer period of an individual's life span.[162]

Health services in most developing countries are organised to primarily tackle acute communicable diseases. These services are often not ideally developed to promote effective care and prevention for NCDs.[12] As a result, unfortunately, there are now many 'poorer' developing countries that face a double burden, since the levels of infectious diseases (e.g. HIV/AIDS, tuberculosis, malaria, etc) continue to be high, in addition to increasing levels of NCDs.[48, 163]

3.3. Diabetes burden in the Eastern Mediterranean Region

In the WHO's Eastern Mediterranean Region (EMR) (Figure **3.1**), the problem of T2DM is mounting. There has been a rapid increase of the disease prevalence rates in both sexes in the EMR.[114] The majority of countries in this region have witnessed massive and rapid socioeconomic developments over the last four decades. These improvements in social and economic standards have been recognised as the major reason for the epidemiological transition of risk and

disease burden in the region.[112, 164-166] The WHO has estimated that around 47% of the EMR's burden of disease is due to NCDs and that this figure is expected to rise to 60% by 2020.[114]

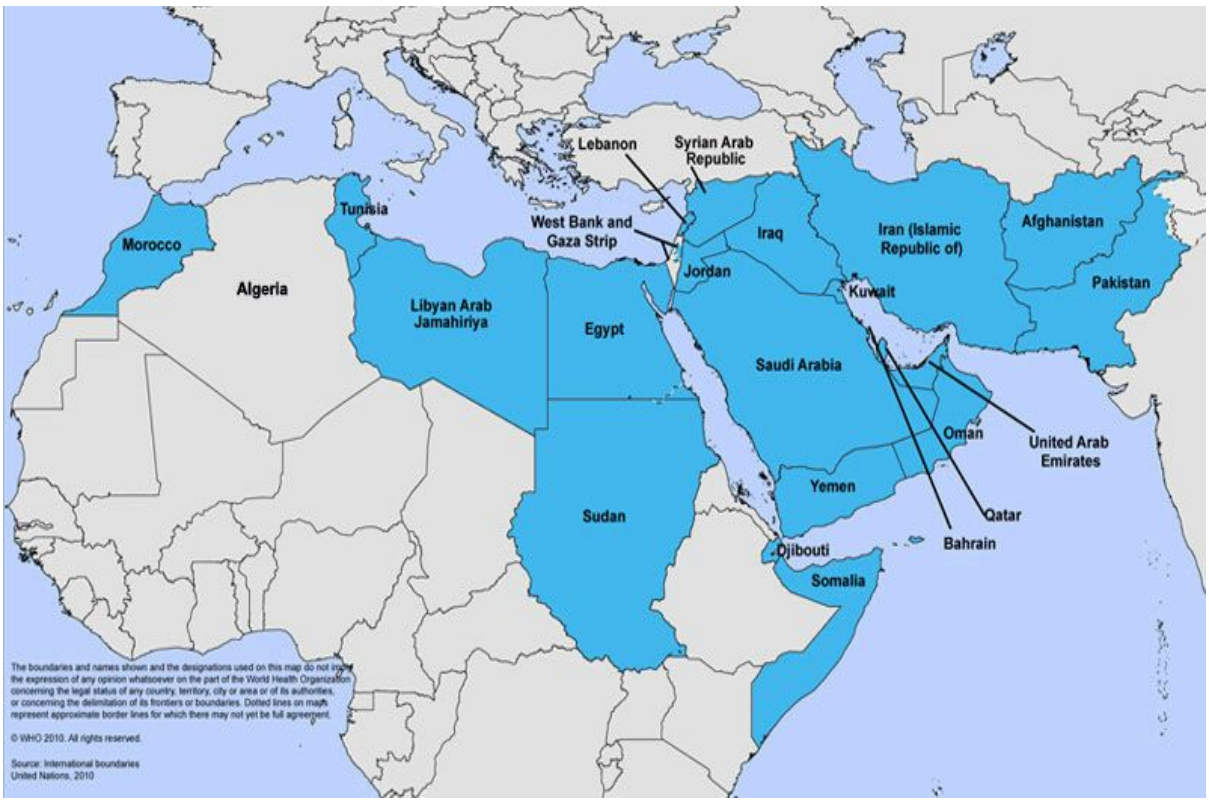


Figure 3.1. Map of the WHO's Eastern Mediterranean Region (EMR)

The prevalence of major risk factors for NCDs have been estimated to be very high in this region.[114] According to estimates of the regional WHO office in EMR in 2004, 14.5% of adults (≥20 year-old) in the region had diabetes, 43% were overweight/obese, and 40% of men were smokers (Table **3.3**).[114] As with most developing countries, many EMR countries have reported the onset of T2DM at the second and third decades of age in a large proportion of cases, and in some countries the disease is emerging in children.[162]

Table 3.3. Distribution of NCD risk factors among adults (≥ 20 years-old) in the countries of the EMR[114]

Risk factor	Regional adjusted mean (%)	Range (%)
Smoking		
Males	40	9-82
Females	13	-
Hypertension	26	7-48
Diabetes	14.5	3-36
Overweight/ obesity	43	11-79
Dyslipidaemia	50	4-57
Physical inactivity	79	18-97

The IDF's region of *Middle East and North Africa (MENA)*, which is similar to the WHO's EMR with inclusion of Algeria and exclusion of Somalia and Djibouti, has been recognised as the major hot spot for diabetes in the world. According to the IDF, MENA had the highest estimated prevalence of diabetes (12.5%) globally in 2011, and will remain to have the highest predicted prevalence (14.3%) by 2030. This is equivalent to 32.8 million people with diabetes in 2011 and 60 million people in 2030.[9] In 2012, diabetes has resulted in 356,586 estimated deaths in MENA, and approximately US$ 12 billion have been spent on treating diabetes in the region.[167]

The majority of countries in EMR were found to have national guidelines for the prevention and management of diabetes, and more than 50% of these countries reported having diabetes control plans. However, according to the WHO, although preventive strategies exist in many EMR countries, these strategies are not being rationally or widely utilised.[162]

Among all countries in the EMR, the countries of the Gulf Cooperation Council (GCC) have the highest levels of diabetes, and are almost constantly among the top 10 countries with the highest diabetes prevalence globally. Therefore, the next section focuses on prevalence rates of diabetes and the risk factors studied in this thesis (obesity and smoking) in the GCC countries.

3.4. Prevalence of diabetes, obesity and smoking in the countries of Gulf Cooperation Council

3.4.1. Overview

The Gulf Cooperation Council (GCC) was established in 1981 between six countries located on the coast of the Arabian Gulf (Figure **3.2**). These countries are Saudi Arabia, Bahrain, Kuwait, Oman, Qatar, and United Arab Emirates (UAE). These countries declared that the GCC was established in view of the special relations between them, their similar political systems, and common objectives.[168] People of these countries have many familial inter-relations, and share many similarities in environments, lifestyle, and social and cultural habits.[169]

Figure 3.2. Map showing the GCC and neighbouring countries

Compared to Saudi Arabia, all the remaining five countries are small and have small population sizes. The total area of GCC countries is 2,672,700 km^2, with Saudi Arabia alone constituting an area of approximately 2,250,000 km^2.[168] In 2002, the total population of all GCC countries has been estimated to be around 32 million. The population of Saudi Arabia alone constituted around 22 million, compared to around 3.5 million in UAE, 2.5 million in Oman, 2.5 million in Kuwait, 685,000 in Qatar, and 672,000 in Bahrain.[168]

The GCC countries are known to be the major source of oil in the world, with the strongest economies among countries of the EMR. The gross domestic product (GDP) of these countries in 2008 has been estimated to be 1060 billion US dollars, with an average GDP per capita of 28,300 US dollars.[168] UAE has been ranked to have the second highest GDP per capita in the world in 2009.[170] The GCC countries have witnessed substantial social and economic developments in the recent decades, with great changes toward sedentary lifestyles and 'western' dietary habits of their populations.[171] These countries are now considered a major focus for diabetes globally. According to the IDF, all the GCC countries, except Oman, are among the top 10 countries with the highest prevalence of diabetes in the world in 2011 and 2030.[9]

In the next subsection, the published national population-based studies of prevalence of diabetes, obesity, and smoking in the GCC countries (except Saudi Arabia) are presented. Then, section 3.5. discusses in more detail the

Saudi context in terms of demography, health care system, levels of NCDs, diabetes care, and the relevant studies on the prevalence of diabetes, obesity and smoking.

3.4.2. Published studies on the prevalence of diabetes, obesity, and smoking in the GCC countries

A comprehensive literature review was conducted for the national population-based studies that reported the prevalence of T2DM and the two risk factors studied in this thesis (obesity and smoking) in the GCC countries. The search was carried out using Medline database with relevant search terms (appendix 1). Results of these prevalence studies are shown in Tables **3.4**–**3.6**.

The inclusion criteria for studies were the following: a) a nationwide population-based cross sectional survey; b) multistage stratified random sampling techniques; c) both men and women were included; d) prevalence of outcome of interest (i.e. T2DM, obesity, and smoking) was reported; and e) diagnostic criteria of T2DM and definition of obesity were clearly stated.

The exclusion criteria were a) a study that covered a subnational sample of population (e.g. covered only one region of the country, or only one sex); b) a study that reported the prevalence of self-reported diabetes or self-measurement of weight and height; and c) duplicate papers that used the same data but reported the results for different age ranges (in this case, the most recent paper that reported the prevalence for adults was selected).

In general, all these studies used good sampling techniques and covered large sample sizes of both sexes with good response rates. They used standard global criteria for diagnosis of T2DM (WHO and ADA criteria) and obesity (BMI ≥30 kg/m^2). Thus, the studied samples and results were most likely reliable and representative of each country's population.

Most of the selected studies excluded pregnant women, but did not differentiate between type 1 and type 2 diabetes. In this thesis, the reported prevalence rates of diabetes *in adults* were considered as being for T2DM, as T2DM constitutes around 90% of all diagnosed cases of diabetes and is the most common type of diabetes in adults.

Prevalence of T2DM in these studies ranges between 9.8–29.4%[172-178] (Table **3.4**). The highest prevalence was reported in Bahrain[177] but this study covered an older study population (40–69 years) than other studies in the remaining countries (≥20 years). UAE had the second highest prevalence (21.4%),[174] while Oman reported the lowest prevalence in two studies (9.8% and 11.6%).[175, 178] The prevalence in all studies was almost equal in both sexes or was slightly higher in women, except in Bahrain where the prevalence in women (35.3%) was considerably higher than men (25.4%).[177]

Studies showed very high prevalence rates of obesity in the GCC countries (Table **3.5**). The studies were based on BMI (≥ 30 kg/m^2) for diagnosis of obesity and none of them used other measures, such as WC or WHR. Prevalence of obesity ranges between 19-47.5%[172-174, 179-182] with prevalence rates of more than 45% in Kuwait[172] and Qatar[173]. However, one study in Oman[180] reported a prevalence of 47.9% but that was for overweight (BMI ≥ 25 kg/m^2) and obesity combined. The lowest prevalence (19%) was reported in Oman, but it should be noted that data of this study were old (for year 1991), although the study was published in 2004.[179] Prevalence of obesity in the GCC countries was substantially higher in women than men, as reported by almost all studies.

For smoking prevalence, there were only three studies (from Oman, Bahrain and Kuwait) found to be conducted at national level[183-185] (Table **3.6**). No published studies were obtained for Qatar and UAE. In these three studies, the prevalence of 'active' smoking (defined as smoking at the time of survey) was measured. The highest overall prevalence was in Bahrain (21.2%)[184] followed by Kuwait (17%)[185], whereas it was much lower in Oman (7%)[183]. However, the study in Oman covered an older population (40–69 years) than studies in Bahrain (≥15 years) and Kuwait (≥18 years). In all studies, the prevalence of smoking in men was much higher than women. This is an expected finding, since female smoking in the GCC countries is not acceptable in their conservative social cultures.

Table 3.4. Studies on the prevalence of diabetes in the GCC countries

Study (year published)	Country	Sample size			Age (years)	Diagnostic criteria	Prevalence of diabetes (%)		
		men	*women*	*total*			*men*	*women*	*total*
Al Rashdan et al. [172] 2010	Kuwait	918	1362	2280	20-65	ADA 1997 FPG	-	-	18.1
Bener et al. [173] 2009	Qatar	571	546	1117	≥ 20	WHO 1999 OGTT if FPG < 7 mmol/l	15.2	18.1	16.7
Malik et al. [174] 2005	UAE	2498	3346	5844	≥ 20	WHO 1999 OGTT if FPG < 7 mmol/l	20.4	22.3	21.4
Al-Lawati et al. [175] 2002	Oman	2905	2933	5838	≥ 20	WHO 1999 FPG	11.8	11.3	11.6
Abdella et al. [176] 1998	Kuwait	1105	1898	3003	≥ 20	WHO 1985 OGTT if FPG ≥ 6.1 mmol/l	14.7	14.8	14.8
Al-Mahroos et al. [177] 1998	Bahrain	1195	834	2029	40-69	WHO 1985 OGTT	25.4	35.3	29.4
Asfour et al. [178] 1995	Oman	2133	2963	5096	≥ 20	WHO 1985 OGTT	9.7	9.8	9.8

Table 3.5. Studies on the prevalence of obesity in the GCC countries

Study (year published)	Country	Sample size			Age (years)	Prevalence of obesity (%) BMI ≥30 kg/m^2		
		men	*women*	*total*		*men*	*women*	*total*
Al Rashdan et al. [172] 2010	Kuwait	918	1362	2280	20-65	39.2	53.0	47.5
Bener et al. [173] 2009	Qatar	571	546	1117	≥ 20	-	-	45.2
Malik et al. [174] 2005	UAE	2498	3346	5844	≥ 20	24.0	40.0	33.0
Al-Lawati et al. [179] 2004 (data for year 1991)	Oman	2128	2958	5086	≥ 20	10.5	25.1	19.0
Al-Riyami [180] 2003	Oman	3074	3356	6430	≥ 20	42.0*	46.0*	47.9*
Musaiger et al. [181] 2001	Bahrain	298	216	514	30-79	21.2	48.7	35.0
Al-Mahroos et al. [182] 2001	Bahrain	1168	845	2013	≥ 20	25.3	33.2	29.3

* Prevalence estimates are for overweight and obesity combined (BMI ≥25 kg/m^2)

Table 3.6. Studies on the prevalence of active smoking in the GCC countries

Study (year published)	Country	Sample size			Age (years)	Definition of active smoking	Prevalence of active smoking (%)		
		men	*women*	*total*			*men*	*women*	*total*
AlRiyami et al. [183] 2004	Oman	3506	3505	7011	40-69	Smoking at the time of survey	13.4	0.5	7.0
Hamadeh et al. [184] 1992	Bahrain	4785	4497	9282	≥ 15	Smoking at the time of survey	33.1	9.2	21.2
Memon et al. [185] 2000	Kuwait	1798	2061	3859	≥ 18	Smoking at the time of survey and had smoked more than 100 cigarettes in their lifetime	34.4	1.9	17.0

3.5. Prevalence of diabetes, obesity and smoking in Saudi Arabia

3.5.1. Introduction

The Kingdom of Saudi Arabia occupies most of the Arabian Peninsula. It is one of the largest countries in the Middle East Region, extending between the Red Sea in the west to the Arabian Gulf in the east. Saudi Arabia has diverse geography with coastal areas in the east and west (coastline of around 2650 km), high rugged mountains mainly in the south and south-west, but the sandy desert areas remain to occupy most parts of land. Climate conditions are extremely hot and harsh at summer times, with temperatures reaching 50°C and more, and dry cold at winter with minimum temperatures of less than 0°C in some regions. Riyadh is the Capital City of the country, located in its centre. The Kingdom is divided into 13 administrative regions (provinces) as illustrated in Figure **3.3**.

Figure 3.3. Administrative regions of Saudi Arabia

Saudi Arabia is one of the strongest economies in its region, as it is ranked the first in the list of oil-producing countries globally. Oil was first discovered in Saudi Arabia in 1930s and the country now has the largest reserves of petroleum in the world, and is the largest exporter. The petroleum sector accounts for roughly 80% of budget revenues, 45% of GDP, and 90% of export earnings. As a result, Saudi Arabia witnessed a massive improvement in

socioeconomic development in the past five decades, with great progress having been made in health, education, housing and the environment. There is now an extensive network of modern roads, highways, airports, seaports and huge industrial cities and complexes for petrochemical, desalination and other plants. The industrial sector is the dominant source of wealth, creating around 51% of GDP with most of this from oil and gas mining; the service sector accounts for 43% of GDP and agriculture for 5%.[186] Presence of the two Holy Mosques in Mecca and Medina makes Saudi Arabia one of the most popular destinations to all Muslims all over the world. This may also contribute to the Saudi economy income, as many millions of people come to visit these places during Hajj (the Muslim pilgrimage to Mecca) and all-round the year.

3.5.2. Demography

The population of Saudi Arabia was estimated in the last completed national census, held in 2004, to be 22,678,262. The age and sex distribution of the Saudi population is shown in the 2004 population pyramid in Figure **3.4**. The Kingdom has a relatively young population, where those who aged less than 15 years constitute 39.9% of the total Saudi population, compared to 56.6% aged 15-64 years, and 3.5% aged ≥ 65 years.[187]

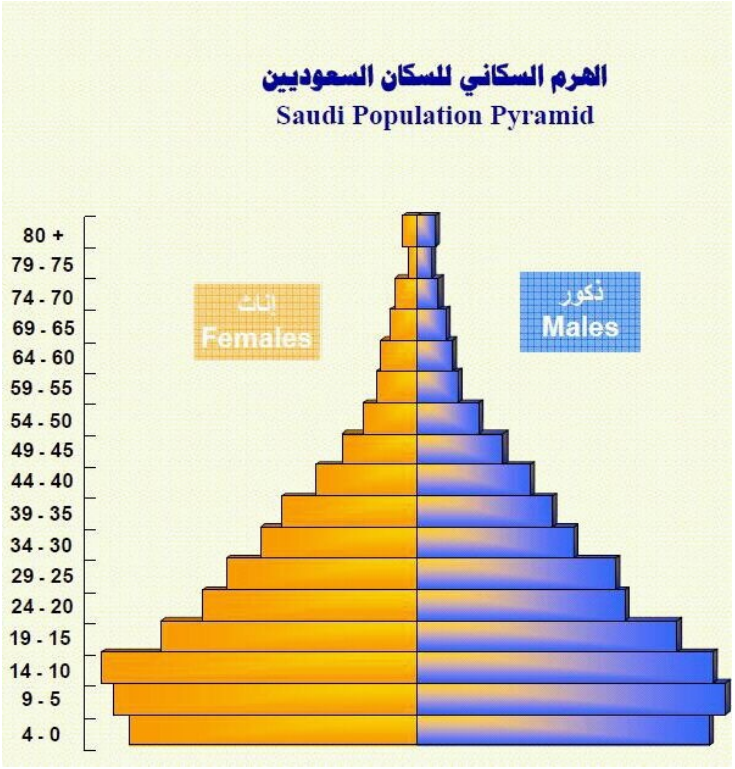


Figure 3.4. The Saudi population pyramid, 2004[187]

Table **3.7** shows the major demographic indicators in the last few years, as estimated by the Saudi Ministry of Health.[188]

Table 3.7. Major demographic indicators of the Saudi national population[188]

Indicator	2004	2005	2006	2007
Crude birth rate/ 1000 population	25.3	25.3	24.9	24.5
Crude death rate/ 1000 population	3.8	3.8	4.0	3.9
Infant mortality rate/ 1000 live births	19.1	18.5	18.6	17.4
Maternal mortality rate/ 100,000 live births	12.0	12.0	14.6	14.6
Life expectancy at birth (years)	73.6	72.5	73.1	73.3

Crude birth and death rates fell from 49/1000 population and 23/1000 population in 1960[189] to 24.5/1000 population and 3.9/1000 population respectively, in 2007.[188] Furthermore, infant mortality greatly decreased from 170/1000 live births in 1960[189] to 17.4/1000 live births in 2007.[188] In contrast, life expectancy notably increased from 44 years in 1960[189] to 73.3 years in 2007.[188]

National censuses in Saudi Arabia do not account for ethnic groups of the Saudi-national population. However, other sources estimated that Arabs constitute more than 90% of them, and less than 10% are descended from Afro-Asian origins, mainly black Africans, Turks, Iranians, Indonesians, Indians, Russians and others.[190] These ethnic minorities primarily immigrated as pilgrims hundreds of years ago and then resided permanently in some regions of the country.[190]

The population growth rate between 1992 and 2004 was estimated to be 2.5%, which is less than that between 1974 and 1992 (3.7%). This decrease was attributed to decreased birth rate, mainly due to improved level of education, increased access to contraceptives and older age at marriage than in the past.[187] As a result, the population in the ≤15 year age group decreased by 18.9% from 1992 to 2004. On the other hand, the population in the ≥65 year age group increased by 6.7% during the same period, due to improved health services and increased life expectancy of population.[187]

The 2004 census also showed that around two thirds of the Saudi population live in the three most urbanised regions of the country (Riyadh, Mecca, and Eastern Province). The total Saudi population living in urban areas increased from 49% in 1974 to 80% in 2004. Rate of illiteracy among Saudis fell by half

from 28.4% in 1992 to 14.7% in 2004.[187] Around 86% of Saudi families have one car or more, 90% of them have television, and 25% of them had internet access in 2004.[187] According to the World Bank, the Saudi GDP per capita in 2009 was US$ 23,429, which is one of the highest in the world.[170]

Saudi Arabia (and other GCC countries) has a large population of foreign workers (expatriates). In the 2004 census, it has been estimated that around 25% (6,150,922) of the Saudi population were non-Saudi nationals.[187] During the past five decades (the post-oil era), Saudi Arabia has been highly dependent on foreign labour. Later, with the progressive increase in the national population size and the considerable improvements in education and training, a large proportion of foreign labour in professional, administrative and technical work positions have been replaced by Saudi nationals. Nevertheless, expatriates still comprise the majority of employees in some occupations, mainly agriculture, cleaning and domestic service industries. The 2004 estimates showed that the main bulk of the foreign population is formed of people from South Asian origin (Indians, Pakistanis, Bangladeshis and Sri Lankans), Arabs (mainly Egyptians, Yemenis, Syrians and Sudanese), Turkish, and Pacific and Southeast Asia (mainly Indonesians and Filipinos).[187] However, in terms of net migration, Saudi Arabia has almost a stable situation. It has been estimated that the net migration rate in Saudi Arabia was -0.6 migrant/ 1000 population in 2012.[191]

Also, data on the socioeconomic status of population and regional disparities/ inequalities are limited from Saudi Arabia. However, the 2004 census reported some socioeconomic indicators of population by region (e.g. level of education, type of housing, and main occupational groupings).[187] Table **3.8** summarises these indicators in the three most urbanised regions (Riyadh, Mecca and Eastern Province) in addition to two terminal regions (Jazan and Northern Borders). In general, the level of education is better in the three main regions compared to the other two terminal regions. However, the differences in the main occupational groupings are small. There are slightly higher proportions of people working in ‘high-class’ (e.g. management and professional scientific) occupations in the three main regions. In contrast, proportions of people working in ‘lower-class’ (e.g. agriculture and manual) occupations are slightly higher in terminal regions. In terms of housing type, there is a higher proportion

of ‘villa’ households in Northern Borders Region, and a higher proportion of ‘flat’ households in the three main regions, but this could be mainly attributed to regional differences in the population density and relative costs of households.

Table 3.8. Some socioeconomic indicators by region from the national census, 2004

	Riyadh	Mecca	Eastern Province	Jazan	Northern Borders
Level of education (% population aged ≥10 years)					
Illiterate	10.5	14.1	9.9	26.2	18.3
University	10.9	10.4	9.1	5.9	7.1
Post-graduate	0.8	1.1	0.4	0.1	0.1
Main occupational groupings (% population aged ≥15 years)					
Directors & managers	11.5	11.0	9.8	6.9	8.4
Specialists in professional and technical fields	14.7	13.5	12.6	10.1	10.2
Workers in service sector	10.7	11.6	11.6	12.8	12.0
Workers in agriculture and manual jobs	4.1	4.9	4.6	9.2	8.1
Type of housing (% households)					
Traditional house	12.5	31.2	17.8	73.2	20.2
Villa	27.7	7.9	27.6	9.5	34.4
Flat	34.4	51.1	42.6	8.2	18.4

3.5.3. Overview of the Saudi health care system

The health care system in Saudi Arabia started in 1925 when a ‘public health department’ was established in Mecca and was responsible for sponsoring and monitoring free health care for the population and pilgrims through establishing a number of hospitals and dispensaries in the main cities.[192, 193] The network of health services started to expand after the establishment of the Ministry of Health (MOH) in 1951. However, health services were predominantly curative and delivered by an extending network of dispensaries and hospitals in most regions of the Kingdom. Preventive health care was carried out by some regional ‘health offices’ while some of the common communicable diseases (e.g. TB, leishmaniasis, and malaria) were controlled through separate programmes.[192] Further important development in the health care system was introduced when the primary health care (PHC) system was established in the early 1980s. Since that time, preventive care started to become a major integral role of PHC which currently covers all regions of the country.[192, 193]

Currently, the national health care system in Saudi Arabia is mainly run by the MOH, which provides free-of-charge primary, secondary, and tertiary health care across the whole country. MOH has a decentralised organisational and administrative structure.[192] There are 20 health regions, each led by a Regional Director and having a number of health sectors. Each health sector includes at least one general hospital and a number of primary health care centres (PHCCs), school health services and health offices. The policies, plans and programmes of the MOH are implemented through this structure. The curative, preventive, and rehabilitative services are also provided by other governmental and private sectors.[192] In the last few years, there has been a big advance in the size and quality of health care services in KSA. There is currently a network of around 2000 PHCCs and more than 200 hospitals, including tertiary and specialist hospitals.[192] The MOH budget was approximately 3% of the total national budget in 1970, and this increased to 5% in 1992, 8% in 2001,[189] and 12% in 2011.[194]

PHCCs represent the leading and largest component of the Saudi health care system, where approximately 83% of public health sector attendances occur in PHC clinics.[195] They are distributed throughout the country and serve as the patient's first point of contact with the national health system. The centres form a network closely linked to the general hospitals, which in turn are linked to tertiary care services by a referral and feedback system.[192] The health centres implement the various aspects of PHC which include primary, secondary and tertiary preventive services, in addition to curative health care. Moreover, they carry out population and family censuses within their catchment areas, maintain patient health records, survey schools in their areas and conduct routine home visits. The essential services provided by a PHCC include maternal and child health, immunisation, management of chronic diseases (e.g. hypertension and diabetes), dental health, provision of essential drugs, environmental health (e.g. water safety and food hygiene), health education and disease control.[192]

The MOH hospitals are also distributed all over the country and provide a wide range of emergency and advanced medical and surgical services. The health care services within hospitals vary according to their levels (secondary general hospitals and tertiary referral and specialist hospitals).[193] During the last few

years, many types of complex surgical procedures have been made in the Saudi hospitals as first in the Middle East region. Examples include conjoint twins separation, liver transplantation and some advanced open heart surgeries.[188]

In addition to PHCCs and hospitals, there are also some other health care institutions which provide specific health services. For instance, a number of chest/ TB hospitals, physiotherapy and rehabilitation centres and anti-smoking centres are distributed in different regions.[188]

3.5.4. Non-communicable diseases in Saudi Arabia

Because of the massive improvement of health care services along with the marked socio-economic advances in the past few decades, the predominant disease pattern in Saudi Arabia has shifted from communicable to non-communicable diseases.[192] This is consistent with the 'epidemiological transition' that has been taking place in most developing countries, as described in section 3.1.1. In the period of 1920s-1960s, the main health concern in Saudi Arabia was the control of various infectious diseases such as TB, leishmaniasis, schistosomiasis, malaria, measles, etc. Although some sporadic cases and outbreaks of these diseases remain, they are no longer the major cause of ill health in the Kingdom. During the last 30-40 years, there has been sharp elevation in the levels of several non-communicable health problems, such as diabetes, cardiovascular disease, cancer, and road traffic accidents (RTA).[19, 188, 195, 196] As described earlier in section 3.1.1, this increase in the burden of NCDs can mainly be attributed to changes in the population lifestyle and dietary habits toward a modern/western lifestyle with sedentary behaviours and increased access to high calorie and unhealthy foods.

Prevalence of hypertension and hyperlipidaemia in Saudi Arabia has been estimated at 26% and 19.3% respectively according to the WHO Stepwise sureveillance (STEPS) in 2005.[19] Of the 413 deaths per 100,000 in 2002, 144 (35%) were due to cardiovascular disease.[196] Neoplasms account for approximately 5% of hospital reported deaths.[188] In addition, RTA is a major problem faced by the health care system in Saudi Arabia, and it has been estimated that of all the deaths that occur in the MOH hospitals, more than 80%

are due to road traffic crashes.[195] Diabetes and its risk factors (e.g. obesity and smoking) have also been reported at very high levels, and this is discussed in detail in section 3.5.6.

In 2003, the Saudi MOH established the "General Directorate of Non-communicable Diseases" with a principal aim of preventing NCDs and their complications through various measures. These measures include, for example, enhancing the public awareness toward NCDs, their risk factors and complications, and population screening for early diagnosis of NCDs.[197] The Directorate also initiates and coordinates national strategies, plans and campaigns for control and prevention of NCDs. There are several units/ programmes that follow the Directorate, such as the National Diabetes Programme (NDP), Diet and Physical Activity Programme, Cardio-vascular Disease Control Programme, Cancer Control Programme, Premarital Screening Programme and others.[197]

3.5.5. Diabetes health care in Saudi Arabia

Most diabetes health care is provided to patients within PHCCs. Each patient diagnosed with diabetes has to be registered in his/her PHCC for regular follow up, health education, and treatment by general practitioners. Each patient has a specific diabetes record in the PHCC. The record contains information on the patient's vital signs, urine and blood investigation results, treatment and health education advices, all recorded regularly (usually monthly). Oral hypoglycaemic drugs and insulin are all available in PHCCs. Patients are referred to secondary or tertiary care levels if further evaluation or management is needed. In addition, there are 20 "Diabetic Clinics" distributed all over the 20 health regions of Saudi Arabia. Patients are also referred regularly to these clinics for further evaluation by specialist doctors. In 2007, for example, more than 400,000 visits to these clinics were recorded by MOH.[188] Data on T2DM patients are forwarded from health sectors to the NDP in MOH.

The NDP is the central unit within the General Directorate of Non-communicable Diseases that contains the national morbidity and mortality statistics of patients diagnosed with diabetes (all types). In addition, the NDP initiates and coordinates national strategies and campaigns for diabetes control and prevention. Important roles of the NDP include, for example, health

promotion, screening of high risk groups of population, ongoing supervision of diabetes health services in PHCCs, hospitals and diabetes clinics (*personal communication, Dr M. Al-Hamid, the Head of NDP, 2012*). Although the establishment of the NDP in Saudi Arabia is an exremely important step, it remains a 'young' programme, which needs time for several future developments in terms of reliable population-based data on diabetes. For example, in relation to this thesis, cross sectional data on prevalence of T2DM and its risk factors could not be obtained from NDP because, as mentioned earlier, all data in the NDP are related to the diagnosed 'cases' of the disease only. There were no diabetes population-based surveys carried out by NDP at a national level. Furthermore, a national diabetes registry is not currently available, although development of one is now in process (*personal communication, Dr M. Al-Hamid, the Head of NDP, 2012*).

The public health planners in Saudi Arabia (and other GCC countries) have started to realise the massive and progressively growing burden of diabetes in their countries. Currently, Saudi Arabia adopts the GCC Action Plan for prevention and control of diabetes, which was established by all the GCC countries in 2007.[198] This action plan has been set for the 10-year period of 2008-2018. It aims to achieve several objectives related to the prevention of diabetes (primary, secondary and tertiary prevention), in addition to improving the health care services offered to diabetic individuals and supporting the relevant research. The objective of primary prevention aims to reduce the prevalence of T2DM, mainly through reducing the levels of its risk factors, such as obesity, physical inactivity and smoking. Several strategies have been set, including setting policy reduction targets for obesity and smoking prevalence to be achieved by each member country by 2018. These policy targets are discussed in detail in chapter 8.

In Saudi Arabia, the Diet and Physical Activity Programme[199] has already developed in late 2011 a national strategy for diet and physical activity, which is compatible with the WHO's Global Strategy on Diet, Physical Activity and Health.[200] The Programme has also established in 2012 a 'national committee' for diet and physical activity, chaired by the MOH and includes a number of relevant departments (e.g. schools, universities, food industry, media, etc) that can assist in implementing the strategy. Elements of the strategy include, for

example, increasing the community awareness of the importance of physical activity and healthy diet, integrating physical activity and healthy diet in school curriculums and environments, and increasing and improving the outdoor and indoor spaces for public walking and exercise.[199]

Moreover, the Tobacco Control Programme (TCP)[201] in the Saudi MOH (established in 2002) aims to reduce the levels of active and passive tobacco smoking in the Kingdom. The main preventive strategies of the TCP are raising the awareness of people on the smoking health hazards, monitoring the relevant legislations (e.g. prohibition of smoking in public areas and workplaces), and offering free help and consultation to those who decide to quit smoking (through the Tobacco Control Clinics).

3.5.6. Published studies on the prevalence of type 2 diabetes, obesity and smoking in Saudi Arabia

A comprehensive literature review was carried out on the prevalence studies of T2DM, obesity and smoking in Saudi Arabia through Medline database. The reference lists of relevant articles were checked to identify other studies. Moreover, personal communications were made with the head of the Saudi NDP to obtain more relevant information and guidance to further studies.

The search strategy used in Medline is shown in appendix 1. Inclusion and exclusion criteria were similar to those used for studies from the GCC countries (as discussed in section 3.4.2).

3.5.6.1. Prevalence studies of type 2 diabetes in Saudi Arabia

Literature review identified five national population-based studies. These studies were carried out between 1989 and 2005 and covered both sexes of the Saudi population. They varied in the age groups included and diagnostic methods and criteria (Table **3.9**).

The most recent published study was the WHO's STEPwise Surveillance (STEPS) of NCDs risk factors[19] in 2005. In this study, individuals aged 15-24 years were included, in addition to the recommended age of the WHO STEPS approach (25-64 years). An overall prevalence of 15.8% and 14.9% was reported in men and women aged 15-64 years respectively, using the ADA 1997/ WHO 1999 diagnostic criteria (fasting plasma glucose ≥7 mmol/l). However, the reported overall prevalence for those aged 25-64 years was 20.1% in men and 18.3% in women. Results showed significant increasing prevalence rates with increasing age in both sexes. The age-specific prevalence rates were very similar for men and women across all age groups, except for the oldest age group (55-64 years), where women had a higher prevalence (49.7%) than men (39.5%).

Another study was conducted by Al-Nozha et al.[18] over a five-year period between 1995 and 2000. They studied around 17,000 adult Saudi subjects aged 30-70 years. Diagnosis of diabetes was based on the ADA 1997 criteria with measuring only fasting blood glucose. This study showed that the overall

prevalence of diabetes in the Saudi population was 23.7% which was significantly higher among men (26.2%) than women (21.5%), and among those living in urban areas (25.5%) than the residents of rural areas (19.5%). Again, the reported prevalence of diabetes increased significantly with increasing age in both men and women, and there were no noticeable differences in the age-specific prevalence for all age groups of both sexes.

Earlier studies included relatively younger age groups and showed lower overall prevalence rates.[35, 36, 202] In one study that was carried out during 1992-1995,[36] the total prevalence in those aged >14 years was reported to be 5.6% and 4.5% among men and women respectively, using the WHO 1985 criteria with measuring both fasting blood glucose and OGTT to define diabetes (fasting blood glucose ≥7.8 mmol/l and/or 2 hour OGTT ≥11.1 mmol/l). In another study, Al-Nuaim[202] studied a large sample of individuals aged ≥15 years and reported a significantly higher prevalence among residents in urban (men 5.1%, women 4.9%) than rural settings (men 4.5%, women 4.5%), using random (not fasting) blood glucose of ≥11.1 mmol/l to define diabetes. Osman et al.[35] reported a higher prevalence of 13.2% among subjects aged ≥18 years, with a fasting blood glucose of ≥7.0 mmol/l used as a cut-off value to diagnose diabetes.

In general, all these studies used good sampling techniques of multistage stratified random sampling of all regions of the Kingdom with probability proportionate to population size of each region. They covered large nationwide sample sizes of households and considered both sexes. The reported response rates in these studies were excellent. With the exception of Al-Nuaim study, in which the response rate was 69%, the other studies reported response rates ranging from 92-98%. Thus, the studied samples were most likely reliable and representative of the total Saudi population. The studies used standardised methods, tools, and criteria for measuring blood glucose and diagnosis of diabetes.

Nevertheless, the data periods in these studies overlap, and they covered different age ranges of the Saudi population, used different diagnostic criteria to define diabetes, and reported the prevalence rates in different age-group intervals. These differences may make it difficult to compare between the

results. However, generally, there was a rise in diabetes prevalence in Saudi Arabia over time, as reported by these studies. Such an observed rise could be mainly explained by three factors. First, the levels of risk factors for developing diabetes (e.g. obesity, physical inactivity, smoking, etc) had, in parallel, increased over time (as discussed in the next two sections). Second, the change in the diagnostic criteria of diabetes from the old fasting glucose and OGTT cut-offs to the new lower fasting values might contribute to this rise, as the new criteria probably classified more individuals to be diabetics compared to the old criteria. Third, the incidence of diabetes in the Saudi population might increase over time leading to this elevation in the disease prevalence.

Osman et al.[35] reported only the overall prevalence of diabetes for the total population without providing age- and sex-specific prevalence rates. Moreover, Al-Nuaim[202] used 'random' blood glucose (no fasting glucose) measurements to diagnose diabetes, which might lead to missing of significant numbers of individuals with diabetes. However, although measuring random glucose can be considered a limitation by today's standards, such a method was recommended by the WHO, at the time of the study, to be used in epidemiological studies.[203]

As mentioned in section 3.4.2, most of diabetes prevalence studies excluded pregnant women from their population samples. However, these studies did not differentiate between type 1 and type 2 diabetes. In this thesis, the reported prevalence rates of diabetes *in adults* were considered as being for T2DM, as T2DM constitutes approximately 90% of all diagnosed cases of diabetes and is the most common type of diabetes in adults.

3.5.6.2. Prevalence studies of obesity in Saudi Arabia

Five nationwide population-based studies of obesity prevalence have been identified through literature review. All these studies used BMI to define obesity (BMI ≥30 kg/m^2). Like the diabetes prevalence studies, these studies were also carried out between 1989 and 2005 and covered both sexes of Saudis (Table **3.10**).

The WHO STEPS study[19] reported a mean BMI of 27.0 kg/m^2 in men and 29.1 kg/m^2 in women aged 15-64 years. The prevalence of obesity among men and women in 2005 was 28.3% and 43.8% respectively. Al-Nozha et al.[34] reported

an overall prevalence of obesity of 35.6% among those aged 30-70 years during 1995-2000, which was significantly higher in women (44%) than men (26.4%).

In another study conducted during 1990-1993 among those aged ≥20 years, Al-Nuaim et al.[37] reported an overall obesity prevalence of 22.1%. Again, it was significantly higher among women (26.6%) than men (17.8%). Moreover, Osman et al.[35] reported an overall obesity prevalence of 20.8% during 1989-1994 (15.6% in men and 24.9% in women). Warsy and El-Hazmi[36] reported an overall prevalence of obesity of 15.8% which was significantly higher in women (18.6%) than men (11.9%).

As with the diabetes prevalence studies, these studies covered large samples of both sexes with excellent response rates from all regions of Saudi Arabia, using multistage stratified random methods and probability proportionate to size. They used standardised tools to measure BMI, which is recommended by WHO as the most useful population-level measure of obesity. However, BMI has its own limitations that have been described earlier in chapter 2.

On the other hand, the data periods in these studies overlap, and they covered samples with different age ranges, and reported their results in different age group bands. In addition, Al-Nuaim[37] reported only age-specific prevalence rates of obesity (no sex-specific).

3.5.6.3. Prevalence studies of smoking in Saudi Arabia

There are more than 30 published studies investigating the prevalence of smoking in Saudi Arabia during the last three decades. Unfortunately, the majority of these studies were carried out among only men from certain population subgroups (e.g. school students, medical students, physicians, etc) and were limited only to some cities or provinces. According to these studies, the prevalence of current smoking among Saudis ranges from 2.4-53% (median 17.5%).[204]

There are three nationwide population-based studies[19, 38, 39] on current smoking among adults of both sexes in Saudi Arabia, conducted between 1990-2005 (Table **3.11**). The overall prevalence of active smoking in these studies ranges

from 11.6–12.8%. As expected, the prevalence of smoking was substantially higher among men than women as reported by two studies[19, 39], since female smoking in Saudi Arabia is considered socially unacceptable and stigmatised.[39] However, recent data from subnational surveys suggested that female smoking prevalence in Saudi Arabia is increasing, particularly among some specific subgroups (e.g. university students). In these surveys, smoking prevalence ranges between 4.2%[205] and 9.1%[206], and the 'water-pipe' tobacco was the commonest type consumed, as it is often readily available, and is perceived as 'fashionable'.[205] There are no recent surveys that measured the prevalence of female smoking at the national level.

In general, these studies used representative nationwide population-based samples through multistage stratified random sampling techniques and probability proportionate to size. As with diabetes and obesity prevalence studies, these studies covered both sexes and different age ranges of the Saudi population.

Nevertheless, it is not easy to collect information on smoking in Saudi Arabia, particularly among women and in some regions where smoking represents a social and religious stigma, even for men. Some people may hide their smoking, particularly during an interview or in the presence of other family members if they are young or female.[39] Therefore, as documented by Jarallah et al.[39], smoking prevalence in Saudi Arabia may have been underestimated in prevalence studies. Furthermore, the data periods in these studies overlap, and they used different definitions for self-reported active smoking (Table **3.11**) through interviews or questionnaires, and none of them used biomedical validation of smoking status.

In total, this chapter reveals the massive and growing global burden of T2DM and its risk factors, particularly on developing countries, including Saudi Arabia. As this thesis uses a modelling approach to estimate and predict T2DM prevalence trends in Saudi Arabia, the next chapter presents a comprehensive theoretical discussion on epidemiological modelling.

Table 3.9. Summary of the published national studies on type 2 diabetes prevalence in Saudi Arabia

Study (year published)	Year conducted	Sample size			Age (years)	Diagnostic criteria	T2DM prevalence (%)			Age groups (years)	Male prevalence (%)	Female prevalence (%)
		Males	Females	Total			Males	Females	Total			
WHO STEPS (2005) [19]	2005	2312	2340	4652	15-64	WHO 1999 FPG	15.8 (20.1)*	14.9 (18.3)*	15.3 (19.2)*	15-24	2.0	2.4
										25-34	2.8	4.5
										35-44	13.7	14.8
										45-54	31.0	31.1
										55-64	39.5	49.7
Al-Nozha et al. (2004) [18]	1995-2000	-	-	16,917	30-70	ADA 1997 FPG	26.2	21.5	23.7	30-39	13.0	11.6
										40-49	23.9	22.4
										50-59	33.5	34.3
										60-70	36.2	36.9
Osman et al. (2000) [35]	1989-1994	2673	3590	6253	≥ 18	ADA 1997 FPG	-	-	13.2	-	-	-
Warsy and El-Hazmi (1999) [36]	1992-1995	6162	8498	14,660	> 14	WHO 1985 OGTT	5.63	4.53	4.99	14-29	0.38	0.99
										30-44	7.01	5.03
										45-59	21.06	22.09
										> 60	28.75	24.37
Al-Nuaim (1997) [202]	1990-1993	6873	6304	13,177	≥ 15	Random Plasma Glucose (RPG). DM if RPG >11.1 mmol/l. OGTT if RPG 5.5–11.1mmol/l	12.0 (U)** 7.0 (R)**	14.0 (U) 8.0 (R)	-	15-20	2.0(U); 1.0 (R)	2.0(U); 1.0 (R)
										21-30	3.0(U); 2.0(R)	5.0(U); 3.0(R)
										31-40	9.0(U); 4.0(R)	15.0(U); 8.0 (R)
										41-50	28.0(U); 17.0(R)	36.0(U); 11.0(R)
										51-60	39.0(U); 22.0(R)	49.0(U); 26.0(R)
										> 60	35.0(U); 19.0 (R)	42.0(U); 29.0(R)

* Prevalence rate for population aged 25-64 years ** U: urban; R: rural

Table 3.10. Summary of the published national studies on obesity prevalence in Saudi Arabia

Study (year published)	Year conducted	Sample size			Age (years)	Obesity prevalence (%) (BMI ≥ 30 kg/m^2)			Age groups (years)	Male prevalence (%)	Female prevalence (%)
		Males	Females	Total		Males	Females	Total			
WHO STEPS (2005) [19]	2005	2244	2345	4589	15-64	28.3 (31.5) *	43.8 (50.4) *	36.2 (41.2) *	15-24	17.8	19.6
									25-34	27.1	39.5
									35-44	34.5	54.7
									45-54	32.9	58.8
									55-64	31.0	53.2
Al-Nozha et al. (2004) [34]	1995-2000	-	-	17,232	30-70	26.4	44.0	35.6	30-39	25.2	40.2
									40-49	30.3	50.2
									50-59	27.8	45.9
									60-70	22.1	39.0
Osman et al. (2000) [35]	1989-1994	2673	3590	6253	≥ 18	15.6	24.9	20.8	18 - <21	9.0	16.5
									21 - <31	10.4	22.1
									31 - <40	20.7	32.7
									≥ 40	20.8	33.2
Warsy et al. (1999) [36]	1992-1995	6646	9064	15,710	> 14	13.1	20.3	15.8	14-19	4.7	4.5
									20-29	9.1	13.2
									30-39	15.9	26.9
									40-49	19.2	36.0
									50-59	16.4	28.7
Al-Nuaim (1997) [37]	1990-1993	5407	5244	10,651	≥ 20	17.8	26.6	22.1	20-29	14.7 (both sexes combined)	
									30-39	24.8 (both sexes combined)	
									40-49	33.2 (both sexes combined)	
									50-59	26.3 (both sexes combined)	

* Prevalence rate for population aged 25-64 years

Table 3.11. Summary of the published national studies on smoking prevalence in Saudi Arabia

Study (year published)	Year conducted	Sample size			Age (years)	Definition of active smoking	Smoking prevalence (%)			Age groups (years)	Male prevalence (%)	Female prevalence (%)
		Males	Females	Total			Males	Females	Total			
WHO STEPS (2005) [19]	2005	2336	2414	4750	15-64	-	24.2 (23.6) *	1.4 (1.5) *	12.6 (12.2) *	15-24	26.0	0.96
										25-34	31.7	1.3
										35-44	27.4	1.4
										45-54	19.2	2.2
										55-64	13.1	1.1
Al-Nozha et al. (2004) [38]	1995-2000	-	-	17,232	30-70	Smoking in the last one year before survey	-	-	12.8	-	-	-
Jarallah et al. (1999) [39]	1990-1993	-	-	8,310	≥ 15	Smoking one or more cigarettes daily for 6 months or more before survey	21.1	0.9	11.6	15-20	6.7 (both sexes combined)	
										21-30	13.7 (both sexes combined)	
										31-40	15.8 (both sexes combined)	
										41-50	12.2 (both sexes combined)	
										51-60	8.2 (both sexes combined)	
										61-70	8.0 (both sexes combined)	

* Prevalence rate for population aged 25-64 years

Chapter 4. Epidemiological Modelling

As stated in chapter 1, this thesis used the approach of modelling to study the trends and projections of the prevalence of T2DM in Saudi Arabia. Therefore, this chapter presents a theoretical discussion on modelling in terms of definition, uses, types, structure, and limitations. In addition, this chapter also discusses the steps involved in developing a model, and the existing diabetes models in the literature.

4.1. What is a model?

In brief, a model is a simplification of reality.[207] The National Research Council[208] defined a model as *"… a replicable, objective sequence of computations used for generating estimates of quantities of concern…"*. According to the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Task Force on Good Research Practices - Modelling Studies,[22] a model is defined as *"an analytic methodology that accounts for events over time and across populations based on data drawn from primary and/or secondary sources"*. So, a model is a logical mathematical framework that permits the integration of facts and values, and that links these data to outcomes that are of interest to health-care decision makers.

4.2. What are the uses of models in epidemiology and public health?

Models have been extensively used in the fields of epidemiology and public health. They are used mainly to guide policy decisions in many areas that affect human life and health.[21] For instance, models can be used to predict the trends in a disease prevalence and mortality under alternative health policy scenarios or to compare the effectiveness and cost-effectiveness of different treatments.[209] Since models combine data from various local sources with trial based effectiveness evidence, they can form a helpful tool for decision making process.[21] Models permit policy makers to examine and compare between various future policy options and intervention scenarios within a population; hence they provide a platform for appropriate planning and resource allocation.[22, 23]

One of the most important advantages of modelling is its ability to use different types of inputs from various sources and to reveal the logical connection between these inputs and outputs of interest.[22] A model combines and integrates into a coherent whole different types of data from prevalence studies, prospective studies, controlled trials, meta-analyses, routine surveillance, expert opinions, and assumptions.[207] However, different types of data sources are associated with varying data quality, and this can result in uncertainty of the model parameters. Thus, models and their results should be represented as *aids* to decision making, not as statements of scientific fact,[22] i.e. model results should never be presented as unconditional claims of estimates or effectiveness. Rather, the model outputs should be represented as conditional upon the input data and assumptions.[22, 23] In other words, models should eliminate the random noise, which exists in 'real-world' situations and focus solely on the relationship between inputs and outcomes.[210] Therefore, models must be subjected to sensitivity analyses to identify the impact of potential uncertainties around the different input parameters on the results.[22]

4.3. Why model type 2 diabetes?

As mentioned in chapter 3, T2DM is a global health concern and is associated with substantial morbidity and mortality.[45] The disease imposes enormous social and economic burdens on both individuals and health care budgets.[6] Such a burden is heavier in developing countries, which are facing a dramatic increase in T2DM levels, and where the health care systems and policies are not well organised to tackle the growing problem.[12]

Policy makers in T2DM prevention and control programmes are required to make decisions and to allocate resources, which should be important and have lasting consequences for a large number of the population.[211] Unfortunately, there is limited evidence regarding epidemiological studies or clinical trials that measured disease progression and the impact of interventions on the disease prevalence and longevity.[28] When such information is not available, the logical analytical framework offered by modelling can be a helpful tool. Models can be used to gain insights about the likely future trends in the levels of T2DM and related risk factors, and to quantify the impact of reducing such risk factors in preventing the disease and its complications.[28, 211]

Diabetes modelling studies have been widely used to provide different types of useful information for policy makers. Some models have been used to forecast the future burden of diabetes and impact of some interventions (e.g. risk factor modifications, treatments) on the future disease levels.[28, 212] Other models, such as the United Kingdom Prospective Diabetes Study (UKPDS), estimated the likely occurrence of major complications of diabetes (e.g. ischaemic heart disease, myocardial infarction, stroke, renal failure, blindness, etc) over a lifetime and calculated health economic outcomes, such as quality adjusted life expectancy.[26] Moreover, other models have been intended for assessment of budgetary impact of diabetes in terms of the direct health care costs associated with the main diabetic complications.[211]

One of the most common types of models used for chronic diseases (including T2DM) is a "Markov model". This particular type/ class of modelling is also used in this thesis. Therefore, the next section presents a brief discussion of Markov models, their general structure and limitations.

4.4. Overview of Markov models

4.4.1. Background

Based on their analytical methodology and their use of time, models can generally follow one of two broad classes. First, *simple decision trees*, which are very useful for modelling events or health states that do not occur repeatedly and the likelihood of the event does not change over time.[213] This modelling approach fits well for acute and short-term conditions (e.g. bacterial infection, antibiotic therapy, adverse events in a hospitalised patient). Second, *Recursive trees*, which involve health states that can repeat over time. The model starts with a cohort of individuals and follows them for a specific time period. In each time cycle (e.g. one year), individuals have a risk (probability) of developing the outcome. The probability of developing the outcome may change every year.[213, 214] Markov modelling is a logical extension of recursive trees for more complex events occurring over time. Hence, Markov modelling is ideal for chronic diseases such as T2DM.[214]

4.4.2. General structure of a Markov model

Figure **4.1** illustrates a very simple general structure of a Markov model.[215] The model starts with a cohort of patients/persons that are followed over some specified time (i.e. the time horizon of analysis). The time horizon is divided into equal increments of time, referred to as *Markov cycles*.[214] A Markov model assumes that an individual is always in one of a finite number of discrete health states referred to as *Markov states* (illustrated in Figure **4.1** as ovals). All events of interest are modelled as transitions from one state to another (illustrated in Figure **4.1** as arrows). Therefore, a Markov model is classified as a *state-transition model*. During each Markov cycle, an individual may make a transition from one state to another, or may remain in the same state in consecutive cycles (illustrated in Figure **4.1** as arrows leading from a state to itself).[214, 216, 217] In most models, only certain transitions are allowed. For instance, an individual with T2DM assigned to "Diseased" health state is not allowed to make a transition back to "Well" state, assuming that the remission rate is zero. In addition, of course, a person in "Dead" state cannot make a transition to any other state. Thus, "Dead" state is referred to as an *absorbing state*, where the entire cohort will have been absorbed by this state after a sufficient number of cycles have passed.[214]

The relative size of of the "starting states" can usually be determined from population demographic trends or prevalence studies. State transitions are expressed as *transition probabilities (TPs)*, which are assumed to take place for each cycle of the model. Transition probabilities are abstracted from literature or may represent experts' assessment.[216] In the literature, state transitions are most commonly expressed as "rates". Rates can, theoretically, range from zero to infinity and are expressed per unit time. On the other hand, probabilities range from zero to one and have time built into them implicitly. To convert rates into probabilities, the following formula is generally used: $P[t] = 1 - e^{-rt}$, where P is transition probability; t is time units; and r is rate.[216, 217] However, this formula mostly produces probabilities of transition *between* states. The probability of staying in the *same* state in a given cycle will be simply 1 minus the probability of leaving that particular state, because the probability of moving to states in each cycle must sum to 1 (since an individual must be in one and only one state at any given time).[216, 217]

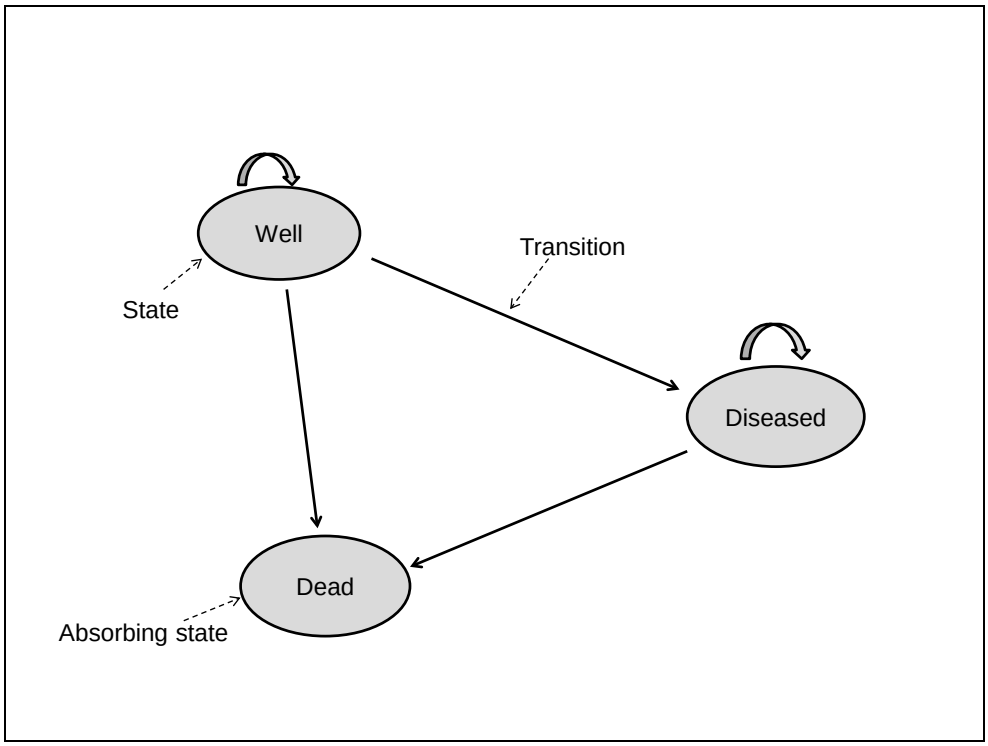


Figure 4.1. Simple illustration of the general structure of a Markov model[215]

4.4.3. Limitations of Markov models

The most important limitation of Markov models is the loss of memory of prior states, which is referred to as the *Markovian assumption* or *Markov property*. This restriction specifies that the behaviour of the process subsequent to any cycle depends only on its description in that cycle; and that knowing only the present health state of an individual is sufficient to project the future states. In other words, all individuals in a given state at a given time have the same prognosis, regardless of how they reached their present state or how long they spent in the previous state.[214, 217]

As previously stated, data for modelling are obtained from various sources. As this may be considered an advantage, it can also be a limitation. Such different types of data sources are associated with varying data quality, and this can result in uncertainties of some modelling parameters. Thus, all Markov models should be subjected to appropriate sensitivity analyses to identify the impact of uncertainty of different parameters on the modelling results.[22]

4.5. What are the steps of developing a model?

Figure **4.2** demonstrates a flow chart of the most important steps in developing a model.

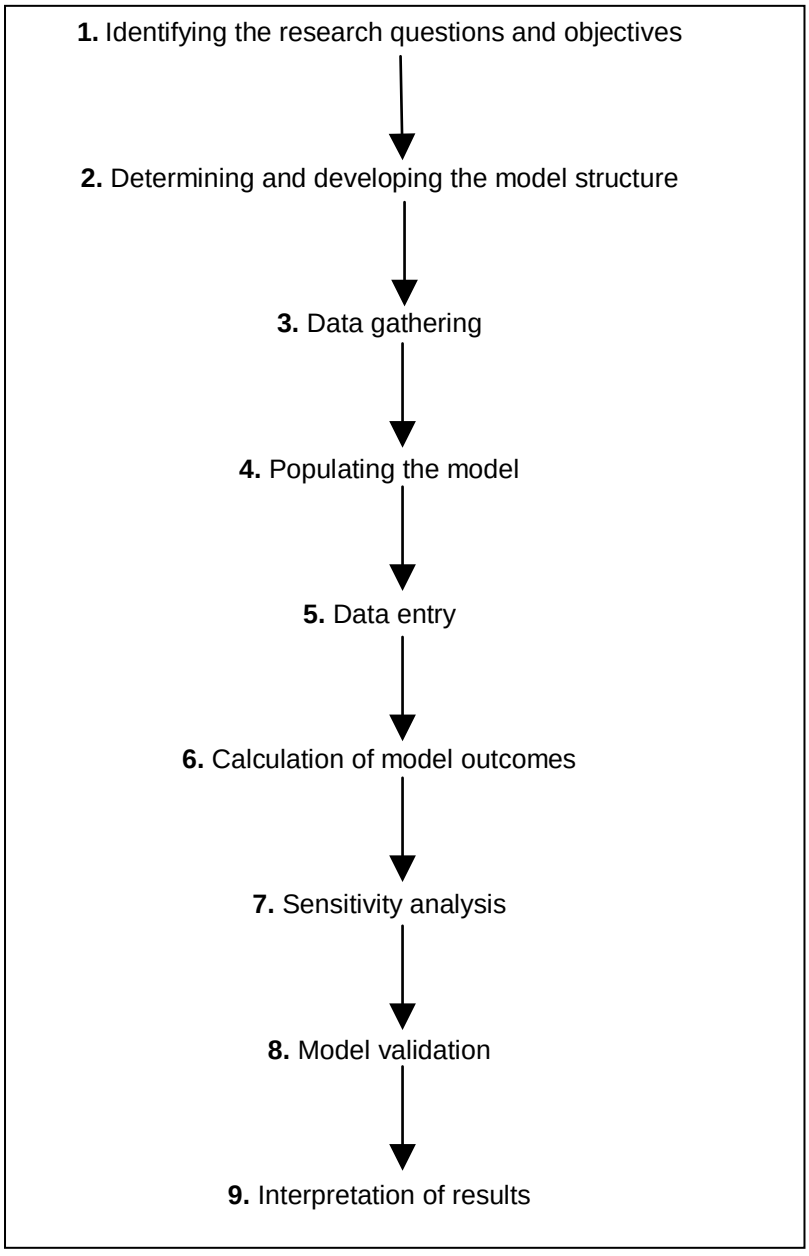


Figure 4.2. Flow chart for the steps of developing a model

Identifying the research questions and objectives is the first step in developing a model. The research question must be clearly stated. In addition, the competing interventions, target population, length of follow up and outcome measures must also be explicitly defined.[218]

After defining the research problem, the appropriate ***model structure*** should be determined. This step is primarily based on understanding of the nature and progression of the health event of interest.[218] In general, disease modelling (particularly chronic disease modelling) combines two major components: the disease natural history and different interventions in order to answer policy questions.[209] Natural history of chronic diseases can be very complex. At the same time, a model structure should be as simple as possible. Therefore, the ISPOR Task Force recommended that "it is not necessary to model the full complexity of a disease if the decision can be informed by a more aggregated structure, in terms of disease states or population subgroups".[22]

The structure of a model should be consistent both with a coherent theory of the modelled disease and with available evidence regarding causal linkages between variables.[22] However, this does not mean that all causal linkages must have been proven by, for example, showing that the effect size is statistically significant ($p<0.05$). Instead, it means that the linkages assumed are not contradicted by available evidence and are consistent with widely accepted theories.[22]

The structure of a model should reflect the time dependence of events being modelled. As previously discussed, in a simple decision tree, the likelihood of a modelled event is mostly time-independent (i.e. does not change over time).[213, 214] On the other hand, recursive trees and Markov models fit well for chronic conditions with prolonged or continuous exposure to a risk.[210, 217] The modelled disease in this thesis (T2DM) is a typical example for such chronic health events.

It is important to indicate that the level of complexity (e.g. number of health states, number of modelled outcomes) of a chronic disease model depends on the amount of data available to inform the model parameters.[209] Therefore, if the available modelling data are limited, some explicitly-justified compromises/

assumptions might be needed regarding, for example, the way of modelling a chronic disease epidemiology and natural history.[209, 219]

Data gathering is the next step after determining the suitable modelling structure. It was discussed earlier that models are flexible regarding the types of required data. Modelling data can be obtained from different sources which vary in terms of data amount and quality.[22, 207] These data sources may be health records, clinical trials, literature (e.g. meta-analyses), databases, etc. If there are no reliable data on some variables, expert opinions and assumptions can be useful.[22, 218] One of the recommendations of the ISPOR Task Force[22] was that "a model should not be faulted because existing data fall short of ideal standards of scientific rigor. Decisions will be made, with or without the model. To reject the model because of incomplete evidence would imply that a decision with neither the data nor the model is better than a decision with the model but without the data. With the model, the available evidence can be used in a logical way to inform the decision; without the model, an opportunity to utilise the available evidence within the logical framework will have been forgone". However, it is essential that all data sources are described with their strengths and limitations, and any assumptions must also be clearly addressed, since the modelling results are conditional upon such data inputs and assumptions.[22]

Populating the model and then ***data entry*** are the stages where the collected data are incorporated into the model. There are two basic steps that should be undertaken regarding populating a model. First is setting up the transition probabilities (TPs) of the model. TPs represent the tendency of an individual to make a transition from one state to another or the likelihood that an event will occur in a given length of time.[214] TPs are derived mainly from published sources, such as clinical trials and systematic reviews. Examples of information that can be used to set up TPs include mortality rates, RRs, incidence rates of a disease, and response to a treatment.[217] The second important step in populating a model is determining the types of outcome parameters. This depends largely on the nature of the modelled health event. For instance, in some diabetes forecasting models, the major modelling outcome would be the projected prevalence of diabetes and the number of diabetic individuals.[220] In comparison, models of other chronic diseases (e.g. ischaemic heart disease) may use different outcome parameters that consider quality of life or duration of

survival of patients (e.g. Quality Adjusted Life Years "QALYs", Disability Adjusted Life Years "DALYs", Deaths Prevented or Postponed "DPPs", and Life Years Gained "LYG").[23,213]

After data entry, the next stage of analysis work can be started for ***calculation of model outcomes***. The analysis work is an iterative process, and the key modelling variables should be tested using different values/ ranges (scenarios).[209, 213, 221] This process is known as ***sensitivity analysis***, which must be a vital part of all modelling studies.[22] Sensitivity analysis is essential to deal with the problem of uncertainty of some model variables, which can originate from uncertain values or subjective estimates and assumptions.[21]

There are two broad types/ techniques of sensitivity analysis: *one-way (univariate)* and *multi-way (multivariate)*. In the one-way (univariate) sensitivity analysis, only one variable is examined at a time. After the base-case scenario is estimated, the outcome variable is re-estimated holding all parameters constant apart from the one parameter chosen. This method can be applied repeatedly to as many variables in a model as desired.[222] One commonly used subtype of univariate sensitivity analysis is the *"threshold analysis"*. In this type of analysis, the size of one input parameter is changed over a range, followed by determining the level above or below which the conclusions change, i.e. the 'threshold' point at which there is no better alternative than others. Threshold analysis is commonly used in models with cost effectiveness analyses.[222]

In the multi-way (multivariate) sensitivity analysis, more than one modelling variable are examined simultaneously. It can be two-way, three-way or n-way analysis.[222] For example, a two-way analysis examines varying values of a range for two parameters at the same time. Both of these parameters should be common to the interventions assessed and, eventually, the impact of changes on the outcomes of two mutually exclusive interventions is assessed.[222]

One subtype of the multi-way sensitivity analysis is referred to as *"analysis of extremes"* method. This method has been used in several modelling studies, including this thesis as discussed in detail in chapter 5. In this type of sensitivity analysis, the best and worst estimates of a variable (or a number of variables) are incorporated and the model is then run to produce extreme estimates of the output.[219, 222] However, a common criticism to the 'analysis of extremes' method

is that the choice of 'extreme values' is mostly arbitrary,[223] and it is unlikely that all of the extreme values of key modelling parameters will occur simultaneously.[222]

A second subtype of multi-way sensitivity analysis is known as *"probabilistic sensitivity analysis"*, which is a relatively complex process, in which all input parameters are considered as random quantities and therefore are associated with a probability distribution.[224, 225] Uncertainties in the model inputs are formulated by a joint probability distribution and then the induced uncertainties in the outputs are analysed.[225]

Moreover, another example of multi-way sensitivity analysis is the *"scenario analysis"*, in which a number of interesting values for some of the modelling parameters are examined under different scenarios in order to evaluate the expected outcomes of each scenario.[224] Scenario analysis was also used in this thesis as discussed in chapters 5,6, 7, and 8.

Model validation is an important step in order for a model to earn the acceptance of decision makers and health care providers.[226] The ISPOR Task Force grouped model validation approaches into three main categories.[22] First, *internal validation* through internal testing and 'debugging'. This type of validation can be performed by using null or extreme input values to check if they result in the expected output values.[22] The second type of validation is *between-model validation*, in which a model is validated against other models addressing the same problem (convergent validity).[22, 227] The third type is *external validation* that compares a model's outputs with observed data. However, models are based on evidence available at the time they are constructed. Thus, as discussed earlier, models should never be regarded as complete, immutable or statements of scientific facts. They should be subjected to repeated updates as new evidence becomes available regarding their structure and input parameters.[22]

4.6. Existing diabetes models in the literature

4.6.1. Background

For many years, large-scale randomised controlled trials on diabetes clinical outcomes and impact of interventions have been the main data source for clinicians and decision makers involved in diabetes care. Nevertheless, although such trials remain a vital source of information, they often do not provide data on the long-term (>5-10 years) scale. In addition, the results of a clinical trial are directly applicable only to the population recruited and the protocol used.[228, 229] Alternatively, clinicians and policy makers have traditionally had to rely on their own judgement. However, there are wide variations in practice patterns of clinicians, and it is impossible for the human mind to address the complexity, variability and uncertainties of health and disease.[229] In addition, as discussed in chapter 3, the global prevalence rates of diabetes and its risk factors are progressively increasing, and countries need to gain insights on the future trends in the disease levels. Therefore, the logical analytic framework of modelling, as a valuable tool to provide this information, has been largely accepted by leading diabetes organisations, such as the American Diabetes Association (ADA).[229]

There is now a growing utilisation of computer modelling technology to study various clinical and epidemiological aspects of diabetes.[229] There is a large body of published literature that describes several diabetes models and presents their results.[26-32] These models used different methodologies, obtained data from different types of sources, and reported different outcome measures.

4.6.2. Published diabetes models

4.6.2.1. Clinical and economic diabetes models

As discussed earlier, this thesis aims mainly to study the past, current, and future trends in the prevalence of T2DM in Saudi Arabia, which has a relatively limited amount of data on T2DM epidemiology and risk factors. The majority of published diabetes models have utilised data and presented results that are related to the 'clinical' and 'health economics' aspects of T2DM (e.g. modelling the disease clinical progression and complications, modelling the health care

costs of diabetes, and modelling the cost-effectiveness of some drug treatments and interventions).[24, 25] In addition, many models have not used the 'general population' or 'total diabetic population' as their population of interest. Rather, these models have studied 'sub-samples' of diabetics (e.g. those diabetic patients with a certain complication) in order to model and project certain outcomes, costs, intervention impact, etc.[230] Table **4.1** presents a brief list of some examples of published diabetes models with different output parameters related primarily to the disease complications and health economics.

Table 4.1. Summary of examples of published diabetes models with their main output parameters

	Name of model/ authors	Type	Setting and/or study population	Main output parameter(s)
1	The CORE Diabetes Model [28, 226, 231]	Markov model (internet-based, interactive computer model)	Type 1 and type 2 diabetic populations	• Development of long-term diabetes complications • Life expectancy • Quality adjusted life expectancy • Total health care costs of patients with the complications
2	The UKPDS Outcomes Model [26]	Probabilistic discrete-time model (implemented in software) Consists of several sub-models, each for one complication	Type 2 diabetic populations	• Estimated 1st occurrence of each of 7 diabetes-related complications • Life expectancy • Quality adjusted life expectancy • Costs of complications in people with T2DM
3	Eastman et al. [232, 233]	Markov model Consists of several sub-models for complications	United States, Incident T2DM cases aged 25-74 years	• Occurrence of T2DM complications
4	EAGLE [27]	Markov model	Type 1 and type 2 diabetics in many European countries	• Long-term effects of diabetes treatment and related costs in type 1 and type 2 diabetes
5	The Global Diabetes Model (GDM) [29]	Continuous, stochastic microsimulation model	Individuals with diabetes and representative diabetic populations	• Predicted complications, survival, utilities, and medical care costs
6	JADE [234]	Probabilistic discrete-event simulation model	United Kingdom, Type 2 diabetic population (UKPDS participants)	• projected long-term impacts on life expectancy and occurrence of complications of diabetes when using different HbA1c thresholds for intensifying treatment of T2DM
7	Saaddine et al. [235]	Markov model	United States, US population with diagnosed diabetes, age ≥40 years	• Projected number of people with diabetic eye complications for the years 2005-2050

Table 4.1 (cont.). Summary of examples of published diabetes models with their main output parameters

	Name of model/ authors	Type	Setting and/or study population	Main output parameter(s)
8	The Cardiff Stochastic Simulation Cost-Utility Model (DiabForecaster) [236]	Discrete-event simulation model	Cardiff, United Kingdom, Large cohort of T2DM patients	• Total costs • Total number of clinical events • Quality-adjusted life years (QALYs)
9	The CDC Diabetes Cost-effectiveness Group Model [237]	Markov model	United States, Cohort of newly diagnosed T2DM patients aged ≥25 years	• Cost per QALY for multiple interventions
10	Zhou et al. [238]	Discrete-event simulation model	Wisconsin, United States, Cohort of T2DM patients	• Predicted mortality • Predicted prevalence rates of multiple complications and comorbidities of T2DM • Predicted average undiscounted total direct medical costs

4.6.2.2. Diabetes prevalence forecasting models

There are fewer models that have attempted to study the trends in the prevalence of T2DM and forecast its future burden on specific populations. For the purpose of comparison with the model used in this thesis, Table **4.2** provides a more detailed list of only those relevant models, which had a similar main output parameter as that used in this thesis (the projected population prevalence of diabetes). This list of 'diabetes prevalence forecasting models' was obtained through searching Medline (1980 - week 46 of 2012) using the following search strategy for titles and keywords: ['diabetes OR type 2 diabetes' AND 'prevalence' AND 'model$ OR diabetes model$ OR prevalence model$ OR project$ OR forecast$'] and through cross referencing of relevant articles. The electronic search yielded a total of 2410 articles. The vast majority of search results (2336 articles) were excluded as being irrelevant after skimming of the titles. Abstract reviews of the remaining 74 articles resulted in excluding 65 articles, leaving 9 articles for inclusion. Additional 3 articles were obtained through cross-referencing. Articles were included if they used modelling approaches, covered a defined general population or total/ large cohort of type 2 diabetics, and reported projections (forecasts) of diabetes prevalence among the main modelling outputs. However, the data sources and results of these models are not presented in Table **4.2**, as this brief list aims basically to compare the main structure and data input requirements of these models against the model in this thesis. In addition, the list does not include those models which were built to produce 'global' predictions of diabetes prevalence, such as the previously discussed models[9, 14-17, 20] in chapter 3.

Table 4.2. Summary of diabetes models with 'the projected diabetes prevalence' as a main output parameter

	Name of model / authors	Type	Setting and/or study population	Main data inputs used to construct the model	Main output parameter(s)	Main variables used to inform the projections of T2DM prevalence	Sensitivity analysis	Validation
1	Holman et al. [30] (the APHO* Diabetes Prevalence Model)	--	United Kingdom, Population of England aged ≥16 years with diagnosed and undiagnosed diabetes	• Current and projected estimates of population structure (by age, sex and ethnicity) • Age- and sex-specific prevalence rates for self-reported physician diagnosed diabetes • Undiagnosed diabetes prevalence based on HbA_{1c} • Prevalence and future projections of obesity and overweight	• Projected prevalence of diabetes (2010-2030)	• Demographic changes • Trends in the population rates of overweight and obesity	Multi-variate sensitivity analysis: 95% CIs of diabetes prevalence estimates, and other data input parameters	Results of the model compared with results from the general practitioner diabetes registers and the PBS Diabetes Prevalence Model
2	Boyle et al. [31]	Multiple discrete states dynamic models	United States, US adult population aged 18-79 years	• Current and projected estimates of population structure, mortality rates, net migration, and births • Current and projected estimates of diabetes incidence, and prevalence of diabetes and 'prediabetes'	• Projected annual diagnosed diabetes incidence (2008-2050) • Projected annual total diabetes prevalence (2008-2050)	• Trends in diabetes incidence and mortality	Results presented in different scenarios based on different values of incidence and mortality risk	Not reported

* The Association of Public Health Observatories

Table 4.2 (cont.). Summary of diabetes models with 'the projected diabetes prevalence' as a main output parameter

	Name of model / authors	Type	Setting and/or study population	Main data inputs used to construct the model	Main output parameter(s)	Main variables used to inform the projections of T2DM prevalence	Sensitivity analysis	Validation
3	Lau et al. [32] (The Alberta Diabetes Model)	Life table model	Alberta (Canada), Population of Alberta	• Age- and sex-specific diabetes prevalence for the last observed year • Historical age- and sex-specific incidence and mortality rates • Future projections of prevalence, incidence and mortality • Current and projected estimates of population structure • Detailed health care cost data	• Projected prevalence of diagnosed diabetes (2008-2035) • Projected health care costs of diabetes (2008-2035)	• Demographic changes • Changes in incidence and mortality	Not reported	Not reported
4	Huang et al. [239]	Markov model (consists of multiple modules)	United States, Diabetic men and women aged 24-85 years	• Prevalence and incidence of diabetes for the baseline year • Total population structure and projections by age, sex and ethnicity • Population mortality data • Estimated lifetime costs for prevalent and incident cohorts (for all drugs and treatment options) • Initial distribution of BMI categories • Yearly transitions across BMI categories (estimated from longitudinal data)	• Projected incidence and prevalence of obesity and diabetes (2009-2034) • The direct spending on diabetes care and complications (2009-2034)	• Demographic changes • Trends in the population rates of overweight and obesity	Not reported	Not reported

Table 4.2 (cont.). Summary of diabetes models with 'the projected diabetes prevalence' as a main output parameter

	Name of model / authors	Type	Setting and/or study population	Main data inputs used to construct the model	Main output parameter(s)	Main variables used to inform the projections of T2DM prevalence	Sensitivity analysis	Validation
5	Magliano et al. [240]	Multi-state life-tables	Australia, population aged ≥ 25 years	• Age- and sex-specific incidence rates of diabetes • All-cause mortality in those with diabetes • All-cause mortality in those without diabetes	• Lifetime risk of diabetes • The number of years lived free of, and the number of years lived with diabetes for the Australian adult population from the year 2000, and • Projected prevalence of diabetes to the year 2025	• Demographic changes • Incidence and mortality rates (assumed that the observed rates during 2000 - 2005 remain constant over the modelling period)	95% CIs for the age-specific diabetes incidence, diabetes prevalence and the RR for mortality associated with diabetes	Not reported
6	Mainous et al. [212]	Multi-state Markov model	United States, US population aged >20 years	• Population data and projections • Prevalence of diagnosed diabetes and total diabetes burden (diagnosed and undiagnosed) • Proportion of the population at risk of developing diabetes • Diabetes mortality estimates [all-cause mortality among individuals with diabetes (either diagnosed or undiagnosed)]	• Estimated future diabetes (diagnosed and undiagnosed) prevalence in 2011, 2021, and 2031	• Demographic factors • Incidence • Mortality • Migration • The trends in proportion of adults at high risk of diabetes (based on a national published multivariable diabetes risk score)	Results presented under various assumed values (increase and then decrease by 10%, 20%, 30%) of the proportion of adults at high risk of diabetes, and the mortality	Not reported

Table 4.2 (cont.). Summary of diabetes models with 'the projected diabetes prevalence' as a main output parameter

	Name of model / authors	Type	Setting and/or study population	Main data inputs used to construct the model	Main output parameter(s)	Main variables used to inform the projections of T2DM prevalence	Sensitivity analysis	Validation
7	Martinsen et al. [241]	--	Greenland, Total population	• Current and projected estimates of population structure aged ≥35 years • Current and projected estimates of obesity prevalence • Base year's prevalence of T2DM (≥35 years) • Base year's prevalence of multiple complications of diabetes	• Projected prevalence of T2DM (1999-2014) • Projected prevalence of complications (1999-2014)	• Demographic changes • Temporal changes in obesity prevalence	Results presented based on two assumed scenarios for the BMI distribution trends	Not reported
8	Narayan et al. [242]	Markov model	United States, Total population	• Age-, sex-, and ethnicity-specific diabetes incidence, 2004 • Age-, sex-, and ethnicity-specific diabetes prevalence, 2004 • US population data, 2004 • Census projections of the US live births, mortality rates, and net migration • RR of mortality for people with diabetes	• Prevalence of diagnosed diabetes in the US for 2005-2050	• Incidence rate of diabetes in 2004	95% CIs for uncertainty in the model transition rates, including incidence	Not reported

Table 4.2 (cont.). Summary of diabetes models with 'the projected diabetes prevalence' as a main output parameter

	Name of model / authors	Type	Setting and/or study population	Main data inputs used to construct the model	Main output parameter(s)	Main variables used to inform the projections of T2DM prevalence	Sensitivity analysis	Validation
9	Honeycutt et al. [220]	Markov model	United States, US men and women with diagnosed diabetes	• Estimated diagnosed diabetes prevalence and incidence • The relative risk of mortality from diabetes compared with no diabetes • Current and projected estimates of current population structure (by age, sex and ethnicity), live births, net migration • The mortality rate of the general population	• Projected number of people with diagnosed diabetes (2000-2050) • Projected incidence and prevalence of diagnosed diabetes in the US (2000-2050)	• Demographic changes	Model run with lower and upper bounds on 95% CIs for 2000 prevalences, 2000 incidence rates, and RRs	Results compared to previous forecasts of the same population – this model resulted in higher forecasts
10	Bagust et al. [211, 243]	Markov model (consists of multiple modules for outcomes and costs)	United Kingdom, Type 2 diabetic populations	• Total population structure and projections by age and sex • Prevalence of the major complications of diabetes • The annual excess cost of T2DM in population	• Projected incidence and prevalence of T2DM • Long-term complications in people with T2DM • Health care costs of complications of T2DM	• Demographic changes	Results presented based on +/- 1 standard error of the proportional reduction in cardiovascular mortality reported by UKPDS	Not reported

Table 4.2 (cont.). Summary of diabetes models with 'the projected diabetes prevalence' as a main output parameter

	Name of model / authors	Type	Setting and/or study population	Main data inputs used to construct the model	Main output parameter(s)	Main variables used to inform the projections of T2DM prevalence	Sensitivity analysis	Validation
11	Ruwaard et al. [244]	--	Netherlands, Total population	• Base year's estimates and future projections of diabetes prevalence and incidence, and population life expectancy	• Projected number of diabetic individuals (1980-2005) • Projected prevalence of diabetes (1980-2005)	• Trends in diabetes incidence and population life expectancy	Results presented based on different variants of prevalence, incidence, and reduction of life expectancy	The model prevalence estimates were compared with previous available cross-sectional data for 1980
12	Helms [245]	--	United States, Total population	• Age-specific prevalence of diabetes, 1987 • Age-specific incidence rate of diabetes • US population data and projections	• Projected prevalence of diabetes, 1990-2050 • Projected number of people with diabetes, 1990-2050	• Estimated incidence of diabetes	Not reported	Not reported

The diabetes prevalence forecasting models listed in Table **4.2** predicted the future prevalence of diabetes in different populations. However, these models varied in the type/ structure, data inputs used for model building, and the variables used to inform the projections of diabetes prevalence. For example, two of the most recent models in the list [the APHO Diabetes Prevalence Model[30] (for England) and the model of Boyle et al.[31] (for the US)] have some differences in the parameters used to project the future diabetes prevalence.

Briefly, the APHO Diabetes Prevalence Model predicted the total diabetes prevalence (diagnosed and undiagnosed) for the population of England aged ≥16 years for 2009, 2010, 2015, 2020, 2025, and 2030.[30] The first main set of data inputs used in this model was the current and projected population data (by age, sex, ethnic group, and deprivation) from the Office for National Statistics (ONS). The population data used in the model were based on the ONS populations by ethnic group for 2002-2007. Trends in the proportion of the population in sex specific age groups during 2002-2007 were extrapolated to 2030 using linear regression. Then, these proportions were applied to the 2006 based population projections produced by the ONS. It was assumed that the changes in the population by ethnic group found in 2002-2007 would continue to apply from 2008 to 2030.[30] The second set of data inputs was the age- and sex-specific prevalence rates for self-reported physician diagnosed diabetes, which were obtained from the Health Survey for England (HSE), 2006. Undiagnosed diabetes was also obtained from HSE 2006 and was defined as HbA_{1c} of ≥6.5% (≥48 mmol/ mol) in the absence of a self-reported diagnosis of diabetes. To take account of differences in the prevalence by ethnic group, the model used data from HSE 2004, which included a booster sample of people from minority ethnic groups. Trends in the prevalence of overweight (BMI 25–29.9 kg/ m^2) and obesity (BMI ≥30 kg/ m^2) were obtained from the HSEs 2003–2008, and were assumed to continue to 2030. These trends in overweight and obesity were used to inform the projections in diabetes prevalence.[30] Moreover, the model also used different RRs for estimations. For instance, sex-specific RRs by ethnicity were used for some ethnic minorities such as south Asian (Indian, Pakistani and Bangladeshi) men and women. Also, RRs of having diabetes if overweight or obese were incorporated in the estimation of future diabetes prevalence.[30] The APHO Diabetes Prevalence Model estimated that

the diabetes prevalence in 2010 was 7.4% among those aged ≥16 years, and was predicted to rise to 8.0% in 2015 and 9.5% in 2030. The estimated prevalence of diabetes was higher in men (8.6%) than women (6.3%) and among people from South Asian (14.0%) and Black (9.8%) ethnic groups than in White, mixed and other ethnic groups (6.9%).[30]

In comparison, Boyle et al.[31] constructed a series of dynamic models to project the future burden of diabetes among US adults (18-79 years) up to 2050. A three-state model partitioned the US population into 'no diabetes', 'undiagnosed diabetes', and 'diagnosed diabetes'. Then, a four-state model divided the state of 'no diabetes' into high-risk (prediabetes) and low-risk (normal glucose) states. The data inputs used for modelling included population data and projections up to 2050 from the US Census Bureau, initial year prevalence of diabetes in the US, and incidence rate estimates of diagnosed diabetes for the US adult population aged 18-79 years from 1980-2007 obtained from the Centres for Disease Control and Prevention (CDC). Projections in the incidence of diabetes for 2008-2050 were estimated using logistic regression. In addition, the model included literature-derived estimates of the rates of transition from having no diabetes, prediabetes, and undiagnosed diabetes to having diagnosed diabetes, as well as the risk of mortality associated with different glycaemic and diabetic states. Boyle et al. used primarily two sets of variables to inform the projected future diabetes prevalence. First, the trends in the incidence of diabetes, from which they assumed three projection scenarios (low incidence, middle incidence, and high incidence) for 2008-2050, based on the mean incidence rates from logistic regression. The second set contained the RR of death for individuals with undiagnosed diabetes and the RR of death for those with diagnosed diabetes (both versus those without diabetes). Again, the authors assumed two different sets of such RRs (high and low) from two different studies in the US. The modelling results of the future diabetes prevalence were presented in four scenarios: two low incidence scenarios (with high and with low mortality risk) and two middle incidence scenarios (with high and with low mortality risk). Assuming low incidence and relatively high diabetes mortality, the model projected the total diabetes prevalence (diagnosed and undiagnosed) to increase from 14% in 2010 to 21% of the US adult population by 2050. On the other hand, if recent increases in diabetes incidence continue and diabetes

mortality is relatively low, the projected prevalence will increase to 33% by 2050. Moreover, a middle-ground scenario projected a prevalence of 25% to 28% by 2050. The model also quantified the potential effect of a hypothetical preventive intervention offered to all people with impaired fasting glucose (who constitute a group with a high risk for future development of diabetes). The authors argued that if half of the people with impaired fasting glucose participated in an intervention and their incidence was reduced by 50%, it would be roughly equivalent to a 25% reduction in all people with impaired fasting glucose. Therefore, it was assumed that the hypothetical intervention would reduce by 25% the annual incidence of diabetes in people with impaired fasting glucose. For example, using the projected middle incidence scenario and low mortality risk, the model projected that nearly 3.5 million incident cases would be reported in 2050 with no intervention, and around 3.2 million incident cases would be reported with intervention. That is equivalent to a net reduction of approximately 345,000 incident cases of diabetes by 2050 with such a hypothetical intervention.

In general, this chapter offers a theoretical background of epidemiological models of T2DM, their uses, structure, and limitations. It also presents a review of the existing diabetes models in literature. In the next chapter, the Saudi IMPACT Diabetes Forecast Model (used in this thesis) is described in detail, including data sources, assumptions used, methods, and justification of its use (over the other diabetes prevalence forecast models) to study diabetes prevalence trends and projections in Saudi Arabia.

Chapter 5. The Saudi IMPACT Diabetes Forecast Model: data inputs, data sources, and methods

This chapter presents an extensive description and discussion of the model developed and used in this thesis (the Saudi IMPACT Diabetes Forecast Model), data inputs used to construct the model, data sources with their strengths and limitations, assumptions, and methods of estimating and projecting T2DM prevalence in Saudi Arabia.

5.1. Introduction

The IMPACT model was first developed in 1996, and was used in many settings to estimate the changes in coronary heart disease (CHD) mortality attributable to medical and surgical treatments, and risk factor changes.[219, 246-249] The IMPACT model studied diabetes as one of several risk factors for CHD. Later, the model was further developed to study diabetes prevalence as an output, based on trends in some main risk factors, and to provide some policy scenarios to quantify the impact of reducing the levels of such risk factors on the projected diabetes prevalence. The 'IMPACT Diabetes Forecast Model' has been successfully used and validated in four developing countries in the EMR (Turkey, Syria, Tunisia, and Palestinian areas), as part of the project: MEDiterranean studies of Cardiovascular disease and Hyperglycaemia: analytical Modelling of Population Socio-economic transitions (MEDCHAMPS).[219]

The IMPACT Diabetes Forecast Model used in MEDCHAMPS is a Markov model implemented in Microsoft Excel spreadsheets. It works in the same method of Markov modelling as that described earlier in chapter 4. The model integrates information on population, obesity and smoking trends. The model assumes that the population is divided into three distinct (discrete) pools (health states): those who are obese, those who are smokers, and those who are 'healthy' (i.e. non-obese, non-smoker, and non-diabetic). From these health states, the model estimates and predicts the trends in diabetes prevalence over a specified time period. It also estimates the decline in the projected diabetes

prevalence, which might be attributed to changes in the levels of obesity and smoking as risk factors (Figure **5.1**).[219]

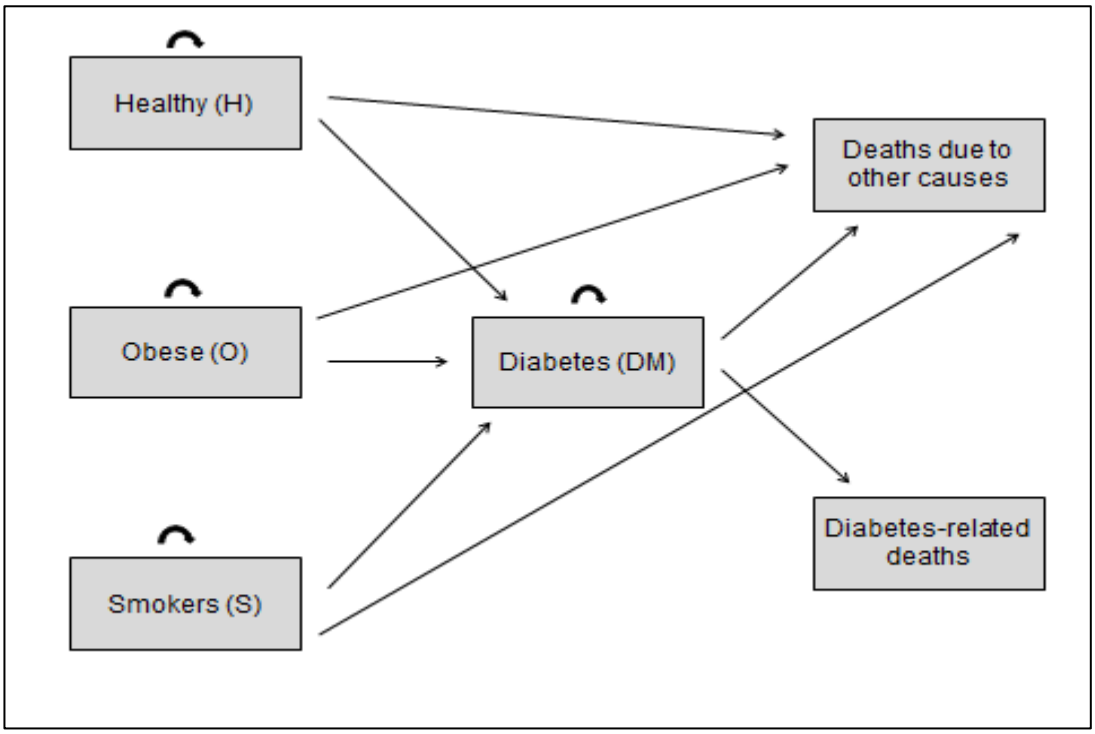


Figure 5.1. General structure of the IMPACT Diabetes Forecast Model

As a 'discrete-state' Markov model, the IMPACT Diabetes Forecast Model assumes that every individual in the population is in one (and only one) health state in each modelling cycle (one year). As illustrated in Figure **5**.**1**, the model assumes that individuals make transitions from the three main health states (healthy, obese, and smokers), or remain in the same state during each modelling cycle. Individuals in these three main states can make transitions to the (diabetes) state (i.e. they develop diabetes), or die due to other causes. Individuals in the (diabetes) states can die as a result of diabetes or diabetes-related conditions (such as cardiovascular disease) or due to other causes. Diabetic individuals cannot make the transition back to the three main states, assuming a zero remission rate. Generally, the transition from (healthy) to (diabetes) states is informed by the *incidence of diabetes*, while the transition from (obese) to (diabetes) states is informed by the *(diabetes incidence X relative risk of diabetes in 'obese' individuals)*, and the transition from (smokers) to (diabetes) states is informed by the *(diabetes incidence X relative risk of diabetes in 'smokers')*. Moreover, the transitions from any of the model states (healthy, obese, smokers and diabetes) to the state of (deaths due to other

causes) are informed by the *total mortality rate*. On the other hand, the transition from the (diabetes) state to the state of (diabetes-related deaths) is informed by the *case fatality rate*.

Because the modelling was originally intended for developing countries, the IMPACT Diabetes Forecast Model was designed to use a relatively small amount of data inputs that should be obtainable from such countries with only limited available local data. The main data input requirements are a) cross sectional data on T2DM, obesity and smoking prevalence, b) population structure by age and sex, and c) population demographic trends. In addition, other data items are required, such as RRs of T2DM in obese and in smokers, but most of such data can be obtained from the literature, and will be subject to extensive sensitivity analyses, which will take in consideration the uncertainties around such parameters. If some data are unavailable, the model can use reasonable assumptions.

However, the most crucial piece of data required is the incidence of T2DM, which is a key model parameter. Diabetes incidence is usually very difficult to obtain and is not expected to have local estimates for most countries worldwide,[219] and is widely variable between different countries and regions. Thus, the model adapted Barendregt's (DISMOD) method[157], which estimates a baseline diabetes incidence based on the diabetes prevalence and general mortality, that are usually available in many developing countries. Detailed description of the DISMOD method, in addition to the model structure, assumptions made and data sources are discussed later in this chapter. The IMPACT Diabetes Forecast Model was validated by comparing its estimates to observed estimates for each participating country. The validation results were good for all countries, and the model estimates were reasonably close to observed estimates for men and women at different time points (*Personal communication, Martin O'Flaherty, 2012*).

It is important to mention that this thesis constructed the Saudi IMPACT Diabetes Forecast Model based on the general structure of the original IMPACT model. However, as discussed in chapter 1, this thesis undertook a number of 'original' substantial developments and improvements to the original IMPACT model, mainly to the sections of sensitivity analyses, validation and 'what if'

policy options. These developments are discussed in more detail in section 5.4 of this chapter, chapter 6, and chapter 8. In brief, as previously mentioned in chapter 1, the original IMPACT model, examined the uncertainties around the modelling parameters by applying only the 'analysis of extremes' method. In comparison, the Saudi IMPACT Diabetes Forecast Model used, in addition, the method of 'scenario analysis' to explore uncertainties in the future trends of key model inputs. Also, in the original IMPACT model, there were only two policy reduction targets (one for obesity prevalence and another for smoking prevalence), and both of them were 'theoretical/ hypothetical' targets. On the other hand, the Saudi IMPACT Diabetes Forecast Model used existing local policy targets, in addition to other international targets set by leading authorities, and therefore should offer more comprehensive and 'realistic' intervention options for policy makers. Furthermore, the original IMPACT model was validated only by comparing its estimates to the observed data, while this thesis undertook, in addition, a substantially detailed 'concurrent validation', by comparing the model estimates to other existing models of the same purpose, such as that of the most recent IDF Diabetes Atlas,[9] a recent Global Burden of Disease (GBD) project,[20] and other studies.[14-17]

Choosing the structure of the IMPACT Diabetes Forecast Model as a 'base/ foundation' for building the model in this thesis can be justified by its successful use and validation in four countries of the Eastern Mediterranean Region, in which Saudi Arabia is located. The model was originally developed for use in this particular region which, as discussed earlier, has alarming levels of T2DM and its risk factors (e.g. obesity and smoking). In addition, the model takes into consideration the paucity of information in such developing countries, and therefore the required data inputs for modelling should be attainable from them. The risk factors studied by the IMPACT Diabetes Forecast Model (obesity and smoking) are common health problems in these countries and there are reasonably good local population data on these risk factors. It has been mentioned in chapter 1 that reliable prevalence data on obesity and smoking in Saudi Arabia are available at different time points. Therefore, these data were used to estimate the likely trends and projections of the levels of these two risk factors over time. In contrast, there are no sufficient data on the prevalence of

other risk factors (physical activity and diet). Only one national study[19] has reported the prevalence of physical activity and dietary patterns.

The other existing diabetes models (discussed in chapter 4) were originally designed for use in developed populations, that have different occurrence and levels of T2DM and its risk factors. In addition, most of these models have different output parameters, and therefore require several types of data inputs, which are unlikely to be available from developing countries. Furthermore, none of these models was validated in the EMR region or any other developing countries.

5.2. Structure of the Saudi IMPACT Diabetes Forecast Model software

The Saudi IMPACT Diabetes Forecast Model is a Markov model implemented in Microsoft Excel spreadsheets, specifically created for this thesis. The model's workbook is structured in 'tabs'.[250] The main tabs of the model are summarised in Table **5.1**.

Table 5.1. Summary of the general workbook structure of the Saudi IMPACT Diabetes Forecast Model

Name of tab(s)	Description
About	General information on the model and names of the development team
Data Input	Data entry facility for entering country specific data
Dashboard	Tabular and graphical presentation of the main model outputs
Outputs	Tables of the model's output numbers
Validation	Summary and graphical presentation of validation of the model
Sensitivity Analysis	Setting up different scenarios and summary of the effect of change in values of the important parameters on the model outputs
Age and sex specific Markov chains	Perform the calculations for each age group and sex in the model

The 'Data Input' tab is the major one to be filled in by the user. Information in almost all the other tabs are dependent on data entered into the 'Data Input' tab. Figures 5.2-5.6 show screenshots of the sections in this tab. Cells in white colour (unshaded) are the only cells that must be filled in by the user. The starting year of the model's time horizon must be entered and the model then automatically fills in all the following years (time horizon was set up for 30 years in the model). In the Saudi IMPACT Diabetes Forecast Model, the time horizon starts from 1992 and ends at 2022. The starting year of modelling (1992) was selected based on the timing of the earliest available local population-based data on diabetes prevalence, as the available population surveys from Saudi Arabia started at the early 1990s (as discussed in chapter 3).

The 'Data Input' tab consists of two main sections. Section 1 (figure 5.2) is for population structure data, where the numbers of the Saudi population for each year, sex and age group are entered. The age groups covered by the model are six, starting from 25 year-old and are ordered in 10-year-intervals (i.e. 25-34,

35-44, 45-54, 55-64, 65-74 and 75+ years). The model calculates the total numbers of population for each year and sex, and for both sexes combined.

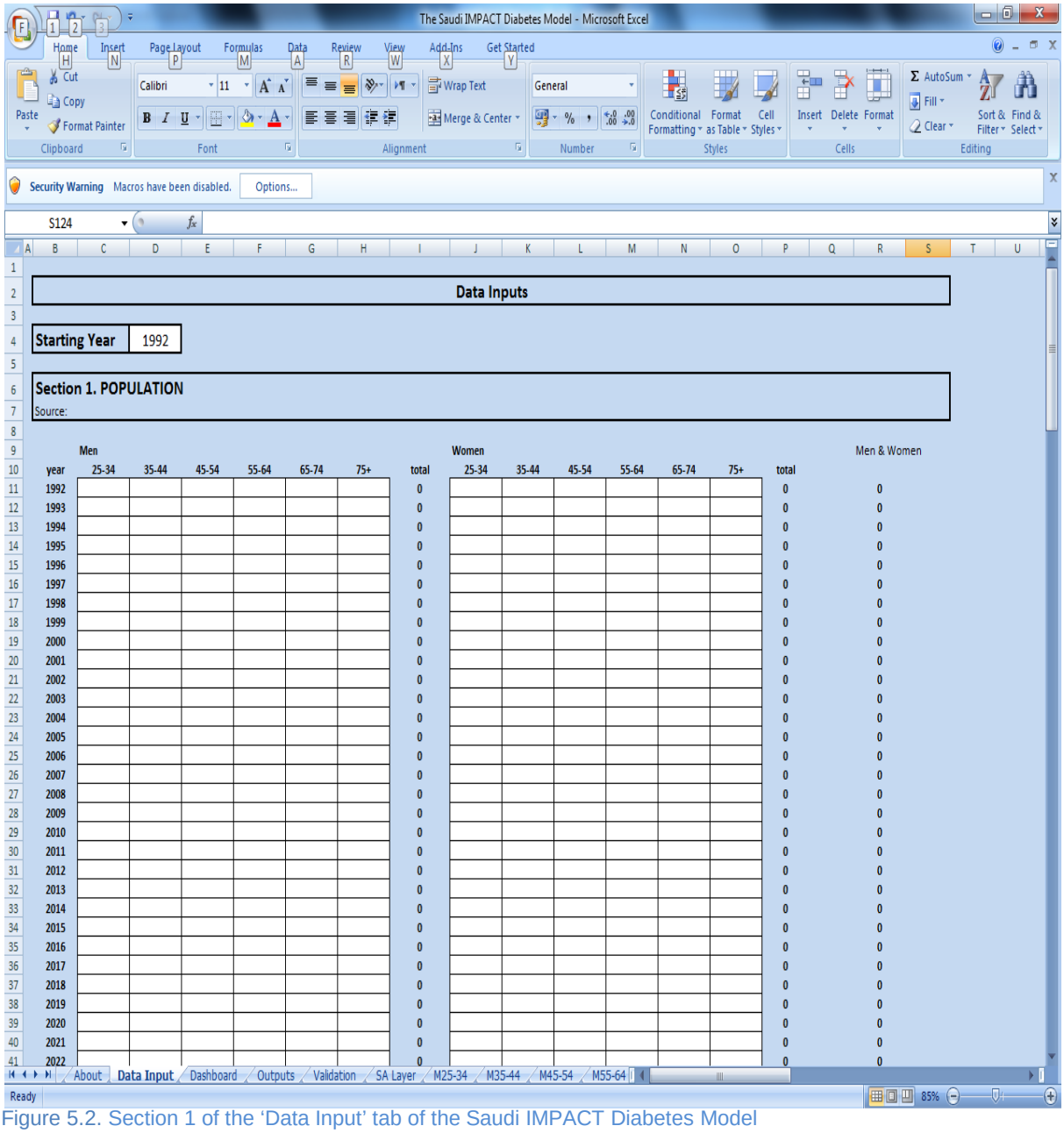


Figure 5.2. Section 1 of the 'Data Input' tab of the Saudi IMPACT Diabetes Model

Section 2 is designed for morbidity data, and is divided into four subsections. The first subsection (figure 5.3) is for the entry of T2DM prevalence for the starting year of modelling (1992). The prevalence must be entered for each sex and age group of population.

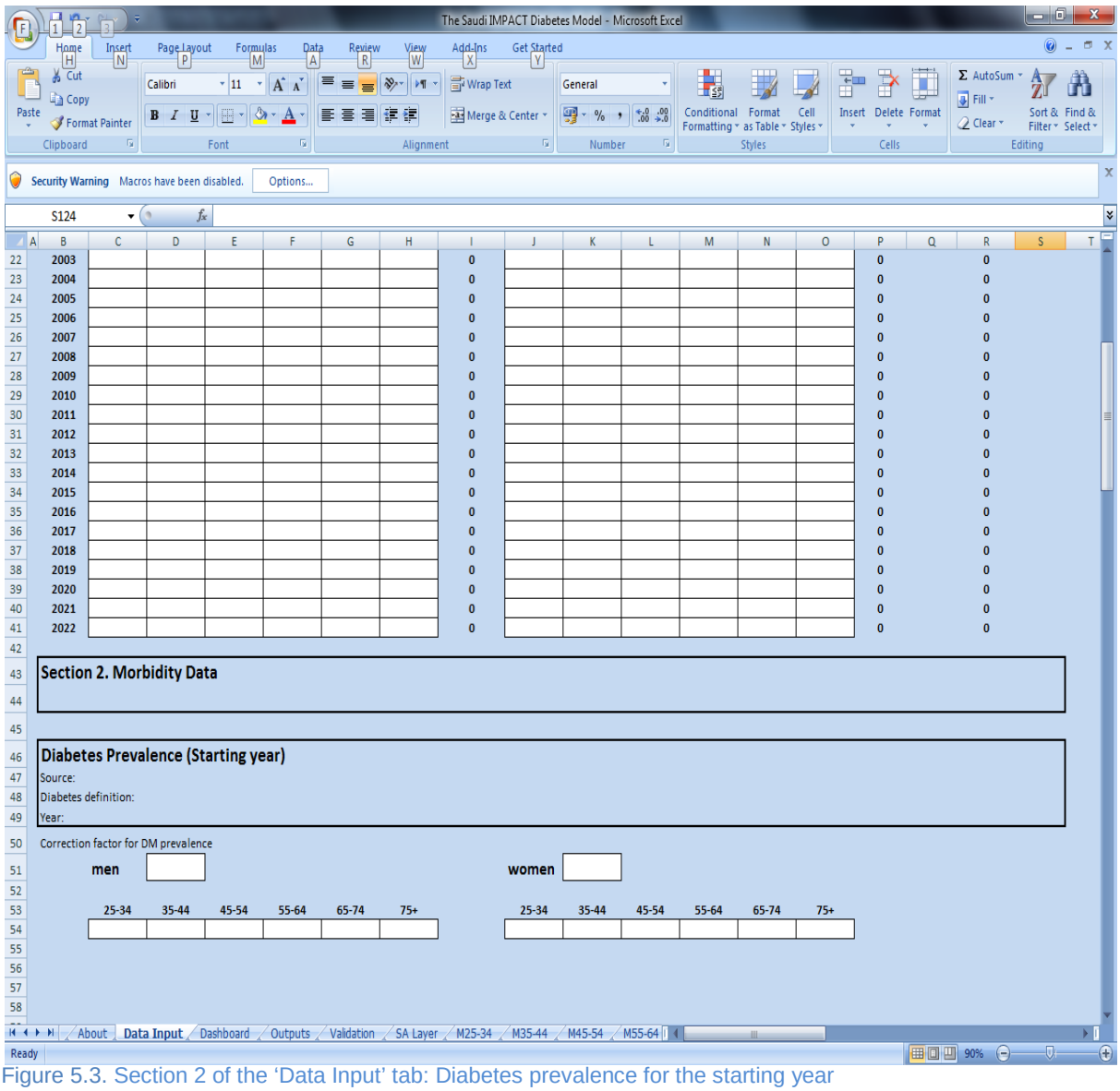


Figure 5.3. Section 2 of the 'Data Input' tab: Diabetes prevalence for the starting year

The second subsection (figure 5.4) is for data on obesity prevalence trends which must be entered for each sex and age group and for all years (1992-2022). The model calculates the weighted average of obesity prevalence of each year, for each sex and for both sexes combined, by dividing the total prevalence of each year on the number of population at the same period as a denominator.

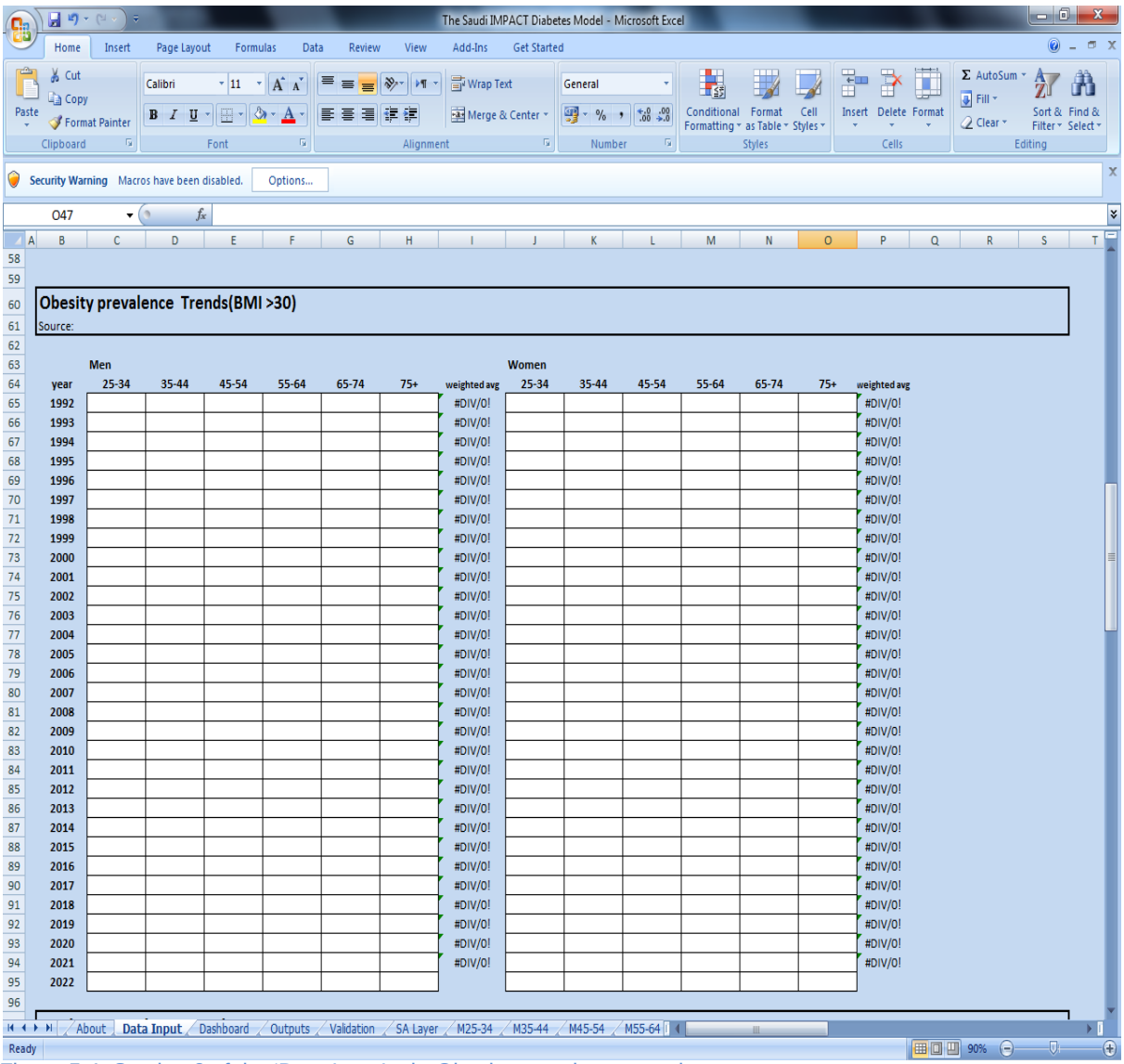


Figure 5.4. Section 2 of the 'Data Input' tab: Obesity prevalence trends

In the third subsection (figure 5.5), smoking prevalence trends are entered for each sex and age group and for all years (1992-2022). The last subsection (figure 5.6) is for the other essential parameters for modelling (transition parameters). These parameters are sex- and age-specific diabetes incidence, case fatality rate and total mortality, which were derived for the Saudi population by using the DISMOD model software (discussed in detail in section 5.3.2.5).

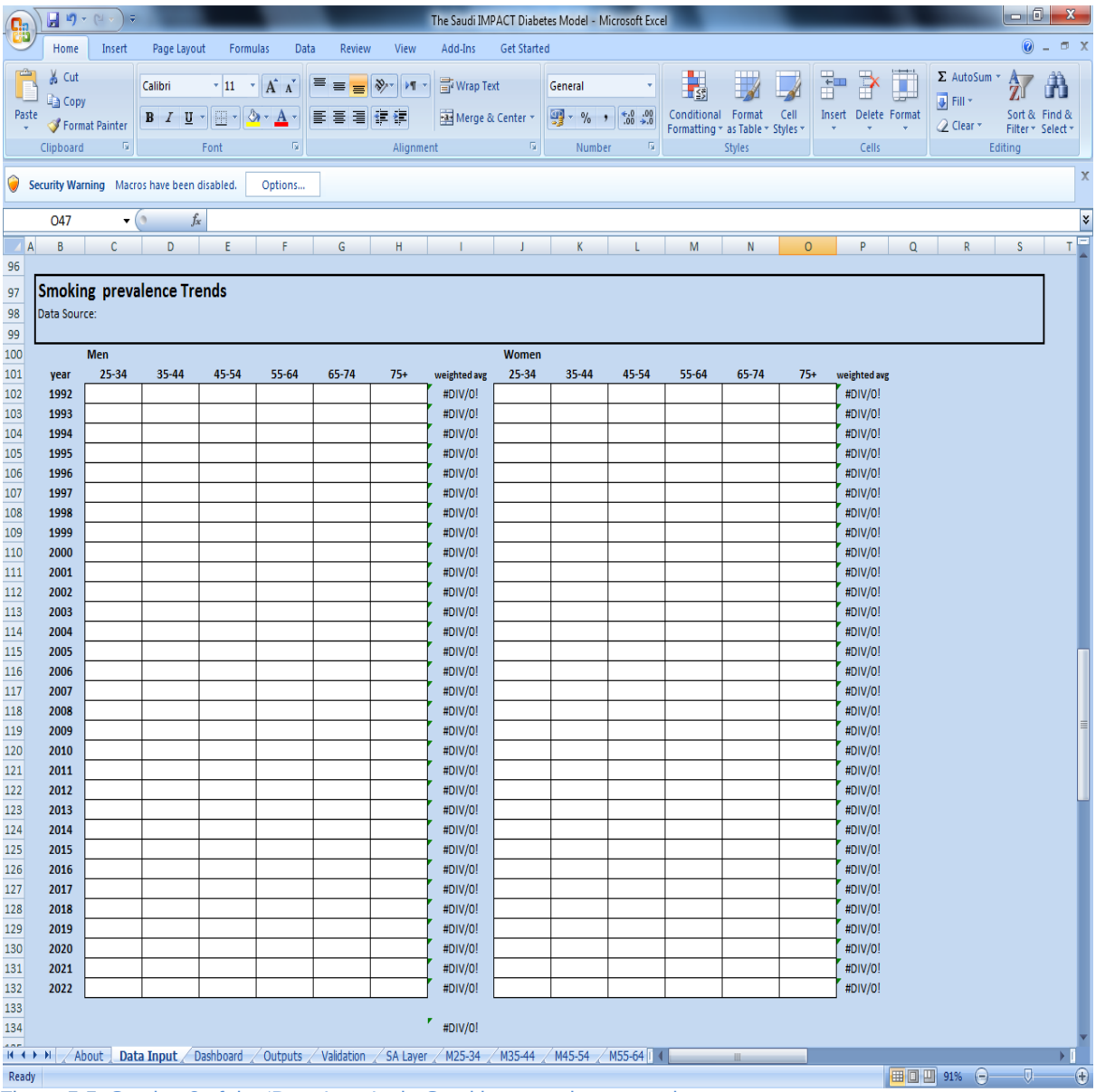


Figure 5.5. Section 2 of the 'Data Input' tab: Smoking prevalence trends

Some important information (e.g. data sources, diabetes definition, etc) can be documented for each section in the 'Data Input' tab, and the features of Microsoft Excel also enable the user to insert comments on any particular section or cell in order to document or clarify any related special information.

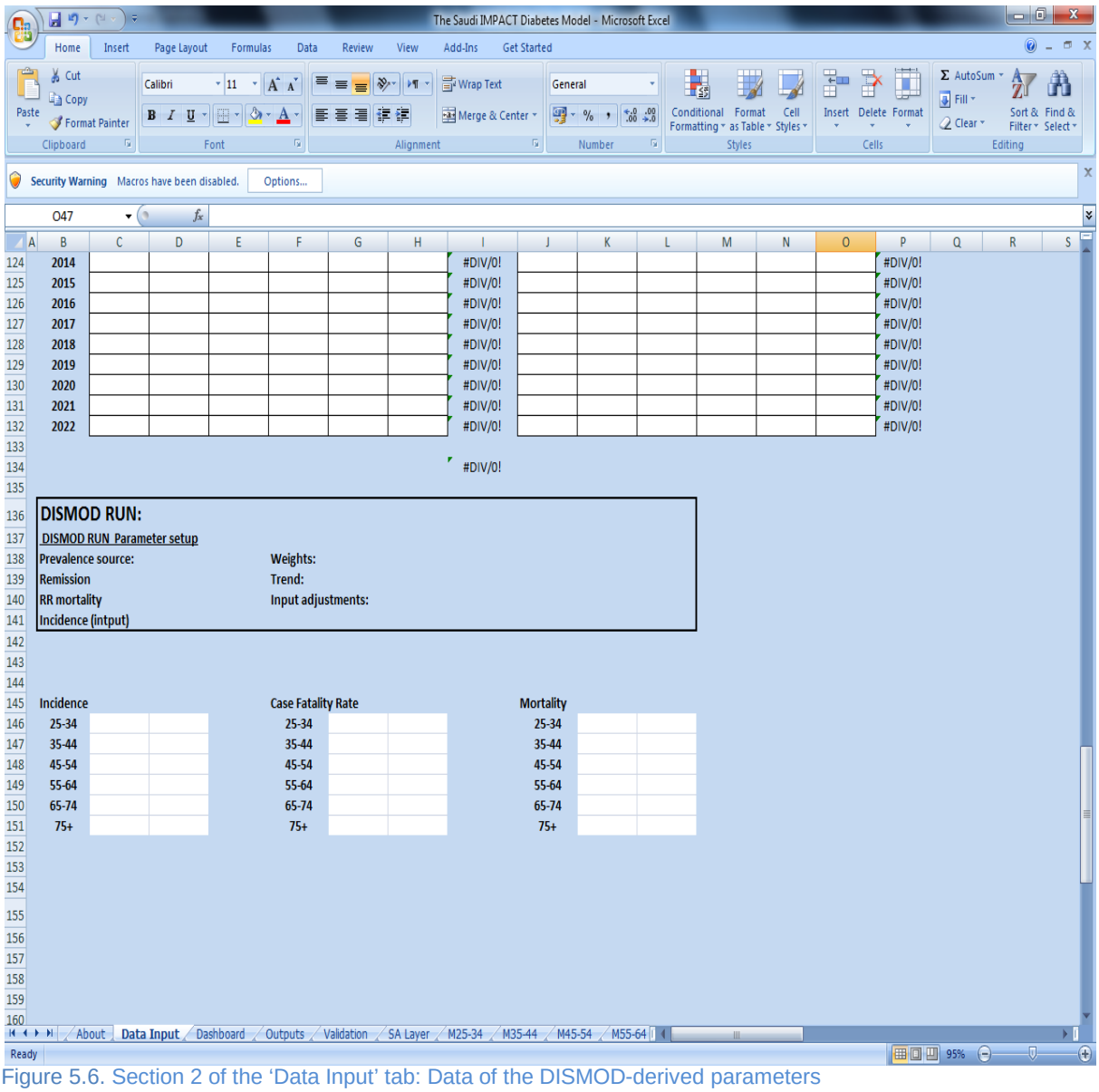


Figure 5.6. Section 2 of the 'Data Input' tab: Data of the DISMOD-derived parameters

5.3. Data inputs into the Saudi IMPACT Diabetes Forecast Model: description, sources and assumptions

5.3.1. Introduction

As previously mentioned in chapter 4, modelling data can be obtained from a wide range number of sources, which can include assumptions and expert opinions.

The Saudi IMPACT Diabetes Forecast Model required various data from different sources, such as population structure, demographic trends, total mortality, prevalence of obesity and smoking, and trends in the levels of these two risk factors over time. Unfortunately, some required data from Saudi Arabia were scarce and patchy, even for population structure and mortality, which

should be routine data as in more developed countries. For other types of data, such as prevalence of T2DM and risk factors, the published national surveys were reliable and used validated and standardised measuring tools. However, these studies presented their findings in different formats. For instance, the 'age' variable of study populations varied in terms of the whole age range of participants and the age-group intervals.

The shortage/variations in data from Saudi Arabia made it necessary to develop some 'reasonable' assumptions and to perform some approaches such as inter- and extrapolation of some model parameters. However, this is not critical for the successful development of a valid model[219] and, as described in chapter 4, it is natural for the majority of models to utilise a wide range of data inputs, including assumptions, from various sources.[22] However, all assumptions and sources of modelling data should be explicitly stated for all modelling studies, because model results are conditional upon data inputs and assumptions.[22, 210]

5.3.2. Description of data inputs and their sources

The basic data required to build the Saudi IMPACT Diabetes Forecast Model are a) the Saudi population structure by age and sex; b) future projections in population structure over the time horizon of model; c) prevalence of T2DM for the starting year of modelling (1992); d) prevalence of obesity and smoking for as many time points as possible; and e) trends in prevalence of obesity and smoking over time. The other types of data (parameters) required to set up the transition probabilities between the model states are either estimated through some specific approaches implemented in DISMOD (incidence, case fatality, and total mortality) or obtained from literature (RRs of T2DM in obese and in smoking individuals).

Sources of all modelling data inputs and their advantages and limitations are summarised in Table **5.2**. Next, the following sections present a detailed description of the data items included in the modelling process.

Table 5.2. Summary of data sources for the Saudi IMPACT Diabetes Forecast Model with their strengths and limitations

Information	Data source(s)	Strengths and limitations
Population structure	Central Department of Statistics and Information (CDSI) [251]	**Strengths:** • Available online. • Population structure stratified by age group and sex. **Limitations:** • Available only for two years (1992 and 2004).
Projections in population structure	United Nations, Department of Economic and Social Affairs [252]	**Strengths:** • Available online. • Population structure stratified by age group and sex. • Population projections estimated based on the local censuses from the CDSI. **Limitations:** • Population projections only available in 5-year period intervals.
Prevalence of T2DM, obesity and smoking	Published national surveys in the literature [19, 34, 36, 37, 39]	**Strengths:** • Nationwide and population-based. • Large sample sizes. • Good sampling techniques - representative national samples from both sexes and all regions of the country. • Very good response rates. • Standardised methods, tools, and criteria for diagnosis of T2DM and obesity. **Limitations:** • Some studies did not report prevalence by age group, sex, or both. • For obesity studies, all of them relied on BMI to diagnose obesity – none of them used WC or WHR. • For smoking studies, they used different definitions for ‘active smoking’.

Table 5.2. (cont.). Summary of data sources for the Saudi IMPACT Diabetes Forecast Model with their strengths and limitations

Information	Data source(s)	Strengths and limitations
Projections in obesity and smoking prevalence	Assumptions (Linear interpolation + projecting by the observed annual rate of increase)	**Strengths:** • Observed data on obesity and smoking suggest linear trend. • Linear increase in obesity prevalence compatible with linear increase in mean BMI as estimated by WHO [13]. **Limitations:** • Extremely high (probably implausible) projections of obesity in some age groups.
T2DM incidence and case fatality + total mortality	DISMOD model [157]	**Strengths:** • Simple concept of Markov modelling. • Previously validated and used for countries in EMR. • Used successfully by leading global studies (e.g. Global Burden of Disease Study) • Free software. • Supplements parameters of disease epidemiology from partial data. • Provides 'internally consistent' estimates of incidence, case fatality, and mortality. **Limitations:** • Assumes a 'steady' population, with stable incidence and mortality over time. • Assumes independence of the all-other-causes mortality from diabetes.

Table 5.2. (cont.). Summary of data sources for the Saudi IMPACT Diabetes Forecast Model with their strengths and limitations

Information	Data source(s)	Strengths and limitations
Relative risk of T2DM in obese	Guh et al. [97] (systematic review and meta-analysis)	**Strengths:** • Pooled RRs estimated from large prospective cohort studies. • Pooled RRs estimated by comparing the risk of T2DM in obese (BMI ≥30 kg/m^2) with those with 'normal' weight. **Limitations:** • The studies included were from developed countries only. • Pooled RRs reported as sex-specific only (no age-specific). • Potential publication bias.
Relative risk of T2DM in smokers	Willi et al. [130] (systematic review and meta-analysis)	**Strengths:** • Pooled RR estimated from large prospective cohort studies. • Pooled RR adjusted for several covariates. • Included studies from developed and developing countries. **Limitations:** • Reported only one adjusted pooled RR for both men and women (no sex- or age-specific RRs). • Potential publication bias.

5.3.2.1. Population structure

The structure of the adult Saudi population aged 25-75+ years (by age group and sex) was obtained from the Central Department of Statistics and Information (CDSI); an affiliate of the Ministry of Economy and Planning in Saudi Arabia. The CDSI was established around 50 years ago to be the main official authority for population statistics in Saudi Arabia.[251]

Three completed national censuses have been conducted by CDSI to-date: in 1974, 1992 and 2004. Detailed data of these censuses were available on the CDSI website (http://www.cdsi.gov.sa/english/).[251]

The Saudi population structure in each census was stratified by sex and five-year age groups (<1, 1-4, 5-9, 10-14, 15-19, up to 80+ years). Since the time period covered by the model in this thesis was 1992-2022, data of the 1974 census were not used. A linear interpolation approach was used to 'fill in the gaps' between the census data for 1992 and 2004. The 'average' estimates of population structure were calculated between these two available time points, assuming a linear increase in population. For example, to calculate population in 1993, the formula: $(11*\alpha_1+\alpha_2)/12$ was used; where α_1 is population in 1992 and α_2 is population in 2004. Similarly, for year 1994, the formula: $(10*\alpha_1+2\alpha_2)/12$ was used, and so on. These formula calculations were applied to each single age group of population for each individual year.

5.3.2.2. Projections in population structure

There were no available local data on the Saudi population structure from 2005 onwards. Therefore, data were obtained from the United Nations; Department of Economic and Social Affairs (UN-ESA), Population Estimates and Projections Section.[252] The UN-ESA provides *"World Population Prospects"*, with a wide range of detailed country-specific indicators of populations for most countries in the world. Data were available online (http://esa.un.org/wpp/) with a long list of available indicators and another list of countries. After selecting one indicator and one country from each list, the period range of interest (from 1950 up to 2100) can also be selected. One of the listed indicators is "population by five-year age group and sex" and the estimates of this indicator are displayed in five-year intervals (i.e. 1990, 1995, 2000, etc).[252]

Sources of data and method of estimation are documented on the website for each country, which is a strength of this particular data source.[252] Estimates and projections of the UN-ESA for Saudi Arabia are most likely reliable, since they were based on the available local data and indicators. As reported in the website, the total Saudi population for 2010 was estimated to be consistent with the 1974 and 2004 censuses, taking into account the subsequent trends in fertility, mortality and international migration. Such trends and population projections were estimated using sophisticated statistical methods, such as 'probabilistic projections' using Bayesian hierarchal modelling. These methods and related assumptions are explicitly documented in detail on the website.[252]

The Department of Health Statistics in the Saudi Ministry of Health often relies on these UN population data for estimating different health parameters in the Kingdom *(Personal communication, Statistics Department staff, February 2011)*. Moreover, the UN population projections were widely used by leading global organisations, such as the IDF[9], and several other studies[14-16] to estimate and predict diabetes prevalence in countries.

The population structure for 2005-2009 was obtained through linear interpolation (similar approach as that described in section 5.3.2.1), since local data for 2004 were available, and the 2010 estimates were provided by the UN-ESA. Estimated population structure was then calculated through the same interpolation approach for every year up to 2022.

The Saudi population structure (1992 - 2022) that was used as an input into the Saudi IMPACT Diabetes Forecast Model is summarised in Table **5.3**.

Table 5.3. Data input into the Saudi IMPACT Diabetes Forecast Model: Structure of population of Saudi Arabia, 1992-2022 (*)

Year	Men- age groups (years)						Women- age groups (years)					
	25-34	**35-44**	**45-54**	**55-64**	**65-74**	**75+**	**25-34**	**35-44**	**45-54**	**55-64**	**65-74**	**75+**
1992	1988608	1265062	561736	305582	149294	97116	1158266	685776	368854	205322	110180	77585
1993	2042141	1333903	603824	313209	154106	99411	1210719	727225	387551	215229	117693	79507
1994	2095674	1402743	645911	320836	158918	101705	1263172	768674	406248	225135	125206	81429
1995	2149206	1471584	687999	328464	163730	104000	1315625	810122	424945	235042	132720	83351
1996	2202739	1540425	730086	336091	168542	106295	1368078	851571	443642	244948	140233	85273
1997	2256272	1609265	772174	343718	173354	108589	1420531	893020	462339	254855	147746	87195
1998	2309805	1678106	814262	351345	178166	110884	1472984	934469	481036	264762	155259	89118
1999	2363337	1746947	856349	358972	182977	113179	1525436	975917	499732	274668	162772	91040
2000	2416870	1815787	898437	366599	187789	115473	1577889	1017366	518429	284575	170285	92962
2001	2470403	1884628	940524	374227	192601	117768	1630342	1058815	537126	294481	177799	94884
2002	2523936	1953469	982612	381854	197413	120063	1682795	1100264	555823	304388	185312	96806
2003	2577468	2022309	1024699	389481	202225	122357	1735248	1141712	574520	314294	192825	98728
2004	2631001	2091150	1066787	397108	207037	124652	1787701	1183161	593217	324201	200338	100650
2005	2641168	2146125	1136823	436590	217198	125043	1837418	1241468	633848	344334	209282	105375
2006	2651334	2201100	1206858	476072	227358	125435	1887134	1299774	674478	364467	218225	110100
2007	2661501	2256075	1276894	515554	237519	125826	1936851	1358081	715109	384601	227169	114825
2008	2671667	2311050	1346929	555036	247679	126217	1986567	1416387	755739	404734	236113	119550
2009	2681834	2366025	1416965	594518	257840	126609	2036284	1474694	796370	424867	245056	124275
2010	2692000	2421000	1487000	634000	268000	127000	2086000	1533000	837000	445000	254000	129000
2011	2701400	2450200	1569200	694400	284200	130600	2134400	1596600	895000	469800	267000	134600
2012	2710800	2479400	1651400	754800	300400	134200	2182800	1660200	953000	494600	280000	140200
2013	2720200	2508600	1733600	815200	316600	137800	2231200	1723800	1011000	519400	293000	145800
2014	2729600	2537800	1815800	875600	332800	141400	2279600	1787400	1069000	544200	306000	151400
2015	2739000	2567000	1898000	936000	349000	145000	2328000	1851000	1127000	569000	319000	157000
2016	2790200	2573200	1949800	1007400	383800	150200	2395400	1898800	1180400	611400	336000	165400
2017	2841400	2579400	2001600	1078800	418600	155400	2462800	1946600	1233800	653800	353000	173800
2018	2892600	2585600	2053400	1150200	453400	160600	2530200	1994400	1287200	696200	370000	182200
2019	2943800	2591800	2105200	1221600	488200	165800	2597600	2042200	1340600	738600	387000	190600
2020	2995000	2598000	2157000	1293000	523000	171000	2665000	2090000	1394000	781000	404000	199000
2021	3029200	2611200	2186600	1370400	572600	181400	2698000	2138600	1457000	836800	426800	211400
2022	3063400	2624400	2216200	1447800	622200	191800	2731000	2187200	1520000	892600	449600	223800

(*) Results for (1993-2003, 2005-2009, 2011-2014, 2016-2019, and 2021-2022) were obtained through interpolation. Results for 2010, 2015, and 2020 were obtained from the World Population Prospects, United Nations.

5.3.2.3. Prevalence of type 2 diabetes, obesity and smoking

The major sources of data on prevalence of T2DM, obesity and smoking in Saudi Arabia were the published national surveys.[19, 34, 36, 37, 39] Different sources were utilised for literature review, including the MEDLINE database, in addition to cross referencing and personal contacts. The literature review strategy is presented in appendix 1, and the selected surveys have been discussed earlier in chapter 3.

As previously discussed in chapter 3, all studies were population-based and were carried out at the national level, covering all regions of Saudi Arabia, with good sampling sizes and techniques and high response rates. Hence, they were most likely representative of the population of Saudi Arabia. In addition, they used standard validated measuring and diagnostic tools such as the criteria of WHO or ADA for diagnosis of diabetes[41]; and BMI for definition of obesity.[87] On the other hand, some of these studies reported only the overall prevalence rate without providing the age- and sex-specific rates.[38] Moreover, all obesity studies depended only on BMI for diagnosis of obesity[19, 34, 36, 37], which has some limitations, as discussed in chapter 2. For smoking studies, different definitions of active smoking were used across different studies.[19, 35, 39] However, it was assumed that these different definitions would not affect the prevalence results substantially.

The Saudi IMPACT Diabetes Forecast Model requires data on the T2DM prevalence for each sex and age group of the population in the starting year of model (1992) only. In addition, the model also needs similar data on obesity and smoking prevalence for each single year of its time horizon (1992-2022). For the T2DM prevalence in 1992, the study of Warsy and El-Hazmi[36] was used as a source of data. However, as previously described in chapter 3, the study of Warsy and El-Hazmi, in addition to four obesity studies[34-37] and two smoking studies[38, 39], were carried out over a "period range" – e.g. 1990-1993 and 1995-2000, and their results were reported in age group intervals that were different from the model. Furthermore, one obesity study[37] and one smoking study[39] provided only the age-specific prevalence rates (no sex-specific). Therefore, some assumptions were necessary in order to make the age group intervals homogeneous for all studies and to obtain 'single year' prevalence rates.

Moreover, assumptions were required to obtain sex- and age-specific rates for all studies.

Firstly, it was assumed that the reported prevalence rates applied roughly to the midpoint of the period range. For instance, the study of Al-Nozha et al.[34] on obesity was conducted over the period of 1995-2000, so it was assumed that the results apply for 1997. Similarly, the results of Jarallah et al. study[39] on smoking, conducted during 1990-1993, were assumed to apply for 1992 and so on. However, the only exception to this assumption was the use of the study of Warsy and El-Hazmi[36] for obtaining the starting year (1992) diabetes prevalence, although it was conducted over the period range of 1992-1995. Warsy and El-Hazmi used the WHO 1985 diagnostic criteria, with fasting blood glucose and OGTT, to define T2DM. On the other hand, there were two more potential studies for obtaining the 1992 diabetes prevalence[35, 202], but neither study was used as a source for the starting year prevalence, due to limitations in either the diagnostic definition used or the presentation of reported results. The first study was that of Al-Nuaim[202], which was conducted during 1990-1993. As mentioned in chapter 3, that study used 'random' blood sugar (not fasting or OGTT) to diagnose T2DM. The second study was that of Osman et al.[35] which was carried out over the period of 1989-1994. Unfortunately, this study reported only the total population diabetes prevalence without presenting the age- and sex-specific prevalence rates.

Secondly, the age group bands of studies were managed to be compatible with the model's age groups. One of studies (the WHO STEPS study)[19] had the same age bands as those of the model, however only up to 64 years (i.e. 25-34, 35-44, 45-54, 55-64 years). For other studies, assumptions were made to consider the overlap between the model's age groups and those reported by studies. For example, in Al-Nozha et al. study[34], the prevalence rate of the age group 35-44 years was assumed to be the average of prevalence for the study age groups of 30-39 and 40-49 years, while the prevalence rate of the age group 45-54 years was assumed to be equal to the average of that reported for age groups 40-49 and 50-59 years. Similarly, in the study of Warsy and El-Hazmi[36], the prevalence rate for the age group 25-34 years was assumed to be the average of the reported prevalence rates for the reported age groups of 14-29 and 30-44 years. Also, the prevalence rate of the age group 35-44 years was

assumed to be the average of prevalence for the reported age groups 30-44 and 45-59 years.

Thirdly, for studies that reported only the age-specific prevalence, the "sex ratio" of prevalence was calculated from other similar studies and assumed to be the same for them. For example, for obesity studies, the sex ratio was calculated for each age group in the study of Warsy and El-Hazmi[36] and applied these age-specific ratios to Al-Nuaim study[37], which was the only obesity survey that did not report sex-specific prevalence rates. On the other hand, for smoking studies, the sex ratios were calculated from the WHO STEPS[19] study and were applied to Jarallah et al. study.[39] It was assumed that such sex ratios were unlikely to differ substantially between different studies.

Finally, the results of one obesity study and one smoking study were excluded as inputs into the model, because their data were insufficient for modelling. The first excluded study was that of Osman et al.,[35] which included relatively younger age groups (18-20, 21-30, 31-40 and ≥40 years) and, therefore, the previous assumptions could not be applied on this particular study in order to obtain similar age groups as the model. The second excluded study was that of Al-Nozha et al.,[38] which originally measured the prevalence of coronary artery disease in Saudi Arabia for both sexes and all age groups between 30-70 years. This study determined also the prevalence of the major modifiable risk factors for coronary artery disease (including smoking). However, unfortunately, it reported only the overall smoking prevalence without age- or sex-specific rates. Attempts to contact the authors (by email and telephone) to obtain any further data were unsuccessful.

Therefore, four studies on obesity prevalence and two studies on smoking prevalence were made compatible to the model's requirements after applying the previous assumptions to their reported results. They provided prevalence rates of obesity and smoking for the Saudi population during the period from 1992-2005. Interpolation was performed in order to obtain results of the missing years within this range. However, there were significant and unexplained differences in the reported prevalence rates of obesity between Al-Nuaim study[37] (results for 1992) and the study of Warsy and El-Hazmi[36] (results for 1993) across almost all age groups of both sexes, although both studies were

conducted at almost the same time. For example, the prevalence in men aged 55-64 years was 9.5% in Al-Nuaim study, and 16.4% in the other study. Moreover, the prevalence of obesity in women aged 35-44 years was 18.6% in Al-Nuaim study, while it was 31.5% in Warsy study. However, no obvious differences were found in the quality of data of both surveys. Table **5.4** summarises the most important features of these two studies. Although the response rate in Al-Nuaim study was lower than that in Warsy et al. study, this, alone, seems unlikely to explain such considerable differences in results. Thus, the average of prevalence rates from these two studies was calculated for each sex and age group, and was assumed to apply for 1992.

Table 5.4. Comparison of Al-Nuaim and Warsy et al. studies on obesity prevalence in Saudi Arabia

Study	Sample size	Sampling method	Response rate	Definition of obesity	Measurement method
Al-Nuaim[37]	10,651 (50.8% males and 49.2% females)	Multistage stratified cluster sampling of all regions of Saudi Arabia with probability proportionate to size	69%	BMI ≥ 30 kg/m^2	- Trained physicians in primary care centres - standardised measurement tools
Warsy & El-Hazmi[36]	14,660 (42% males and 58% females)	Multistage stratified cluster sampling of all regions of Saudi Arabia with probability proportionate to size	95%	BMI ≥ 30 kg/m^2	- Household visits of trained members - standardised measurement tools

Another problem faced with the prevalence surveys was the highest limit of age groups covered, even after applying the previous assumptions. The oldest age group obtained from these surveys was 55-64 years. Thus, two of the model's age groups were missing (65-74 and 75+ years). However, the only exception was the study of Warsy and El-Hazmi[36], which was used to obtain the diabetes prevalence for 1992. In that study, the last reported age group was 'open-ended' (≥60 years), and therefore, the diabetes prevalence rates for the age groups 65-74 and 75+ years were assumed to be equal to that reported for the age group ≥60 years.

The approach to overcome the limitation of missing older age groups was to search for the required data from other neighbouring countries, and to extrapolate the prevalence for the missing two age groups. This extrapolation

was based on assuming a similar pattern of prevalence in these two oldest age groups in relation to the previous age group (55-64 years). The Gulf Cooperation Council (GCC) countries have similar cultures, environments and population characteristics in terms of lifestyle and socioeconomic status.[169] Details of the published national surveys on obesity and smoking in these countries have been discussed earlier in chapter 3. Again, unfortunately, almost all surveys from these countries did not cover older age groups of population (≥65 years). However, there were two good published studies from Oman (for obesity and smoking prevalence rates) that included older age groups, and were used for extrapolation.

The first study was that of Al-Lawati et al.[179], which compared two national surveys for prevalence of overweight (BMI 25–29.9 kg/m^2) and obesity (BMI ≥30 kg/m^2) in 1991 and 2000. Both of these surveys covered nationally representative samples of Omanis aged ≥20 years. There were 5,086 participants (2,128 men and 2,958 women) in the 1991 survey, and 6,400 participants (3,069 men and 3,331 women) in the 2000 survey. The response rates were above 90% in both surveys. Tools and methods of measurement of weight and height (to calculate BMI) were well calibrated and standardised. The results of these two surveys were reported for each sex and in 10-year-intervals (20-29, 30-39, 40-49, 50-59, 60-69, 70-79, and 80+ years). Prevalence rates of obesity were reported separately from those of overweight. Similar previous assumptions were first applied to obtain similar age groups to the Saudi IMPACT Diabetes Forecast Model. For instance, the prevalence rate for the age group 25-34 years was assumed to be the average of the reported prevalence rates for the age groups of 20-29 and 30-39 years, etc. Table **5.5** presents an example of the results of the obesity prevalence among Omani men before and after applying these assumptions.

Table 5.5. The results of two Omani surveys[179] on obesity prevalence in men before and after the applying of assumptions

The reported results			**Results with assumptions**	
The 1991 survey			The 1991 survey	
Age group (yrs)	**Prevalence (%)**		**Age group (yrs)**	**Prevalence (%)**
20-29	6.60		25-34	9.55
30-39	12.50		35-44	14.50
40-49	16.50	→	45-54	14.55
50-59	12.60		55-64	10.55
60-69	8.50		65-74	5.15
70-79	1.80		75+	0.90
80+	0			
Overall	10.5			
The 2000 survey			The 2000 survey	
Age group (yrs)	**Prevalence (%)**		**Age group (yrs)**	**Prevalence (%)**
20-29	11.00		25-34	15.35
30-39	19.70		35-44	21.40
40-49	23.10	→	45-54	21.50
50-59	19.90		55-64	18.15
60-69	16.40		65-74	12.20
70-79	8.00		75+	6.50
80+	5.00			
Overall	16.7			

After obtaining a similar age group pattern as the model, the available data from Saudi Arabia for 1992 were extrapolated using the Omani data for 1991. For instance, the proportion of difference between prevalence rates for the age groups 55-64 and 65-74 was calculated for each sex in the Omani population in 1991, through dividing the prevalence of older age group by that of younger age group (e.g. for men, 5.15 / 10.55 = 0.4882). Next, this difference proportion was multiplied by the prevalence for the age group 55-64 of the Saudi population, to eventually obtain the prevalence for the age group 65-74 years in 1991 (e.g. for men, 0.4882 X 12.9 = 6.30). Similar methods were applied to the Omani data in 2000 to obtain prevalence rates of obesity in the missing age groups of both sexes in Saudi Arabia for 2000. Data for 1993-1999 were estimated through linear interpolation. Figure **5.7** compares between the data from Oman and Saudi Arabia after applying the previous assumptions.

Moreover, there was only one national smoking survey from the GCC countries which covered older age groups. This study was again from Oman (Al Riyami et al.)[183], carried out in 2000 and covered a nationally representative sample of Omanis aged ≥20 years. The total sample size was 7011 (3,506 males and 3,505 females). The definition of current smoking was 'smoking at the time of survey'. Prevalence rates were reported for each sex and age group (20-29, 30-39, 40-49, 50-59, 60-64, and ≥65 years). First, the age groups were arranged in regular 10-year-intervals (20-29, 30-39, 40-49, 50-59, 60-69, 70-79 and 80+ years). It was assumed that the prevalence for the age group 60-69 was the average of that reported for 60-64 and 65+ years (For men, [7.4 + 7.9] / 2 = 7.7% and for women, [2.2 + 0.8] / 2 = 1.5%). The prevalence rates for the age groups 70-79 and 80+ years were assumed to be equal to that reported for the age group 65+ (7.9% for men and 0.8% for women). Next, a similar approach was performed as with the obesity survey in order to obtain similar age groups as the model. Table **5.6** illustrates an example of the results in men before and after applying the assumptions.

Table 5.6. The results of an Omani survey[183] on smoking prevalence in men before and after the applying of assumptions

The reported results			**Results with assumptions**	
Age group (yrs)	**Prevalence (%)**		**Age group (yrs)**	**Prevalence (%)**
20-29	11.50		25-34	14.50
30-39	17.50		35-44	18.10
40-49	18.70	→	45-54	16.65
50-59	14.60		55-64	11.15
60-69	7.70		65-74	7.80
70-79	7.90		75+	7.90
80+	7.90			
Overall	13.4			

Again, the available Saudi data for 2000 were extrapolated in the same method applied for the obesity survey in order to obtain prevalence of smoking for the missing age groups in both sexes. However, there were no other studies measuring smoking prevalence in the oldest age groups from neighbouring countries. Hence, prevalence rates for the two oldest age groups in the Saudi population in 1992 (starting year of the model) were extrapolated using the same previous study from Oman, assuming a similar prevalence pattern by age

to that of 2000. Linear interpolation was performed to estimate the values for the period 1993-1999. Figure **5.8** showed a comparison between the data from Oman and Saudi Arabia after applying the previous assumptions. It could be observed that the smoking prevalence tended to be considerably higher among younger age groups of men (25-34 and 35-44 years) in Saudi Arabia in 2000 (25% and 22% respectively), compared to their Omani counterparts (14.5% and 18.1% respectively). However, the prevalence rates were very comparable for older men in the age groups of 45-54 and 55-64 years (15.3% and 10.9% respectively in Saudi Arabia, compared to 16.7% and 11.2% respectively in Oman). Therefore, the two countries seem to have different smoking prevalence for young men, but the prevalence tends to be similar in older men. This observation might justify the use of the previous Omani study to extrapolate smoking prevalence in the two oldest age groups in Saudi Arabia. The reported smoking prevalence among women of all age groups in both countries was extremely low, despite some minor differences, and was unlikely to have a significant impact on the results of extrapolation for women.

Table **5.7** summarises the diabetes prevalence data (for 1992), in addition to the four studies on obesity prevalence and the two studies on smoking prevalence in Saudi Arabia, which were used as inputs into the Saudi IMPACT Diabetes Forecast model. These studies also formed a basis for future projections in prevalence of these risk factors, as discussed in the next section.

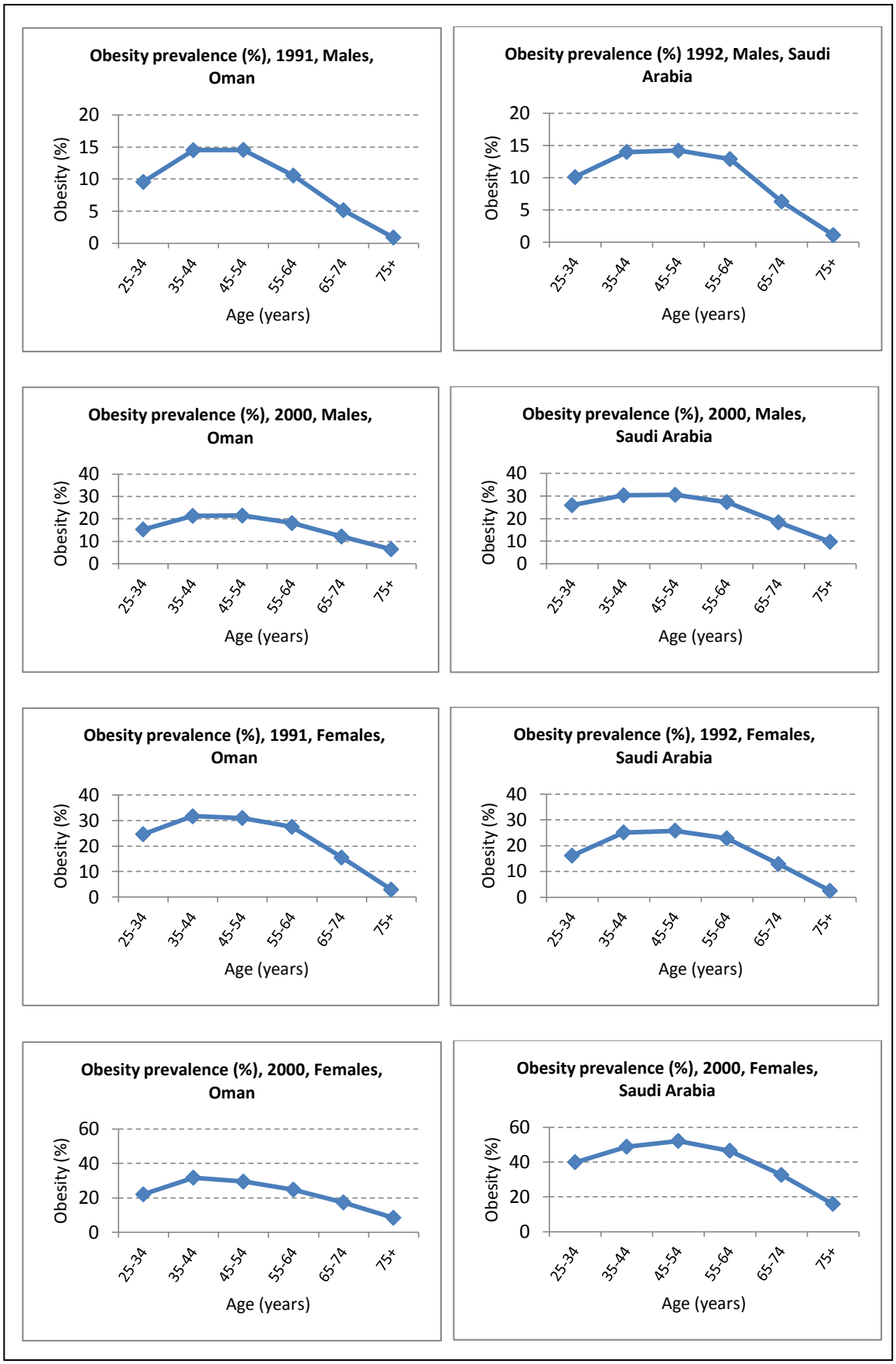


Figure 5.7. Comparison of obesity prevalence (%) between Oman and Saudi Arabia for 1991, 1992 and 2000

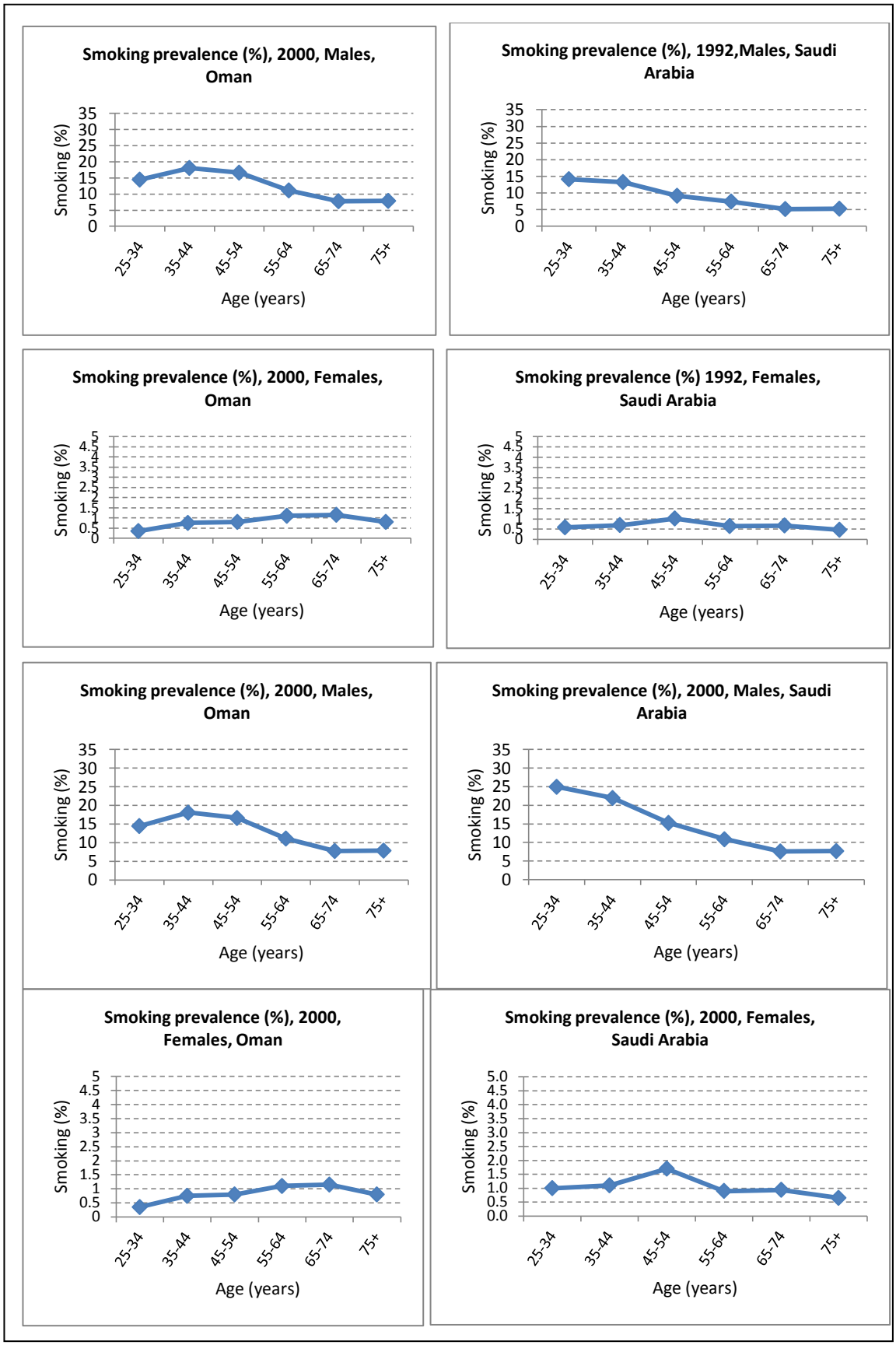


Figure 5.8. Comparison of smoking prevalence (%) between Oman and Saudi Arabia for 2000

Table 5.7. Summary of the results of prevalence studies on diabetes, obesity and smoking (%) in Saudi Arabia after applying assumptions

Year/ period midpoint	Study	Men age groups (years)						Women age groups (years)					
		25-34	35-44	45-54	55-64	65-74	75+	25-34	35-44	45-54	55-64	65-74	75+
Diabetes (Starting year)													
1992	Warsy & El-Hazmi [36]	3.7	7.0	21.1	24.9	28.8	28.8	3.0	5.0	22.1	23.2	24.4	24.4
Obesity													
1992	Al-Nuaim [37] Warsy & El-Hazmi [36]	10.1	14.0	14.2	12.9	6.3	1.1	16.1	25.1	25.8	22.8	12.9	2.5
1997	Al-Nozha et al.[34]	25.2	27.8	29.1	25.0	13.8	6.5	40.2	45.2	48.1	42.5	25.2	10.9
2005	WHO STEPS [19]	27.1	34.5	32.9	31.0	19.8	10.3	39.5	54.7	58.8	53.2	36.8	17.3
Smoking													
1992	Jarallah et al.[39]	14.2	13.3	9.2	7.5	5.2	5.3	0.6	0.7	1.0	0.7	0.7	0.5
2005	WHO STEPS [19]	31.7	27.4	19.2	13.1	7.8	7.9	1.3	1.4	2.2	1.1	0.9	0.7

5.3.2.4. Projections in the obesity and smoking prevalence

For projections in the prevalence of obesity and smoking in men and women aged 25-64 years, a linear trend was assumed by applying the 'observed' annual rate of increase in prevalence during the period 1992-2005. However, for the two oldest age groups (65-74 and 75+ years), the future projections were estimated through applying the annual rate of increase during 1992-2000 for obesity and smoking prevalence.

The annual rate of increase in prevalence was estimated by dividing the net difference in prevalence for each sex and age group during the time period over the duration (number of years) of the same time period. For example, the annual rate of increase during 1992-2005 was calculated as follows:
[prevalence rate in 2005 - prevalence rate in 1992] / 13.

The annual rates of increase for each sex and age group are summarised in Table **5.8**.

Table 5.8. The observed annual rates of increase in prevalence of obesity and smoking (%) for men and women in Saudi Arabia(*)

	Men – age groups (years)						Women – age groups (years)					
	25-34	**35-44**	**45-54**	**55-64**	**65-74**	**75+**	**25-34**	**35-44**	**45-54**	**55-64**	**65-74**	**75+**
Obesity	1.50	1.85	1.72	1.66	1.51	1.09	2.10	2.78	3.05	2.80	2.46	1.68
Smoking	1.35	1.08	0.77	0.43	0.30	0.30	0.05	0.05	0.09	0.03	0.03	0.02

(*) Rates of change in obesity and smoking prevalence for age groups 25-64 years were calculated for the period 1992-2005. Rates of change in obesity prevalence for age groups 65 - ≥75 years were calculated for the period 1991-2000. Rates of change in smoking prevalence for age groups 65 - ≥75 years were calculated for the period 1992-2000.

The decision of applying a linear increasing trend in obesity and smoking prevalence was justified by observing the same linear trend from the available local data during 1992-2005 in almost all age groups of both sexes (Table 5.7). Furthermore, the assumed projections in obesity prevalence were also supported by recent estimates of trends in mean BMI by the WHO Global Burden of Disease Study (GBD), 2011[13], which also showed a linear increasing trend in mean BMI in Saudi Arabia. In the GBD Study, trends and their

uncertainties of mean BMI were estimated for adults aged ≥20 years in 199 countries and territories all over the world for the period 1980-2008. Data were obtained from published and unpublished health examination surveys and epidemiological studies. For Saudi Arabia, studies used[19, 34-36] were similar to those reviewed in this thesis (chapter 3), in addition to two unpublished data from the WHO and one study[253] with subnational sample. For each sex, a complex multi-level Bayesian hierarchical model was used to estimate mean BMI by age, country, and year. The model was based on many sophisticated statistical equations described in detail by the authors.[13] In general, trends over time were modelled as non-linear, consisting of a linear trend plus a smooth non-linear trend, with both components were modelled hierarchically. Time-varying country-level covariates were used to inform the estimates. The covariates used were national income (natural logarithm (Ln) per-head gross domestic product converted to international dollars in 1990), urbanisation (proportion of population that lived in urban areas), and national availability of multiple food types (from the food balance sheets of the Food and Agriculture Organization (FAO) of the United Nations).[13] The results of mean BMI in Saudi Arabia (1980-2008) as estimated by the GBD Study are summarised in Table **5.9**.

Table 5.9. Trends in mean BMI (and uncertainty intervals) in Saudi Arabia (1980-2008) as estimated by the GBD Study[13], 2011

Year	Mean BMI (kg/m^2)	
	Men	Women
1980	25.0 (23.8 - 26.3)	26.3 (24.8 - 27.8)
1990	25.9 (25.6 - 26.2)	27.3 (26.9 - 27.8)
2000	27.0 (26.6 - 27.4)	28.5 (28.0 - 29.0)
2008	27.9 (27.2 - 28.6)	29.6 (28.7 - 30.5)

- Capping of the projected obesity prevalence

The projected obesity prevalence reached very high and probably implausible values with the previously discussed assumption of a linear increase in prevalence over time, based on the observed annual rate of increase. These substantially high prevalence rates were more prominent in women, where the projected prevalence in 2022 reached 87% in women aged 35–44 years, 98% in those aged 45–54 years, and 85% in those aged 55–64 years.

Capping of the projected obesity prevalence at a specific level was performed to overcome this limitation. This assumed capping of prevalence was based on recent data from the United States[254] (published in 2012), which revealed that the total obesity prevalence (BMI ≥30 kg/m^2) in the US adult men and women for 2009-2010 did not differ significantly from that of 2003–2008. This 'stability' or 'slowing / levelling off' of obesity prevalence in the US was reported after the observed linear increase in the previous years. All the past and current data on obesity prevalence were obtained from one source of information, which is the National Health and Nutrition Survey (NHANES). The NHANES started in 1960, covering nationally-representative samples, and continued to release data in two-year cycles since 1999.

Moreover, several other countries also reported the same slowing / levelling off in the previous obesity trends. The National Obesity Observatory[255] (NOO) in the UK (www.noo.org.uk) has published data on trends in the prevalence of adult obesity (BMI ≥30 kg/m^2) during 1995–2009 from many developed countries around the world. Unfortunately, many of these countries have missing prevalence data for most years within that period. However, countries with the most complete data have also suggested a possible degree of levelling off of obesity prevalence during the last 10–13 years. Examples of such countries include England, Italy and Sweden (Table **5.10**).

Table 5.10. Some international data on adult obesity prevalence trends (%)[255]

	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
England	16.0	17.0	18.0	19.0	20.0	21.0	22.0	23.0	23.0	23.0	23.0	24.0	24.0	24.5	23.0
Italy	–	–	–	–	8.8	8.6	8.5	8.5	9.0	–	9.9	10.2	9.9	9.9	–
Sweden	–	–	7.9	8.1	8.1	9.2	9.2	10.2	9.7	9.8	10.7	9.6	10.2	–	–

In addition, Rokholm et al.[256] have recently reviewed 52 studies on obesity prevalence (BMI ≥30 kg/m^2) trends from different countries around the world. They found that the global obesity epidemic has generally showed levelling off since the early 2000s. The studies reviewed were from different countries in Europe, North America and Asia. The regional difference in obesity prevalence trends was not confirmed by the review, although some countries, particularly Asian (e.g. Iran and Bangladesh), remained to show increasing trends in prevalence. However, there were concerns regarding the low quality of studies from these countries.[256] Furthermore, stability and signs of a decrease in obesity prevalence were found in some other countries of the region (e.g. Hong Kong, China). Thus, the authors concluded that the levelling off seems fairly homogeneous across the world regions. Nevertheless, this review was constrained by some limitations. For instance, it did not include studies from some world regions (e.g. Africa, Middle East and South America). In addition, concerns about the representativeness of samples used in studies and the potential publication biases might have affected the findings.

In general, the causes of such levelling off of the global obesity prevalence trends in recent years are not completely clear, and are likely to have complex roots, in spite of some attempts to attribute these changes to certain environmental and socioeconomic factors.[254] Of course, the accelerated global modernisation, urbanisation and adopting 'western' lifestyles, with decreased physical activity and consuming energy dense foods, remains the first

suggested cause for the worldwide epidemic of obesity. Thus, based on assuming this as a cause, the levelling off could be the result of public health campaigns, which may have been able to stabilise the population's energy balance by influencing food and exercise habits.[256] However, this inference cannot be confirmed, since there is no available evidence for the effectiveness of the public health campaigns in many developing countries that have already been observed to witness levelling off of obesity prevalence trends. In addition, as previously discussed in chapter 2, the aetiology of obesity is complex and associated with several other demographic, genetic and socioeconomic factors. Therefore, Rokholm et al. indicated that the currently observed changes in the obesity trends can provide an opportunity for further investigations into the causes of the obesity epidemic. If the pattern of exposure to a putative cause over time corresponds to the change in obesity trend, the factor would qualify for further analysis. However, a sufficient time lag between exposure to a putative cause and changes in the obesity trends may be important to be considered.[256]

The decision to perform capping of the projected obesity prevalence in Saudi Arabia for this thesis could be justified primarily by two reasons. First is to avoid the probable implausibility of reaching a point when every individual in some age groups of the Saudi population becomes 'obese' as a result of assuming a continuing linearity in trends over time. Second, the previously mentioned literature seems supportive to this decision, although there was no specific evidence from Saudi Arabia or Middle East, but, at least, some other developing countries in Asia have been observed to witness levelling off of obesity trends during the last years.[256] However, it is important to indicate that sensitivity analyses, which were performed for modelling in this thesis (as presented in chapters 6, 7 and 8), provided uncertainty values for the output results. Moreover, the main model outputs were compared with and without capping, so that the effect of capping on the predicted prevalence of diabetes could be quantified.

An important consideration in the decision of capping was the level of obesity prevalence at which the capping should be performed. The available evidence, as reviewed by Rokholm et al.[256], showed that the global levelling off of obesity trends was fairly homogeneous for men and women, in spite of the differences

in the sex-specific ‘values’ of prevalence at which the levelling off occurred. Furthermore, the recently observed levelling off does not imply that an absolute biological limit / threshold has been reached in various populations around the world. For example, the latest observed levelling off values in the UK[255] (≈ 21-24%) and the US[254] (≈ 30-40%) have been already well surpassed in Saudi Arabia.

Therefore, the assumption used in this thesis was to cap the projected obesity trends at the highest ‘observed’ value in any age group for each sex separately. The trend was fixed from that cap point on, for that sex-age group. Then, the other age groups were allowed to reach the cap point for the sex, and when the cap value is reached, the trend was also fixed from that point onwards. As shown in Table **5.11**, the highest observed value for obesity prevalence in men was 34.5% in those aged 35-44 years. On the other hand, the highest observed value in women was 58.8% in the age group 45-54 years. So, the capping point was assumed to be **35%** in men and **60%** in women.

Prevalence rates of obesity in Saudi Arabia from 1992-2022, after applying all the previously discussed assumptions, are summarised in Table **5.11**, while those of smoking are summarised in Table **5.12**.

Table 5.11. Data input into the Saudi IMPACT model: Prevalence rates of obesity (%) in Saudi Arabia, 1992-2022 (*)

Year	Men- age groups (years)						Women- age groups (years)					
	25-34	35-44	45-54	55-64	65-74	75+	25-34	35-44	45-54	55-64	65-74	75+
1992	10.06	14.00	14.18	12.94	6.30	1.10	16.13	25.05	25.81	22.77	12.85	2.45
1993	13.08	16.76	17.16	15.35	7.81	2.19	20.94	29.08	30.26	26.71	15.31	4.13
1994	16.11	19.52	20.15	17.76	9.31	3.27	25.76	33.11	34.72	30.66	17.78	5.82
1995	19.14	22.28	23.13	20.17	10.82	4.36	30.57	37.14	39.18	34.61	20.24	7.50
1996	22.17	25.04	26.12	22.59	12.33	5.44	35.39	41.17	43.64	38.55	22.71	9.18
1997	25.20	27.80	29.10	25.00	13.83	6.53	40.20	45.20	48.10	42.50	25.17	10.86
1998	25.44	28.64	29.58	25.75	15.34	7.61	40.11	46.39	49.44	43.84	27.63	12.55
1999	25.68	29.48	30.05	26.50	16.84	8.70	40.03	47.58	50.78	45.18	30.10	14.23
2000	25.91	30.31	30.53	27.25	18.35	9.78	39.94	48.76	52.11	46.51	32.56	15.91
2001	26.15	31.15	31.00	28.00	18.63	9.89	39.85	49.95	53.45	47.85	33.36	16.18
2002	26.39	31.99	31.48	28.75	18.91	9.99	39.76	51.14	54.79	49.19	34.18	16.45
2003	26.63	32.83	31.95	29.50	19.19	10.10	39.68	52.33	56.13	50.53	35.03	16.73
2004	26.86	33.66	32.43	30.25	19.48	10.21	39.59	53.51	57.46	51.86	35.89	17.01
2005	27.10	34.50	32.90	31.00	19.77	10.32	39.50	54.70	58.80	53.20	36.77	17.29
2006	27.51	**35.14**	33.47	31.51	20.07	10.43	40.33	56.22	**60.59**	54.69	37.68	17.59
2007	27.92	**35.79**	34.04	32.04	20.37	10.55	41.18	57.78	**62.44**	56.22	38.61	17.88
2008	28.34	**36.45**	34.63	32.57	20.68	10.66	42.05	59.38	**64.34**	57.79	39.56	18.18
2009	28.76	**37.13**	**35.22**	33.11	20.99	10.78	42.93	**61.03**	**66.30**	59.41	40.53	18.49
2010	29.19	**37.82**	**35.83**	33.65	21.31	10.89	43.83	**62.73**	**68.32**	**61.07**	41.53	18.80
2011	29.63	**38.52**	**36.44**	34.21	21.63	11.01	44.76	**64.47**	**70.40**	**62.78**	42.56	19.12
2012	30.08	**39.23**	**37.07**	34.78	21.96	11.13	45.70	**66.26**	**72.54**	**64.53**	43.60	19.44
2013	30.53	**39.96**	**37.71**	**35.35**	22.29	11.25	46.66	**68.10**	**74.75**	**66.34**	44.68	19.76
2014	30.98	**40.70**	**38.36**	**35.94**	22.62	11.38	47.64	**69.99**	**77.03**	**68.20**	45.78	20.10
2015	31.45	**41.46**	**39.01**	**36.53**	22.96	11.50	48.64	**71.94**	**79.37**	**70.10**	46.91	20.43
2016	31.92	**42.23**	**39.69**	**37.14**	23.31	11.62	49.67	**73.93**	**81.79**	**72.07**	48.06	20.78
2017	32.40	**43.01**	**40.37**	**37.75**	23.66	11.75	50.71	**75.99**	**84.28**	**74.08**	49.25	21.13
2018	32.88	**43.81**	**41.06**	**38.38**	24.02	11.88	51.78	**78.10**	**86.85**	**76.15**	50.46	21.48
2019	33.38	**44.62**	**41.77**	**39.02**	24.38	12.01	52.87	**80.26**	**89.49**	**78.29**	51.70	21.84
2020	33.88	**45.44**	**42.49**	**39.66**	24.75	12.14	53.98	**82.49**	**92.22**	**80.48**	52.98	22.21
2021	34.39	**46.29**	**43.22**	**40.32**	25.12	12.27	55.12	**84.78**	**95.02**	**82.73**	54.28	22.59
2022	34.90	**47.14**	**43.96**	**40.99**	25.50	12.40	56.27	**87.14**	**97.92**	**85.04**	55.62	22.97

(*) prevalence rates in bold were capped at 35% in men and 60% in women

Table 5.12. Data input into the Saudi IMPACT model: Prevalence rates of smoking (%) in Saudi Arabia, 1992-2022 (*)

Year	Men- age groups (years)						Women- age groups (years)					
	25-34	35-44	45-54	55-64	65-74	75+	25-34	35-44	45-54	55-64	65-74	75+
1992	14.16	13.30	9.18	7.45	5.20	5.30	0.59	0.70	1.02	0.65	0.68	0.47
1993	15.51	14.38	9.95	7.88	5.50	5.60	0.64	0.75	1.11	0.68	0.71	0.49
1994	16.86	15.47	10.72	8.32	5.81	5.91	0.70	0.81	1.20	0.72	0.75	0.52
1995	18.21	16.55	11.49	8.75	6.11	6.21	0.75	0.86	1.29	0.75	0.78	0.54
1996	19.56	17.64	12.26	9.19	6.42	6.52	0.81	0.92	1.38	0.79	0.81	0.56
1997	20.91	18.72	13.03	9.62	6.72	6.82	0.86	0.97	1.47	0.82	0.84	0.58
1998	22.26	19.81	13.80	10.06	7.02	7.12	0.92	1.02	1.56	0.86	0.88	0.61
1999	23.60	20.89	14.58	10.49	7.33	7.43	0.97	1.08	1.66	0.89	0.91	0.63
2000	24.95	21.98	15.35	10.93	7.63	7.73	1.03	1.13	1.75	0.93	0.94	0.65
2001	26.30	23.06	16.12	11.36	7.65	7.75	1.08	1.18	1.84	0.96	0.94	0.65
2002	27.65	24.15	16.89	11.80	7.68	7.78	1.14	1.24	1.93	1.00	0.94	0.65
2003	29.00	25.23	17.66	12.23	7.70	7.80	1.19	1.29	2.02	1.03	0.94	0.65
2004	30.35	26.32	18.43	12.67	7.72	7.82	1.25	1.35	2.11	1.07	0.94	0.65
2005	31.70	27.40	19.20	13.10	7.75	7.85	1.30	1.40	2.20	1.10	0.94	0.65
2006	32.13	27.70	19.35	13.16	7.77	7.87	1.30	1.40	2.20	1.10	0.94	0.65
2007	32.56	28.00	19.50	13.21	7.79	7.90	1.30	1.40	2.20	1.10	0.94	0.65
2008	33.00	28.30	19.65	13.27	7.82	7.92	1.30	1.40	2.21	1.10	0.94	0.65
2009	33.45	28.61	19.80	13.33	7.84	7.94	1.30	1.40	2.21	1.10	0.94	0.65
2010	33.90	28.92	19.95	13.39	7.86	7.97	1.30	1.40	2.21	1.10	0.94	0.65
2011	34.35	29.23	20.11	13.45	7.89	7.99	1.30	1.40	2.21	1.10	0.94	0.65
2012	34.82	29.55	20.26	13.50	7.91	8.02	1.30	1.41	2.21	1.10	0.94	0.65
2013	35.29	29.87	20.42	13.56	7.94	8.04	1.31	1.41	2.22	1.10	0.94	0.65
2014	35.76	30.19	20.57	13.62	7.96	8.07	1.31	1.41	2.22	1.10	0.94	0.65
2015	36.25	30.52	20.73	13.68	7.99	8.09	1.31	1.41	2.22	1.10	0.94	0.65
2016	36.74	30.85	20.89	13.74	8.01	8.11	1.31	1.41	2.22	1.10	0.94	0.65
2017	37.23	31.19	21.05	13.80	8.03	8.14	1.31	1.41	2.22	1.10	0.95	0.65
2018	37.73	31.53	21.22	13.86	8.06	8.16	1.31	1.41	2.23	1.10	0.95	0.65
2019	38.24	31.87	21.38	13.92	8.08	8.19	1.31	1.41	2.23	1.11	0.95	0.65
2020	38.76	32.21	21.54	13.98	8.11	8.21	1.31	1.41	2.23	1.11	0.95	0.65
2021	39.28	32.56	21.71	14.04	8.13	8.24	1.31	1.41	2.23	1.11	0.95	0.65
2022	39.81	32.92	21.88	14.10	8.16	8.26	1.31	1.41	2.23	1.11	0.95	0.65

5.3.2.5. The transition parameters (diabetes incidence, case fatality, and total mortality)

A. Introduction

The Saudi IMPACT Diabetes Forecast Model used the incidence of T2DM, case fatality, and total mortality as crucial data inputs for the modelled Saudi population to inform the transitions between the different health states. Nevertheless, reliable data on these three parameters from Saudi Arabia were not available. In fact, such data (particularly incidence of T2DM) are also not available for most countries all over the world. This lack of incidence estimates globally is attributed to the difficulty in describing the epidemiology and natural history of T2DM.[157] The disease is well known for its gradual and asymptomatic onset. A large proportion of patients hardly experience any symptom of T2DM in the early stages of disease and may remain asymptomatic with an 'occult' disease for years. As a result of this complicated case definition and a high prevalence of undiagnosed cases, the global estimates of T2DM incidence and prevalence are highly variable. These estimates are often dependent on factors other than the true occurrence of disease (e.g. patient awareness and level of case finding).[157] Most available studies on incidence of diabetes in some countries are too small to yield reliable estimates, because it is difficult and expensive to conduct large studies with adequate follow-up durations.[157]

Moreover, the observed mortality due to T2DM (diabetes-related mortality) is mostly unavailable, or is presumed to be underestimated. This is because that mortality estimates of T2DM are mostly obtained from death certificates, which are mostly based on the concept of a single 'underlying' cause of death. However, in case of T2DM, death may occur as a result of several associated complications, such as cardiovascular disease and/or chronic renal failure, which are often recorded as the underlying cause of death.[157]

Therefore, in this thesis, a previously validated method was used in order to estimate such vital modelling parameters for the Saudi population. This method was that proposed by Barendregt et al. to estimate diabetes incidence in Netherlands.[157] The method is used to obtain age- and sex-specific estimate of T2DM incidence that is consistent with previously estimated prevalence and

mortality. It combines both a prevalence estimate and a mortality estimate in an incidence-prevalence-mortality (IPM) model, known as DISMOD, in order to obtain an estimate of diabetes incidence.

IPM models of disease processes are mainly used to overcome limitations of empirical observed data of some diseases, including T2DM. Of course, empirical observed data are the gold standard for obtaining epidemiological information, but such data are often incomplete or of dubious validity.[257] Moreover, the validity of observed estimates tends to vary even for an individual disease. For example, in instances where incidence is more difficult to observe than mortality, more incident cases than deaths are likely to be missed. Consequently, incidence data will be less complete than those on mortality, making these two parameters internally inconsistent.[257] IPM models exploit the causal structure of a disease process (i.e. incidence has to precede prevalence, and cause-specific mortality can only follow being diseased). In other words, any prevalent case must have become incident at some younger age, and any person dead with a disease must have been an incident case previously and have been prevalent. This causal structure is then incorporated into a mathematical model (DISMOD) in order to estimate data that are missing from an observational set. Eventually, jointly estimated incidence, prevalence, and mortality rates, using a causal model, are therefore internally consistent.[157, 257, 258]

The following sections discuss in detail the DISMOD model, which was used in this thesis to estimate the incidence of T2DM, case fatality, and total mortality in Saudi Arabia; its conceptual basis, data inputs, outputs, advantages and limitations.

B. DISMOD

(i) Conceptual basis, data inputs and outputs

DISMOD (stands for DISease MODelling) is a multistate generic mathematical disease model, implemented in software, which is made available to the public domain by the WHO: (http://www.who.int/healthinfo/global_burden_disease/tools_software/en/).

DISMOD was used extensively by the WHO for the Global Burden of Disease (GBD) Study since 1990, and also by many other subsequent country studies in the world. It was designed to measure the causes and patterns of disease in populations with only partial and insufficient data, through supplementing the data by exploiting the causal relations between the various variables that describe a disease process.[157, 257, 258] These 'logical' relations can be expressed as a formal model of a generic disease process. Such a formal disease model allows estimation of an internally consistent description of disease epidemiology from partial data.

DISMOD is based on the common conceptual disease model in figure 5.9. It is a continuous time Markov process (discussed in chapter 4), which describes the population as being in different states, while transition hazards determine how people move from one state to another. It follows an initially disease-free cohort over time and applies the transition hazards.[157, 258] Population is partitioned into two independent (discrete) main states: susceptibles and cases. Cases may die from their disease, while both cases and susceptibles are at risk of dying from all other causes. Therefore, there are four main transition hazards between states: incidence, case-fatality, all-other-causes mortality and remission.[257] However, mortality from all other causes poses a problem, as it is an input to the model, but often is not known. It can be estimated from the total mortality and the diabetes-specific mortality, but, again, the latter is mostly not known. Hence, DISMOD assumes that hazards are not affected by the presence or absence of other hazards that act on the same population.[258] Based on this assumption, the mortality from all other causes is assumed to be independent of diabetes (i.e. it is the same for both diabetic and non-diabetic individuals in the population). This implies that incidence, case fatality and remission are not affected by value of mortality from all other causes. So, DISMOD set the value of mortality from all other causes to 'zero', leaving it out of the model's equations, and estimates the disease incidence and other rates.[258]

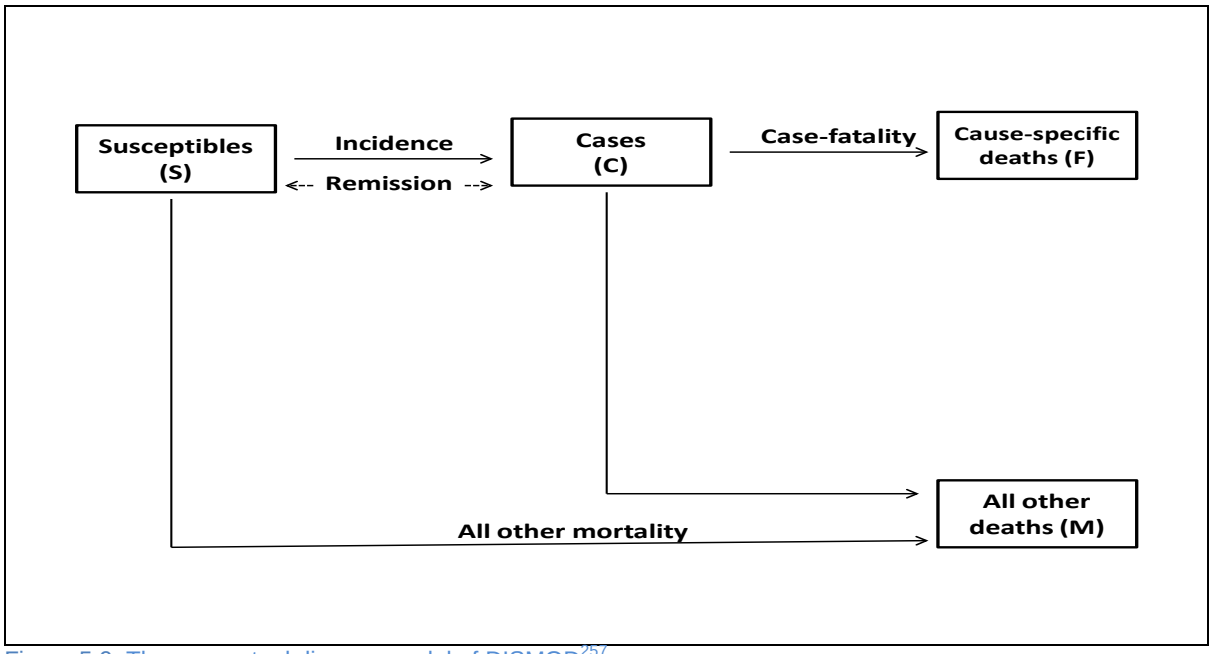


Figure 5.9. The conceptual disease model of DISMOD[257]

By assuming independence of the mortality from all other causes, the diabetes-related mortality in DISMOD stands for all excess mortality caused by diabetes (which includes deaths due to diabetes-related conditions/ complications, such as cardiovascular disease).[258] Since valid estimates on diabetes-related mortality are not available from most countries in the world, including Saudi Arabia, an alternative method to estimate it was proposed for DISMOD by Baan et al.[259] In brief, the method was developed in order to provide an 'adjusted' relative risk estimate of *mortality in diabetics as compared to the* ***general population.*** This relative risk estimate (in this section, is abbreviated as $\mathbf{RR_{adj}}$) is an equivalent to the all excess mortality caused by diabetes. The method estimates the RR_{adj} by using a commonly available parameter of diabetes (i.e. prevalence) in addition to the 'typical' relative mortality risk for diabetes (in this section, is abbreviated as **RR**), which is equal to: *(Total mortality rate for diabetics / Total mortality rate for* ***non-diabetics****)*.

Because the RR_{adj} (which is equivalent to diabetes-related mortality rate) includes all excess mortality for diabetics, it is therefore independent from all other mortality. So, it can be used (unlike the specific mortality restricted to diabetes) in an IPM model that assumes independence from the non-diabetes-related mortality.[157] The proposed formula of the Baan et al. method is:

$$\mathrm{RRadj} = \frac{RR}{pRR+(1-p)} \qquad (1)$$

Where p is the prevalence of diabetes.

The age- and sex-specific prevalence of diabetes in Saudi Arabia (for the starting year of modelling; 1992) is available (Table **5.7**), and the RR can be obtained from literature. Baan et al.[259] reviewed 12 studies that reported age- and sex-specific relative mortality risks for diabetes (RRs) in different countries. In general, they compared these studies and found that the reported RRs were similar in spite of differences between these studies in design, population and time. In order to estimate the incidence of diabetes in the Netherlands, Baan et al. used RRs from the Verona Diabetes Study[260] (population-based) from Italy, which used the 'non-diabetic' population as the reference population.

Briefly, the Verona Diabetes Study[260] aimed to determine the prevalence of known diabetes mellitus on the 31st December 1986, and to assess all-cause mortality in the subsequent 5 years (1987-1991) in Verona, a mid-size town of the north-east Italy. A total of 5996 diabetic patients were identified (overall prevalence 2.61%) mainly from Family Physicians in Verona. Mortality was assessed by matching all death certificates of Verona in 1987-1991 with the diabetic cohort. The total 'observed' deaths in the diabetic cohort by the 31st December 1991 (1260 patients) were compared with the 'expected' deaths at the same time point (863 individuals), using as a reference the non-diabetic population of Verona. This reference population was obtained from the Social Health Unit (SHU) of Verona, which is part of the National Health System. In Italy, all Family Physicians in a particular area follow the SHU of the same area, and each citizen is assigned by law to one Family Physician. Thus, the records of the Family Physicians were most likely complete for the population in Verona. By comparing the "observed / expected" mortalities, an overall standardised mortality ratio (SMR) of 1.46 (95% CI: 1.38–1.54) was obtained. SMRs were also calculated for each age group and sex of the study population.[260]

Using the age- and sex-specific SMRs from the Verona Diabetes Study,[260] the relative risk for diabetes mortality (RR_{adj}) was estimated for the Saudi population in 1992 (Table **5.13**), through the Baan et al. formula[259] described above. The decision to use RRs from the Verona Diabetes Study for this thesis was based on a previous effective use of such RRs for countries in the same region of Saudi Arabia. These RRs were used for the same purpose in the

MEDCHAMPS project, for the four participating countries from the EMR; namely Turkey, Syria, Palestine and Tunisia. The RR_{adj} was calculated specifically for the population of each of these countries, using the RRs from the Verona Diabetes Study, and the results of all models from these countries were good when validated against observed data (*personal communication, Martin O'Flaherty, 2012*). However, extensive sensitivity analyses were performed in order to assess the potential effects of uncertainty in diabetes incidence, case fatality and total mortality (that were estimated using these RRs) on the model outputs.

Table 5.13. The estimated RR_{adj} for the Saudi population

Age group (years)	Sex	RR from Verona Study[260]	Diabetes Prevalence in Saudi Arabia[36]	RR_{adj} for Saudi population
25-34	men	2.33	3.70%	2.22
	women	3.43	3.01%	3.20
35-44	men	2.33	7.01%	2.13
	women	3.43	5.03%	3.06
45-54	men	2.33	21.06%	1.82
	women	3.43	22.09%	2.23
55-64	men	2.13	24.91%	1.66
	women	2.33	23.23%	1.78
65-74	men	1.5	28.75%	1.31
	women	2.27	24.37%	1.73
75+	men	1.13	28.75%	1.09
	women	1.32	24.37%	1.22

DISMOD needs a minimum of three input variables in order to estimate the epidemiological parameters of a disease. In this thesis, the available variables for Saudi Arabia were prevalence of T2DM for 1992 (derived from the study of Warsy and El-Hazmi[36]), remission and RR_{adj}. Remission of T2DM was assumed to be zero, though some evidence has emerged showing that 'resolution' of diabetes was reported after bariatric surgeries.[261] In this thesis, however, it was assumed that the remission rate is not likely to affect the incidence estimates substantially.

In addition to the previous three disease input variables, DISMOD needs total mortality rates and population structure for the population under study. For

Saudi Arabia, population structure for 1992 was available from a national census, as discussed in section 5.3.2.1. Local data on the sex- and age-specific total mortality rates were not available from Saudi Arabia. Thus, such data (for 1992) were obtained from the life tables of the WHO Global Health Observatory (GHO) Data Repository (http://apps.who.int/ghodata/).[262] All input variables into DISMOD are by age, and the estimations are performed separately for men and women.[258] After providing data inputs, DISMOD runs its calculations based on a set of differential equations that describe the disease process. These equations were described in detail by Barendregt et al.[258] DISMOD provides different outputs (disease parameters), that are 'internally-consistent' for the modelled population, based on the inputs provided.

As indicated, all the input variables of the Saudi population were specific to the starting year of modelling (1992). DISMOD, as an IPM model, assumes that a modelled population is in 'equilibrium' or a 'steady state', i.e. there are no trends in the disease transition parameters (incidence, case fatality and total mortality), and these parameters remain constant over time. So, an important assumption used in the Saudi IMPACT Diabetes Forecast Model was that diabetes incidence and other parameters obtained from DISMOD were 'stable' for the Saudi population during the modelling period (1992-2022). However, sensitivity analysis could deal with uncertainties in the model results that might originate from this assumption.

The DISMOD outputs (parameters) used in the Saudi IMPACT Diabetes Forecast Model are incidence of diabetes, case fatality rate for diabetes, and total mortality for the Saudi population with and without diabetes. Table **5.14** summarises the data inputs into DISMOD and the outputs used for modelling.

Table 5.14. Summary of the data inputs and outputs of DISMOD

Men

	Data inputs			Data outputs		
Age groups (years)	Prevalence rate (%)	Remission rate (%)	RR_{adj}	Incidence rate (per 1000 population)	Case fatality rate (%)	Total mortality rate (per 1000 population)
25-34	3.70	0	2.22	12.90	0.15	0.10
35-44	7.01	0	2.13	17.70	0.39	0.50
45-54	21.06	0	1.82	18.90	0.67	1.10
55-64	24.91	0	1.66	20.70	1.20	2.50
65-74	28.75	0	1.31	22.40	1.35	3.30
75+	28.75	0	1.09	26.70	2.10	6.10

Women

	Data inputs			Data outputs		
Age groups (years)	Prevalence rate (%)	Remission rate (%)	RR_{adj}	Incidence rate (per 1000 population)	Case fatality rate (%)	Total mortality rate (per 1000 population)
25-34	3.01	0	3.20	12.90	0.16	0.10
35-44	5.03	0	3.06	15.00	0.43	0.50
45-54	22.09	0	2.23	15.90	0.62	1.00
55-64	23.23	0	1.78	16.70	0.96	1.80
65-74	24.37	0	1.73	19.70	1.90	4.10
75+	24.37	0	1.22	30.70	4.62	11.60

(ii) The DISMOD computational basis for the outputs

The total mortality for people with and without diabetes is estimated by DISMOD from the 'observed' average population total mortality, the relative risk of mortality for diabetics (RR_{adj}) and diabetes prevalence using the following equations:[157]

$m = pm^1 + (1 - p)m^0$ (2) and

$m^1 = m^0 RR$ (3)

By substituting equation 3 in equation 2, the mortality of the non-diabetics will be as follows:

$$m^0 = \frac{m}{pRR+1-p} \quad (4)$$

Thus, the diabetes-related mortality rate (m^0) in a population with a diabetes prevalence of p will be calculated as follows:

$m^d = pm^0$ (RR – 1) = $\frac{p(RR-1)m}{pRR+1-p}$ (5) - *(This is the same as the population attributable risk times total mortality)*.

Where *p* = prevalence of diabetes; *RR* = relative risk on total mortality, given exposure to diabetes; *m* = average total mortality rate; m^0 = total mortality rate of non-diabetics; m^1 = total mortality rate of diabetics; m^d = diabetes-related mortality rate of the mixed population.

Given this mortality rate in the population and the prevalence of diabetes, the incidence at age "*a"* can be written as a function of prevalence at "*a"* and "*a+1"*, and mortality at "*a"*, as follows:

$$i_a = \frac{p_{a+1}\,(1- m_a^d) - p_a + m_a^d}{1- p_a} \qquad (6)$$

This method produces a "population incidence", i.e. for both exposed and unexposed people to the risk factors under study in this thesis (obesity and smoking). However, the Saudi IMPACT Diabetes Forecast Model needs incidence in the unexposed population to inform the transition between the (healthy) and (diabetes) states.

The incidence of a disease in a population is a weighted sum of the incidence among the exposed and the incidence among the unexposed to a risk factor,[263] as follows:

$$i_p = i_e \times p + i_u \times (1 - p) \qquad (7)$$

Where i_p is the population incidence, i_e is the incidence amongst the exposed, i_u is the incidence amongst the unexposed and *p* is risk factor prevalence.

The incidence in the exposed is equal to the incidence in the unexposed times the RR, as follows:

$$i_e = RR \times i_u \qquad (8)$$

Replacing equation 8 in equation 7:

$$i_p = RR \times i_u \times p + i_u \times (1 - p) \qquad (9)$$

Therefore, I_u can be calculated as follows:

$$i_u = \frac{i_p}{(p \times RR - p) + 1} \qquad (10)$$

Table **5.15** summarises the age- and sex- specific incidence rates (I_u), that were calculated through equation 10 and used in the Saudi IMPACT Diabetes Forecast Model.

Table 5.15. Age- and sex-specific incidence rates *(I_u)* used in the Saudi IMPACT Diabetes Forecast Model

Age groups (years)	Diabetes incidence rate	
	Men	Women
25-34	0.0082	0.0045
35-44	0.0098	0.0039
45-54	0.0105	0.0040
55-64	0.0119	0.0046
65-74	0.0165	0.0080
75+	0.0251	0.0240

(iii) Advantages and limitations of DISMOD

As previously discussed, DISMOD was specifically designed for situations with insufficient data on a disease epidemiology, in order to supplement the partial data by exploiting the causal relations between the various variables that describe a disease process.[257] It is based on a 'logical' mathematical description of a disease process and natural history, and it produces 'internally-consistent' parameters of the disease epidemiology in the modelled population. DISMOD was validated by comparing its results for some types of cancers in Netherlands against both the 'observed' data and an 'artificial/ hypothetical' dataset that was internally consistent. This validation resulted in practically reproducible results of the two datasets.[257] In addition, as mentioned earlier, DISMOD has been used by the WHO for the GBD Study since 1990, and also for many country-specific studies around the world. It is embedded in free software, which is accessible through the WHO website:
(http://www.who.int/healthinfo/global_burden_disease/tools_software/en/).

On the other hand, DISMOD has some limitations. As mentioned earlier, one of the important limitations of DISMOD is the assumption of a 'steady' modelled population with constant trends of transition hazards over time. Therefore, occurrence of trends in incidence, for example, might lead to discrepancies between the estimates of diabetes prevalence in the Saudi IMPACT Diabetes

Forecast Model and the actual prevalence. In other words, if the true incidence of T2DM has increased in Saudi Arabia since 1992, then the model projections of the disease prevalence would most likely be underestimated. However, as discussed above, the sensitivity analysis provides different results based on different values of incidence and mortality, and, hence, deals with the potential uncertainties around such parameters. A second limitation of DISMOD is the assumption of a "zero" value of the excess mortality from other diseases. Although this assumption is convenient, it might not be appropriate in the case of diabetes. Diabetic individuals also suffer from an increased risk of dying from diseases other than diabetes (e.g. cardiovascular disease). Therefore, as discussed earlier, the developers of DISMOD constructed a diabetes-related mortality rate (RR_{adj}), which is assumed to include all excess mortality for diabetics, and is independent from all other mortality.

5.3.2.6. The transition parameters (Relative risks of diabetes in obese and in smokers)

The (diabetes incidence X RR of developing diabetes if 'obese') was used to inform the transition of individuals from the model's (obese) state to the (diabetes) state. Similarly, the (diabetes incidence X RR of developing diabetes if a smoker) was used to inform the transition from (smoker) state to (diabetes) state. As expected, these RRs were not available from Saudi Arabia as well as most developing countries. Therefore, such RRs were derived from literature.

There are several prospective studies that have assessed the association between obesity and incidence of T2DM[97] and between smoking and incidence of T2DM.[130] These studies were carried out in different countries/ populations (mostly developed countries), and provided incidence/ RR estimates of developing diabetes in 'obese' individuals and in smokers. However, there are two relatively recent systematic reviews[97, 130] that synthesized the results of multiple original studies and conducted meta-analyses to estimate pooled RRs. These two systematic reviews/ meta-analyses have been discussed previously in chapter 2. The pooled RRs estimated by such reviews were used in the Saudi IMPACT Diabetes Forecast Model as transition parameters, as shown in Table **5.16**.

Table 5.16. Relative risk estimates used to inform transitions in the Saudi IMPACT Diabetes Forecast Model

	Result		Used in the model to inform transition		Reference
	Men	*Women*	*from*	*to*	
RR of having diabetes if obese (BMI ≥ 30 kg/m^2)	6.74	12.41	'obese' state	'diabetes' state	Guh et al.[97]
RR of having diabetes if smoker	1.44	1.44	'smokers' state	'diabetes' state	Willi et al.[130]

It is important to note that the pooled RRs estimated by Guh et al.[97] were reported only as sex-specific (no age-specific RRs). So, these RRs were used for all age groups of each sex. In addition, Willi et al.[130] reported only one adjusted pooled RR for both men and women (no sex- or age-specific RRs). Therefore, the reported RR was assumed to apply equally for men and for women of all age groups. Furthermore, the reported diabetes RRs for obese and for smokers were assumed to be constant over the whole modelling period (1992-2022).

5.3.2.7. Setting up the transition probabilities in the Saudi IMPACT Diabetes Forecast Model

The transition hazards estimated by DISMOD (incidence, case fatality, and total mortality) were all expressed as rates. It has been discussed in chapter 4 that Markov models use transition probabilities (TPs), rather than rates, to describe the transitions between the health states in the model. While rates can take values from zero to infinity and are expressed per unit time, probabilities range from zero to one and have time built into them implicitly.[217] To convert rates into probabilities, the following formula is generally used:

$$P[t] = 1 - e^{-rt} \qquad (11)$$

Where P is transition probability; t is time units; and r is rate. However, this formula produces probabilities of transition between states. The probability of staying in the same state in a given cycle will typically be equal to 1 minus the probability of leaving that particular state, because the probability of moving to states in each cycle must sum to 1 (since individuals must be in one and only

one state at any given time).[216, 217] Table **5.17** summarises the results of converting the output rates of DISMOD to TPs.

Table 5.17. Results of converting the values of transition hazards from rates to transition probabilities

Age group (years)	Incidence		Case fatality		Total mortality	
	Rate	Transition probability	Rate	Transition probability	Rate	Transition probability
Men						
25 – 34	0.0082	0.0082	0.0015	0.0015	0.0001	0.0001
35 – 44	0.0098	0.0098	0.0039	0.0039	0.0005	0.0005
45 – 54	0.0105	0.0104	0.0067	0.0067	0.0011	0.0011
55 – 64	0.0119	0.0118	0.0120	0.0119	0.0025	0.0025
65 – 74	0.0165	0.0163	0.0135	0.0134	0.0033	0.0033
75+	0.0251	0.0248	0.0210	0.0208	0.0061	0.0061
Women						
25 – 34	0.0045	0.0045	0.0016	0.0016	0.0001	0.0001
35 – 44	0.0039	0.0039	0.0043	0.0043	0.0005	0.0005
45 – 54	0.0040	0.0040	0.0062	0.0062	0.0010	0.0010
55 – 64	0.0046	0.0046	0.0096	0.0096	0.0018	0.0018
65 – 74	0.0080	0.0080	0.0190	0.0188	0.0041	0.0041
75+	0.0240	0.0237	0.0462	0.0451	0.0116	0.0115

In the Saudi IMPACT Diabetes Forecast Model, as illustrated previously in Figure **5.1**, there are six distinct states (including two death states) and nine possible transitions between them. In addition, there are four probabilities of staying in each of the four health states: healthy (H), obese (O), smokers (S), and diabetics (DM). Table **5.18** illustrated a transition matrix for the 'allowable' transitions between the states of the model.

Table 5.18. The allowable transitions in the Saudi IMPACT Diabetes Forecast Model

Transition from / **to**	H	O	S	DM	Deaths (no DM)	Deaths (DM)
H	$1-TP_{HDM}$ - TP_{HD-}			TP_{HDM}	TP_{HD-}	
O		1- TP_{ODM} - TP_{OD-}		TP_{ODM}	TP_{OD-}	
S			1- TP_{SDM} – TP_{SD-}	TP_{SDM}	TP_{SD-}	
DM				1- TP_{DMD-} – TP_{DMD+}	TP_{DMD-}	TP_{DMD+}
Deaths (no DM)						
Deaths (DM)						

These allowable TPs are specific to each age group of each sex. Six of these TPs represent the transition hazards which were estimated through DISMOD and were already converted to probability values (Table **5.17**). First, the TP of moving from the H state to the DM state (TP_{HDM}) is equal to the *incidence* of diabetes. Second, the TP of moving from the DM state to the state of diabetes-specific deaths (TP_{DMD+}) is equal to the *case fatality*. Third, all the four TPs of moving from the H, O, or S states to the state of deaths for other causes (TP_{HD-}, TP_{OD-}, TP_{SD-}, TP_{DMD-}) are equal to the *total mortality* estimated by DISMOD. Another two TPs are estimated by incorporating the RRs of diabetes in obese and in smoking individuals (Table **5.16**). The TP of moving from the O state to the DM state (TP_{ODM}) is equal to: [incidence of diabetes X RR of diabetes in obese individuals]. On the other hand, the transition probability of moving from the S state to the DM state (TP_{SDM}) is equal to: [incidence of diabetes X RR of diabetes in smokers]. Finally, as discussed earlier, the probability of staying at the same state as the previous cycle is equal to 1 minus the probability of leaving that particular state.

To illustrate these calculations, the transition probabilities for men aged 25–34 years are presented here as an example. Table **5.19** summarises the transition parameters for this age group of men.

Table 5.19. Transition parameters for men aged 25-34 years

Parameter	Value for men aged 25–34 years
Incidence	0.0082
Case fatality	0.0015
Mortality	0.0001
RR of diabetes in obese	6.7
RR of diabetes in smokers	1.44

Based on these transition parameters, the TPs for men aged 25–34 years were estimated as summarised in Table **5.20**.

Table 5.20. Summary of calculations of transition probabilities for men aged 25-34 years

Transition from	**Transition to** H	O	S	DM	Deaths (no DM)	Deaths (DM)
H	1- 0.0082 - 0 = **0.9918**			**0.0082**	**0.0001**	
O		1- 0.0549 – 0 = **0.9451**		0.0082 X 6.7 = **0.0549**	**0.0001**	
S			1- 0.0118 – 0 = **0.9882**	0.0082 X 1.44 = **0.0118**	**0.0001**	
DM				1- 0.0001 – 0.0015 = **0.9985**	**0.0001**	**0.0015**
Deaths (no DM)						
Deaths (DM)						

However, the major output of the Saudi IMPACT Diabetes Forecast Model is the trends in diabetes, in terms of both the numbers of individuals with diabetes and the prevalence of the disease. Thus, the model used for its estimations the TPs of moving to the DM state from the other states, i.e. TP_{HDM}, TP_{ODM}, TP_{SDM}, and the probability of staying in the same DM state. In addition, the model also used the two transition hazards to the death states (i.e. case fatality and total mortality). The 'typical' TPs of staying in the same health state were not utilised by the model. The model used another approach to estimate the size (number of individuals) in each health state at every modelling cycle. This approach

incorporated the parameter of ‘population attributable risk’ for estimations (discussed in detail in the next section, which illustrates an example of the model calculations of sizes of states for men aged 25-34 years).

As previously discussed, the Saudi IMPACT Diabetes Forecast Model performs calculations separately for each sex and age group of the Saudi population. The model software (Microsoft Excel) contains a number of ‘tabs’ which present these calculations. Each separate tab was assigned for one age group of one sex. For example, the calculations for men aged 25-34 years were presented in one tab, while that for women aged 25-34 years in another tab, and so on. The age- and sex-specific calculations determined the size of each model state for each year (cycle) of the modelling period (1992-2002).

Table **5.21** presents the results of these calculations for men in the age group 25-34 years, and Table **5.22** illustrates an example of the calculation methods for year 1994.

Table 5.21. Example of calculations of a Markov chain for men aged 25-34 years

year	Population	Obesity prevalence	Smoking prevalence	H	O	S	DM	Deaths (DM)	Deaths (no DM)	DM prevalence
1992	1,988,608	10.1%	12.7%	1,492,571	173,184	249,374	73,479			3.7%
1993	2,042,141	13.1%	13.5%	1,449,039	225,346	269,796	97,960	110	199	4.8%
1994	2,095,674	16.1%	14.1%	1,403,487	277,518	289,010	125,658	257	403	6.0%
1995	2,149,206	19.1%	14.7%	1,356,016	329,674	306,885	156,631	445	613	7.3%
1996	2,202,739	22.2%	15.2%	1,306,734	381,782	323,294	190,929	680	828	8.7%
1997	2,256,272	25.2%	15.6%	1,255,751	433,810	338,115	228,596	966	1,048	10.1%
1998	2,309,805	25.4%	16.6%	1,247,234	427,960	364,943	269,667	1,309	1,273	11.7%
1999	2,363,337	25.7%	17.5%	1,237,894	421,904	392,325	311,214	1,713	1,504	13.2%
2000	2,416,870	25.9%	18.5%	1,227,755	415,665	420,253	353,196	2,180	1,741	14.6%
2001	2,470,403	26.2%	19.4%	1,216,838	409,266	448,724	395,574	2,709	1,982	16.0%
2002	2,523,936	26.4%	20.4%	1,204,961	402,348	477,679	438,948	3,302	2,229	17.4%
2003	2,577,468	26.6%	21.3%	1,192,521	395,642	507,207	482,098	3,960	2,482	18.7%
2004	2,631,001	26.9%	22.2%	1,179,521	389,161	537,309	525,009	4,682	2,740	20.0%
2005	2,641,168	27.1%	23.1%	1,144,370	371,165	557,961	567,672	5,469	3,003	21.5%
2006	2,651,334	27.5%	23.3%	1,124,009	357,494	560,910	608,921	6,320	3,267	23.0%
2007	2,661,501	27.9%	23.5%	1,104,105	344,559	563,928	648,908	7,233	3,532	24.4%
2008	2,671,667	28.3%	23.6%	1,084,633	332,365	567,014	687,654	8,206	3,798	25.7%
2009	2,681,834	28.8%	23.8%	1,065,568	320,916	570,165	725,185	9,236	4,065	27.0%
2010	2,692,000	29.2%	24.0%	1,046,883	310,212	573,377	761,528	10,323	4,333	28.3%
2011	2,701,400	29.6%	24.2%	1,028,198	300,028	576,461	796,712	11,465	4,602	29.5%
2012	2,710,800	30.1%	24.3%	1,009,859	290,597	579,599	830,746	12,659	4,873	30.6%
2013	2,720,200	30.5%	24.5%	991,825	281,886	582,780	863,709	13,904	5,144	31.8%
2014	2,729,600	31.0%	24.7%	974,082	273,913	586,005	895,600	15,199	5,416	32.8%
2015	2,739,000	31.4%	24.8%	956,614	266,693	589,270	926,423	16,541	5,689	33.8%
2016	2,790,200	31.9%	25.0%	957,407	273,582	603,026	956,185	17,930	5,962	34.3%
2017	2,841,400	32.4%	25.2%	957,563	280,761	616,814	986,262	19,363	6,242	34.7%
2018	2,892,600	32.9%	25.3%	957,079	288,248	630,626	1,016,646	20,841	6,526	35.1%
2019	2,943,800	33.4%	25.5%	955,955	296,062	644,454	1,047,329	22,365	6,815	35.6%
2020	2,995,000	33.9%	25.6%	954,187	304,219	658,289	1,078,305	23,935	7,109	36.0%
2021	3,029,200	34.4%	25.8%	945,000	306,890	667,740	1,109,569	25,551	7,409	36.6%
2022	3,063,400	34.9%	25.9%	935,532	310,174	677,194	1,140,499	27,214	7,712	37.2%

Table 5.22. Example showing the calculation methods used to determine the sizes of the model states, for men aged 25-34 years in 1994

Health state/ information	Source/ Method of calculation
Population	As estimated by linear interpolation (Table 5.3) = **2,095,674**
Prevalence of obesity	As estimated by linear interpolation (Table 5.11) = **16.1%**
Prevalence of smoking	= The 'original' smoking prevalence in 1994 as estimated by linear interpolation (Table 5.12) – [The 'original' smoking prevalence in 1994 as estimated by linear interpolation (Table 5.12) X obesity prevalence in 1994] = 0.169 – [0.169 X 0.161] = **14.1%**
Size of the H state	= Population – O state – S state – DM state = 2,095,674 – 277,518 – 289,010– 125,658 = **1,403,487**
Size of the O state	= [obesity prevalence X population] – [size of DM state in 1994 X ((obesity prevalence X RR of DM if obese – 1) / (obesity prevalence X RR of DM if obese -1) + 1))] = [0.161 X 2,095,674] – [125,658 X ((0.161 X 6.7 – 1) / (0.161 X 6.7 – 1) + 1))] = **277,518**
Size of the S state	= [smoking prevalence X population] – [size of DM state in 1994 X ((smoking prevalence X RR of DM if smoker – 1) / (smoking prevalence X RR of DM if smoker -1) + 1))] = [0.141 X 2,095,674] – [125,658 X ((0.141 X 1.44 – 1) / (0.141 X 1.44 – 1) + 1))] = **289,010**
Size of the DM state	= Size of H state in 1993 X TP(H→DM) + Size of O state in 1993 X TP(O→DM) + Size of S state in 1993 X TP(S→DM) + Size of DM state in 1993 X TP(DM→DM) = 1,449,039 X 0.008 + 225,346 X 0.055 + 269,796 X 0.012 + 97,960 X 0.999 = **125,658**

Table 5.22 (cont.). Example showing the calculation methods used to determine the sizes of the model states, for men aged 25-34 years in 1994

Health state/ information	Source/ Method of calculation
Size of the state of DM-related deaths	= (Size of DM state in 1993 X TP of case fatality) + Size of the state of DM-related deaths in 1993 = (97,960 X 0.0015) + 110 = **257**
Size of the state of deaths due to other causes	= Size of the state of deaths due to other causes in 1993 + [Size of H state in 1993 X TP of total mortality + Size of O state in 1993 X TP of total mortality + Size of S state in 1993 X TP of total mortality + Size of DM state in 1993 X TP of total mortality] = 199 + [1,449,039 X 0.0001 + 225,346 X 0.0001 + 269,796 X 0.0001 + 97,960 X 0.0001] = **403**
Diabetes prevalence	= Size of the DM state / population in 1994 = 125,658 / 2,095,674 = **6.0%**

As shown in Table **5.22**, the model performs its calculations through the concept of transitions between 'discrete' Markov states, as discussed earlier. Nevertheless, the methods of calculation were different for both smoking prevalence and the sizes of the risk factor states (O and S states). These different methods of calculation were used to handle the issue of 'overlaps' between the model health states.

Since the model states are discrete, an individual can only be in one (and only one) state during a modelling cycle (one year). Therefore, the presence of any individual in the (O) state implies that this individual is obese, but not a smoker and not diabetic. In other words, the size of the (O) state, for example, represents only those obese individuals who are not smokers and not diabetics at the same time.

In order to handle such overlaps, there were three different methods of calculation performed by the model. The first method was to deal with the overlap between the (O) and (S) states. The 'original' prevalence of smoking, which was obtained through linear interpolation (Table **5.12**), was multiplied by the obesity prevalence. This multiplication was assumed to yield the proportion of population who were both obese and smokers at the same time. Then, such a proportion was subtracted from the 'original' prevalence of smoking, to leave in the (S) state only those individuals who were smokers but not obese.

The second method of calculation was performed to handle the overlap between the (O) and (DM) states. This method used the population attributable risk (PAR) for obesity to eliminate this potential overlap.

PAR is one of the commonly used "measures of impact" in epidemiology. It is defined as the excess rate of disease in the total study population of exposed and non-exposed individuals that is attributable to a particular exposure, assuming a causal relationship between exposure and disease.[264] If the prevalence of exposure (p) and the relative risk (RR) are available, PAR is conventionally calculated as follows:

$$PAR = \frac{p\,(RR-1)}{p\,(RR-1)+1}$$

In the context of this thesis, assuming a causal relationship between obesity and diabetes, the calculated PAR yielded the excess rate of diabetes in the total population (obese and non-obese) that was attributed to obesity. The model calculated the number of diabetes cases (in the DM state) in whom the disease was assumed to be 'caused' by obesity, through multiplying PAR by the size of DM state. Then, the number of such cases was subtracted from the total obese individuals in population. This calculation method was assumed to leave in the (O) state only those obese individuals who were non-diabetics.

The third method of calculation was applied to remove the overlap between the (S) and (DM) states. This method used the same previous approach of PAR, which was assumed to leave in the (S) states only those people who were smokers, but not diabetics.

Therefore, by applying these three methods (approaches) of calculation, the study population was assumed to be partitioned in discrete Markov states without overlaps.

5.4. Sensitivity analyses

In chapter 4, it has been discussed that sensitivity analysis should be a vital part in all modelling studies.[22] Modelling data are mostly obtained from different sources and might be of different qualities. In addition, models commonly use assumptions and expert opinions. Thus, modelling input parameters could be subject to uncertainties, which might result in uncertain outputs. Simply, sensitivity analysis refers to estimation and presentation of model results under various scenarios,[209] as a way of handling the uncertainties around the key model parameters. In the Saudi IMPACT Diabetes Forecast Model, several types of sensitivity analyses have been performed. As previously mentioned, substantial original developments were undertaken to the section of sensitivity analyses in this thesis, in order to involve additional and more rigorous types than that used in the original IMPACT model. These types of sensitivity analyses are summarised in the following three sections.

5.4.1. Analysis of extremes

The model used the '*analysis of extremes*' method of sensitivity analysis. As discussed in chapter 4, this method is commonly used in modelling studies, and

is a type of multi-way (multivariate) analysis. It consists of examining different (higher and lower) values of multiple parameters simultaneously, and presenting the impact of such 'extreme' values on the output results of the model. So, the 'best' values estimated through the base-case scenario are presented with ranges of minimum and maximum uncertainty limits.

In the Saudi IMPACT Diabetes Forecast Model, all model parameters (except population structure) were set at 20% higher and 20% lower values than the base-case scenario. The model was run with this distribution of extreme values and the uncertainty limits were estimated accordingly. In chapters 6, 7 and 8, all the results are presented with such uncertainty limits (in brackets or presented separately in tables).

However, it has been discussed in chapter 4 that the extreme uncertainty values in this method of sensitivity analysis are mostly decided arbitrarily. In this thesis, the range of uncertainty (20% higher and 20% lower) was decided, as it is relatively 'conservative', because it is wider (though not much wider) than the 95% CIs of the point estimates reported in some national surveys of obesity and smoking prevalence.[19, 34, 37, 39]

5.4.2. Modelling scenarios with capped versus uncapped projections in the obesity trends

As indicated earlier, capping was performed for the assumed increasing linear trends in obesity prevalence in Saudi Arabia. Detailed discussion has been provided in section 5.3.2.4, regarding the justification and assumed levels of capping used in the model. There was no evidence for a specific biological threshold/ limit at which capping could be done, and therefore the capping points in this thesis (35% in men and 60% in women) were decided arbitrarily. So, such a decision of capping remains uncertain, although it might seem more realistic than reaching extremely high and probably implausible prevalence rates as a result of assuming linear increasing projections of obesity. Therefore, the modelling outputs are presented in this thesis (chapters 6, 7 and 8) with different scenarios of capped versus uncapped trends in obesity prevalence rates. The quantified effects (impact) of capping on the main modelling outputs are presented as a form of sensitivity analysis.

5.4.3. Modelling scenarios with inclusion versus exclusion of the two oldest age groups of population

It has been discussed earlier that the available 'observed' data from Saudi Arabia on obesity and smoking prevalence did not cover the population age groups of ≥65 years. The oldest age groups reported in these surveys were in the range of 60-64 years. Therefore, the trends in prevalence of obesity and smoking for the age groups 65-74 and ≥75 years were obtained through extrapolating the available data using similar population-based information from Oman. However, again, such a method of extrapolation remains uncertain. Although the two countries are neighbouring and might share many similar population and lifestyle characteristics, there might be still some significant differences in the prevalence of these risk factors. Hence, in order to handle this type of uncertainty, modelling outputs are presented with inclusion of these two oldest age groups in the modelled Saudi population, and then with exclusion of them.

Overall, this chapter provides an extensive description and discussion of the Saudi IMPACT Diabetes Forecast Model, its structure and data sources, assumptions, and methodology (including the different methods of sensitivity analyses). The next chapter presents the model results (outputs) for the past and current estimated T2DM prevalence (1992-2013).

Chapter 6. Past and current trends in the estimated prevalence of type 2 diabetes in Saudi Arabia

In chapter 5, the Saudi IMPACT Diabetes Forecast Model was described, along with the data sources and their strengths and limitations. Also, data inputs into the model, methods, and the assumptions used were discussed. This chapter presents the results (outputs) of the model for the period 1992-2013. Minimum and maximum values [uncertainty intervals (UI)] of the outputs are presented in brackets in this chapter, chapter 7, and chapter 8 as a form of sensitivity analysis. As discussed earlier, these uncertainty values were estimated using the 'analysis of extremes' method, through running the model with all parameters set to values of 20% lower and 20% higher than the 'best' estimates of the model. This chapter also presents the results of validation of the Saudi IMPACT Diabetes Forecast Model against local observed data and another model.

As mentioned in chapter 5, the results of the Saudi IMPACT Diabetes Forecast Model are presented in different scenarios as part of dealing with uncertainties around some parameters, particularly among obesity trends projections under different assumptions. These scenarios are summarised in Table **6.1**.

Table 6.1. The different four scenarios to present the results of the Saudi IMPACT Diabetes Forecast Model

	Description
Scenario 1	Modelling results for the population aged *25-64* years, *with* capping
Scenario 2	Modelling results for the population aged *25-64* years, *without* capping
Scenario 3	Modelling results for the population aged *25-75+* years, *with* capping
Scenario 4	Modelling results for the population aged *25-75+* years, *without* capping

6.1. Trends in the prevalence of type 2 diabetes in Saudi Arabia during 1992 - 2013

In this section, the trends in prevalence of T2DM in Saudi Arabia during the period of 1992–2013 are presented, as estimated by the Saudi IMPACT Diabetes Forecast Model. These results are presented based on the four scenarios discussed in Table **6.1**.

6.1.1. The overall and sex-specific prevalence of diabetes and numbers of diabetic individuals in the Saudi population

6.1.1.1. Results based on scenario 1: population aged 25-64 years, with capping

Assuming linearly increasing trends in the prevalence of smoking and obesity in Saudi Arabia (obesity prevalence capped at 35% in men and 60% in women), the model estimated that the overall diabetes prevalence in the Saudi population aged 25-64 years would increase from 8.5% (UI: 6.8–10.2%) to 30.8% (UI: 25.2–36.2%) during the period of 1992–2013 (Figure **6.1**). The number of individuals with T2DM was estimated to increase nearly eight-fold, from 555,101 (UI: 355,265–799,346) in 1992 to 4,090,778 (UI: 2,669,048–5,761,060) in 2013 (Table **6.2**).

In men, diabetes prevalence was estimated to increase substantially by 263% during the same period; from 8.7% (UI: 6.9–10.4%) to 31.6% (UI: 26.2–36.5%) (Figure **6.3**). This is equivalent to an increase of 2,101,687 individuals (UI: 1,399,606-2,896,341); from 356,567 (UI: 228,203-513,456) in 1992 to 2,458,253 (UI: 1,627,808-3,409,797) in 2013 (Table **6.2**).

In comparison, in women, diabetes prevalence was estimated to increase also by 263%; from 8.2% (UI: 6.6–9.9%) in 1992 to 29.8% (UI: 23.7–35.7%) in 2013 (Figure **6.3**). The total number of women with diabetes was estimated to increase by 1,433,991 (UI: 914,178-2,065,373); from 198,534 (UI: 127,062-285,890) in 1992 to 1,632,525 (UI: 1,041,240-2,351,262) in 2013 (Table **6.2**).

6.1.1.2. Results based on scenario 2: population aged 25-64 years, without capping

Under the assumption that the obesity and smoking trends in Saudi Arabia would continue to increase by the same 'observed' annual rates till 2013 (without capping of the projected obesity prevalence), the overall prevalence of diabetes in the Saudi population aged 25-64 years was estimated to increase to 31.4% (UI: 25.5–37.0%) by 2013 (Figure **6.2**). The total number of individuals with diabetes was estimated to increase to 4,161,646 (UI: 2,703,025–5,887,412) (**Table 6.3**).

In men, the estimated relative increase in diabetes prevalence during 1992-2013 was 267%, where the prevalence reached 31.9% (UI: 26.3–37.0%) in 2013 (Figure **6.4**). The number of men with diabetes was estimated to increase by a total of 2,124,221 (UI: 1,410,334-2,937,711) during the same period, and reached 2,480,788 (UI: 1,638,536-3,451,167) in 2013 (Table **6.3**).

On the other hand, diabetes prevalence was estimated to increase by 273% in women aged 25-64 years during the same period, with a prevalence reaching 30.6% (UI: 24.3–37.0%) in 2013 (Figure **6.4**). The number of women with diabetes increased by 1,482,323 (UI: 937,426-2,150,355), and was estimated to be 1,680,858 (UI: 1,064,488 - 2,436,245) in 2013 (Table **6.3**).

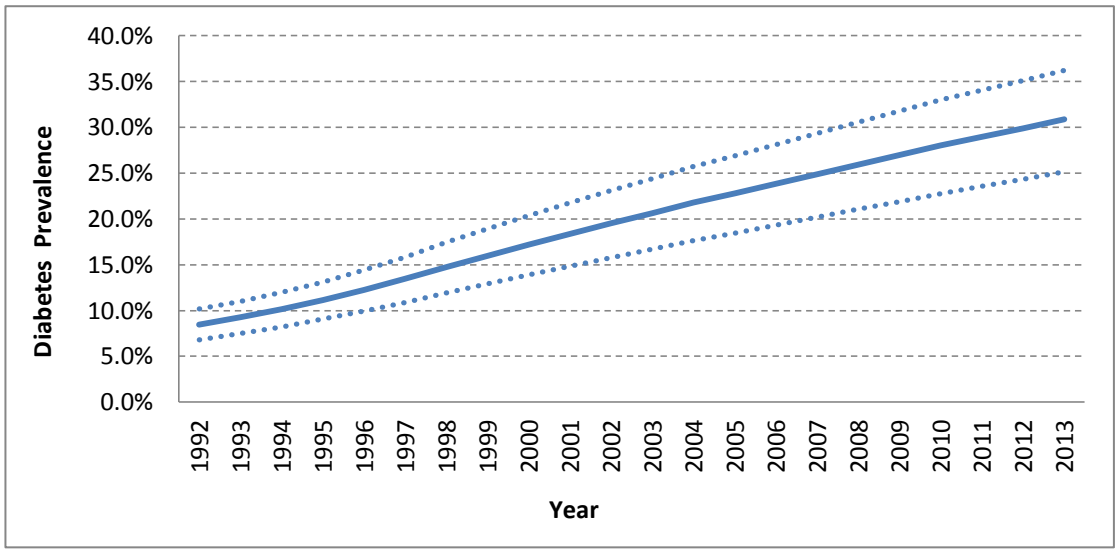


Figure 6.1. *(Scenario 1)* Trends in the estimated diabetes total prevalence (and uncertainty values) for population aged 25-64 years, with capping of projected obesity prevalence, Saudi Arabia (1992-2013)

[*Solid line:* point (best) estimates; *Dotted lines:* minimum and maximum uncertainty estimates. Diagnostic criteria: WHO 1985]

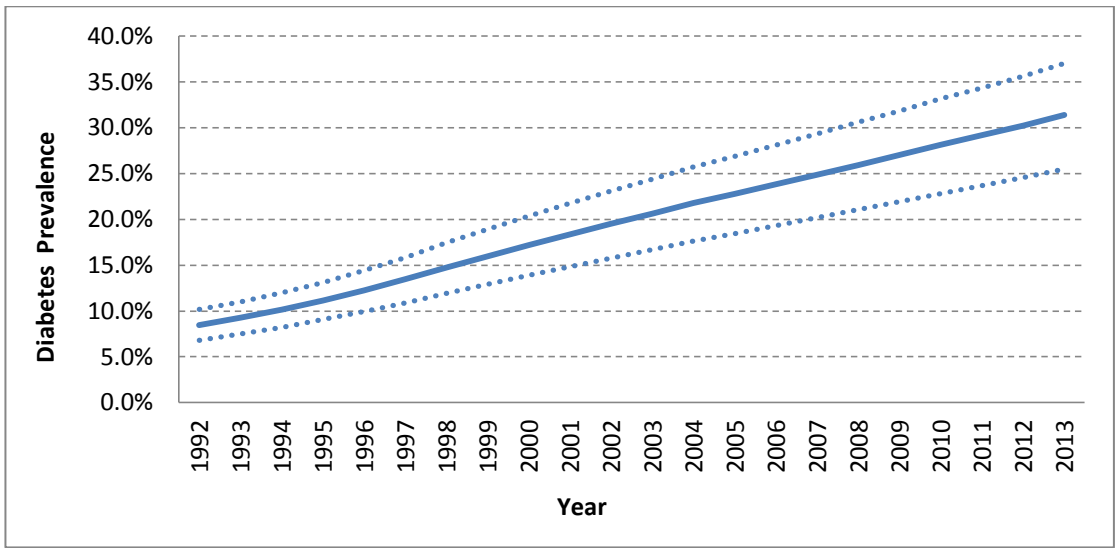


Figure 6.2. *(Scenario 2)* Trends in the estimated diabetes total prevalence (and uncertainty values) for population aged 25-64 years, without capping of projected obesity prevalence, Saudi Arabia (1992-2013)

[*Solid line:* point (best) estimates; *Dotted lines:* minimum and maximum uncertainty estimates. Diagnostic criteria: WHO 1985]

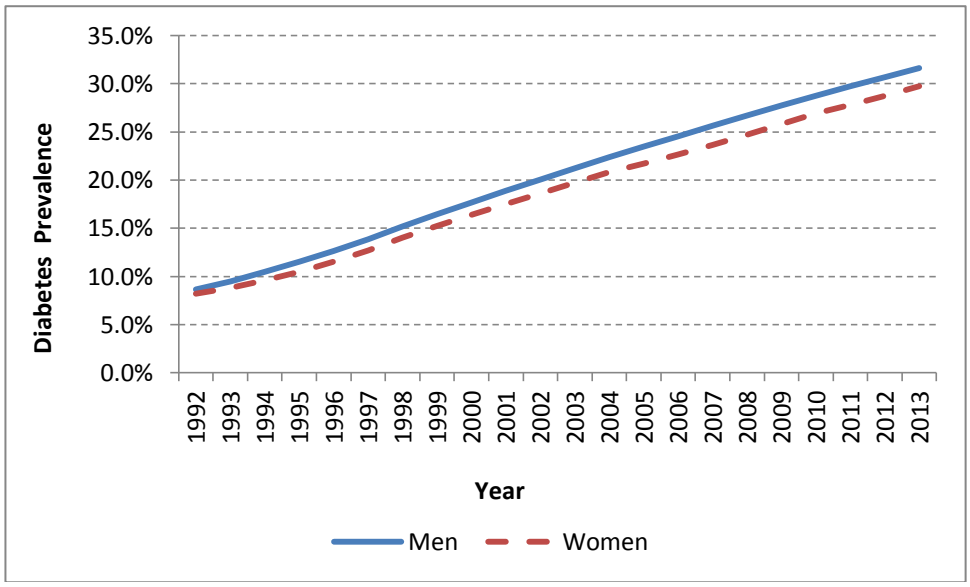


Figure 6.3. *(Scenario 1)* Trends in the estimated diabetes prevalence (and uncertainty values) for men and women aged 25-64 years, with capping of projected obesity prevalence, Saudi Arabia (1992-2013)

[Diagnostic criteria: WHO 1985]

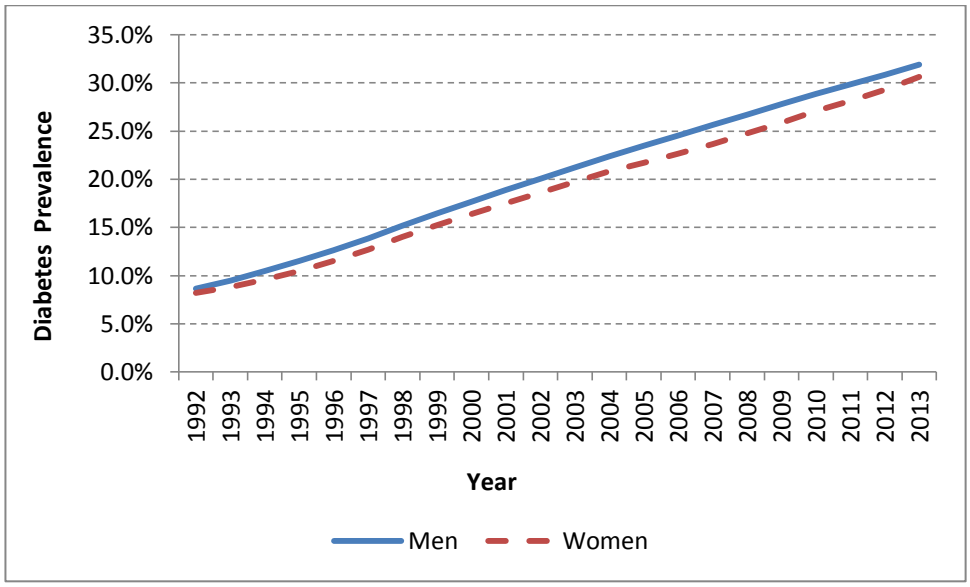


Figure 6.4. *(Scenario 2)* Trends in the estimated diabetes prevalence (and uncertainty values) for men and women aged 25-64 years, without capping of projected obesity prevalence, Saudi Arabia (1992-2013)

[Diagnostic criteria: WHO 1985]

Table 6.2. *(Scenario 1)* Estimated numbers of individuals with diabetes for population aged 25-64 years, with capping of projected obesity prevalence, Saudi Arabia (1992-2013)

Year	Men	Uncertainty intervals		Women	Uncertainty intervals		Total	Uncertainty intervals	
	best estimate	minimum	maximum	best estimate	minimum	maximum	best estimate	minimum	maximum
1992	**356,567**	228,203	513,456	**198,534**	127,062	285,890	**555,101**	355,265	799,346
1993	**408,141**	263,675	580,974	**223,907**	144,786	319,582	**632,047**	408,462	900,556
1994	**467,098**	303,390	660,351	**255,030**	165,718	362,454	**722,128**	469,108	1,022,805
1995	**533,753**	347,522	752,099	**292,164**	190,015	414,860	**825,917**	537,536	1,166,960
1996	**608,378**	396,230	856,623	**335,532**	217,821	477,096	**943,910**	614,051	1,333,719
1997	**691,204**	449,663	974,229	**385,328**	249,268	549,398	**1,076,532**	698,930	1,523,628
1998	**782,428**	507,950	1,105,147	**441,714**	284,474	631,952	**1,224,142**	792,424	1,737,098
1999	**876,174**	568,323	1,238,508	**499,184**	320,653	715,520	**1,375,358**	888,976	1,954,029
2000	**972,353**	630,739	1,374,194	**557,746**	357,800	800,153	**1,530,098**	988,538	2,174,346
2001	**1,070,872**	695,152	1,512,085	**617,405**	395,908	885,882	**1,688,277**	1,091,060	2,397,967
2002	**1,172,669**	762,283	1,653,293	**678,039**	434,987	972,392	**1,850,709**	1,197,270	2,625,685
2003	**1,276,966**	831,325	1,797,526	**742,248**	476,108	1,064,869	**2,019,214**	1,307,433	2,862,396
2004	**1,383,668**	902,232	1,944,626	**809,890**	519,239	1,162,872	**2,193,558**	1,421,471	3,107,499
2005	**1,492,677**	974,955	2,094,423	**880,746**	564,326	1,265,759	**2,373,423**	1,539,281	3,360,181
2006	**1,605,155**	1,050,040	2,249,187	**957,051**	612,612	1,377,025	**2,562,206**	1,662,652	3,626,212
2007	**1,720,653**	1,127,290	2,408,033	**1,039,602**	664,582	1,497,682	**2,760,255**	1,791,872	3,905,715
2008	**1,838,481**	1,206,386	2,569,629	**1,127,634**	719,947	1,626,100	**2,966,115**	1,926,334	4,195,729
2009	**1,958,525**	1,287,282	2,733,720	**1,220,878**	778,651	1,761,594	**3,179,403**	2,065,933	4,495,315
2010	**2,080,436**	1,369,825	2,899,594	**1,318,305**	840,233	1,902,341	**3,398,741**	2,210,058	4,801,934
2011	**2,203,645**	1,453,763	3,066,126	**1,418,010**	903,900	2,044,620	**3,621,654**	2,357,662	5,110,747
2012	**2,329,163**	1,539,553	3,235,404	**1,521,141**	970,272	2,190,658	**3,850,304**	2,509,825	5,426,062
2013	**2,458,253**	1,627,808	3,409,797	**1,632,525**	1,041,240	2,351,262	**4,090,778**	2,669,048	5,761,060

Table 6.3. *(Scenario 2)* Estimated numbers of individuals with diabetes for population aged 25-64 years, without capping of projected obesity prevalence, Saudi Arabia (1992-2013)

Year	Men	Uncertainty intervals		Women	Uncertainty intervals		Total	Uncertainty intervals	
	best estimate	minimum	maximum	best estimate	minimum	maximum	best estimate	minimum	maximum
1992	**356,567**	228,203	513,456	**198,534**	127,062	285,890	**555,101**	355,265	799,346
1993	**408,141**	263,675	580,975	**223,907**	144,787	319,584	**632,048**	408,462	900,559
1994	**467,096**	303,389	660,349	**255,029**	165,717	362,452	**722,125**	469,106	1,022,801
1995	**533,749**	347,520	752,096	**292,161**	190,013	414,856	**825,910**	537,532	1,166,952
1996	**608,370**	396,226	856,612	**335,528**	217,818	477,090	**943,898**	614,044	1,333,701
1997	**691,195**	449,658	974,216	**385,321**	249,263	549,387	**1,076,516**	698,921	1,523,603
1998	**782,414**	507,943	1,105,125	**441,705**	284,469	631,937	**1,224,119**	792,411	1,737,061
1999	**876,159**	568,315	1,238,485	**499,173**	320,647	715,504	**1,375,332**	888,962	1,953,989
2000	**972,336**	630,729	1,374,168	**557,737**	357,794	800,139	**1,530,072**	988,524	2,174,307
2001	**1,070,848**	695,139	1,512,048	**617,390**	395,900	885,859	**1,688,238**	1,091,039	2,397,907
2002	**1,172,638**	762,266	1,653,243	**678,020**	434,976	972,362	**1,850,658**	1,197,243	2,625,605
2003	**1,276,932**	831,307	1,797,472	**742,228**	476,096	1,064,838	**2,019,160**	1,307,403	2,862,310
2004	**1,383,630**	902,212	1,944,567	**809,871**	519,228	1,162,844	**2,193,501**	1,421,440	3,107,411
2005	**1,492,630**	974,930	2,094,349	**880,719**	564,310	1,265,716	**2,373,349**	1,539,240	3,360,065
2006	**1,605,099**	1,050,010	2,249,098	**957,018**	612,594	1,376,974	**2,562,118**	1,662,604	3,626,072
2007	**1,720,752**	1,127,333	2,408,229	**1,039,836**	664,693	1,498,091	**2,760,587**	1,792,027	3,906,320
2008	**1,839,500**	1,206,867	2,571,515	**1,129,087**	720,651	1,628,613	**2,968,587**	1,927,518	4,200,129
2009	**1,961,243**	1,288,576	2,738,706	**1,224,641**	780,482	1,768,079	**3,185,884**	2,069,058	4,506,785
2010	**2,085,865**	1,372,417	2,909,527	**1,326,372**	844,193	1,916,147	**3,412,237**	2,216,610	4,825,674
2011	**2,213,241**	1,458,340	3,083,702	**1,434,154**	911,775	2,072,572	**3,647,395**	2,370,116	5,156,273
2012	**2,344,381**	1,546,811	3,263,282	**1,550,214**	984,363	2,241,392	**3,894,596**	2,531,174	5,504,673
2013	**2,480,788**	1,638,536	3,451,167	**1,680,858**	1,064,488	2,436,245	**4,161,646**	2,703,025	5,887,412

6.1.1.3. Results based on scenario 3: population aged 25-75+ years, with capping

Assuming capped trends in obesity prevalence, the model estimated that the overall diabetes prevalence increased by 223% during the period of 1992-2013; from 9.6% (UI: 7.7–11.6%) to 31.0% (UI: 25.4–36.2%) in the Saudi population aged 25-75+ years (Figure **6.5**). There was an estimated increase of 3,712,624 diabetic individuals (UI: 2,446,983-5,181,753) during the same period; from 671,702 (UI: 429,890-967,251) in 1992 to 4,384,326 (UI: 2,876,872-6,149,005) in 2013 (Table **6.4**).

In men, diabetes prevalence increased by 217% during the same period; from 9.8% (UI: 7.8–11.7%) in 1992 to 31.1% (UI: 25.8–35.8%) in 2013 (Figure **6.7**). The number of men with diabetes was estimated to increase by 2,174,619 (UI: 1,459,838-2,974,891); from 427,410 (UI: 273,542-615,470) in 1992 to 2,602,029 (UI: 1,733,380-3,590,360) in 2013 (Table **6.4**).

In women, between 1992 and 2013, there was an estimated relative increase of 220% in the diabetes prevalence; from 9.4% (UI: 7.5–11.2%) to 30.1% (UI: 24.1–36.0%) (Figure **6.7**). This was equivalent to an increase in the number of diabetic women by 1,538,005 (UI: 987,145-2,206,863); from 244,293 (UI: 156,347-351,782) in 1992 to 1,782,297 (UI: 1,143,493-2,558,644) in 2013 (Table **6.4**).

6.1.1.4. Results based on scenario 4: population aged 25-75+ years, without capping

The total diabetes prevalence during 1992-2013 was estimated to increase by 228%, and to reach 31.5% (UI: 25.7–36.9%) in 2013 (Figure **6.6**). The estimated increase in the number of individuals with diabetes was 3,783,491 (UI: 2,480,960-5,308,106), with an estimated total of 4,455,194 (UI: 2,910,849-6,275,357) individuals with diabetes in 2013 (Table **6.5**).

In men, the estimated diabetes prevalence increased by 219%, and reached 31.3% (UI: 25.9 – 36.2%) in 2013 (Figure **6.8**). The number of men with diabetes increased by 2,197,154 (UI: 1,470,566-3,016,260), with an estimated total of 2,624,564 (UI: 1,744,108-3,631,730) in 2013 (Table **6.5**).

In comparison, the estimated diabetes prevalence in women increased by 229% (UI: 17.1–25.9%); with a prevalence of 30.9% (UI: 24.6–37.2%) in 2013 (Figure **6.8**). The estimated number of women with diabetes increased by 1,586,337 (UI: 1,010,394-2,291,845), and reached 1,830,630 (UI: 1,166,741-2,643,627) in 2013 (Table **6.5**).

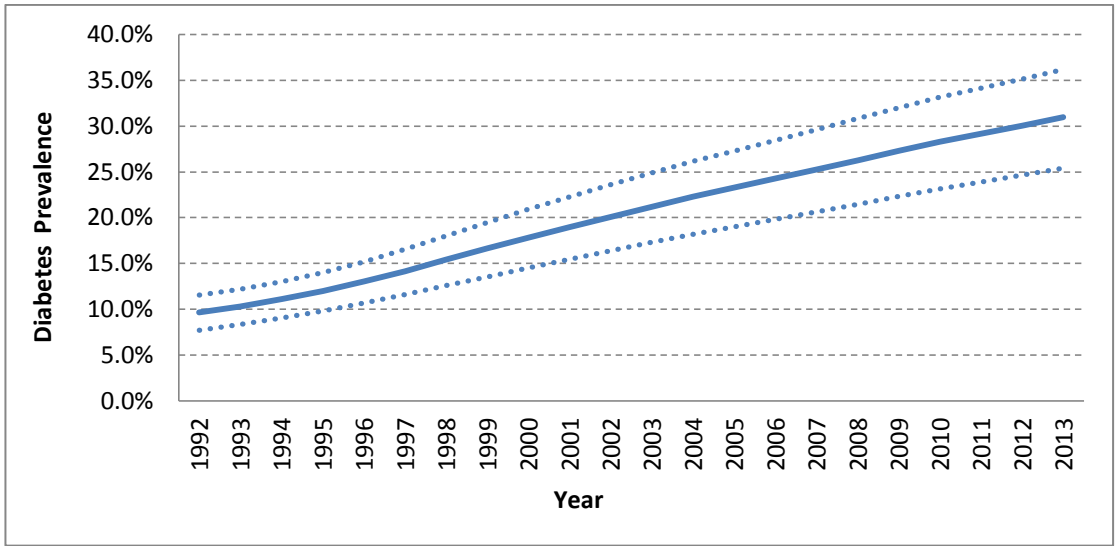


Figure 6.5. *(Scenario 3)* Trends in the estimated diabetes total prevalence (and uncertainty values) for population aged 25-75+ years, with capping of projected obesity prevalence, Saudi Arabia (1992-2013)

[*Solid line:* point (best) estimates; *Dotted lines:* minimum and maximum uncertainty estimates. Diagnostic criteria: WHO 1985]

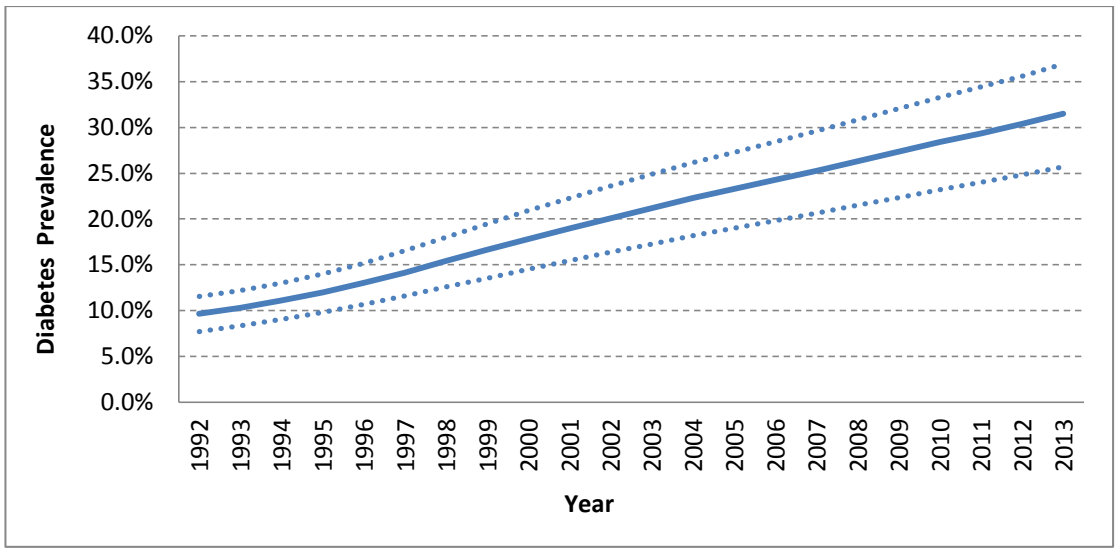


Figure 6.6. *(Scenario 4)* Trends in the estimated diabetes total prevalence (and uncertainty values) for population aged 25-75+ years, without capping of projected obesity prevalence, Saudi Arabia (1992-2013)

[*Solid line:* point (best) estimates; *Dotted lines:* minimum and maximum uncertainty estimates. Diagnostic criteria: WHO 1985]

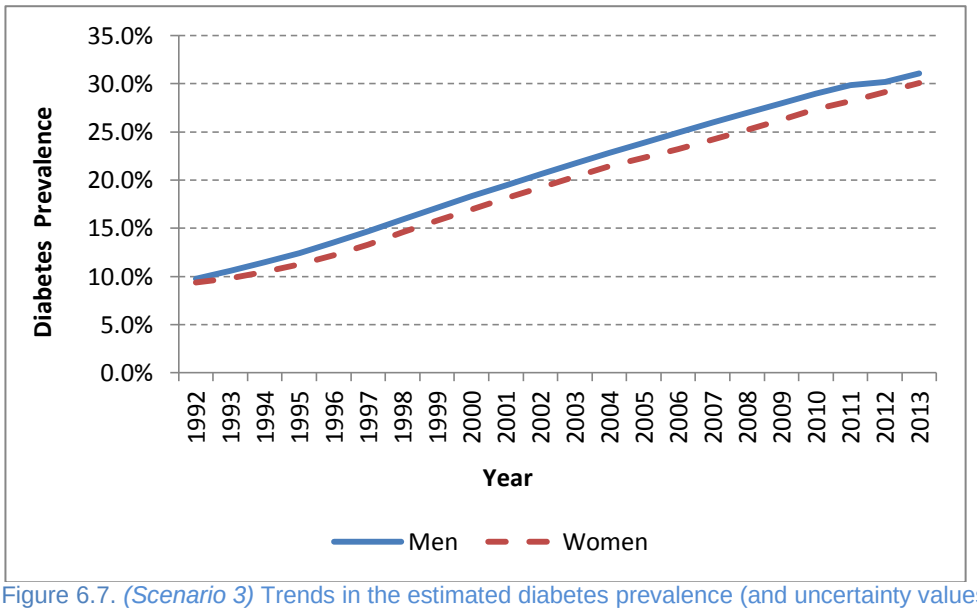


Figure 6.7. *(Scenario 3)* Trends in the estimated diabetes prevalence (and uncertainty values) for men and women aged 25-75+ years, with capping of projected obesity prevalence, Saudi Arabia (1992-2013)

[Diagnostic criteria: WHO 1985]

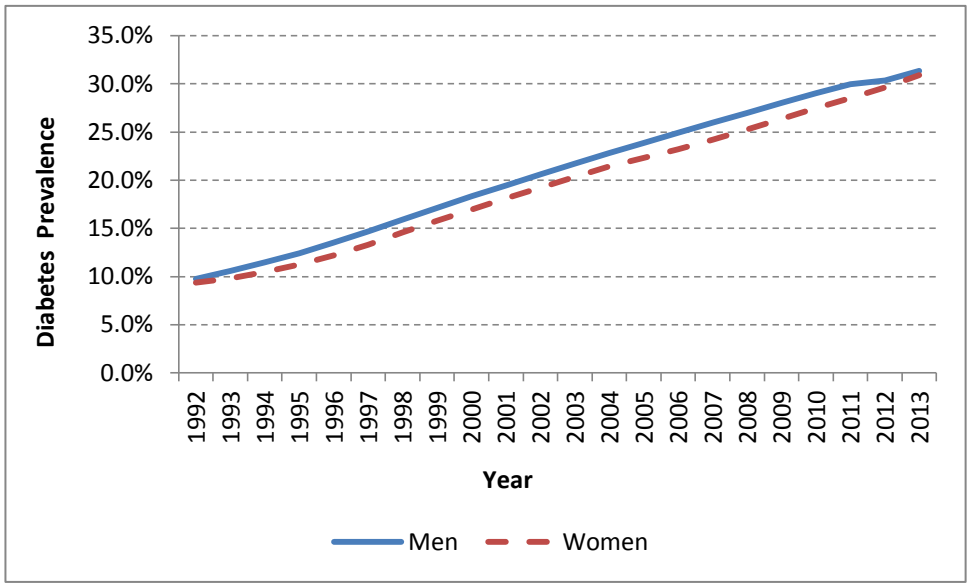


Figure 6.8. *(Scenario 4)* Trends in the estimated diabetes prevalence (and uncertainty values) for men and women aged 25-75+ years, without capping of projected obesity prevalence, Saudi Arabia (1992-2013)

[Diagnostic criteria: WHO 1985]

Table 6.4. *(Scenario 3)* Estimated numbers of individuals with diabetes for population aged 25-75+ years, with capping of projected obesity prevalence, Saudi Arabia (1992-2013)

Year	Men	Uncertainty intervals		Women	Uncertainty intervals		Total	Uncertainty intervals	
	best estimate	minimum	maximum	best estimate	minimum	maximum	best estimate	minimum	maximum
1992	**427,410**	273,542	615,470	**244,293**	156,347	351,782	**671,702**	429,890	967,251
1993	**480,805**	310,902	683,444	**269,273**	174,883	381,670	**750,077**	485,785	1,065,115
1994	**541,673**	352,607	763,251	**300,341**	196,836	421,599	**842,014**	549,443	1,184,849
1995	**610,379**	398,839	855,614	**338,068**	222,439	472,854	**948,448**	621,278	1,328,468
1996	**687,238**	449,766	961,114	**382,894**	251,902	536,146	**1,070,133**	701,669	1,497,260
1997	**772,519**	505,543	1,080,196	**435,145**	285,407	611,806	**1,207,664**	790,950	1,692,002
1998	**866,446**	566,306	1,213,188	**495,045**	323,111	699,910	**1,361,490**	889,417	1,913,099
1999	**963,169**	629,291	1,349,290	**557,086**	362,250	790,999	**1,520,256**	991,541	2,140,289
2000	**1,062,616**	694,458	1,488,415	**621,235**	402,831	884,835	**1,683,852**	1,097,289	2,373,250
2001	**1,164,707**	761,764	1,630,456	**687,419**	444,845	981,156	**1,852,126**	1,206,610	2,611,611
2002	**1,270,219**	831,880	1,776,066	**754,928**	488,167	1,078,031	**2,025,148**	1,320,047	2,854,097
2003	**1,378,180**	903,886	1,924,607	**825,413**	533,393	1,179,207	**2,203,593**	1,437,279	3,103,814
2004	**1,488,504**	977,740	2,075,946	**898,939**	580,529	1,285,043	**2,387,443**	1,558,268	3,360,989
2005	**1,601,101**	1,053,394	2,229,935	**975,441**	629,549	1,395,359	**2,576,542**	1,682,943	3,625,295
2006	**1,717,348**	1,131,504	2,389,244	**1,057,638**	681,906	1,514,627	**2,774,986**	1,813,409	3,903,870
2007	**1,836,780**	1,211,866	2,552,931	**1,146,313**	738,079	1,643,739	**2,983,093**	1,949,945	4,196,669
2008	**1,958,689**	1,294,158	2,719,619	**1,240,693**	797,778	1,781,000	**3,199,382**	2,091,937	4,500,619
2009	**2,082,949**	1,378,328	2,889,019	**1,340,504**	860,946	1,925,690	**3,423,453**	2,239,274	4,814,709
2010	**2,209,197**	1,464,217	3,060,389	**1,444,713**	927,120	2,075,965	**3,653,910**	2,391,337	5,136,355
2011	**2,336,857**	1,551,572	3,232,584	**1,551,415**	995,507	2,228,102	**3,888,271**	2,547,079	5,460,686
2012	**2,467,399**	1,641,095	3,408,502	**1,662,389**	1,067,016	2,385,555	**4,129,788**	2,708,111	5,794,058
2013	**2,602,029**	1,733,380	3,590,360	**1,782,297**	1,143,493	2,558,644	**4,384,326**	2,876,872	6,149,005

Table 6.5. *(Scenario 4)* Estimated numbers of individuals with diabetes for population aged 25-75+ years, without capping of projected obesity prevalence, Saudi Arabia (1992-2013)

Year	Men	Uncertainty intervals		Women	Uncertainty intervals		Total	Uncertainty intervals	
	best estimate	minimum	maximum	best estimate	minimum	maximum	best estimate	minimum	maximum
1992	**427,410**	273,542	615,470	**244,293**	156,347	351,782	**671,702**	429,890	967,251
1993	**480,805**	310,902	683,445	**269,273**	174,883	381,672	**750,078**	485,785	1,065,117
1994	**541,671**	352,605	763,249	**300,340**	196,835	421,597	**842,011**	549,441	1,184,846
1995	**610,376**	398,837	855,610	**338,065**	222,438	472,850	**948,441**	621,274	1,328,460
1996	**687,231**	449,762	961,103	**382,890**	251,900	536,140	**1,070,121**	701,662	1,497,243
1997	**772,510**	505,538	1,080,183	**435,138**	285,403	611,795	**1,207,647**	790,941	1,691,978
1998	**866,432**	566,299	1,213,166	**495,035**	323,105	699,896	**1,361,467**	889,404	1,913,062
1999	**963,154**	629,283	1,349,266	**557,076**	362,244	790,983	**1,520,230**	991,527	2,140,249
2000	**1,062,600**	694,449	1,488,389	**621,226**	402,825	884,821	**1,683,826**	1,097,274	2,373,210
2001	**1,164,683**	761,752	1,630,418	**687,404**	444,837	981,132	**1,852,087**	1,206,589	2,611,551
2002	**1,270,188**	831,863	1,776,015	**754,909**	488,157	1,078,002	**2,025,098**	1,320,020	2,854,017
2003	**1,378,146**	903,868	1,924,552	**825,392**	533,382	1,179,175	**2,203,538**	1,437,250	3,103,728
2004	**1,488,467**	977,719	2,075,887	**898,920**	580,518	1,285,015	**2,387,386**	1,558,237	3,360,902
2005	**1,601,054**	1,053,369	2,229,862	**975,414**	629,534	1,395,317	**2,576,468**	1,682,902	3,625,179
2006	**1,717,293**	1,131,474	2,389,155	**1,057,605**	681,888	1,514,576	**2,774,898**	1,813,361	3,903,731
2007	**1,836,879**	1,211,909	2,553,127	**1,146,547**	738,190	1,644,148	**2,983,425**	1,950,100	4,197,275
2008	**1,959,708**	1,294,639	2,721,506	**1,242,146**	798,482	1,783,514	**3,201,854**	2,093,121	4,505,020
2009	**2,085,667**	1,379,622	2,894,005	**1,344,266**	862,777	1,932,175	**3,429,933**	2,242,398	4,826,180
2010	**2,214,627**	1,466,810	3,070,323	**1,452,780**	931,080	2,089,772	**3,667,407**	2,397,890	5,160,095
2011	**2,346,453**	1,556,150	3,250,159	**1,567,560**	1,003,383	2,256,053	**3,914,012**	2,559,532	5,506,212
2012	**2,482,617**	1,648,353	3,436,381	**1,691,462**	1,081,106	2,436,289	**4,174,079**	2,729,459	5,872,670
2013	**2,624,564**	1,744,108	3,631,730	**1,830,630**	1,166,741	2,643,627	**4,455,194**	2,910,849	6,275,357

6.1.2. Age- and sex-specific prevalence of diabetes and numbers of diabetic individuals

6.1.2.1. Results based on scenario 1: population aged 25-64 years, with capping

Table **6.6** summarises the estimated prevalence rates of diabetes during 1992-2013 for each age group in men and women aged 25-64 years, assuming capped trends in the projected obesity prevalence. The highest relative increase in the estimated diabetes prevalence was in men aged 25-34 years, where it increased substantially by 759%; from 3.7% (UI: 3.0–4.4%) in 1992 to 31.8% (UI: 26.5–36.2%) in 2013. The second highest relative increase in the estimated diabetes prevalence was in women aged 25-34 years (717%), followed by women aged 35-44 years (468%) and men aged 35-44 years (360%). On the other hand, the lowest relative increase was in men aged 55-64 years, where the diabetes prevalence increased by 27%; from 24.9% (UI: 19.9–29.9%) in 1992 to 31.7% (UI: 25.9–37.6%) in 2013. In 2013, the highest estimated diabetes prevalence was 48.6% (UI: 37.2–60.1%) in women aged 55-64 years, followed by a prevalence of 34.0% (UI: 26.8–41.3%) in women aged 45-54 years, while the lowest prevalence was estimated to be 24.5% (UI: 20.1–28.8%) in women aged 25-34 years.

6.1.2.2. Results based on scenario 2: population aged 25-64 years, without capping

The results based on this scenario are presented in Table **6.7**. The highest relative increase in the estimated diabetes prevalence remained as with scenario 1, where men aged 25-34 years had a relative increase of 759%. The second highest relative increase (717%) was also in women aged 25-34 years, in whom the estimated prevalence increased from 3.0% (UI: 2.4–3.6%) in 1992 to 24.5% (UI: 20.1–28.8%) in 2013. The lowest estimated relative increase was again identical to that in scenario 1 (27%) in men aged 55-64 years. In 2013, women aged 55-64 years had the highest estimated diabetes prevalence of 50.2% (UI: 38.0–62.7%), followed by women aged 45-54 years, who had a prevalence of 36.9% (UI: 28.6–45.4%). The lowest estimated diabetes prevalence in 2013 was the same as that estimated through scenario 1, i.e. in women aged 25-34 years [24.5% (UI: 20.1–28.8%)].

Table **6.8** and Table **6.9** present the lower and higher uncertainty values of the estimated diabetes prevalence for each age group in men and women aged 25-64 years, based on scenario 1 and scenario 2. Moreover, Figure **6.9** and Figure **6.10** illustrate a graphical presentation of the trends in the estimated diabetes prevalence over the time period of 1992-2013 for men and women by age group, based on these two scenarios.

Table 6.6. *(Scenario 1)* Estimated prevalence of diabetes per age group (years) in men and women aged 25-64 years, with capping of projected obesity prevalence, Saudi Arabia (1992-2013)

Year	25-34		35-44		45-54		55-64	
	Men	Women	Men	Women	Men	Women	Men	Women
1992	3.7%	3.0%	7.0%	5.0%	21.1%	22.1%	24.9%	23.2%
1993	4.8%	4.0%	8.1%	6.0%	20.5%	21.6%	25.0%	22.6%
1994	6.0%	5.1%	9.3%	7.0%	20.2%	21.3%	25.2%	22.2%
1995	7.3%	6.4%	10.5%	8.1%	20.2%	21.3%	25.6%	22.1%
1996	8.7%	7.7%	11.8%	9.3%	20.4%	21.6%	26.1%	22.4%
1997	10.1%	9.2%	13.1%	10.6%	20.7%	22.1%	26.8%	22.9%
1998	11.7%	10.7%	14.5%	12.0%	21.3%	22.7%	27.6%	23.8%
1999	13.2%	12.1%	15.8%	13.3%	21.9%	23.4%	28.4%	24.8%
2000	14.6%	13.3%	17.1%	14.6%	22.5%	24.2%	29.2%	25.8%
2001	16.0%	14.5%	18.3%	15.9%	23.1%	25.0%	30.1%	26.9%
2002	17.4%	15.5%	19.5%	17.1%	23.8%	25.9%	31.0%	28.2%
2003	18.7%	16.4%	20.7%	18.3%	24.5%	26.8%	32.0%	30.0%
2004	20.0%	17.3%	21.9%	19.5%	25.3%	27.9%	33.0%	32.0%
2005	21.5%	18.2%	23.2%	20.5%	25.5%	28.1%	31.6%	33.3%
2006	23.0%	19.0%	24.4%	21.4%	25.9%	28.6%	30.8%	35.0%
2007	24.4%	19.8%	25.6%	22.4%	26.4%	29.3%	30.4%	37.0%
2008	25.7%	20.6%	26.7%	23.4%	27.0%	30.2%	30.5%	39.3%
2009	27.0%	21.4%	27.8%	24.5%	27.7%	31.1%	30.8%	41.6%
2010	28.3%	22.1%	28.8%	25.6%	28.5%	32.0%	31.4%	44.1%
2011	29.5%	22.9%	30.0%	26.5%	29.1%	32.4%	31.1%	45.9%
2012	30.6%	23.7%	31.1%	27.4%	29.8%	32.9%	31.3%	47.5%
2013	31.8%	24.5%	32.2%	28.4%	30.5%	34.0%	31.7%	48.6%
Relative difference in prevalence	**+759%**	**+717%**	**+360%**	**+468%**	**+45%**	**+54%**	**+27%**	**+109%**

Table 6.7. *(Scenario 2)* Estimated prevalence of diabetes per age group (years) in men and women aged 25-64 years, without capping of projected obesity prevalence, Saudi Arabia (1992-2013)

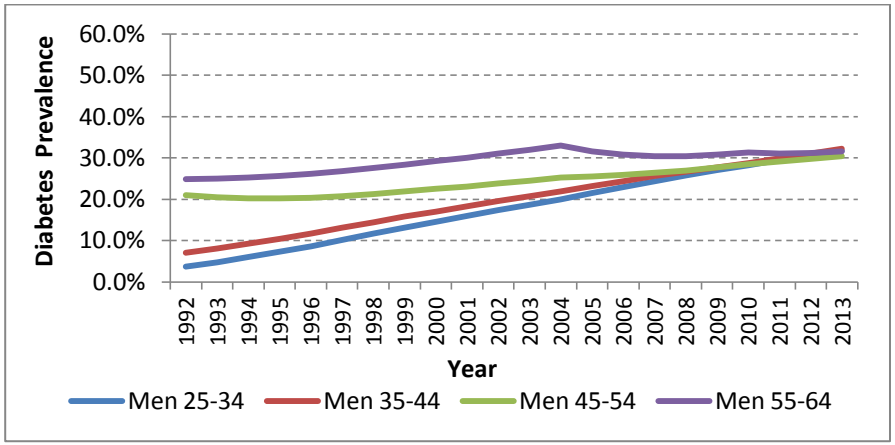
Year	25-34		35-44		45-54		55-64	
	Men	Women	Men	Women	Men	Women	Men	Women
1992	3.7%	3.0%	7.0%	5.0%	21.1%	22.1%	24.9%	23.2%
1993	4.8%	4.0%	8.1%	6.0%	20.5%	21.6%	25.0%	22.6%
1994	6.0%	5.1%	9.3%	7.0%	20.2%	21.3%	25.2%	22.2%
1995	7.3%	6.4%	10.5%	8.1%	20.2%	21.3%	25.6%	22.1%
1996	8.7%	7.7%	11.8%	9.3%	20.4%	21.6%	26.1%	22.4%
1997	10.1%	9.2%	13.1%	10.6%	20.7%	22.1%	26.8%	22.9%
1998	11.7%	10.7%	14.5%	12.0%	21.3%	22.7%	27.6%	23.8%
1999	13.2%	12.1%	15.8%	13.3%	21.9%	23.4%	28.4%	24.8%
2000	14.6%	13.3%	17.1%	14.6%	22.5%	24.2%	29.2%	25.8%
2001	16.0%	14.5%	18.3%	15.9%	23.1%	25.0%	30.1%	26.9%
2002	17.4%	15.5%	19.5%	17.1%	23.8%	25.9%	31.0%	28.2%
2003	18.7%	16.4%	20.7%	18.3%	24.5%	26.8%	32.0%	30.0%
2004	20.0%	17.3%	21.9%	19.5%	25.3%	27.9%	33.0%	32.0%
2005	21.5%	18.2%	23.2%	20.5%	25.5%	28.1%	31.6%	33.3%
2006	23.0%	19.0%	24.4%	21.4%	25.9%	28.6%	30.8%	35.0%
2007	24.4%	19.8%	25.6%	22.4%	26.4%	29.4%	30.4%	37.0%
2008	25.7%	20.6%	26.8%	23.4%	27.0%	30.4%	30.5%	39.3%
2009	27.0%	21.4%	27.9%	24.5%	27.7%	31.5%	30.8%	41.6%
2010	28.3%	22.1%	29.0%	25.6%	28.5%	32.9%	31.4%	44.1%
2011	29.5%	22.9%	30.3%	26.7%	29.2%	33.8%	31.1%	46.1%
2012	30.6%	23.7%	31.6%	27.8%	29.9%	34.9%	31.3%	48.3%
2013	31.8%	24.5%	32.9%	29.0%	30.8%	36.9%	31.7%	50.2%
Relative difference in prevalence	**+759%**	**+717%**	**+370%**	**+480%**	**+46%**	**+67%**	**+27%**	**+116%**

Table 6.8. *(Scenario 1)* Sensitivity analysis: lower (L) and higher (H) uncertainty values of the estimated diabetes prevalence (%) per age group (years) in men and women aged 25-64 years, with capping of projected obesity prevalence, Saudi Arabia (1992-2013)

Year	25-34				35-44				45-54				55-64			
	Men		Women		Men		Women		Men		Women		Men		Women	
	L	H	L	H	L	H	L	H	L	H	L	H	L	H	L	H
1992	3.0	4.4	2.4	3.6	5.6	8.4	4.0	6.0	16.8	25.3	17.7	26.5	19.9	29.9	18.6	27.9
1993	3.9	5.7	3.2	4.8	6.5	9.6	4.8	7.1	16.6	24.3	17.4	25.7	20.3	29.5	18.3	26.7
1994	4.8	7.2	4.1	6.1	7.5	11.0	5.6	8.3	16.5	23.6	17.4	25.2	20.8	29.3	18.2	26.1
1995	5.8	8.7	5.1	7.6	8.5	12.4	6.5	9.6	16.6	23.4	17.5	25.1	21.3	29.4	18.3	25.8
1996	6.9	10.4	6.1	9.3	9.5	13.9	7.5	11.1	16.8	23.5	17.8	25.3	21.9	29.7	18.6	26.0
1997	8.0	12.2	7.2	11.1	10.6	15.5	8.5	12.7	17.2	23.9	18.2	25.8	22.6	30.2	19.1	26.7
1998	9.2	14.1	8.4	13.0	11.7	17.1	9.6	14.4	17.7	24.5	18.7	26.6	23.3	31.0	19.7	27.7
1999	10.4	15.9	9.5	14.7	12.7	18.7	10.6	16.0	18.2	25.2	19.3	27.5	24.1	31.9	20.5	28.9
2000	11.6	17.6	10.5	16.2	13.7	20.2	11.6	17.5	18.7	25.9	19.9	28.4	24.9	32.8	21.3	30.2
2001	12.7	19.2	11.4	17.5	14.7	21.7	12.6	19.1	19.3	26.6	20.5	29.4	25.7	33.7	22.1	31.7
2002	13.8	20.8	12.2	18.7	15.7	23.1	13.6	20.5	19.8	27.3	21.2	30.4	26.5	34.8	23.1	33.3
2003	14.9	22.3	13.0	19.7	16.7	24.5	14.6	22.0	20.4	28.2	22.0	31.6	27.4	35.9	24.3	35.6
2004	16.0	23.7	13.8	20.7	17.7	25.8	15.5	23.5	21.1	29.1	22.8	33.0	28.2	37.0	25.7	38.5
2005	17.3	25.4	14.6	21.7	18.7	27.3	16.3	24.6	21.2	29.4	22.9	33.3	27.0	35.5	26.4	40.6
2006	18.6	27.0	15.3	22.6	19.8	28.7	17.0	25.7	21.5	29.8	23.2	34.0	26.2	34.7	27.5	43.1
2007	19.8	28.5	16.0	23.5	20.8	30.1	17.8	26.9	21.9	30.5	23.6	35.0	25.8	34.6	28.7	46.1
2008	21.0	30.0	16.7	24.4	21.8	31.3	18.6	28.2	22.4	31.3	24.2	36.1	25.7	35.0	30.2	49.2
2009	22.2	31.4	17.3	25.3	22.7	32.5	19.5	29.5	22.9	32.2	24.8	37.3	25.8	35.6	31.8	52.4
2010	23.3	32.7	18.0	26.1	23.6	33.5	20.3	30.7	23.5	33.2	25.5	38.5	26.1	36.5	33.5	55.5
2011	24.4	33.9	18.7	27.0	24.6	34.8	21.1	31.8	24.0	34.0	25.7	39.0	25.8	36.4	34.8	57.5
2012	25.5	35.1	19.4	27.9	25.7	36.0	21.8	32.9	24.5	34.8	26.1	39.7	25.7	36.9	36.1	59.1
2013	26.5	36.2	20.1	28.8	26.7	37.1	22.6	34.1	25.0	35.7	26.8	41.3	25.9	37.6	37.2	60.1

Table 6.9. *(Scenario 2)* Sensitivity analysis: lower (L) and higher (H) uncertainty values of the estimated diabetes prevalence (%) per age group (years) in men and women aged 25-64 years, without capping of projected obesity prevalence, Saudi Arabia (1992-2013)

Year	25-34				35-44				45-54				55-64			
	Men		Women		Men		Women		Men		Women		Men		Women	
	L	H	L	H	L	H	L	H	L	H	L	H	L	H	L	H
1992	3.0	4.4	2.4	3.6	5.6	8.4	4.0	6.0	16.8	25.3	17.7	26.5	19.9	29.9	18.6	27.9
1993	3.9	5.7	3.2	4.8	6.5	9.6	4.8	7.1	16.6	24.3	17.4	25.7	20.3	29.5	18.3	26.8
1994	4.8	7.2	4.1	6.1	7.5	11.0	5.6	8.3	16.5	23.6	17.4	25.2	20.8	29.3	18.2	26.1
1995	5.8	8.7	5.1	7.6	8.5	12.4	6.5	9.6	16.6	23.4	17.5	25.1	21.3	29.4	18.3	25.8
1996	6.9	10.4	6.1	9.3	9.5	13.9	7.5	11.1	16.8	23.5	17.8	25.3	21.9	29.7	18.6	26.0
1997	8.0	12.2	7.2	11.1	10.6	15.5	8.5	12.7	17.2	23.9	18.2	25.8	22.6	30.2	19.1	26.7
1998	9.2	14.1	8.4	13.0	11.7	17.1	9.6	14.4	17.7	24.5	18.7	26.6	23.3	31.0	19.7	27.7
1999	10.4	15.9	9.5	14.7	12.7	18.7	10.6	16.0	18.2	25.2	19.3	27.5	24.1	31.9	20.5	28.9
2000	11.6	17.6	10.5	16.2	13.7	20.2	11.6	17.5	18.7	25.9	19.9	28.4	24.9	32.8	21.3	30.2
2001	12.7	19.2	11.4	17.5	14.7	21.7	12.6	19.0	19.3	26.6	20.5	29.4	25.7	33.7	22.1	31.7
2002	13.8	20.8	12.2	18.7	15.7	23.1	13.6	20.5	19.8	27.3	21.2	30.4	26.5	34.8	23.1	33.3
2003	14.9	22.3	13.0	19.7	16.7	24.5	14.6	22.0	20.4	28.2	22.0	31.6	27.4	35.9	24.3	35.6
2004	16.0	23.7	13.8	20.7	17.7	25.8	15.5	23.5	21.1	29.1	22.8	33.0	28.2	37.0	25.7	38.5
2005	17.3	25.4	14.6	21.7	18.7	27.3	16.3	24.6	21.2	29.4	22.9	33.3	27.0	35.5	26.4	40.6
2006	18.6	27.0	15.3	22.6	19.8	28.7	17.0	25.7	21.5	29.8	23.2	34.0	26.2	34.7	27.5	43.1
2007	19.8	28.5	16.0	23.5	20.8	30.1	17.8	26.9	21.9	30.5	23.7	35.0	25.8	34.6	28.7	46.1
2008	21.0	30.0	16.7	24.4	21.8	31.4	18.6	28.2	22.4	31.3	24.3	36.4	25.7	35.0	30.2	49.2
2009	22.2	31.4	17.3	25.3	22.7	32.6	19.5	29.5	22.9	32.2	25.1	37.9	25.8	35.6	31.8	52.4
2010	23.3	32.7	18.0	26.1	23.7	33.8	20.4	30.8	23.5	33.3	26.1	39.8	26.1	36.5	33.5	55.5
2011	24.4	33.9	18.7	27.0	24.8	35.3	21.2	32.1	24.0	34.1	26.6	41.0	25.8	36.4	34.9	57.9
2012	25.5	35.1	19.4	27.9	26.0	36.7	22.0	33.4	24.6	35.0	27.3	42.5	25.7	36.9	36.5	60.5
2013	26.5	36.2	20.1	28.8	27.1	38.2	23.0	35.0	25.2	36.2	28.6	45.4	25.9	37.6	38.0	62.7



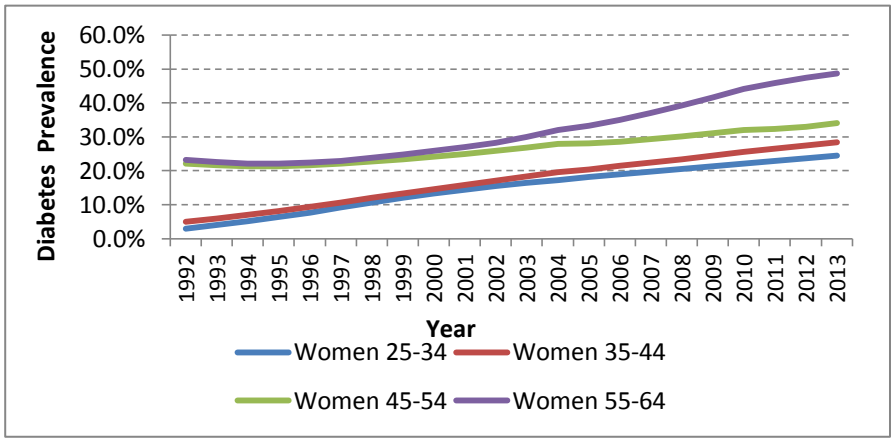
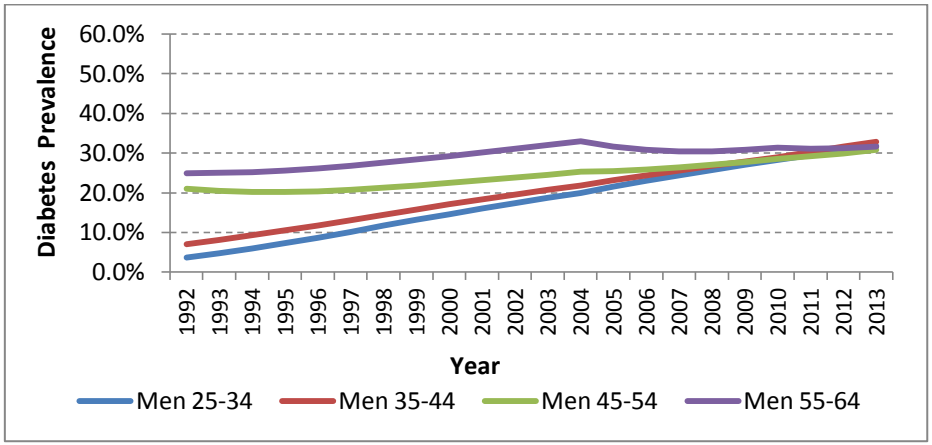


Figure 6.9. *(Scenario 1)* Trends in the estimated prevalence of diabetes per age group (years) in men and women aged 25-64 years, with capping of projected obesity prevalence, Saudi Arabia (1992-2013) [Diagnostic criteria: WHO 1985]



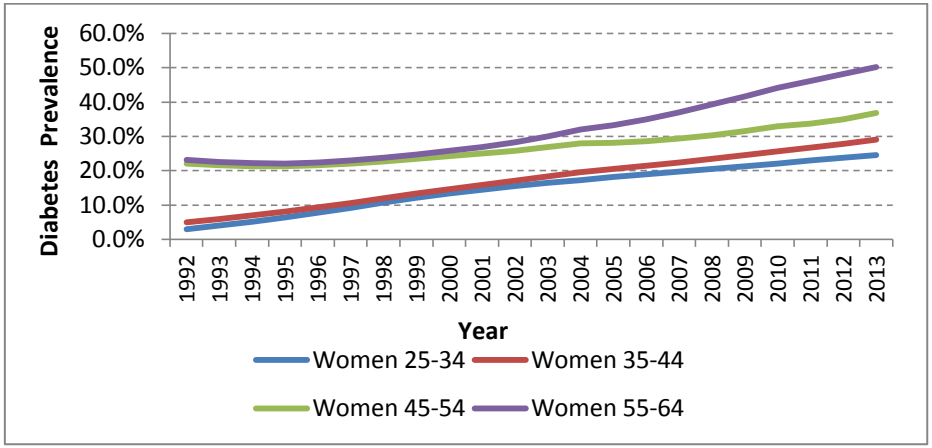


Figure 6.10. *(Scenario 2)* Trends in the estimated prevalence of diabetes per age group (years) in men and women aged 25-64 years, without capping of projected obesity prevalence, Saudi Arabia (1992-2013) [Diagnostic criteria: WHO 1985]

6.1.2.3. Results based on scenario 3: population aged 25-75+ years, with capping

As shown in Table **6.10**, inclusion of the two oldest age groups (65-74 and 75+ years) resulted in an estimated relative increase of 60% in the diabetes prevalence among women aged 65-74 years; from 24.4% (UI: 19.5–29.2%) in 1992 to 39.0% (UI: 32.1–46.1%) in 2013. On the other hand, women aged 75+ years showed minor fluctuations in the results of diabetes prevalence during the same period, with no difference in the estimated prevalence for 1992 and 2013.

6.1.2.4. Results based on scenario 4: population aged 25-75+ years, without capping

The assumption of continuing uncapped linearity in obesity trends had no effect on the results for the two oldest age groups. As presented in Table **6.11**, scenario 4 produced similar results to that obtained by assuming scenario 3.

Table **6.12** and Table **6**.**13** summarise the minimum and maximum uncertainty values in the estimated diabetes prevalence for each sex and age group, based on scenarios 3 and 4. In addition, Figure **6.11** and Figure **6**.**12** presented the trend lines of prevalence obtained by these two scenarios for each age group in men and women.

Table 6.10. *(Scenario 3)* Estimated prevalence of diabetes per age group (years) in men and women aged 25-75+ years, with capping of projected obesity prevalence, Saudi Arabia (1992-2013)

Year	25-34		35-44		45-54		55-64		65-74		75+	
	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
1992	3.7%	3.0%	7.0%	5.0%	21.1%	22.1%	24.9%	23.2%	28.8%	24.4%	28.8%	24.4%
1993	4.8%	4.0%	8.1%	6.0%	20.5%	21.6%	25.0%	22.6%	28.4%	22.7%	29.0%	23.4%
1994	6.0%	5.1%	9.3%	7.0%	20.2%	21.3%	25.2%	22.2%	28.2%	21.6%	29.2%	22.5%
1995	7.3%	6.4%	10.5%	8.1%	20.2%	21.3%	25.6%	22.1%	28.1%	21.0%	29.4%	21.7%
1996	8.7%	7.7%	11.8%	9.3%	20.4%	21.6%	26.1%	22.4%	28.1%	20.9%	29.6%	21.1%
1997	10.1%	9.2%	13.1%	10.6%	20.7%	22.1%	26.8%	22.9%	28.3%	21.4%	29.7%	20.9%
1998	11.7%	10.7%	14.5%	12.0%	21.3%	22.7%	27.6%	23.8%	28.6%	22.3%	29.9%	21.0%
1999	13.2%	12.1%	15.8%	13.3%	21.9%	23.4%	28.4%	24.8%	29.0%	23.7%	30.1%	21.2%
2000	14.6%	13.3%	17.1%	14.6%	22.5%	24.2%	29.2%	25.8%	29.5%	25.4%	30.3%	21.7%
2001	16.0%	14.5%	18.3%	15.9%	23.1%	25.0%	30.1%	26.9%	30.1%	27.4%	30.5%	22.4%
2002	17.4%	15.5%	19.5%	17.1%	23.8%	25.9%	31.0%	28.2%	30.7%	29.5%	30.7%	23.0%
2003	18.7%	16.4%	20.7%	18.3%	24.5%	26.8%	32.0%	30.0%	31.3%	31.1%	30.9%	23.4%
2004	20.0%	17.3%	21.9%	19.5%	25.3%	27.9%	33.0%	32.0%	31.9%	32.5%	31.1%	23.8%
2005	21.5%	18.2%	23.2%	20.5%	25.5%	28.1%	31.6%	33.3%	31.6%	33.4%	31.8%	23.5%
2006	23.0%	19.0%	24.4%	21.4%	25.9%	28.6%	30.8%	35.0%	31.5%	34.3%	32.4%	23.4%
2007	24.4%	19.8%	25.6%	22.4%	26.4%	29.3%	30.4%	37.0%	31.5%	35.1%	32.9%	23.4%
2008	25.7%	20.6%	26.7%	23.4%	27.0%	30.2%	30.5%	39.3%	31.5%	36.0%	33.4%	23.5%
2009	27.0%	21.4%	27.8%	24.5%	27.7%	31.1%	30.8%	41.6%	31.6%	36.8%	33.8%	23.7%
2010	28.3%	22.1%	28.8%	25.6%	28.5%	32.0%	31.4%	44.1%	31.8%	37.6%	34.2%	23.9%
2011	29.5%	22.9%	30.0%	26.5%	29.1%	32.4%	31.1%	45.9%	31.4%	37.9%	33.7%	24.0%
2012	30.6%	23.7%	31.1%	27.4%	29.8%	32.9%	31.3%	47.5%	31.1%	38.3%	33.3%	24.2%
2013	31.8%	24.5%	32.2%	28.4%	30.5%	34.0%	31.7%	48.6%	31.0%	39.0%	33.0%	24.4%
Relative difference in prevalence	**+759%**	**+717%**	**+360%**	**+468%**	**+45%**	**+54%**	**+27%**	**+109%**	**+8%**	**+60%**	**+15%**	**+0%**

Table 6.11. *(Scenario 4)* Estimated prevalence of diabetes per age group (years) in men and women aged 25-75+ years, without capping of projected obesity prevalence, Saudi Arabia (1992-2013)

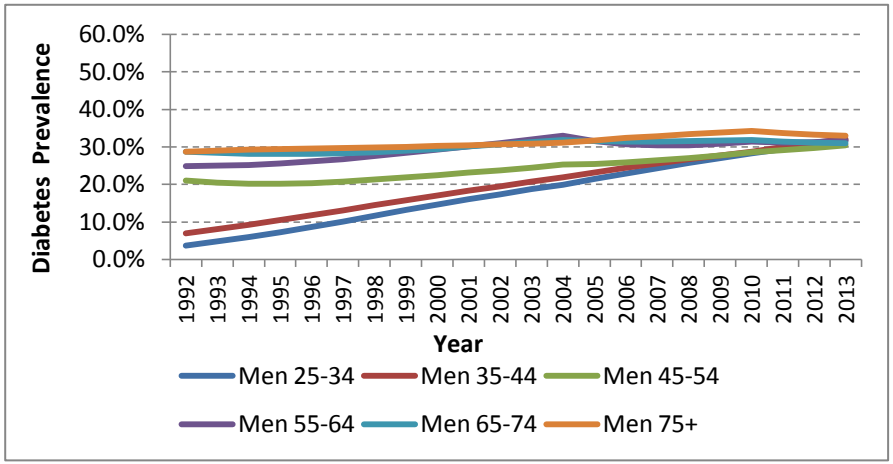
Year	25-34		35-44		45-54		55-64		65-74		75+	
	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
1992	3.7%	3.0%	7.0%	5.0%	21.1%	22.1%	24.9%	23.2%	28.8%	24.4%	28.8%	24.4%
1993	4.8%	4.0%	8.1%	6.0%	20.5%	21.6%	25.0%	22.6%	28.4%	22.7%	29.0%	23.4%
1994	6.0%	5.1%	9.3%	7.0%	20.2%	21.3%	25.2%	22.2%	28.2%	21.6%	29.2%	22.5%
1995	7.3%	6.4%	10.5%	8.1%	20.2%	21.3%	25.6%	22.1%	28.1%	21.0%	29.4%	21.7%
1996	8.7%	7.7%	11.8%	9.3%	20.4%	21.6%	26.1%	22.4%	28.1%	20.9%	29.6%	21.1%
1997	10.1%	9.2%	13.1%	10.6%	20.7%	22.1%	26.8%	22.9%	28.3%	21.4%	29.7%	20.9%
1998	11.7%	10.7%	14.5%	12.0%	21.3%	22.7%	27.6%	23.8%	28.6%	22.3%	29.9%	21.0%
1999	13.2%	12.1%	15.8%	13.3%	21.9%	23.4%	28.4%	24.8%	29.0%	23.7%	30.1%	21.2%
2000	14.6%	13.3%	17.1%	14.6%	22.5%	24.2%	29.2%	25.8%	29.5%	25.4%	30.3%	21.7%
2001	16.0%	14.5%	18.3%	15.9%	23.1%	25.0%	30.1%	26.9%	30.1%	27.4%	30.5%	22.4%
2002	17.4%	15.5%	19.5%	17.1%	23.8%	25.9%	31.0%	28.2%	30.7%	29.5%	30.7%	23.0%
2003	18.7%	16.4%	20.7%	18.3%	24.5%	26.8%	32.0%	30.0%	31.3%	31.1%	30.9%	23.4%
2004	20.0%	17.3%	21.9%	19.5%	25.3%	27.9%	33.0%	32.0%	31.9%	32.5%	31.1%	23.8%
2005	21.5%	18.2%	23.2%	20.5%	25.5%	28.1%	31.6%	33.3%	31.6%	33.4%	31.8%	23.5%
2006	23.0%	19.0%	24.4%	21.4%	25.9%	28.6%	30.8%	35.0%	31.5%	34.3%	32.4%	23.4%
2007	24.4%	19.8%	25.6%	22.4%	26.4%	29.4%	30.4%	37.0%	31.5%	35.1%	32.9%	23.4%
2008	25.7%	20.6%	26.8%	23.4%	27.0%	30.4%	30.5%	39.3%	31.5%	36.0%	33.4%	23.5%
2009	27.0%	21.4%	27.9%	24.5%	27.7%	31.5%	30.8%	41.6%	31.6%	36.8%	33.8%	23.7%
2010	28.3%	22.1%	29.0%	25.6%	28.5%	32.9%	31.4%	44.1%	31.8%	37.6%	34.2%	23.9%
2011	29.5%	22.9%	30.3%	26.7%	29.2%	33.8%	31.1%	46.1%	31.4%	37.9%	33.7%	24.0%
2012	30.6%	23.7%	31.6%	27.8%	29.9%	34.9%	31.3%	48.3%	31.1%	38.3%	33.3%	24.2%
2013	31.8%	24.5%	32.9%	29.0%	30.8%	36.9%	31.7%	50.2%	31.0%	39.0%	33.0%	24.4%
Relative difference in prevalence	**+759%**	**+717%**	**+370%**	**+480%**	**+46%**	**+67%**	**+27%**	**+116%**	**+8%**	**+60%**	**+15%**	**+0%**

Table 6.12. *(Scenario 3)* Sensitivity analysis: lower (L) and higher (H) uncertainty values of the estimated diabetes prevalence (%) per age group (years) in men and women aged 25-75+ years, with capping of projected obesity prevalence, Saudi Arabia (1992-2013)

Year	25-34				35-44				45-54				55-64				65-74				75+			
	Men		Women		Men		Women		Men		Women		Men		Women		Men		Women		Men		Women	
	L	H	L	H	L	H	L	H	L	H	L	H	L	H	L	H	L	H	L	H	L	H	L	H
1992	3.0	4.4	2.4	3.6	5.6	8.4	4.0	6.0	16.8	25.3	17.7	26.5	19.9	29.9	18.6	27.9	23.0	34.5	19.5	29.2	23.0	34.5	19.5	29.2
1993	3.9	5.7	3.2	4.8	6.5	9.6	4.8	7.1	16.6	24.3	17.4	25.7	20.3	29.5	18.3	26.7	23.1	33.3	18.7	26.5	23.5	34.2	19.7	25.8
1994	4.8	7.2	4.1	6.1	7.5	11.0	5.6	8.3	16.5	23.6	17.4	25.2	20.8	29.3	18.2	26.1	23.3	32.4	18.1	24.6	24.1	33.7	19.9	22.8
1995	5.8	8.7	5.1	7.6	8.5	12.4	6.5	9.6	16.6	23.4	17.5	25.1	21.3	29.4	18.3	25.8	23.6	31.6	17.9	23.4	24.6	33.2	20.0	20.6
1996	6.9	10.4	6.1	9.3	9.5	13.9	7.5	11.1	16.8	23.5	17.8	25.3	21.9	29.7	18.6	26.0	23.9	31.1	18.1	23.2	25.0	32.6	20.3	19.5
1997	8.0	12.2	7.2	11.1	10.6	15.5	8.5	12.7	17.2	23.9	18.2	25.8	22.6	30.2	19.1	26.7	24.3	30.8	18.5	23.9	25.5	32.1	20.5	19.2
1998	9.2	14.1	8.4	13.0	11.7	17.1	9.6	14.4	17.7	24.5	18.7	26.6	23.3	31.0	19.7	27.7	24.8	30.8	19.1	25.3	26.0	31.7	20.8	19.5
1999	10.4	15.9	9.5	14.7	12.7	18.7	10.6	16.0	18.2	25.2	19.3	27.5	24.1	31.9	20.5	28.9	25.3	31.0	20.1	27.3	26.5	31.4	21.2	20.2
2000	11.6	17.6	10.5	16.2	13.7	20.2	11.6	17.5	18.7	25.9	19.9	28.4	24.9	32.8	21.3	30.2	25.9	31.5	21.2	29.8	26.9	31.2	21.7	21.3
2001	12.7	19.2	11.4	17.5	14.7	21.7	12.6	19.1	19.3	26.6	20.5	29.4	25.7	33.7	22.1	31.7	26.5	32.2	22.6	32.6	27.4	31.2	22.2	22.5
2002	13.8	20.8	12.2	18.7	15.7	23.1	13.6	20.5	19.8	27.3	21.2	30.4	26.5	34.8	23.1	33.3	27.1	32.9	24.1	35.3	27.8	31.1	22.6	23.4
2003	14.9	22.3	13.0	19.7	16.7	24.5	14.6	22.0	20.4	28.2	22.0	31.6	27.4	35.9	24.3	35.6	27.8	33.5	25.4	37.1	28.2	31.1	23.0	24.0
2004	16.0	23.7	13.8	20.7	17.7	25.8	15.5	23.5	21.1	29.1	22.8	33.0	28.2	37.0	25.7	38.5	28.4	34.1	26.5	38.5	28.6	31.2	23.4	24.5
2005	17.3	25.4	14.6	21.7	18.7	27.3	16.3	24.6	21.2	29.4	22.9	33.3	27.0	35.5	26.4	40.6	28.2	33.8	27.3	39.4	29.4	31.7	23.1	24.2
2006	18.6	27.0	15.3	22.6	19.8	28.7	17.0	25.7	21.5	29.8	23.2	34.0	26.2	34.7	27.5	43.1	28.1	33.6	28.1	40.3	30.2	32.1	22.9	24.2
2007	19.8	28.5	16.0	23.5	20.8	30.1	17.8	26.9	21.9	30.5	23.6	35.0	25.8	34.6	28.7	46.1	28.1	33.6	28.9	41.3	30.9	32.5	22.8	24.4
2008	21.0	30.0	16.7	24.4	21.8	31.3	18.6	28.2	22.4	31.3	24.2	36.1	25.7	35.0	30.2	49.2	28.2	33.7	29.6	42.2	31.6	32.8	22.8	24.6
2009	22.2	31.4	17.3	25.3	22.7	32.5	19.5	29.5	22.9	32.2	24.8	37.3	25.8	35.6	31.8	52.4	28.3	33.9	30.4	43.2	32.2	33.1	22.9	24.9
2010	23.3	32.7	18.0	26.1	23.6	33.5	20.3	30.7	23.5	33.2	25.5	38.5	26.1	36.5	33.5	55.5	28.5	34.2	31.1	44.2	32.7	33.4	23.0	25.2
2011	24.4	33.9	18.7	27.0	24.6	34.8	21.1	31.8	24.0	34.0	25.7	39.0	25.8	36.4	34.8	57.5	28.1	33.8	31.3	44.5	32.5	32.8	23.0	25.4
2012	25.5	35.1	19.4	27.9	25.7	36.0	21.8	32.9	24.5	34.8	26.1	39.7	25.7	36.9	36.1	59.1	27.9	33.6	31.7	45.2	32.2	32.3	23.0	25.6
2013	26.5	36.2	20.1	28.8	26.7	37.1	22.6	34.1	25.0	35.7	26.8	41.3	25.9	37.6	37.2	60.1	27.7	33.6	32.1	46.1	32.1	32.0	23.1	25.9

Table 6.13. *(Scenario 4)* Sensitivity analysis: lower (L) and higher (H) uncertainty values of the estimated diabetes prevalence (%) per age group (years) in men and women aged 25-75+ years, without capping of projected obesity prevalence, Saudi Arabia (1992-2013)

Year	25-34				35-44				45-54				55-64				65-74				75+			
	Men		Women		Men		Women		Men		Women		Men		Women		Men		Women		Men		Women	
	L	H	L	H	L	H	L	H	L	H	L	H	L	H	L	H	L	H	L	H	L	H	L	H
1992	3.0	4.4	2.4	3.6	5.6	8.4	4.0	6.0	16.8	25.3	17.7	26.5	19.9	29.9	18.6	27.9	23.0	34.5	19.5	29.2	23.0	34.5	19.5	29.2
1993	3.9	5.7	3.2	4.8	6.5	9.6	4.8	7.1	16.6	24.3	17.4	25.7	20.3	29.5	18.3	26.8	23.1	33.3	18.7	26.5	23.5	34.2	19.7	25.8
1994	4.8	7.2	4.1	6.1	7.5	11.0	5.6	8.3	16.5	23.6	17.4	25.2	20.8	29.3	18.2	26.1	23.3	32.4	18.1	24.6	24.1	33.7	19.9	22.8
1995	5.8	8.7	5.1	7.6	8.5	12.4	6.5	9.6	16.6	23.4	17.5	25.1	21.3	29.4	18.3	25.8	23.6	31.6	17.9	23.4	24.6	33.2	20.0	20.6
1996	6.9	10.4	6.1	9.3	9.5	13.9	7.5	11.1	16.8	23.5	17.8	25.3	21.9	29.7	18.6	26.0	23.9	31.1	18.1	23.2	25.0	32.6	20.3	19.5
1997	8.0	12.2	7.2	11.1	10.6	15.5	8.5	12.7	17.2	23.9	18.2	25.8	22.6	30.2	19.1	26.7	24.3	30.8	18.5	23.9	25.5	32.1	20.5	19.2
1998	9.2	14.1	8.4	13.0	11.7	17.1	9.6	14.4	17.7	24.5	18.7	26.6	23.3	31.0	19.7	27.7	24.8	30.8	19.1	25.3	26.0	31.7	20.8	19.5
1999	10.4	15.9	9.5	14.7	12.7	18.7	10.6	16.0	18.2	25.2	19.3	27.5	24.1	31.9	20.5	28.9	25.3	31.0	20.1	27.3	26.5	31.4	21.2	20.2
2000	11.6	17.6	10.5	16.2	13.7	20.2	11.6	17.5	18.7	25.9	19.9	28.4	24.9	32.8	21.3	30.2	25.9	31.5	21.2	29.8	26.9	31.2	21.7	21.3
2001	12.7	19.2	11.4	17.5	14.7	21.7	12.6	19.0	19.3	26.6	20.5	29.4	25.7	33.7	22.1	31.7	26.5	32.2	22.6	32.6	27.4	31.2	22.2	22.5
2002	13.8	20.8	12.2	18.7	15.7	23.1	13.6	20.5	19.8	27.3	21.2	30.4	26.5	34.8	23.1	33.3	27.1	32.9	24.1	35.3	27.8	31.1	22.6	23.4
2003	14.9	22.3	13.0	19.7	16.7	24.5	14.6	22.0	20.4	28.2	22.0	31.6	27.4	35.9	24.3	35.6	27.8	33.5	25.4	37.1	28.2	31.1	23.0	24.0
2004	16.0	23.7	13.8	20.7	17.7	25.8	15.5	23.5	21.1	29.1	22.8	33.0	28.2	37.0	25.7	38.5	28.4	34.1	26.5	38.5	28.6	31.2	23.4	24.5
2005	17.3	25.4	14.6	21.7	18.7	27.3	16.3	24.6	21.2	29.4	22.9	33.3	27.0	35.5	26.4	40.6	28.2	33.8	27.3	39.4	29.4	31.7	23.1	24.2
2006	18.6	27.0	15.3	22.6	19.8	28.7	17.0	25.7	21.5	29.8	23.2	34.0	26.2	34.7	27.5	43.1	28.1	33.6	28.1	40.3	30.2	32.1	22.9	24.2
2007	19.8	28.5	16.0	23.5	20.8	30.1	17.8	26.9	21.9	30.5	23.7	35.0	25.8	34.6	28.7	46.1	28.1	33.6	28.9	41.3	30.9	32.5	22.8	24.4
2008	21.0	30.0	16.7	24.4	21.8	31.4	18.6	28.2	22.4	31.3	24.3	36.4	25.7	35.0	30.2	49.2	28.2	33.7	29.6	42.2	31.6	32.8	22.8	24.6
2009	22.2	31.4	17.3	25.3	22.7	32.6	19.5	29.5	22.9	32.2	25.1	37.9	25.8	35.6	31.8	52.4	28.3	33.9	30.4	43.2	32.2	33.1	22.9	24.9
2010	23.3	32.7	18.0	26.1	23.7	33.8	20.4	30.8	23.5	33.3	26.1	39.8	26.1	36.5	33.5	55.5	28.5	34.2	31.1	44.2	32.7	33.4	23.0	25.2
2011	24.4	33.9	18.7	27.0	24.8	35.3	21.2	32.1	24.0	34.1	26.6	41.0	25.8	36.4	34.9	57.9	28.1	33.8	31.3	44.5	32.5	32.8	23.0	25.4
2012	25.5	35.1	19.4	27.9	26.0	36.7	22.0	33.4	24.6	35.0	27.3	42.5	25.7	36.9	36.5	60.5	27.9	33.6	31.7	45.2	32.2	32.3	23.0	25.6
2013	26.5	36.2	20.1	28.8	27.1	38.2	23.0	35.0	25.2	36.2	28.6	45.4	25.9	37.6	38.0	62.7	27.7	33.6	32.1	46.1	32.1	32.0	23.1	25.9



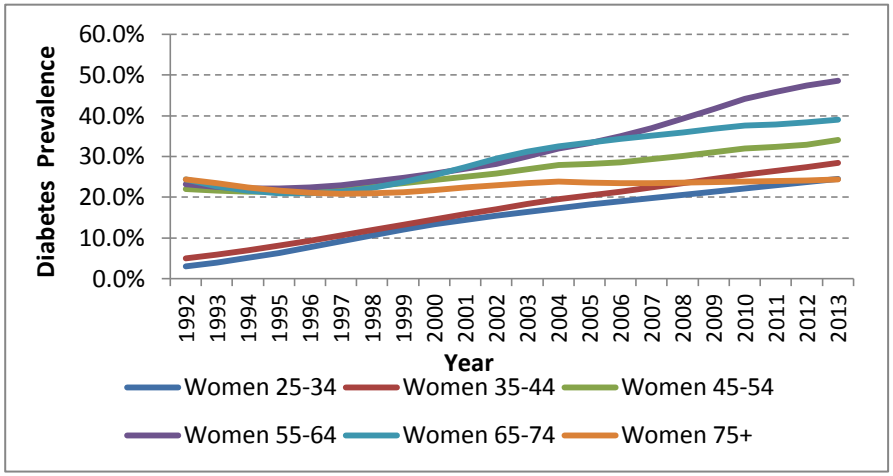
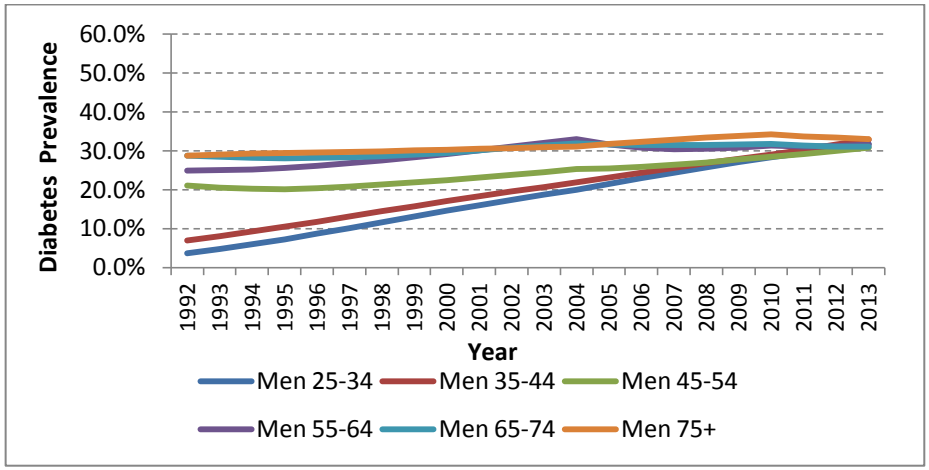


Figure 6.11. *(Scenario 3)* Trends in the estimated prevalence of diabetes per age group (years) in men and women aged 25-75+ years, with capping of projected obesity prevalence, Saudi Arabia (1992-2013) [Diagnostic criteria: WHO 1985]



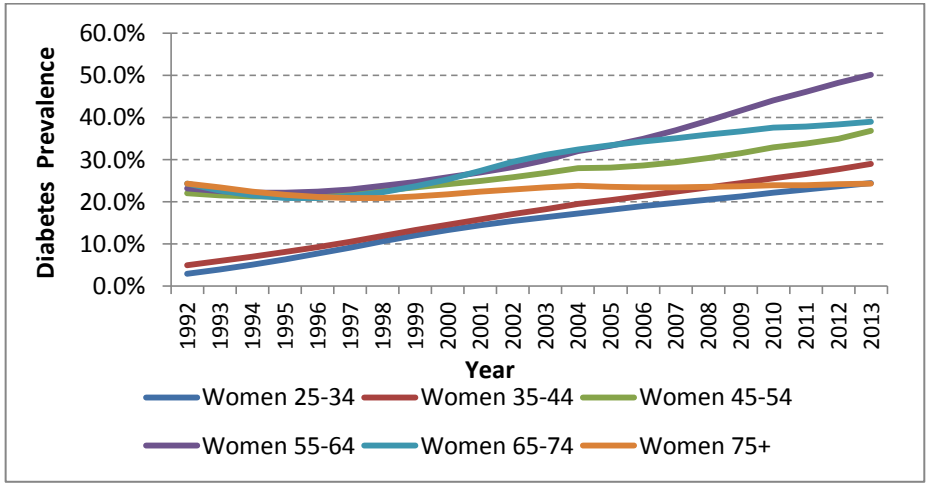


Figure 6.12. *(Scenario 4)* Trends in the estimated prevalence of diabetes per age group (years) in men and women aged 25-75+ years, without capping of projected obesity prevalence, Saudi Arabia (1992-2013) [Diagnostic criteria: WHO 1985]

6.1.3. Quantified effects of the assumed capping of obesity on the modelling results for 2013

Table **6.14** presents the main results of the Saudi IMPACT Diabetes Forecast Model for 2013 based on the different four scenarios described earlier, and provides a summary of the changes in diabetes prevalence estimates due to using different scenarios. The overall estimated population prevalence of diabetes in 2013 was 30.8% based on scenario 1, which calculated the results for the population aged 25-64 years and assumed capped trends in obesity at 35% in men and 60% in women. With scenario 2, the overall population prevalence in 2013 increased by 1.9% to reach 31.4%, by assuming continuous uncapped linear trends in obesity.

Also, the effects of shifting from scenario 1 to scenario 2 were minimal regarding the results of the overall estimated prevalence of diabetes in men and women. In men, the estimated prevalence in 2013 was 31.6% under scenario 1 and 31.9% under scenario 2. On the other hand, diabetes prevalence in women in 2013 was estimated at 29.8% under scenario 1, increasing by 2.7% to reach 30.6% under scenario 2.

Similarly, shifting from scenario 1 to scenario 2 resulted in no or minor relative increases in the estimated diabetes prevalence for each sex and age group. The highest relative increase was 8.5% for women aged 45-54, where the prevalence was 34.0% under scenario 1 and 36.9% under scenario 2.

In scenarios 3 and 4, estimates were calculated after the inclusion of the two age groups of 65-74 and 75+ years, with capped obesity trends in scenario 3 and uncapped trends in scenario 4. Again, shifting from scenario 3 to scenario 4 resulted in minor relative increases of the 2013 diabetes prevalence in the overall population (+1.6%), men (+0.6%) and women (+2.7%). Moreover, this shifting produced similar results of estimated prevalence in the two oldest age groups in men and women.

In general, capping of the assumed linear obesity trends in men and women of the Saudi population resulted in only minor reduction in the estimated prevalence of diabetes during the period of 1992-2013. The most prominent impact of capping was observed in women aged 45-54 years, who had the

highest ‘observed’ and ‘projected’ prevalence of obesity. The estimated prevalence of diabetes in this particular age group showed a relative decrease by around 8% with capping.

Table 6.14. Summary of the main modelling results (2013) for each scenario and the quantified changes as a result of shifting between different scenarios

	Scenario 1	Scenario 2	Quantified relative change (%) as a result of shifting from scenario 1 to scenario 2	Scenario 3	Scenario 4	Quantified relative change (%) as a result of shifting from scenario 3 to scenario 4
Overall population diabetes prevalence (%) in 2013	30.8	31.4	+ 1.9	31.0	31.5	+ 1.6
Overall diabetes prevalence (%) in men in 2013	31.6	31.9	+ 0.9	31.1	31.3	+ 0.6
Overall diabetes prevalence (%) in women in 2013	29.8	30.6	+ 2.7	30.1	30.9	+ 2.7
Estimated prevalence of diabetes (%) per sex and age group in 2013:						
Men 25-34 years	31.8	31.8	No change	31.8	31.8	No change
Men 35-44 years	32.2	32.9	+ 2.2	32.2	32.9	+ 2.2
Men 45-54 years	30.5	30.8	+ 1.0	30.5	30.8	+ 1.0
Men 55-64 years	31.7	31.7	No change	31.7	31.7	No change
Men 65-74 years	-	-	-	31.0	31.0	No change
Men 75+ years	-	-	-	33.0	33.0	No change
Women 25-34 years	24.5	24.5	No change	24.5	24.5	No change
Women 35-44 years	28.4	29.0	+ 2.1	28.4	29.0	+ 2.1
Women 45-54 years	34.0	36.9	+ 8.5	34.0	36.9	+ 8.5
Women 55-64 years	48.6	50.2	+ 3.3	48.6	50.2	+ 3.3
Women 65-74 years	-	-	-	39.0	39.0	No change
Women 75+ years	-	-	-	24.4	24.4	No change

6.2. Validation of the Saudi IMPACT Diabetes Forecast Model

As mentioned in chapter 4, validation is a very important step to test the degree of accuracy/ credibility of a model and to gain the acceptance of health care planners, decision makers and other potential users.[226, 265]

In this thesis, two types of validation were undertaken: a) validation against existing local 'observed' data; and b) concurrent (between-model) validation, where the model results were validated against another model estimating the same output parameter (the GBD model). Results of validation of the Saudi IMPACT Diabetes Forecast Model are discussed in the following two sections.

6.2.1. Validation against local observed data

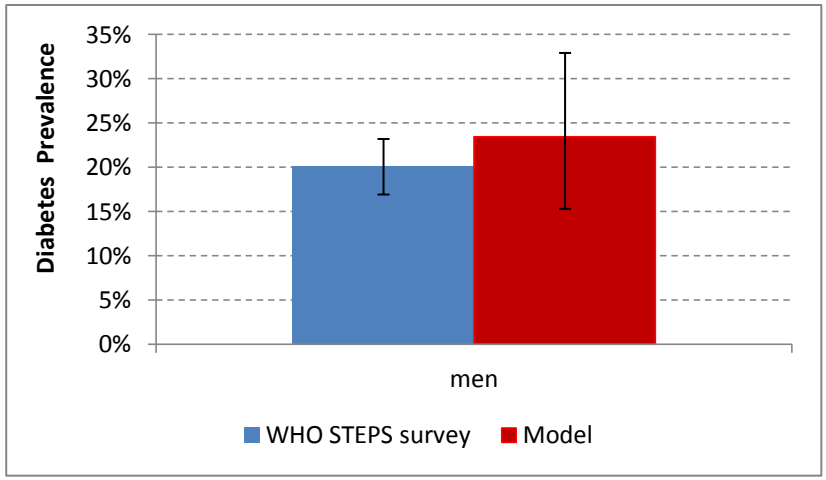
The results of diabetes prevalence as estimated by the model were compared with the 'observed' results from the WHO STEPS survey[19] in Saudi Arabia in 2005. Selection of this particular survey for validation purposes can be justified by two main reasons. First, it was the only available local survey that was not conducted over a 'range' of years. The results of the survey applied for 2005 only, and, therefore, there was no need to use the previously discussed assumption of the 'period midpoint' which was used for data from obesity and smoking surveys. Second, the study population in the WHO STEPS survey was as that covered by the Saudi IMPACT Diabetes Forecast Model (men and women aged 25-64 years). In the other surveys (summarised in Table **3.8**, chapter 3), results were reported using different population denominators with different age ranges (e.g. ≥14 years, ≥18 years, etc), which were not comparable to the model's age limits.

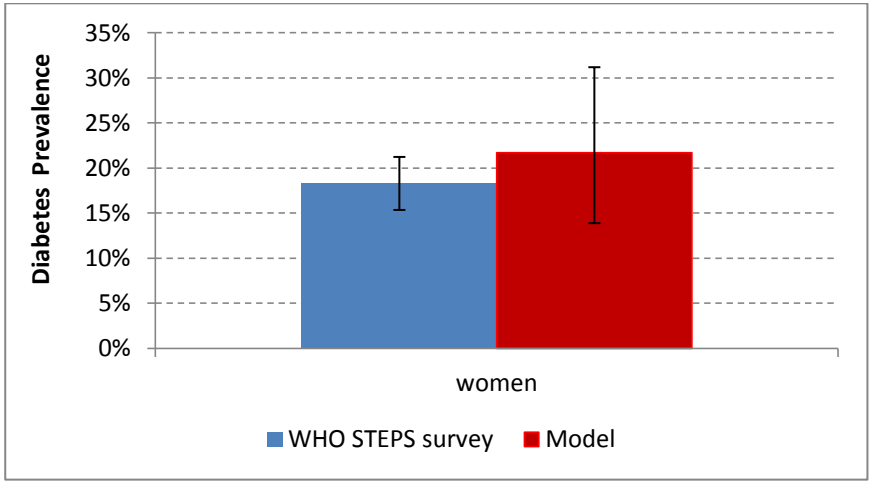
It is important to mention that the model results for 2005 were the same with and without capping of the obesity trends. Therefore, there was no difference in using scenario 1 or scenario 2 of the model for the purpose of validation against the STEPS survey.

Figure **6.13** illustrates the results of validation. The model estimated a diabetes prevalence of 23.0% (UI: 15.0–33.0%) in men aged 25-64 years in 2005, compared to 20.1% (95% CI: 16.9–23.2%) in the STEPS survey. In women, the estimated prevalence by the model was 21.7% (UI: 13.9–31.2%), compared to 18.3% (95% CI: 15.4–21.3%). The total population diabetes prevalence in 2005

was estimated by the model to be 22.8% (UI: 14.8–32.3%), compared to 19.2% (95% CI: 16.1–22.2%) by the STEPS survey.

In general, the model estimates of diabetes prevalence for 2005 were reasonably close to that of the WHO STEPS survey. However, the model tended to slightly overestimate the diabetes prevalence in men (by 2.9 percentage points), women (by 3.4 percentage points) and total population (by 3.6 percentage points), compared to the STEPS survey. The point estimates of the WHO STEPS survey lie within the UIs of the model in this thesis.





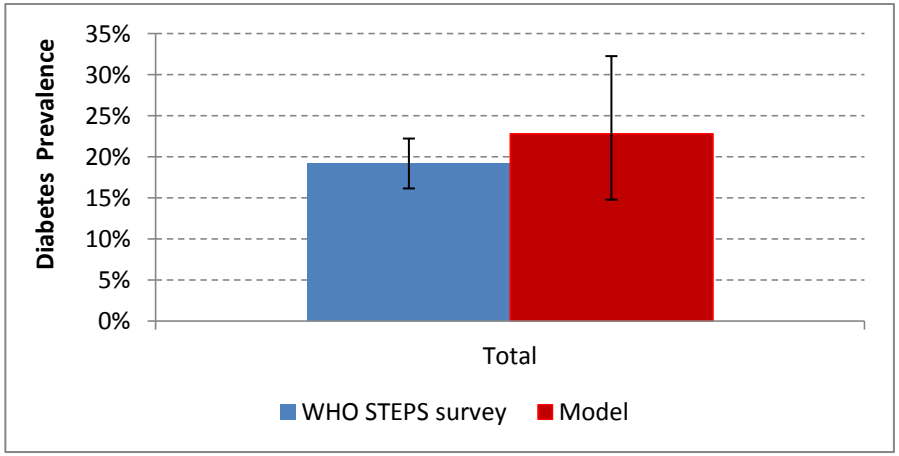


Figure 6.13. Results of the model validation against the WHO STEPS survey (2005) for men, women and total population aged 25-64 years

6.2.2. Validation against another model

The Saudi IMPACT Diabetes Forecast Model produced reasonably comparable estimates of the diabetes prevalence in Saudi Arabia for years 2000 and 2008 to that estimated recently by the WHO Global Burden of Disease (GBD) study, 2011.[20] The GBD model estimated the trends and uncertainties in mean fasting plasma glucose (FPG) and diabetes prevalence during 1980-2008 in adults aged ≥25 years in around 200 countries and territories globally. It used complex multi-level methods of modelling, and incorporated several covariates (including the mean BMI) to inform the estimates of diabetes prevalence. Detailed description and discussion of the methodology and results of the GBD model are presented in chapter 9.

Data sources used by the GBD model for Saudi Arabia included three national population-based surveys.[18, 19, 36] One of these surveys was that of Warsy and El-Hazmi,[36] which was used by the Saudi IMPACT Diabetes Forecast Model to obtain the diabetes prevalence for the starting year of modelling. Another survey was the WHO STEPS survey,[19] which was used in this thesis for validation as discussed earlier. The model results for population aged 25-64 years in 2000 and 2008 were validated against the GBD model, as shown in Figure **6.14**. The model results for 2000 and 2008 did not show any differences by assuming capped obesity trends (scenario 1) or continuing linear trends (scenario 2). Therefore, both scenarios can be used for validation against the GBD model.

The uncertainty intervals reported by the GBD study represented the 2.5–97.5 percentiles of the estimated means of diabetes prevalence. The Saudi IMPACT Diabetes Forecast Model estimated the diabetes prevalence in men at 17.7% (UI: 14.3 – 20.8%) in 2000, compared to 17.5% (UI: 13.6–21.9%) by the GBD study. In women, the estimated prevalence in 2000 was 16.4% (UI: 13.2–19.6%) by the Saudi model and 17.7% (UI: 13.8–21.9%) by the GBD study. On the other hand, the estimated prevalence in 2008 for men was 26.7% (UI: 21.9–31.1%) by the Saudi model, compared to 22.0% (UI: 14.8–30.2%) by the GBD study. For women in 2008, the estimated prevalence was 24.7% (UI: 19.7–29.7%) by the Saudi model, and 21.7% (UI: 14.6–29.9%) by the GBD study.

Generally, the results of the two models in 2000 for men were very similar, whereas for women, the GBD study resulted in a slightly higher (by 1.3 percentage points) estimate than the Saudi IMPACT Diabetes Forecast Model. However, for 2008, the Saudi IMPACT Diabetes Forecast Model tended to produce higher estimates than the other model, in both men (by 4.7 percentage points) and women (by 3.0 percentage points). The point estimates of the GBD model lie within the UIs of the model in this thesis.

In total, in this chapter, the past and current (1992-2013) trends in the diabetes prevalence in Saudi Arabia have been reported, as estimated by the Saudi IMPACT Diabetes Forecast Model. Also, the results of validation of the model against observed data and the recent GBD model have been discussed. The next chapter presents the model outputs of the predicted future diabetes prevalence for the period 2014-2022.

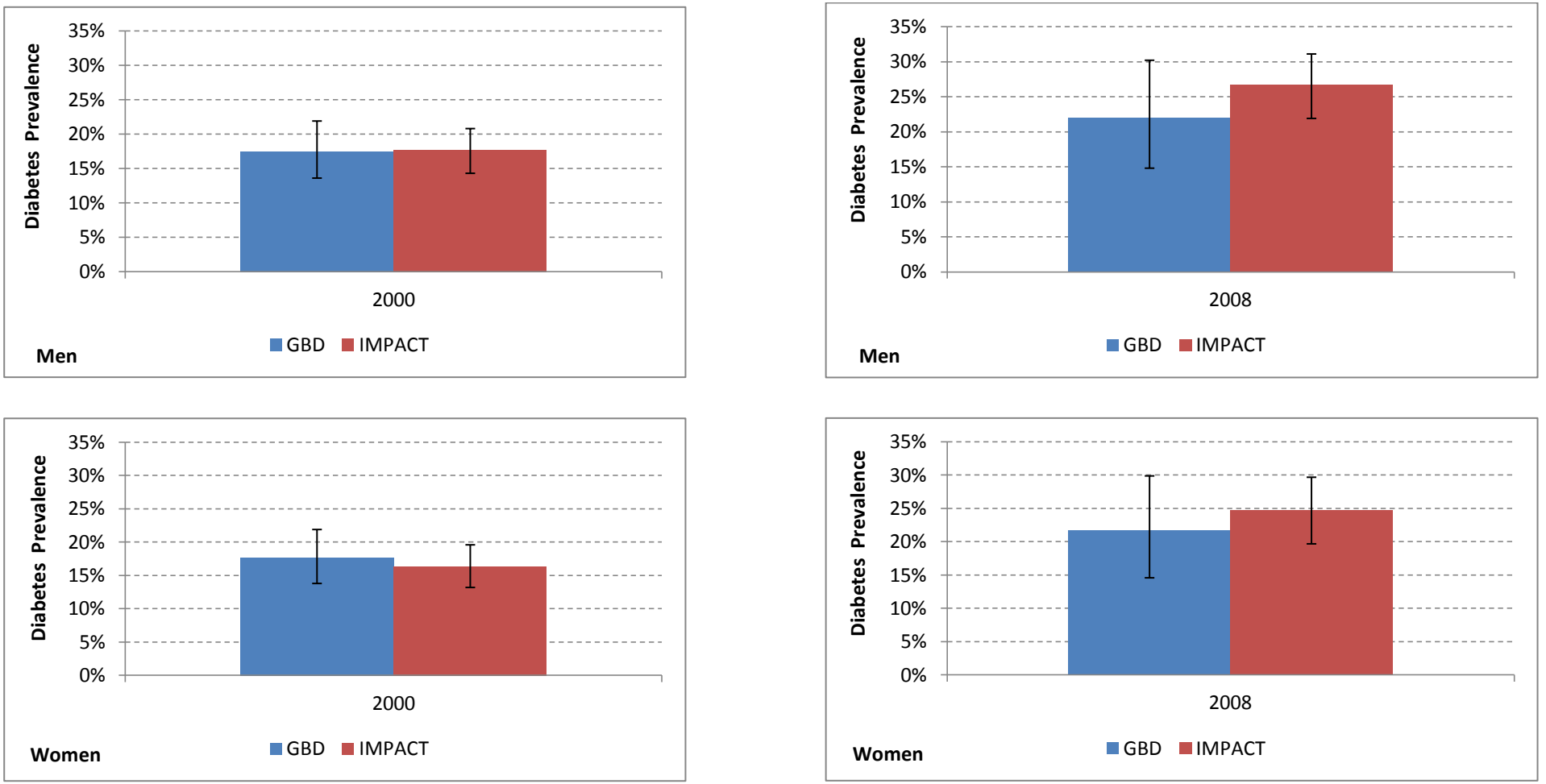


Figure 6.14. Results of the model validation against the GBD study for men and women aged 25-64 years (2000 and 2008)

Chapter 7. Using the Saudi IMPACT Diabetes Forecast Model to predict the future trends in diabetes prevalence in Saudi Arabia

This chapter presents the future trends in diabetes prevalence during 2014-2022, as predicted by the model. In addition, this chapter provides a brief overview of the main results for the whole modelling period (1992-2022). Moreover, this chapter discusses the impact of adjusting the modelling outputs of diabetes prevalence to the more recent diagnostic criteria of T2DM (ADA 1997/ WHO 1999).

7.1. Trends in the prevalence of type 2 diabetes in Saudi Arabia during 2014–2022

The results of the model predictions of the estimated diabetes prevalence in Saudi Arabia during 2014-2022 are presented in this section, based on the four scenarios discussed earlier in chapter 6.

7.1.1. The overall and sex-specific prevalence of diabetes and numbers of diabetic individuals in the Saudi population

7.1.1.1. Results based on scenario 1: population aged 25-64 years, with capping

Diabetes prevalence is estimated to increase by 24% in the Saudi population aged 25-64 years during the nine-year period of 2014-2022, assuming capped obesity trends; from 31.8% (UI: 26.0–37.4%) to 39.5% (UI: 32.5–45.9%) (Figure **7.1**). The estimated number of individuals with diabetes will increase by 2,239,448 (UI: 1,508,444-3,067,650) during the same period; from 4,342,064 (UI: 2,834,922-6,113,433) to 6,581,511 (UI: 4,343,367-9,181,082) (Table **7.1**).

In men, the predicted diabetes prevalence will increase by 21% during the same period; from 32.5% (UI: 27.0–37.6%) in 2014 to 39.2% (UI: 33.2-44.4%) in 2022 (Figure **7.3**). This will be equivalent to an estimated increase of 1,076,527 (UI: 764,029-1,398,513) individuals in the number of men with diabetes; from 2,590,085 (UI: 1,718,194–3,587,497) to 3,666,613 (UI: 2,482,223–4,986,010) (Table **7.1**).

In women, the estimated diabetes prevalence is predicted to increase by 29%; from 30.8% (UI: 24.6–37.1%) in 2014 to 39.8% (UI: 31.7–47.7%) in 2022 (Figure **7.3**). The number of women with diabetes during the same period is predicted to increase by 1,162,920 (UI: 744,416-1,669,136) individuals; from 1,751,978 (UI: 1,116,728–2,525,936) to 2,914,899 (UI: 1,861,144–4,195,073) (Table **7.1**).

7.1.1.2. Results based on scenario 2: population aged 25-64 years, without capping

Assuming continuing uncapped linear trends in obesity prevalence, the estimated overall diabetes prevalence in the total Saudi population aged 25-64 years is predicted to increase by 35% during 2014–2022; from 32.6% (UI: 26.4–38.5%) to 44.1% (UI: 35.4–52.5%) (Figure **7.2**). There is a predicted increase of 2,904,901 (UI: 1,837,274-4,209,704) in the total number of individuals with diabetes; from 4,448,546 (UI: 2,885,782–6,303,886) in 2014 to 7,353,447 (UI: 4,723,056–10,513,591) in 2022 (Table **7.2**).

In men, the predicted diabetes prevalence will increase by 26%; from 32.9% (UI: 27.2–38.2%) in 2014 to 41.3% (UI: 34.4–47.6%) in 2022 (Figure **7.4**). The number of men with diabetes is predicted to increase by 1,236,955 (UI: 840,481-1,691,082) individuals during the same period; from 2,622,048 (UI: 1,733,362–3,646,407) to 3,859,003 (UI: 2,573,843–5,337,489) (Table **7.2**).

In comparison, the predicted diabetes prevalence in women aged 25-64 years during 2014-2022 will increase by 48%; from 32.2% (UI: 25.4–39.0%) to 47.7% (UI: 36.6–58.8%) (Figure **7.4**). The number of diabetic women is predicted to increase by a total of 1,667,946 (UI: 996,793-2,518,622) individuals; from 1,826,498 (UI: 1,152,419–2,657,480) to 3,494,444 (UI: 2,149,212–5,176,102) (Table **7.2**).

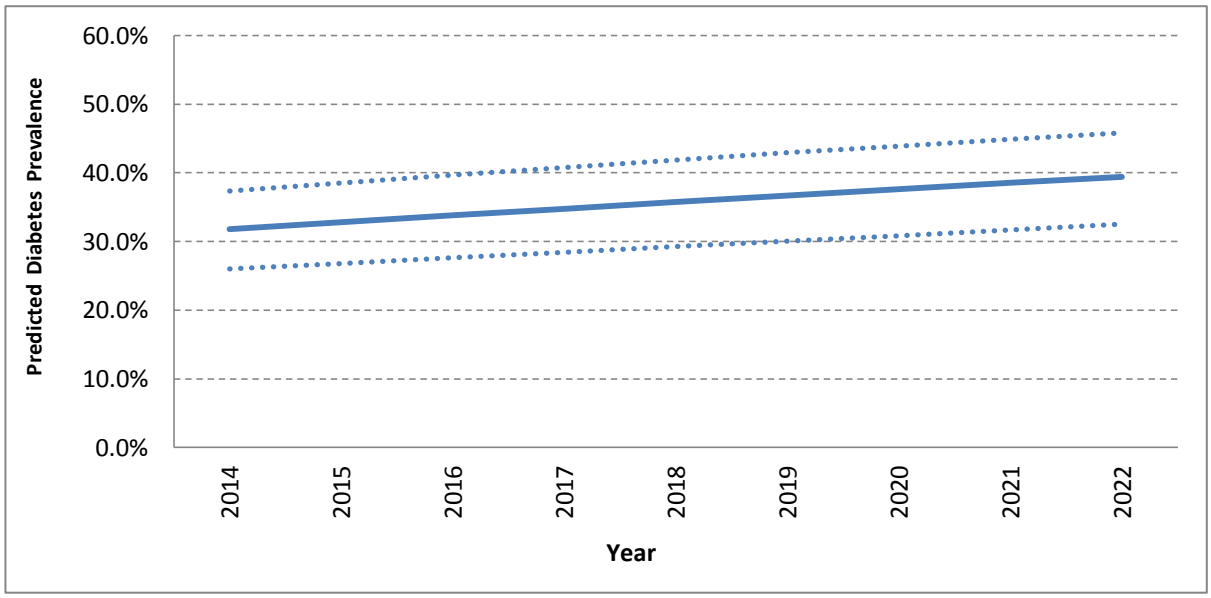


Figure 7.1. *(Scenario 1)* Trends in the predicted diabetes total prevalence (and uncertainty values) for population aged 25-64 years, with capping of projected obesity prevalence, Saudi Arabia (2014-2022)

[*Solid line:* point (best) estimates; *Dotted lines:* minimum and maximum uncertainty estimates. Diagnostic criteria: WHO 1985]

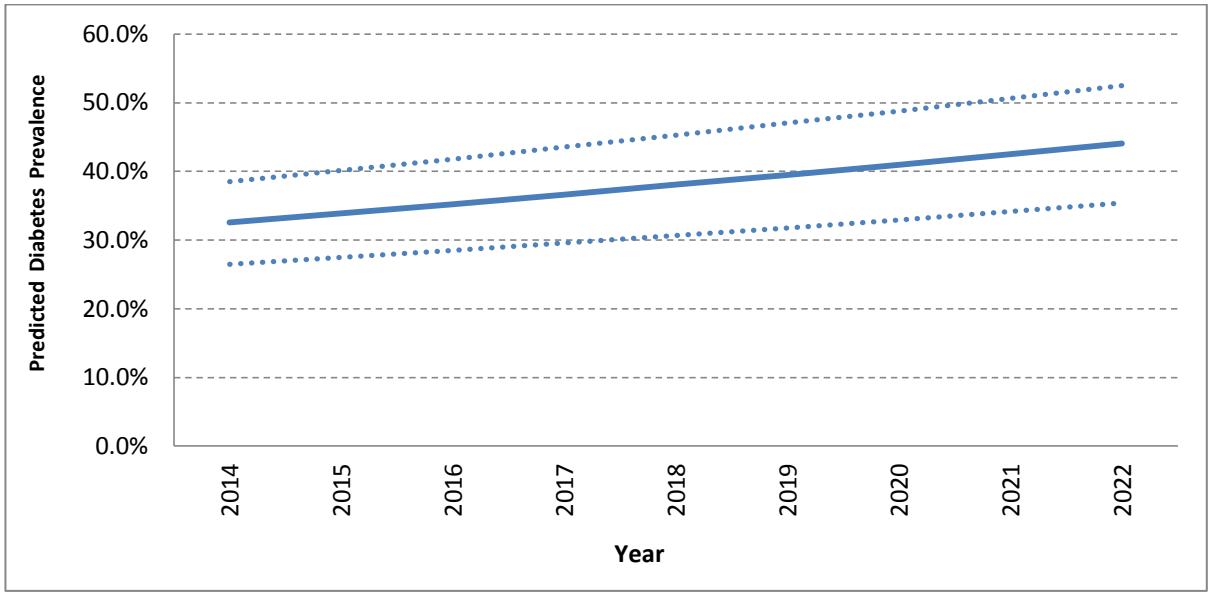


Figure 7.2. *(Scenario 2)* Trends in the predicted diabetes total prevalence (and uncertainty values) for population aged 25-64 years, without capping of projected obesity prevalence, Saudi Arabia (2014-2022)

[*Solid line:* point (best) estimates; *Dotted lines:* minimum and maximum uncertainty estimates. Diagnostic criteria: WHO 1985]

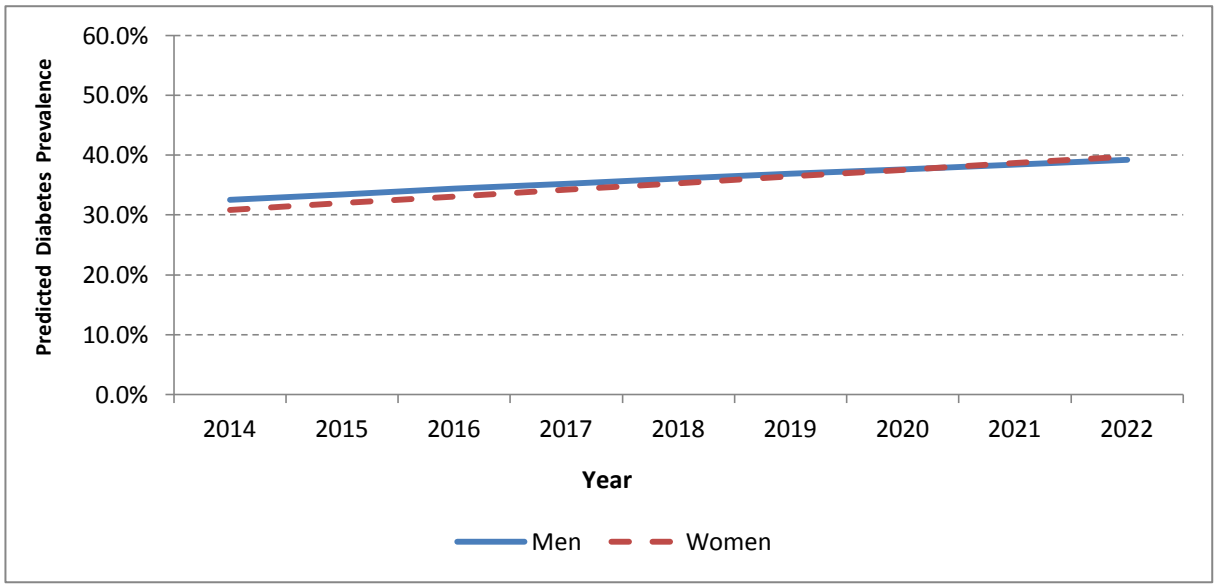


Figure 7.3. *(Scenario 1)* Trends in the predicted diabetes prevalence (and uncertainty values) for men and women aged 25-64 years, with capping of projected obesity prevalence, Saudi Arabia (2014-2022)

[Diagnostic criteria: WHO 1985]

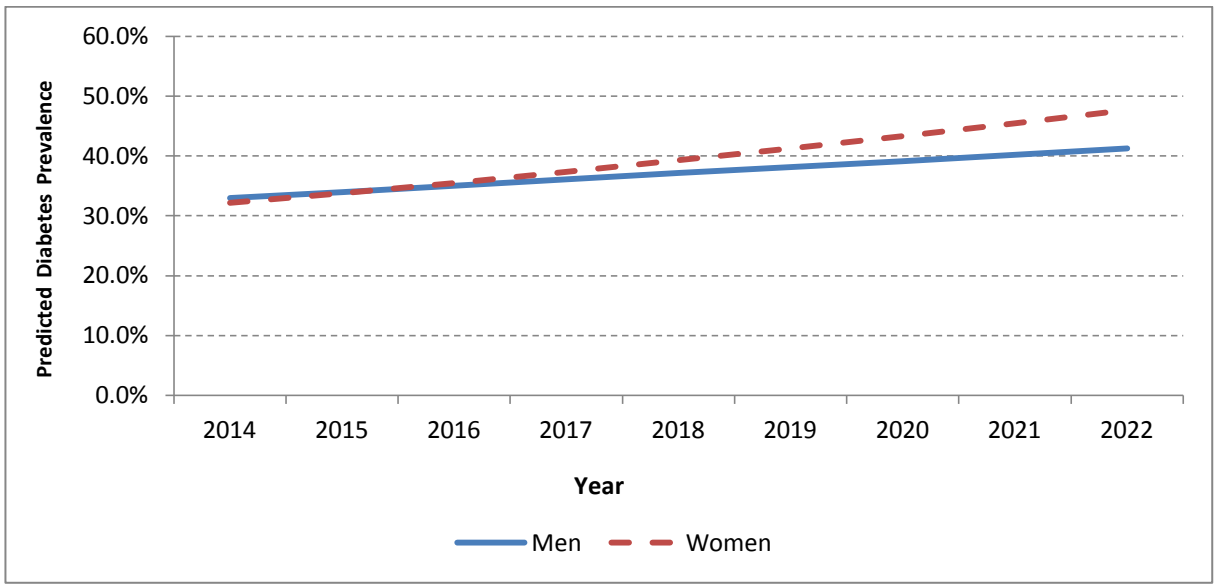


Figure 7.4. *(Scenario 2)* Trends in the predicted diabetes prevalence (and uncertainty values) for men and women aged 25-64 years, without capping of projected obesity prevalence, Saudi Arabia (2014-2022)

[Diagnostic criteria: WHO 1985]

Table 7.1. *(Scenario 1)* Predicted numbers of individuals with diabetes for population aged 25-64 years, with capping of projected obesity prevalence, Saudi Arabia (2014-2022)

Year	Men	Uncertainty values		Women	Uncertainty values		Total	Uncertainty values	
	best estimate	minimum	maximum	best estimate	minimum	maximum	best estimate	minimum	maximum
2014	**2,590,085**	1,718,194	3,587,497	**1,751,978**	1,116,728	2,525,936	**4,342,064**	2,834,922	6,113,433
2015	**2,723,952**	1,810,411	3,767,053	**1,878,845**	1,196,542	2,712,675	**4,602,797**	3,006,953	6,479,727
2016	**2,859,395**	1,904,248	3,947,630	**2,012,150**	1,280,392	2,908,692	**4,871,544**	3,184,640	6,856,322
2017	**2,995,265**	1,999,174	4,127,062	**2,153,212**	1,368,973	3,116,090	**5,148,477**	3,368,147	7,243,152
2018	**3,131,126**	2,094,965	4,304,632	**2,299,815**	1,461,579	3,329,275	**5,430,941**	3,556,545	7,633,907
2019	**3,266,611**	2,191,420	4,479,834	**2,450,178**	1,557,549	3,544,687	**5,716,790**	3,748,969	8,024,521
2020	**3,401,421**	2,288,352	4,652,344	**2,602,917**	1,656,277	3,760,227	**6,004,338**	3,944,629	8,412,571
2021	**3,535,315**	2,385,594	4,821,987	**2,757,005**	1,757,225	3,974,841	**6,292,321**	4,142,819	8,796,828
2022	**3,666,613**	2,482,223	4,986,010	**2,914,899**	1,861,144	4,195,073	**6,581,511**	4,343,367	9,181,082

Table 7.2. *(Scenario 2)* Predicted numbers of individuals with diabetes for population aged 25-64 years, without capping of projected obesity prevalence, Saudi Arabia (2014-2022)

Year	Men	Uncertainty values		Women	Uncertainty values		Total	Uncertainty values	
	best estimate	minimum	maximum	best estimate	minimum	maximum	best estimate	minimum	maximum
2014	**2,622,048**	1,733,362	3,646,407	**1,826,498**	1,152,419	2,657,480	**4,448,546**	2,885,782	6,303,886
2015	**2,767,766**	1,831,135	3,848,122	**1,986,995**	1,248,283	2,903,682	**4,754,761**	3,079,417	6,751,804
2016	**2,917,540**	1,931,691	4,055,448	**2,161,764**	1,352,079	3,172,313	**5,079,303**	3,283,770	7,227,760
2017	**3,070,062**	2,034,447	4,265,798	**2,352,699**	1,464,860	3,466,164	**5,422,761**	3,499,307	7,731,962
2018	**3,224,862**	2,139,189	4,478,273	**2,557,692**	1,586,135	3,779,143	**5,782,554**	3,725,324	8,257,415
2019	**3,381,594**	2,245,742	4,692,318	**2,775,043**	1,715,436	4,107,350	**6,156,637**	3,961,178	8,799,669
2020	**3,539,964**	2,353,942	4,907,540	**3,003,393**	1,852,315	4,448,422	**6,543,357**	4,206,257	9,355,962
2021	**3,699,696**	2,463,625	5,123,613	**3,241,789**	1,996,388	4,801,271	**6,941,485**	4,460,013	9,924,884
2022	**3,859,003**	2,573,843	5,337,489	**3,494,444**	2,149,212	5,176,102	**7,353,447**	4,723,056	10,513,591

7.1.1.3. Results based on scenario 3: population aged 25-75+ years, with capping

Assuming capped trends in the obesity trends, the overall diabetes prevalence in the Saudi population aged 25-75+ years is predicted to increase by 22% during 2014-2022; from 31.9% (UI: 26.2–37.3%) to 38.9% (UI: 32.2–45.2%) (Figure **7.5**). There will be a predicted increase in the number of individuals with diabetes by 2,422,105 (UI: 1,626,531-3,332,590) during the same period; from 4,650,710 (UI: 3,052,901–6,522,822) in 2014 to 7,072,814 (UI: 4,679,432–9,855,412) in 2022 (Table **7.3**).

The predicted diabetes prevalence in men will increase by 18%; from 31.9% (UI: 26.6–36.8%) in 2014 to reach 37.8% (UI: 32.0–42.8%) by 2022 (Figure **7.7**). The number of diabetic men is predicted to increase by a total of 1,158,015 (UI: 818,455-1,514,613) over the same period; from 2,739,864 (UI: 1,828,072–3,776,219) to 3,897,879 (UI: 2,646,527–5,290,833) (Table **7.3**).

In women, the predicted diabetes prevalence will increase by 28%; from 31.1% (UI: 24.9–37.3%) in 2014 to 39.7% (UI: 31.7–47.5%) by 2022 (Figure **7.7**). This will be equivalent to an estimated increase of 1,264,090 (UI: 808,076-1,817,977) individuals in the number of women with diabetes; from 1,910,846 (UI: 1,224,829–2,746,602) to 3,174,935 (UI: 2,032,905–4,564,579) (Table **7.3**).

7.1.1.4. Results based on scenario 4: population aged 25-75+ years, without capping

The predicted diabetes prevalence for the total Saudi population (25-75+ years), assuming continuous uncapped linear trends in obesity, will increase by 33%; from 32.6% (UI: 26.6–38.4%) in 2014 to 43.2% (UI: 34.8–51.3%) in 2022 (Figure **7.6**). The number of individuals with diabetes during the same period is predicted to increase by a total of 3,087,558 (UI: 1,955,361-4,474,645); from 4,757,192 (UI: 3,103,760–6,713,275) to reach 7,844,750 (UI: 5,059,121–11,187,920) (Table **7.4**).

In men, the prevalence of diabetes is predicted to increase by 23%; from 32.3% (UI: 26.8–37.4%) in 2014 to 39.7% (UI: 33.1–45.7%) by 2022 (Figure **7.8**). The number of diabetic men is predicted by the model to increase by 1,318,443 (UI:

894,907-1,807,182); from 2,771,827 (UI: 1,843,240–3,835,129) in 2014 to 4,090,269 (UI: 2,738,147–5,642,311) by 2022 (Table **7.4**).

On the other hand, the diabetes prevalence in women is predicted to increase by 45% between 2014 and 2022; from 32.3% (UI: 25.7–39.1%) to 46.9% (UI: 36.2–57.7%) (Figure **7.8**). The predicted number of women with diabetes will increase by 1,769,115 (UI: 1,060,454-2,667,463); from 1,985,366 (UI: 1,260,520–2,878,146) in 2014 to 3,754,481 (UI: 2,320,974–5,545,609) in 2022 (Table **7.4**).

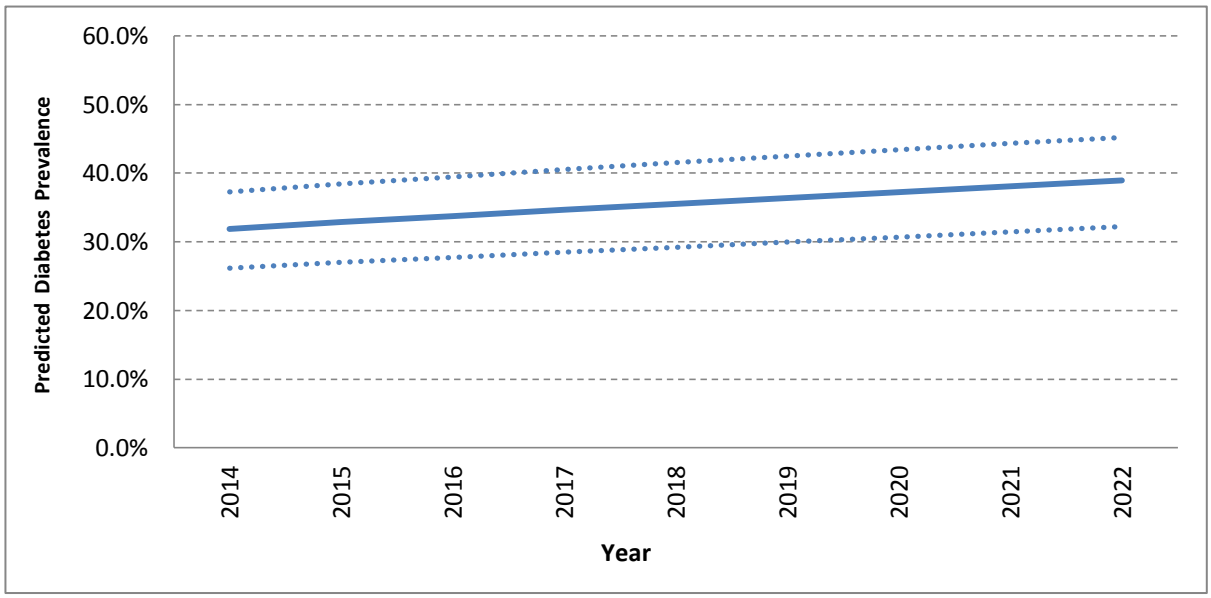


Figure 7.5. *(Scenario 3)* Trends in the predicted diabetes total prevalence (and uncertainty values) for population aged 25-75+ years, with capping of projected obesity prevalence, Saudi Arabia (2014-2022)

[*Solid line:* point (best) estimates; *Dotted lines:* minimum and maximum uncertainty estimates. Diagnostic criteria: WHO 1985]

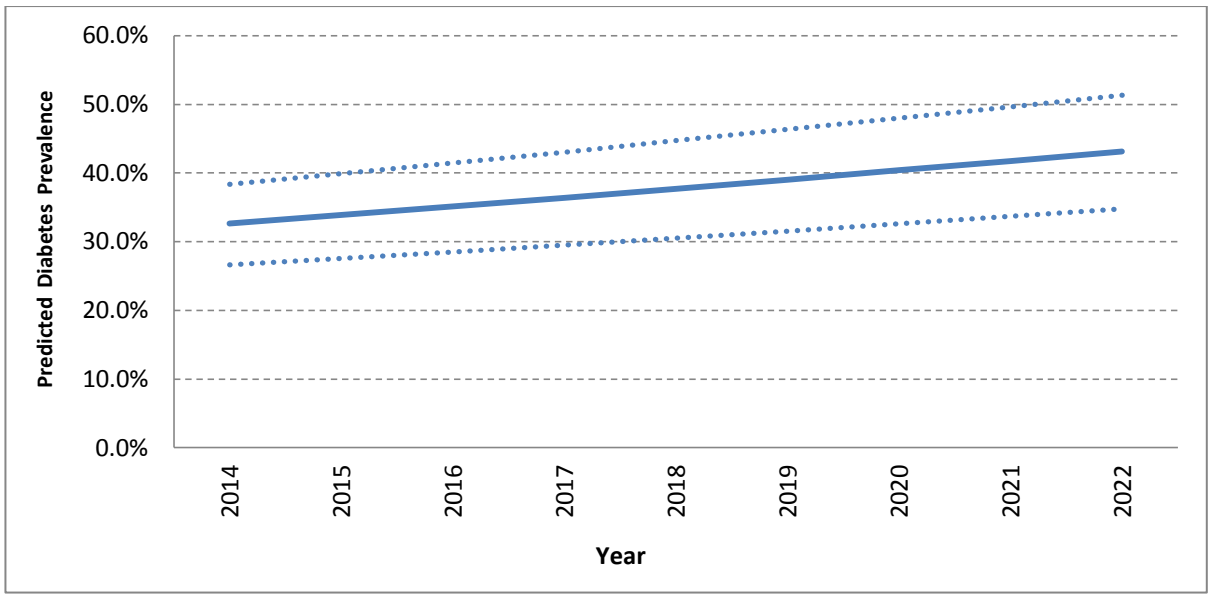


Figure 7.6. *(Scenario 4)* Trends in the predicted diabetes total prevalence (and uncertainty values) for population aged 25-75+ years, without capping of projected obesity prevalence, Saudi Arabia (2014-2022)

[*Solid line:* point (best) estimates; *Dotted lines:* minimum and maximum uncertainty estimates. Diagnostic criteria: WHO 1985]

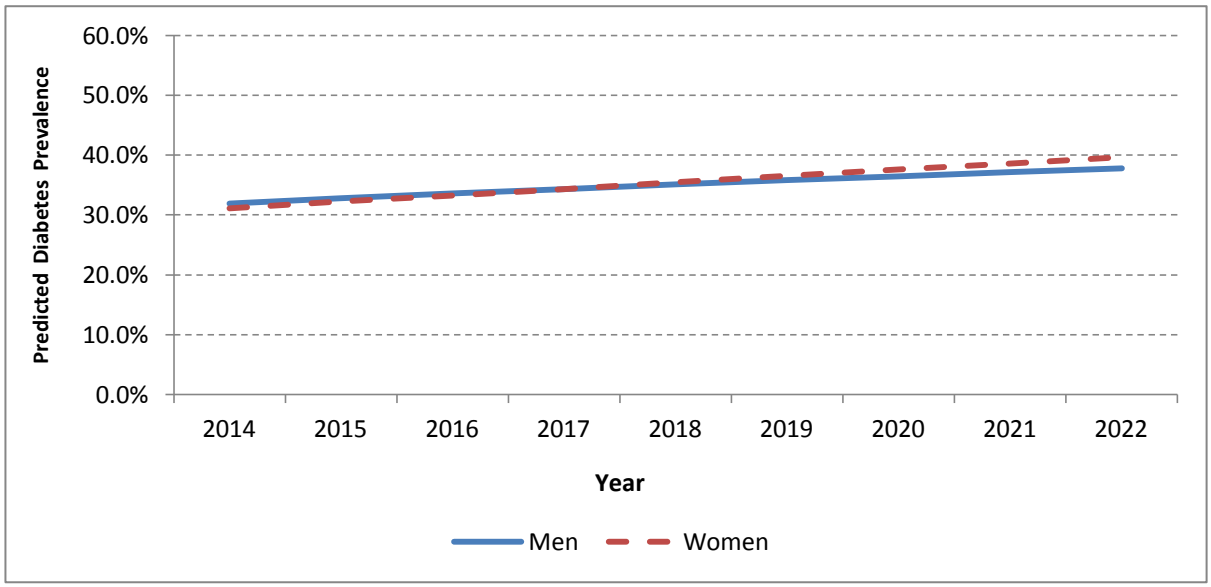


Figure 7.7. *(Scenario 3)* Trends in the predicted diabetes prevalence (and uncertainty values) for men and women aged 25-75+ years, with capping of projected obesity prevalence, Saudi Arabia (2014-2022)

[Diagnostic criteria: WHO 1985]

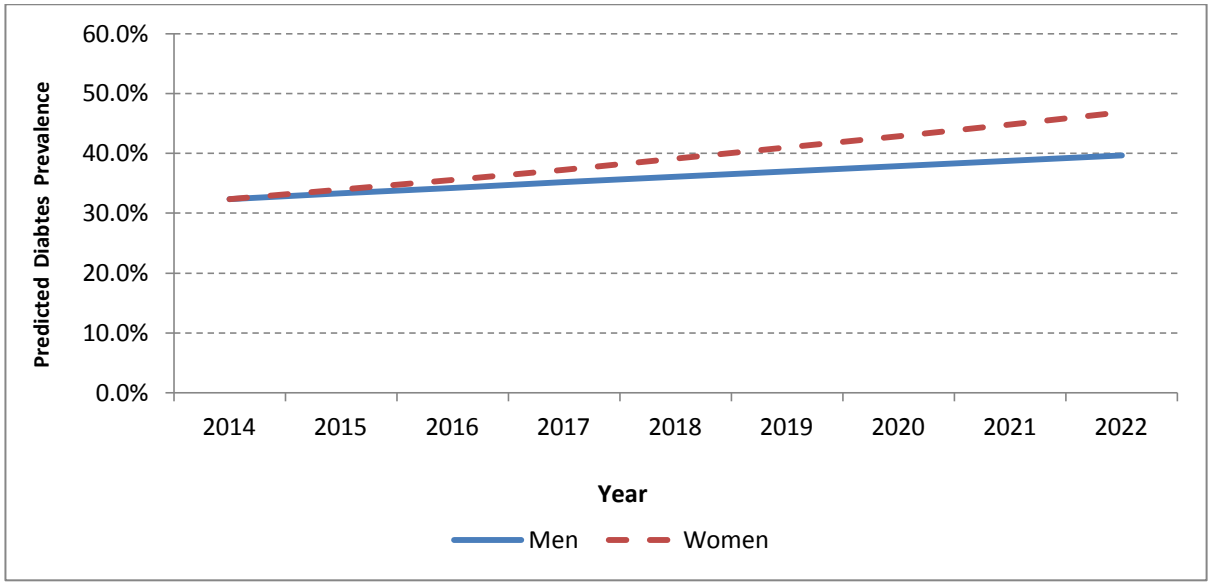


Figure 7.8. *(Scenario 4)* Trends in the predicted diabetes prevalence (and uncertainty values) for men and women aged 25-75+ years, without capping of projected obesity prevalence, Saudi Arabia (2014-2022)

[Diagnostic criteria: WHO 1985]

Table 7.3. *(Scenario 3)* Predicted numbers of individuals with diabetes for population aged 25-75+ years, with capping of projected obesity prevalence, Saudi Arabia (2014-2022)

Year	Men	Uncertainty values		Women	Uncertainty values		Total	Uncertainty values	
	best estimate	minimum	maximum	best estimate	minimum	maximum	best estimate	minimum	maximum
2014	**2,739,864**	1,828,072	3,776,219	**1,910,846**	1,224,829	2,746,602	**4,650,710**	3,052,901	6,522,822
2015	**2,880,151**	1,924,855	3,964,527	**2,047,302**	1,310,802	2,947,281	**4,927,453**	3,235,658	6,911,807
2016	**3,022,391**	2,023,503	4,154,363	**2,190,639**	1,401,101	3,157,820	**5,213,030**	3,424,604	7,312,183
2017	**3,166,556**	2,124,068	4,345,577	**2,342,982**	1,496,789	3,381,925	**5,509,538**	3,620,857	7,727,502
2018	**3,312,045**	2,226,273	4,537,021	**2,501,876**	1,597,088	3,613,331	**5,813,920**	3,823,361	8,150,352
2019	**3,458,346**	2,329,862	4,727,842	**2,665,373**	1,701,279	3,848,112	**6,123,719**	4,031,141	8,575,954
2020	**3,605,036**	2,434,602	4,917,436	**2,831,976**	1,808,712	4,083,972	**6,437,012**	4,243,315	9,001,408
2021	**3,751,764**	2,540,283	5,105,401	**3,000,585**	1,918,813	4,319,758	**6,752,349**	4,459,096	9,425,159
2022	**3,897,879**	2,646,527	5,290,833	**3,174,935**	2,032,905	4,564,579	**7,072,814**	4,679,432	9,855,412

Table 7.4. *(Scenario 4)* Predicted numbers of individuals with diabetes for population aged 25-75+ years, without capping of projected obesity prevalence, Saudi Arabia (2014-2022)

Year	Men	Uncertainty values		Women	Uncertainty values		Total	Uncertainty values	
	best estimate	minimum	maximum	best estimate	minimum	maximum	best estimate	minimum	maximum
2014	**2,771,827**	1,843,240	3,835,129	**1,985,366**	1,260,520	2,878,146	**4,757,192**	3,103,760	6,713,275
2015	**2,923,965**	1,945,579	4,045,596	**2,155,451**	1,362,543	3,138,288	**5,079,416**	3,308,122	7,183,884
2016	**3,080,536**	2,050,945	4,262,181	**2,340,253**	1,472,789	3,421,440	**5,420,789**	3,523,734	7,683,622
2017	**3,241,353**	2,159,341	4,484,313	**2,542,469**	1,592,676	3,731,999	**5,783,822**	3,752,018	8,216,312
2018	**3,405,780**	2,270,496	4,710,662	**2,759,753**	1,721,644	4,063,199	**6,165,533**	3,992,140	8,773,861
2019	**3,573,329**	2,384,184	4,940,326	**2,990,237**	1,859,167	4,410,775	**6,563,566**	4,243,350	9,351,102
2020	**3,743,578**	2,500,192	5,172,632	**3,232,452**	2,004,751	4,772,167	**6,976,031**	4,504,943	9,944,799
2021	**3,916,145**	2,618,314	5,407,028	**3,485,368**	2,157,976	5,146,187	**7,401,513**	4,776,290	10,553,215
2022	**4,090,269**	2,738,147	5,642,311	**3,754,481**	2,320,974	5,545,609	**7,844,750**	5,059,121	11,187,920

7.1.2. Age- and sex-specific prevalence of diabetes and numbers of diabetic individuals

7.1.2.1. Results based on scenario 1: population aged 25-64 years, with capping

Assuming the previously discussed capped projected obesity trends in men and women aged 25-64 years, the highest predicted relative increase in the prevalence of diabetes during 2014-2022 will be in women aged 45-54 years. The prevalence in this age group is predicted to increase by 39%; from 35.6% (UI: 27.8–43.6%) in 2014 to 49.6% (UI: 38.3–60.9%) in 2022. The second highest increase in the diabetes prevalence (34%) is predicted in women aged 35-44 years; from 29.4% (UI: 23.4–35.3%) to 39.4% (UI: 31.5–47.1%). On the other hand, women aged 55-64 years will show relatively stable predicted prevalence rates during this period (Table **7.5**).

7.1.2.2. Results based on scenario 2: population aged 25-64 years, without capping

If the projected trends in obesity continue to increase without capping, the predicted diabetes prevalence during 2014-2022 will show more significant relative increases than that predicted by scenario 1. In women aged 45-54 years, the predicted diabetes prevalence will increase by 75%; from 39.5% (UI: 30.1–49.4%) in 2014 to 69.3% (UI: 50.4–88.9%) in 2022. Moreover, the predicted relative increase in diabetes prevalence during the same period is 55% in women aged 35-44 years, 38% in men aged 45-54 years and 35% in men aged 35-44 years. Women in the age group of 55-64 years, who show stable predicted prevalence of diabetes by scenario 1, are predicted to have a relative increase of 17%; from 52.0% (UI: 39.5–64.8%) in 2014 to reach 61.0% (UI: 45.8–76.8%) by 2022. However, men and women in the youngest age group (25-34 years) will show no difference in the predicted prevalence of diabetes, using both scenarios (Table **7.6**).

Table **7.7** and Table **7**.**8** present the lower and higher uncertainty values of the predicted diabetes prevalence for the age groups, based on scenarios 1 and 2 respectively. In addition, Figure **7.9** and Figure **7**.**10** illustrate a graphical comparison of the predicted prevalence in all age groups, using these two scenarios.

Table 7.5. *(Scenario 1)* Predicted prevalence of diabetes per age group (years) in men and women aged 25-64 years, with capping of projected obesity prevalence, Saudi Arabia (2014-2022)

Year	25-34		35-44		45-54		55-64	
	Men	Women	Men	Women	Men	Women	Men	Women
2014	32.8%	25.3%	33.3%	29.4%	31.3%	35.6%	32.2%	49.5%
2015	33.8%	26.1%	34.3%	30.5%	32.1%	37.4%	32.7%	50.1%
2016	34.3%	26.7%	35.7%	31.9%	33.5%	39.5%	33.0%	49.2%
2017	34.7%	27.3%	36.9%	33.2%	34.8%	41.6%	33.3%	48.9%
2018	35.1%	28.0%	38.1%	34.6%	36.1%	43.7%	33.7%	48.8%
2019	35.6%	28.7%	39.3%	35.9%	37.2%	45.6%	34.2%	49.0%
2020	36.0%	29.4%	40.4%	37.1%	38.2%	47.3%	34.7%	49.3%
2021	36.6%	30.5%	41.3%	38.3%	39.6%	48.5%	35.1%	48.8%
2022	37.2%	31.6%	42.2%	39.4%	40.8%	49.6%	35.5%	48.7%
Relative difference in prevalence	**+13%**	**+25%**	**+27%**	**+34%**	**+30%**	**+39%**	**+10%**	**-2%**

Table 7.6. *(Scenario 2)* Predicted prevalence of diabetes per age group (years) in men and women aged 25-64 years, without capping of projected obesity prevalence, Saudi Arabia (2014-2022)

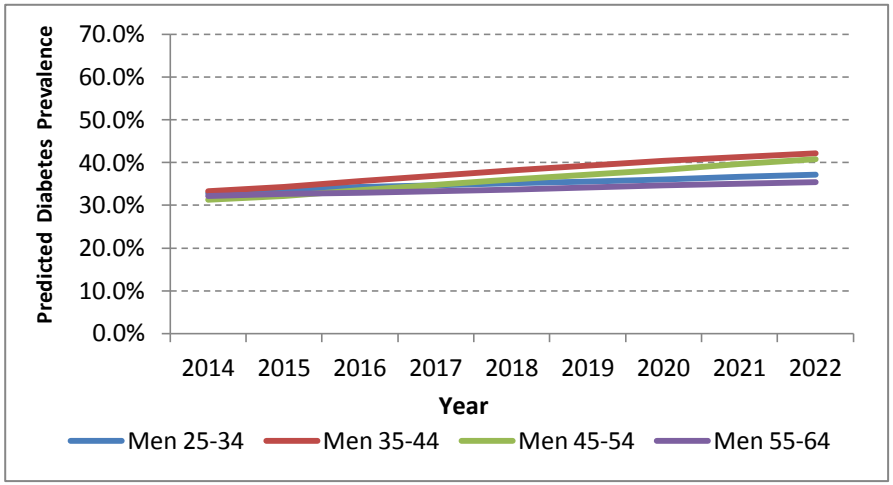
Year	25-34		35-44		45-54		55-64	
	Men	Women	Men	Women	Men	Women	Men	Women
2014	32.8%	25.3%	34.2%	30.5%	31.8%	39.5%	32.2%	52.0%
2015	33.8%	26.1%	35.5%	32.0%	32.8%	42.7%	32.9%	53.7%
2016	34.3%	26.7%	37.1%	34.0%	34.5%	46.4%	33.2%	53.8%
2017	34.7%	27.3%	38.7%	36.0%	36.0%	50.3%	33.7%	54.6%
2018	35.1%	28.0%	40.3%	38.2%	37.6%	54.3%	34.4%	55.8%
2019	35.6%	28.7%	41.8%	40.4%	39.1%	58.4%	35.1%	57.3%
2020	36.0%	29.4%	43.3%	42.6%	40.5%	62.4%	35.8%	58.9%
2021	36.6%	30.5%	44.7%	44.9%	42.3%	65.8%	36.4%	59.7%
2022	37.2%	31.6%	46.0%	47.2%	44.0%	69.3%	37.1%	61.0%
Relative difference in prevalence	**+13%**	**+25%**	**+35%**	**+55%**	**+38%**	**+75%**	**+15%**	**+17%**

Table 7.7. *(Scenario 1)* Sensitivity analysis: lower (L) and higher (H) uncertainty values of the predicted diabetes prevalence (%) per age group (years) in men and women aged 25-64 years, with capping of projected obesity prevalence, Saudi Arabia (2014-2022)

Year	25-34				35-44				45-54				55-64			
	Men		Women		Men		Women		Men		Women		Men		Women	
	L	H	L	H	L	H	L	H	L	H	L	H	L	H	L	H
2014	27.5	37.3	20.8	29.7	27.7	38.2	23.4	35.3	25.7	36.7	27.8	43.6	26.2	38.3	38.1	60.7
2015	28.5	38.3	21.5	30.6	28.6	39.3	24.2	36.6	26.3	37.7	28.9	46.3	26.6	39.0	38.9	61.2
2016	29.0	38.6	22.0	31.3	29.8	40.7	25.3	38.3	27.4	39.4	30.3	49.3	26.7	39.3	38.4	59.8
2017	29.5	39.0	22.5	32.0	31.0	42.1	26.4	39.9	28.5	40.9	31.8	52.1	27.0	39.7	38.3	59.3
2018	30.0	39.4	23.1	32.8	32.2	43.3	27.5	41.5	29.6	42.2	33.3	54.7	27.3	40.2	38.3	59.4
2019	30.4	39.7	23.7	33.6	33.3	44.5	28.5	43.0	30.6	43.4	34.7	56.9	27.7	40.7	38.5	59.6
2020	30.9	40.1	24.3	34.4	34.3	45.5	29.5	44.5	31.5	44.5	36.1	58.7	28.1	41.2	38.7	59.9
2021	31.5	40.7	25.2	35.7	35.3	46.4	30.5	45.8	32.8	45.9	37.2	59.8	28.4	41.5	38.4	59.3
2022	32.2	41.3	26.1	37.0	36.2	47.2	31.5	47.1	33.9	47.1	38.3	60.9	28.8	41.9	38.4	59.3

Table 7.8. *(Scenario2)* Sensitivity analysis: lower (L) and higher (H) uncertainty values of the predicted diabetes prevalence (%) per age group (years) in men and women aged 25-64 years, without capping of projected obesity prevalence, Saudi Arabia (2014-2022)

Year	25-34				35-44				45-54				55-64			
	Men		Women		Men		Women		Men		Women		Men		Women	
	L	H	L	H	L	H	L	H	L	H	L	H	L	H	L	H
2014	27.5	37.3	20.8	29.7	28.2	39.6	24.1	36.7	25.9	37.4	30.1	49.4	26.2	38.4	39.5	64.8
2015	28.5	38.3	21.5	30.6	29.3	41.1	25.2	38.7	26.7	38.8	32.1	54.2	26.6	39.3	40.9	66.8
2016	29.0	38.6	22.0	31.3	30.7	42.9	26.7	41.2	28.0	40.9	34.4	59.6	26.8	39.8	41.0	66.8
2017	29.5	39.0	22.5	32.0	32.1	44.7	28.2	43.8	29.2	42.8	37.0	65.1	27.2	40.4	41.5	68.0
2018	30.0	39.4	23.1	32.8	33.5	46.5	29.8	46.5	30.4	44.7	39.6	70.5	27.6	41.2	42.3	69.7
2019	30.4	39.7	23.7	33.6	34.8	48.2	31.4	49.2	31.6	46.4	42.4	75.7	28.1	42.1	43.3	71.7
2020	30.9	40.1	24.3	34.4	36.1	49.9	33.1	52.1	32.8	48.1	45.2	80.7	28.7	43.0	44.4	73.9
2021	31.5	40.7	25.2	35.7	37.3	51.4	34.8	54.9	34.3	50.1	47.8	84.8	29.2	43.7	44.9	75.0
2022	32.2	41.3	26.1	37.0	38.5	52.9	36.5	57.9	35.7	52.0	50.4	88.9	29.7	44.5	45.8	76.8



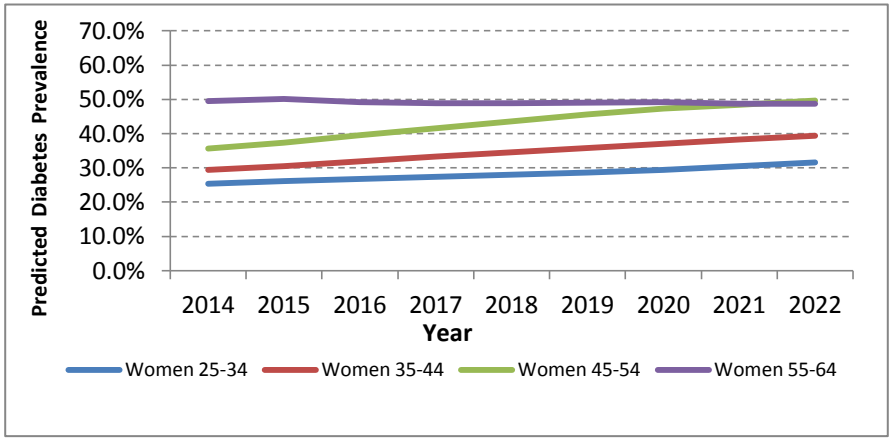
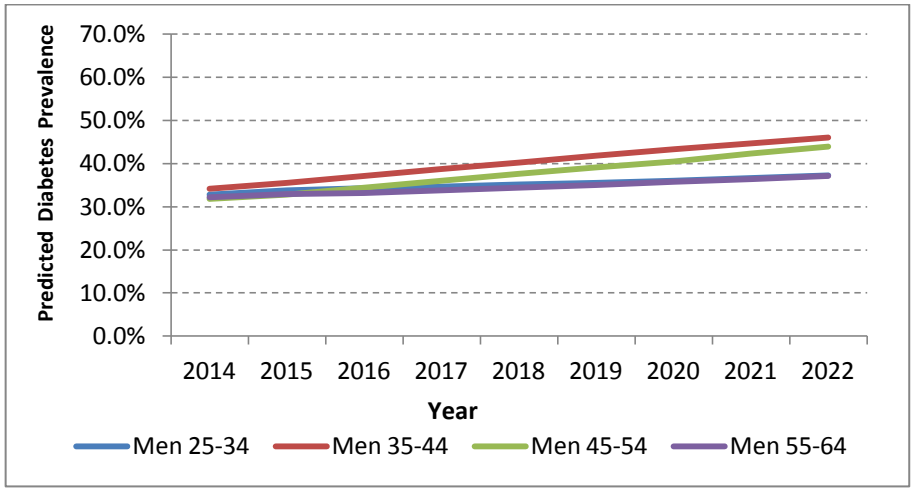


Figure 7.9. *(Scenario 1)* Trends in the predicted prevalence of diabetes per age group (years) in men and women aged 25-64 years, with capping of projected obesity prevalence, Saudi Arabia (2014-2022) [Diagnostic criteria: WHO 1985]



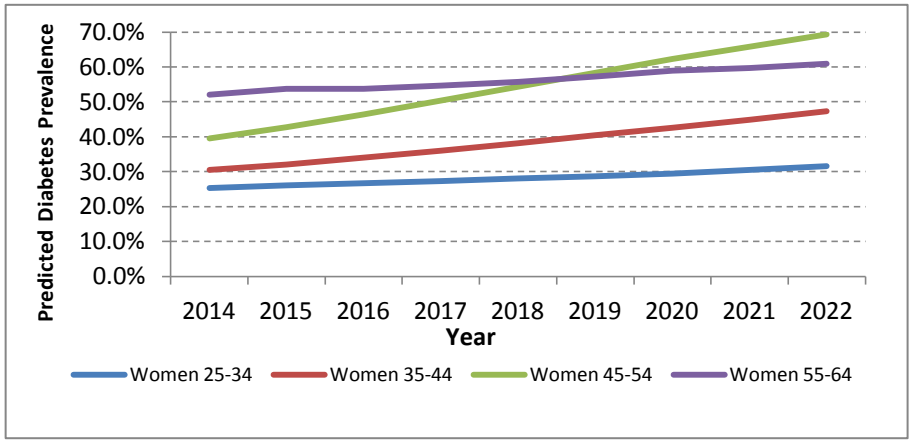


Figure 7.10. *(Scenario 2)* Trends in the predicted prevalence of diabetes per age group (years) in men and women aged 25-64 years, without capping of projected obesity prevalence, Saudi Arabia (2014-2022) [Diagnostic criteria: WHO 1985]

7.1.2.3. Results based on scenario 3: population aged 25-75+ years, with capping

When the two oldest age groups (65-74 and 75+ years) were included in the modelling process (with obesity trends in these age groups extrapolated using Omani data), the model predicted that the diabetes prevalence in women aged 65-74 years will increase by 14%; from 39.7% (UI: 32.6–47.1%) in 2014 to 45.2% (UI: 36.2–54.7%) in 2022. Women aged 75+ years will show relatively stable trends in the predicted diabetes prevalence. On the other hand, men in these two oldest age groups have relative decreasing trends in the predicted diabetes prevalence during the same period, by around 10% (Table **7.9**).

7.1.2.4. Results based on scenario 4: population aged 25-75+ years, without capping

The results of the predicted diabetes prevalence in the two oldest age groups, assuming continuing uncapped linear trends in obesity (Table **7.10**), were similar to that obtained through scenario 3 (with capped obesity trends).

The uncertainty values of the predicted diabetes prevalence based on scenarios 3 and 4 are presented in Table **7.11** and Table **7**.**12**. Moreover, Figure **7.11** and Figure **7**.**12** demonstrate graphically the trends in the diabetes prevalence for each sex and age group, as predicted by applying these two scenarios.

Table 7.9. *(Scenario 3)* Predicted prevalence of diabetes per age group (years) in men and women aged 25-75+ years, with capping of projected obesity prevalence, Saudi Arabia (2014-2022)

Year	25-34		35-44		45-54		55-64		65-74		75+	
	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
2014	32.8%	25.3%	33.3%	29.4%	31.3%	35.6%	32.2%	49.5%	31.1%	39.7%	32.8%	24.6%
2015	33.8%	26.1%	34.3%	30.5%	32.1%	37.4%	32.7%	50.1%	31.2%	40.6%	32.6%	24.9%
2016	34.3%	26.7%	35.7%	31.9%	33.5%	39.5%	33.0%	49.2%	29.9%	40.9%	32.1%	24.8%
2017	34.7%	27.3%	36.9%	33.2%	34.8%	41.6%	33.3%	48.9%	29.1%	41.5%	31.7%	24.8%
2018	35.1%	28.0%	38.1%	34.6%	36.1%	43.7%	33.7%	48.8%	28.8%	42.3%	31.4%	24.9%
2019	35.6%	28.7%	39.3%	35.9%	37.2%	45.6%	34.2%	49.0%	28.7%	43.2%	31.2%	25.2%
2020	36.0%	29.4%	40.4%	37.1%	38.2%	47.3%	34.7%	49.3%	28.8%	44.2%	31.1%	25.5%
2021	36.6%	30.5%	41.3%	38.3%	39.6%	48.5%	35.1%	48.8%	28.3%	44.5%	30.1%	25.3%
2022	37.2%	31.6%	42.2%	39.4%	40.8%	49.6%	35.5%	48.7%	28.1%	45.2%	29.4%	25.3%
Relative difference in prevalence	**+13%**	**+25%**	**+27%**	**+34%**	**+30%**	**+39%**	**+10%**	**-2%**	**-10%**	**+14%**	**-10%**	**+3%**

Table 7.10. *(Scenario 4)* Predicted prevalence of diabetes per age group (years) in men and women aged 25-75+ years, without capping of projected obesity prevalence, Saudi Arabia (2014-2022)

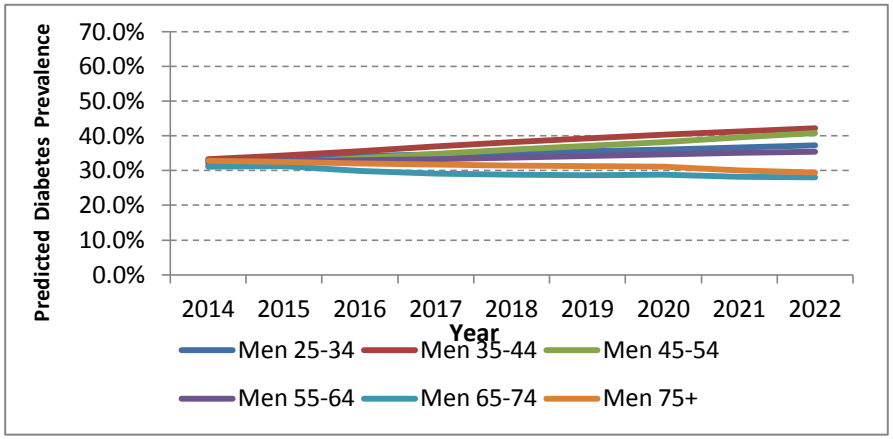
Year	25-34		35-44		45-54		55-64		65-74		75+	
	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
2014	32.8%	25.3%	34.2%	30.5%	31.8%	39.5%	32.2%	52.0%	31.1%	39.7%	32.8%	24.6%
2015	33.8%	26.1%	35.5%	32.0%	32.8%	42.7%	32.9%	53.7%	31.2%	40.6%	32.6%	24.9%
2016	34.3%	26.7%	37.1%	34.0%	34.5%	46.4%	33.2%	53.8%	29.9%	40.9%	32.1%	24.8%
2017	34.7%	27.3%	38.7%	36.0%	36.0%	50.3%	33.7%	54.6%	29.1%	41.5%	31.7%	24.8%
2018	35.1%	28.0%	40.3%	38.2%	37.6%	54.3%	34.4%	55.8%	28.8%	42.3%	31.4%	24.9%
2019	35.6%	28.7%	41.8%	40.4%	39.1%	58.4%	35.1%	57.3%	28.7%	43.2%	31.2%	25.2%
2020	36.0%	29.4%	43.3%	42.6%	40.5%	62.4%	35.8%	58.9%	28.8%	44.2%	31.1%	25.5%
2021	36.6%	30.5%	44.7%	44.9%	42.3%	65.8%	36.4%	59.7%	28.3%	44.5%	30.1%	25.3%
2022	37.2%	31.6%	46.0%	47.2%	44.0%	69.3%	37.1%	61.0%	28.1%	45.2%	29.4%	25.3%
Relative difference in prevalence	**+13%**	**+25%**	**+35%**	**+55%**	**+38%**	**+75%**	**+15%**	**+17%**	**-10%**	**+14%**	**-10%**	**+3%**

Table 7.11. *(Scenario 3)* Sensitivity analysis: lower (L) and higher (H) uncertainty values of the predicted diabetes prevalence (%) per age group (years) in men and women aged 25-75+ years, with capping of projected obesity prevalence, Saudi Arabia (2014-2022)

Year	25-34				35-44				45-54				55-64				65-74				75+			
	Men		Women		Men		Women		Men		Women		Men		Women		Men		Women		Men		Women	
	L	H	L	H	L	H	L	H	L	H	L	H	L	H	L	H	L	H	L	H	L	H	L	H
2014	27.5	37.3	20.8	29.7	27.7	38.2	23.4	35.3	25.7	36.7	27.8	43.6	26.2	38.3	38.1	60.7	27.7	33.8	32.6	47.1	31.9	31.7	23.3	26.3
2015	28.5	38.3	21.5	30.6	28.6	39.3	24.2	36.6	26.3	37.7	28.9	46.3	26.6	39.0	38.9	61.2	27.8	34.0	33.2	48.2	31.8	31.6	23.5	26.6
2016	29.0	38.6	22.0	31.3	29.8	40.7	25.3	38.3	27.4	39.4	30.3	49.3	26.7	39.3	38.4	59.8	26.6	32.7	33.4	48.7	31.4	31.1	23.3	26.5
2017	29.5	39.0	22.5	32.0	31.0	42.1	26.4	39.9	28.5	40.9	31.8	52.1	27.0	39.7	38.3	59.3	25.8	32.1	33.8	49.6	31.1	30.8	23.2	26.7
2018	30.0	39.4	23.1	32.8	32.2	43.3	27.5	41.5	29.6	42.2	33.3	54.7	27.3	40.2	38.3	59.4	25.3	31.9	34.3	50.7	30.8	30.6	23.2	26.9
2019	30.4	39.7	23.7	33.6	33.3	44.5	28.5	43.0	30.6	43.4	34.7	56.9	27.7	40.7	38.5	59.6	25.1	32.0	34.9	51.9	30.6	30.5	23.3	27.3
2020	30.9	40.1	24.3	34.4	34.3	45.5	29.5	44.5	31.5	44.5	36.1	58.7	28.1	41.2	38.7	59.9	25.0	32.3	35.6	53.1	30.5	30.5	23.5	27.7
2021	31.5	40.7	25.2	35.7	35.3	46.4	30.5	45.8	32.8	45.9	37.2	59.8	28.4	41.5	38.4	59.3	24.4	31.9	35.8	53.7	29.5	29.6	23.3	27.6
2022	32.2	41.3	26.1	37.0	36.2	47.2	31.5	47.1	33.9	47.1	38.3	60.9	28.8	41.9	38.4	59.3	24.1	31.9	36.2	54.7	28.7	29.0	23.2	27.7

Table 7.12. *(Scenario 4)* Sensitivity analysis: lower (L) and higher (H) uncertainty values of the predicted diabetes prevalence (%) per age group (years) in men and women aged 25-75+ years, without capping of projected obesity prevalence, Saudi Arabia (2014-2022)

Year	25-34				35-44				45-54				55-64				65-74				75+			
	Men		Women		Men		Women		Men		Women		Men		Women		Men		Women		Men		Women	
	L	H	L	H	L	H	L	H	L	H	L	H	L	H	L	H	L	H	L	H	L	H	L	H
2014	27.5	37.3	20.8	29.7	28.2	39.6	24.1	36.7	25.9	37.4	30.1	49.4	26.2	38.4	39.5	64.8	27.7	33.8	32.6	47.1	31.9	31.7	23.3	26.3
2015	28.5	38.3	21.5	30.6	29.3	41.1	25.2	38.7	26.7	38.8	32.1	54.2	26.6	39.3	40.9	66.8	27.8	34.0	33.2	48.2	31.8	31.6	23.5	26.6
2016	29.0	38.6	22.0	31.3	30.7	42.9	26.7	41.2	28.0	40.9	34.4	59.6	26.8	39.8	41.0	66.8	26.6	32.7	33.4	48.7	31.4	31.1	23.3	26.5
2017	29.5	39.0	22.5	32.0	32.1	44.7	28.2	43.8	29.2	42.8	37.0	65.1	27.2	40.4	41.5	68.0	25.8	32.1	33.8	49.6	31.1	30.8	23.2	26.7
2018	30.0	39.4	23.1	32.8	33.5	46.5	29.8	46.5	30.4	44.7	39.6	70.5	27.6	41.2	42.3	69.7	25.3	31.9	34.3	50.7	30.8	30.6	23.2	26.9
2019	30.4	39.7	23.7	33.6	34.8	48.2	31.4	49.2	31.6	46.4	42.4	75.7	28.1	42.1	43.3	71.7	25.1	32.0	34.9	51.9	30.6	30.5	23.3	27.3
2020	30.9	40.1	24.3	34.4	36.1	49.9	33.1	52.1	32.8	48.1	45.2	80.7	28.7	43.0	44.4	73.9	25.0	32.3	35.6	53.1	30.5	30.5	23.5	27.7
2021	31.5	40.7	25.2	35.7	37.3	51.4	34.8	54.9	34.3	50.1	47.8	84.8	29.2	43.7	44.9	75.0	24.4	31.9	35.8	53.7	29.5	29.6	23.3	27.6
2022	32.2	41.3	26.1	37.0	38.5	52.9	36.5	57.9	35.7	52.0	50.4	88.9	29.7	44.5	45.8	76.8	24.1	31.9	36.2	54.7	28.7	29.0	23.2	27.7



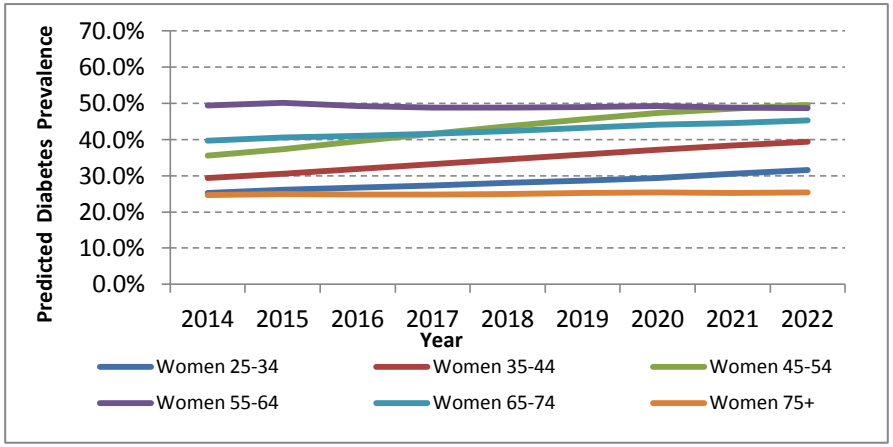
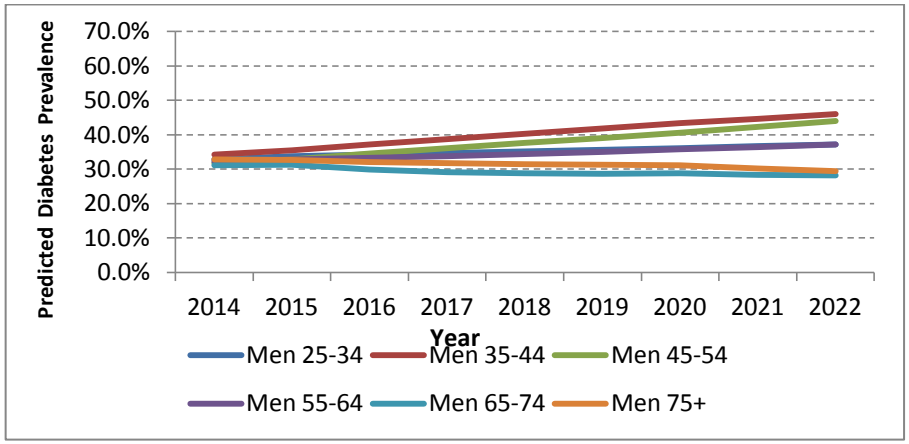


Figure 7.11. *(Scenario 3)* Trends in the predicted prevalence of diabetes per age group (years) in men and women aged 25-75+ years, with capping of projected obesity prevalence, Saudi Arabia (2014-2022) [Diagnostic criteria: WHO 1985]



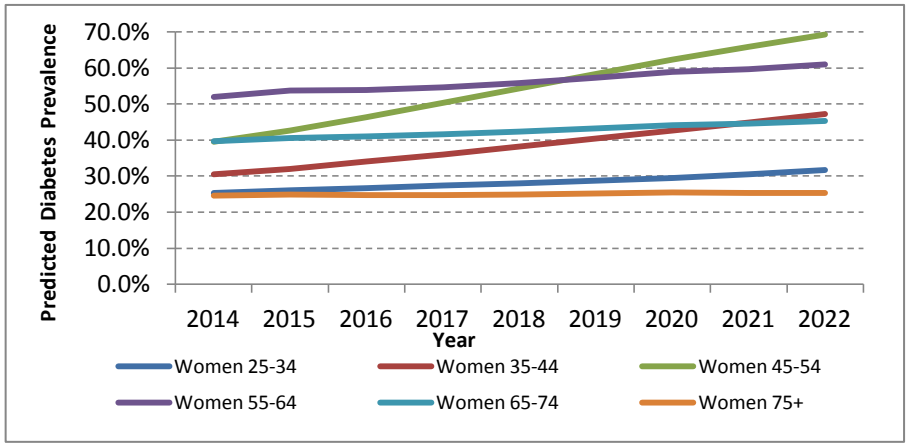


Figure 7.12. *(Scenario 4)* Trends in the predicted prevalence of diabetes per age group (years) in men and women aged 25-75+ years, without capping of projected obesity prevalence, Saudi Arabia (2014-2022) [Diagnostic criteria: WHO 1985]

7.1.3. Quantified effects of the assumed capping of obesity on the modelling results for 2022

Unlike the modelling results for 2013 which have been discussed in chapter 6, the results for 2022 were found to be affected significantly by shifting between different scenarios. As summarised in Table **7.13**, the estimated overall diabetes prevalence for the population aged 25-64 years was 39.5% under scenario 1 (with capped obesity trends), but 44.1% under scenario 2 (with increasing uncapped obesity). Also, the results due to shifting from scenario 1 to scenario 2 showed a relative increase by 5.3% in men and 19.8% in women.

The estimated diabetes prevalence for men and women in the age group 25-34 years was not affected by capping, as the results were similar by shifting from scenario 1 to scenario 2. In the other age groups of men, the quantified relative changes as a result of such a shifting were 9.0% in the age group 35-44 years, 7.8% in the age group 45-54 years and 4.5% in the age group 55-64 years. Importantly, these quantified relative changes were much more prominent in women. Shifting from scenario 1 to scenario 2 resulted in relative increases in the estimated diabetes prevalence by 19.8% in women aged 35-44 years, 39.7% in those aged 45-54 years and 25.3% in the age group 55-64 years.

Adding the two oldest age groups to the model resulted in an estimated population diabetes prevalence of 38.9% in 2022 by scenario 3 (with capped obesity), which increased to 43.2% by scenario 4 (without capping of obesity). In addition, shifting from scenario 3 to scenario 4 resulted in relative increases of diabetes prevalence by 5.0% in men and 18.1% in women.

However, capping had no effect on the estimated results for men and women in the two oldest age groups (65-74 and 75+ years). By shifting from scenario 3 to scenario 4, the estimated diabetes prevalence remained at 28.1% for men aged 65-74 years, 29.4% for men aged 75+ years, 45.2% for women aged 65-74 years and 25.3% in women aged 75+ years.

Table 7.13. Summary of the main modelling results (2022) for each scenario and the quantified changes as a result of shifting between different scenarios

	Scenario 1	Scenario 2	Quantified relative change (%) as a result of shifting from scenario 1 to scenario 2	Scenario 3	Scenario 4	Quantified relative change (%) as a result of shifting from scenario 3 to scenario 4
Overall population diabetes prevalence (%) in 2022	39.5	44.1	+ 11.6	38.9	43.2	+ 11.1
Overall diabetes prevalence (%) in men in 2022	39.2	41.3	+ 5.3	37.8	39.7	+ 5.0
Overall diabetes prevalence (%) in women in 2022	39.8	47.7	+ 19.8	39.7	46.9	+ 18.1
Estimated prevalence of diabetes (%) per sex and age group in 2022:						
Men 25-34 years	37.2	37.2	No change	37.2	37.2	No change
Men 35-44 years	42.2	46.0	+ 9.0	42.2	46.0	+ 9.0
Men 45-54 years	40.8	44.0	+ 7.8	40.8	44.0	+ 7.8
Men 55-64 years	35.5	37.1	+ 4.5	35.5	37.1	+ 4.5
Men 65-74 years	-	-	-	28.1	28.1	No change
Men 75+ years	-	-	-	29.4	29.4	No change
Women 25-34 years	31.6	31.6	No change	31.6	31.6	No change
Women 35-44 years	39.4	47.2	+ 19.8	39.4	47.2	+ 19.8
Women 45-54 years	49.6	69.3	+ 39.7	49.6	69.3	+ 39.7
Women 55-64 years	48.7	61.0	+ 25.3	48.7	61.0	+ 25.3
Women 65-74 years	-	-	-	45.2	45.2	No change
Women 75+ years	-	-	-	25.3	25.3	No change

7.2. Overview of the main results for the whole modelling period (1992-2022)

7.2.1. Comparison of the main results based on scenario 1 and scenario 2

During the 30-year-period of 1992-2022, the estimated diabetes prevalence in the Saudi men and women aged 25-64 years will increase substantially from 8.5% (UI: 6.8–10.2%) to 39.5% (UI: 32.5–45.9%), assuming capped linear trends in obesity prevalence, and to 44.1% (UI: 35.4–52.5%), assuming continuing uncapped linear obesity trends (Figure **7.13** and Figure **7.14**). In men, the diabetes prevalence is estimated to increase from 8.7% (UI: 6.9–10.4%) to 39.2% (UI: 33.2–44.4%) with capped obesity trends, and to 41.3% (UI: 34.4–47.6%) with continuing linearity in obesity trends. On the other hand, in women, diabetes prevalence is estimated to increase from 8.2% (UI: 6.6–9.9%) to 39.8% (UI: 31.7–47.7%) with capping of obesity trends, and to 47.7% (UI: 36.6–58.8%) without such a capping (Figure **7.15** and Figure **7.16**).

Among the population age groups, the assumed capping of the obesity levels had no effect on diabetes prevalence trends in men and women aged 25-34 years, where the estimated relative increases were 905% in men and 953% in women under both scenarios 1 and 2. In comparison, there was a significant effect of capping on the results of the other age groups, particularly among women. For instance, in women aged 45-54 years, diabetes prevalence is estimated to increase by 124% if the obesity trends were capped, and by 214% if such trends were not capped. Similarly, the estimated diabetes prevalence in women aged 55-64 years will increase by 110% with capping, and by 163% with continuing uncapped obesity levels (Figure **7.17**, Figure **7.18**, and Table **7.14**).

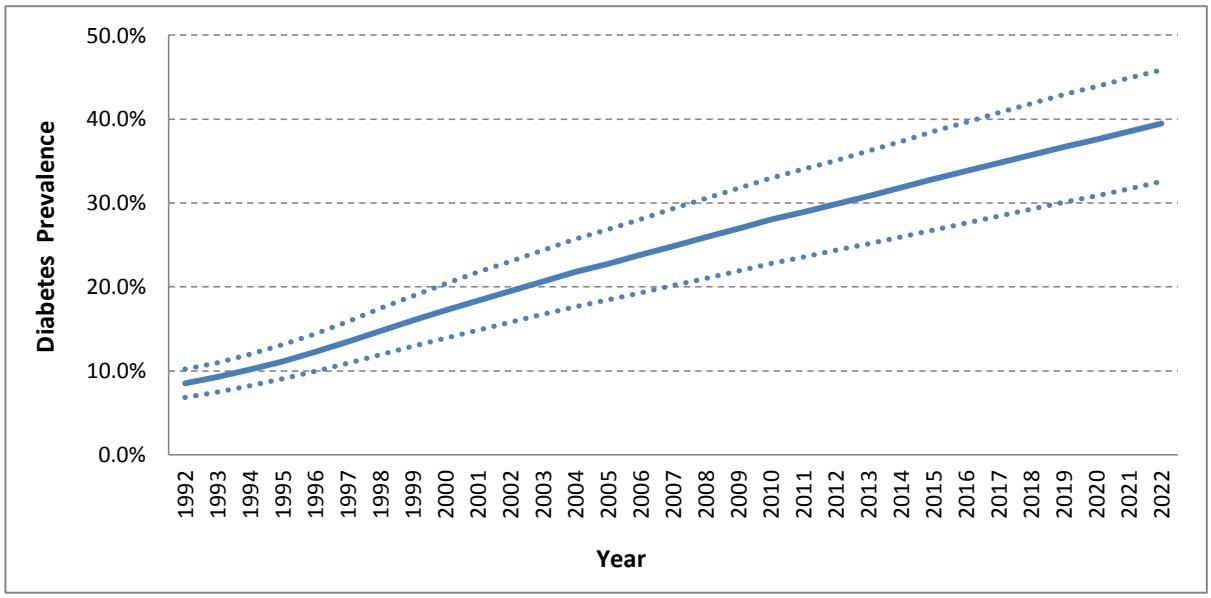


Figure 7.13. *(Scenario 1)* Trends in the estimated diabetes total prevalence (and uncertainty values) for population aged 25-64 years, with capping of projected obesity prevalence, Saudi Arabia (1992-2022)

[*Solid line:* point (best) estimates; *Dotted lines:* minimum and maximum uncertainty estimates. Diagnostic criteria: WHO 1985]

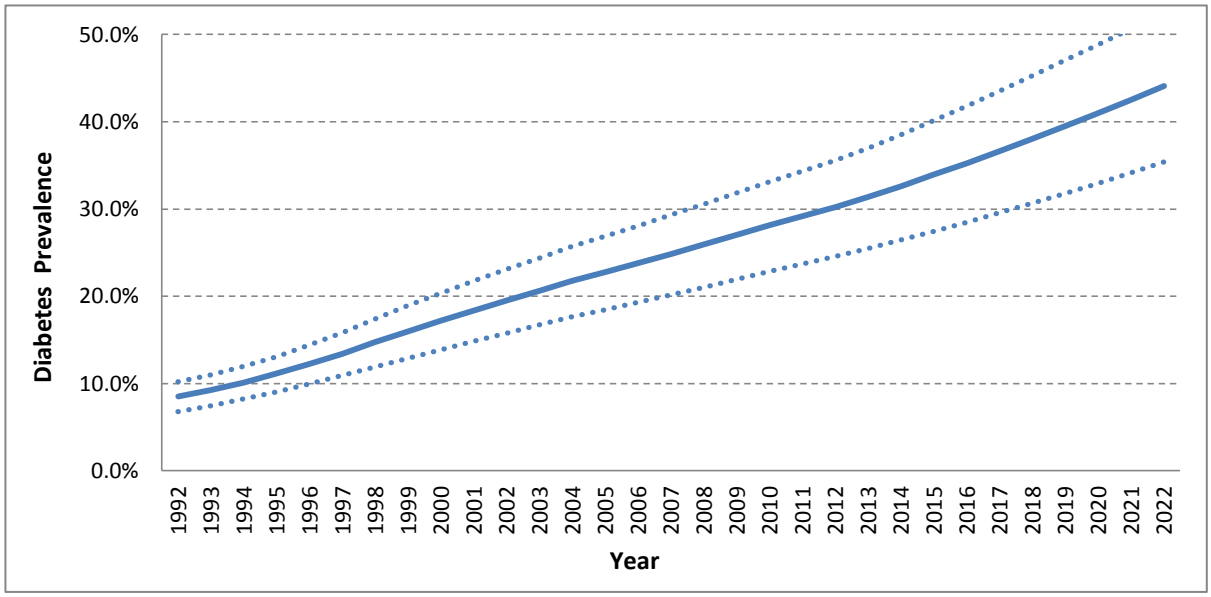


Figure 7.14. *(Scenario 2)* Trends in the estimated diabetes total prevalence (and uncertainty values) for population aged 25-64 years, without capping of projected obesity prevalence, Saudi Arabia (1992-2022)

[*Solid line:* point (best) estimates; *Dotted lines:* minimum and maximum uncertainty estimates. Diagnostic criteria: WHO 1985]

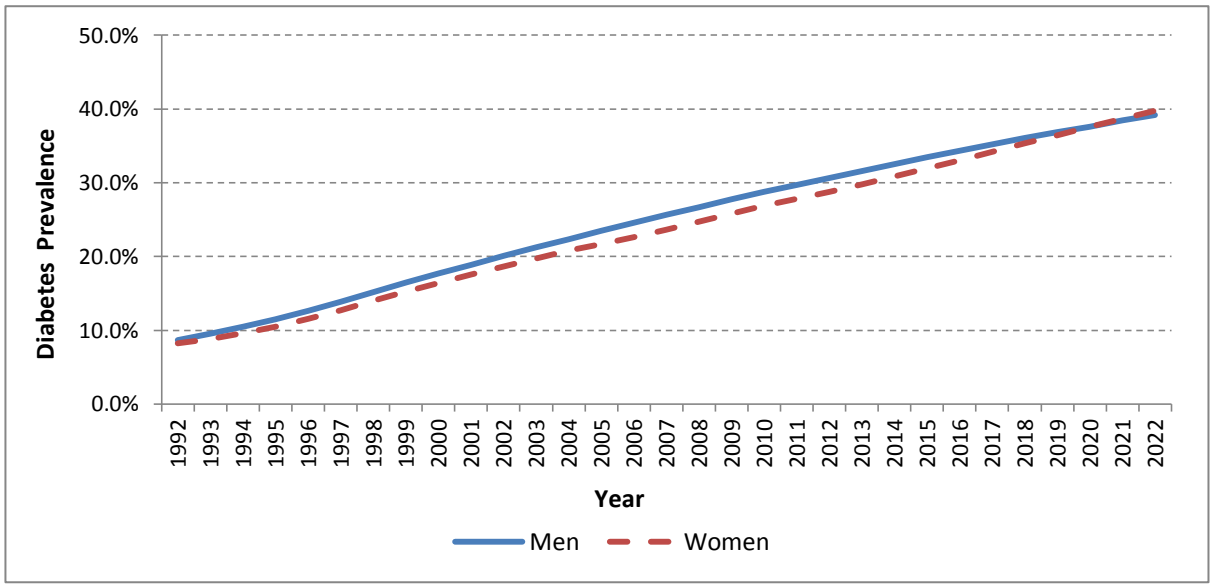


Figure 7.15. *(Scenario 1)* Trends in the estimated diabetes prevalence (and uncertainty values) for men and women aged 25-64 years, with capping of projected obesity prevalence, Saudi Arabia (1992-2022)

[Diagnostic criteria: WHO 1985]

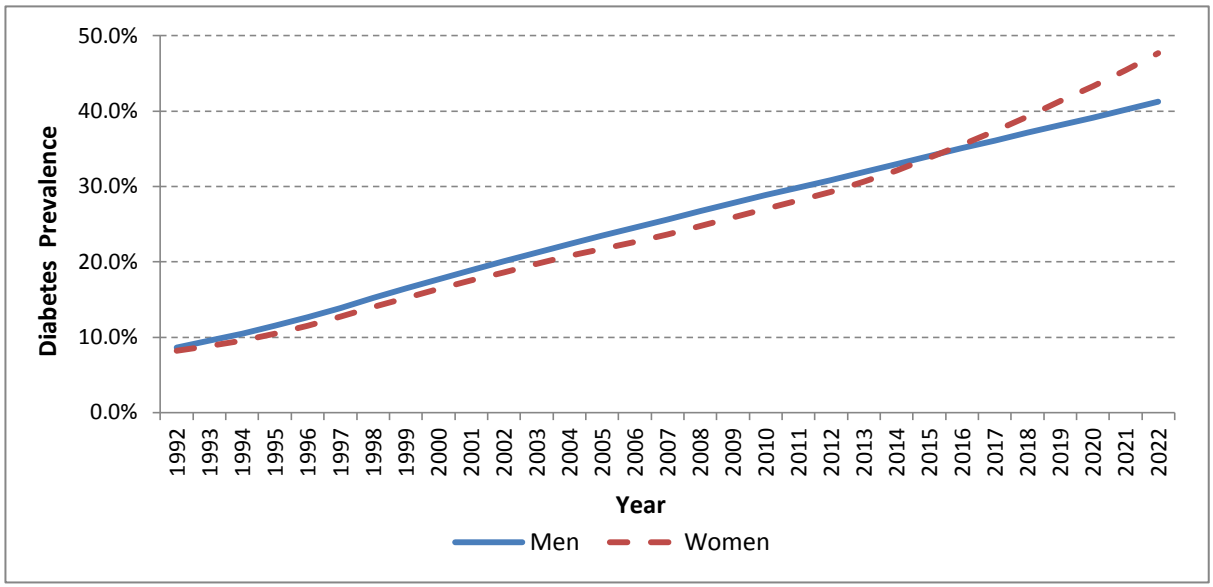
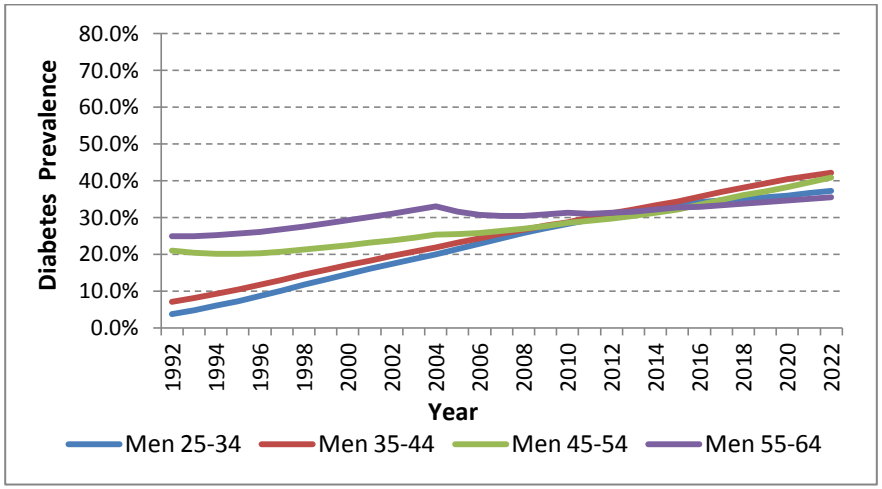


Figure 7.16. *(Scenario 2)* Trends in the estimated diabetes prevalence (and uncertainty values) for men and women aged 25-64 years, without capping of projected obesity prevalence, Saudi Arabia (1992-2022)

[Diagnostic criteria: WHO 1985]



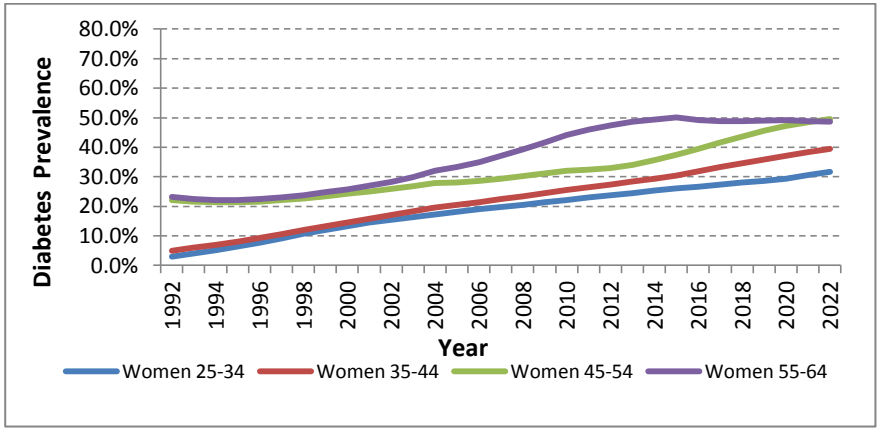
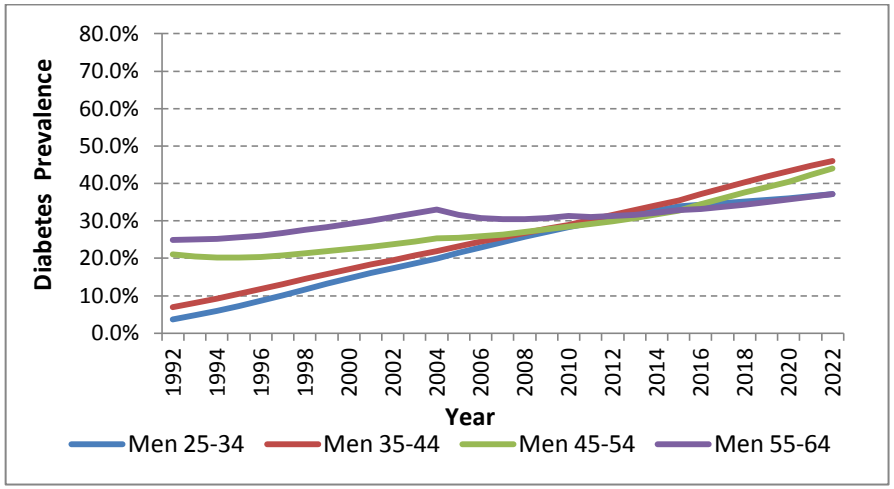


Figure 7.17. *(Scenario 1)* Trends in the estimated prevalence of diabetes per age group (years) in men and women aged 25-64 years, with capping of projected obesity prevalence, Saudi Arabia (1992-2022) [Diagnostic criteria: WHO 1985]



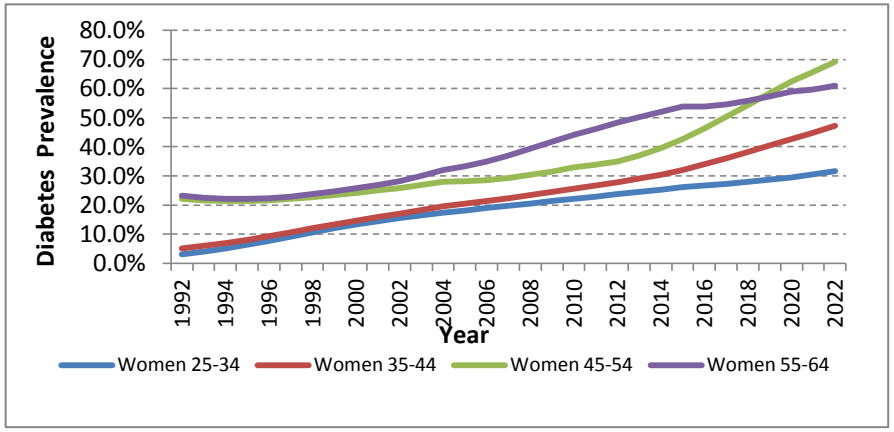


Figure 7.18. *(Scenario 2)* Trends in the estimated prevalence of diabetes per age group (years) in men and women aged 25-64 years, without capping of projected obesity prevalence, Saudi Arabia (1992-2022) [Diagnostic criteria: WHO 1985]

Table 7.14. Summary of the diabetes prevalence rates (%) per sex and age group (years) for the first and last years of modelling, based on the four scenarios

Scenario	Year	25-34		35-44		45-54		55-64		65-74		75+	
		Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
	1992	3.7	3.0	7.0	5.0	21.1	22.1	24.9	23.2				
1	*2022*	37.2	31.6	42.2	39.4	40.8	49.6	35.5	48.7				
	Relative difference	**+905%**	**+953%**	**+502%**	**+688%**	**+93%**	**+124%**	**+43%**	**+110%**				
	1992	3.7	3.0	7.0	5.0	21.1	22.1	24.9	23.2				
2	*2022*	37.2	31.6	46.0	47.2	44.0	69.3	37.1	61.0				
	Relative difference	**+905%**	**+953%**	**+557%**	**+844%**	**+109%**	**+214%**	**+49%**	**+163%**				
	1992	3.7	3.0	7.0	5.0	21.1	22.1	24.9	23.2	28.8	24.4	28.8	24.4
3	*2022*	37.2	31.6	42.2	39.4	40.8	49.6	35.5	48.7	28.1	45.2	29.4	25.3
	Relative difference	**+905%**	**+953%**	**+502%**	**+688%**	**+93%**	**+124%**	**+43%**	**+110%**	**-2%**	**+85%**	**+2%**	**+4%**
	1992	3.7	3.0	7.0	5.0	21.1	22.1	24.9	23.2	28.8	24.4	28.8	24.4
4	*2022*	37.2	31.6	46.0	47.2	44.0	69.3	37.1	61.0	28.1	45.2	29.4	25.3
	Relative difference	**+905%**	**+953%**	**+557%**	**+844%**	**+109%**	**+214%**	**+49%**	**+163%**	**-2%**	**+85%**	**+2%**	**+4%**

7.2.2. Comparison of the main results based on scenario 3 and scenario 4

When the two oldest age groups of the population (65-74 and 75+ years) were included in the modelling, the overall population prevalence of diabetes by 2022 is estimated to reach 38.9% (UI: 32.2–45.2%), assuming capped obesity trends, and 43.2% (UI: 34.8–51.3%) if such trends continue to increase without capping (Figure **7.19** and Figure **7.20**).

In men, the estimated diabetes prevalence in 2022 is 37.8% (UI: 32.0–42.8%) with the assumption of capped obesity, and 39.7% (UI: 33.1–45.7%) with the other assumption of continuing uncapped linearity in obesity. In comparison, women in 2022 will have an estimated diabetes prevalence of 39.7% (UI: 31.7–47.5%) with capping and 46.9% (UI: 36.2–57.7%) without such a capping of obesity levels (Figure **7.21** and Figure **7.22**).

As shown in Figure **7.23**, Figure **7.24**, and Table **7.14**, men and women aged 75+ years would show almost stable pattern of the trends in diabetes prevalence during the modelling period. Also, similar stability is predicted in men aged 65-74 years with a relative difference of -2% in the estimated diabetes prevalence in 1992 and 2022. However, women aged 65-74 years would have a large estimated relative increase in diabetes prevalence (85%) during this period. The results in the two oldest age groups were similar using both scenario 3 (with assumed capped obesity) and scenario 4 (with ongoing increasing obesity).

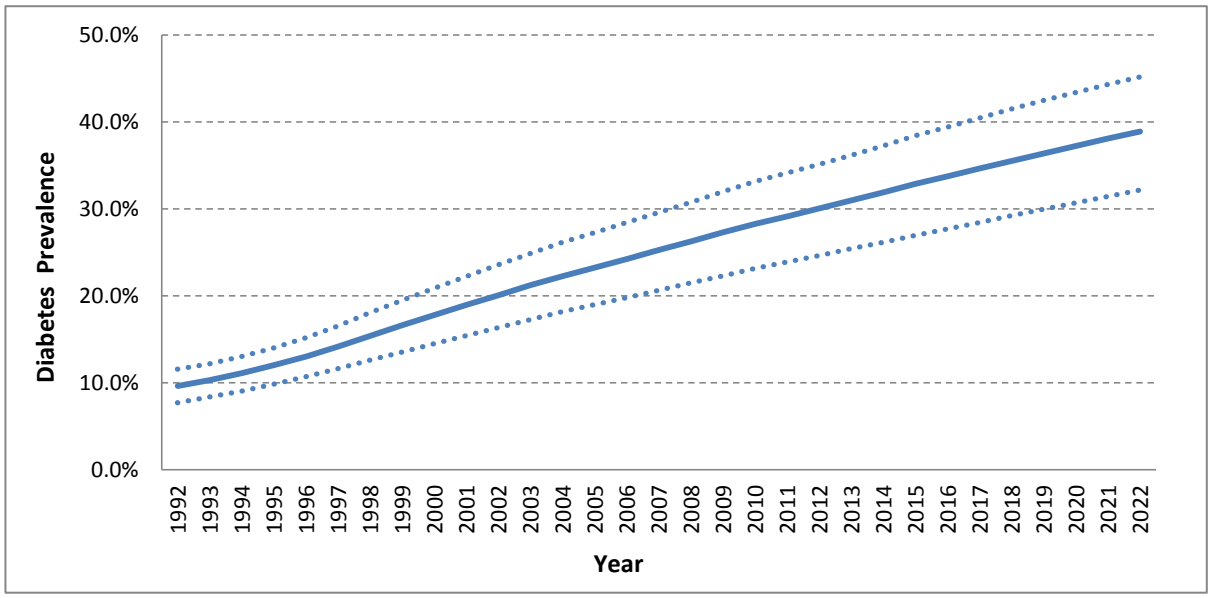


Figure 7.19. *(Scenario 3)* Trends in the estimated diabetes total prevalence (and uncertainty values) for population aged 25-75+ years, with capping of projected obesity prevalence, Saudi Arabia (1992-2022)

[*Solid line:* point (best) estimates; *Dotted lines:* minimum and maximum uncertainty estimates. Diagnostic criteria: WHO 1985]

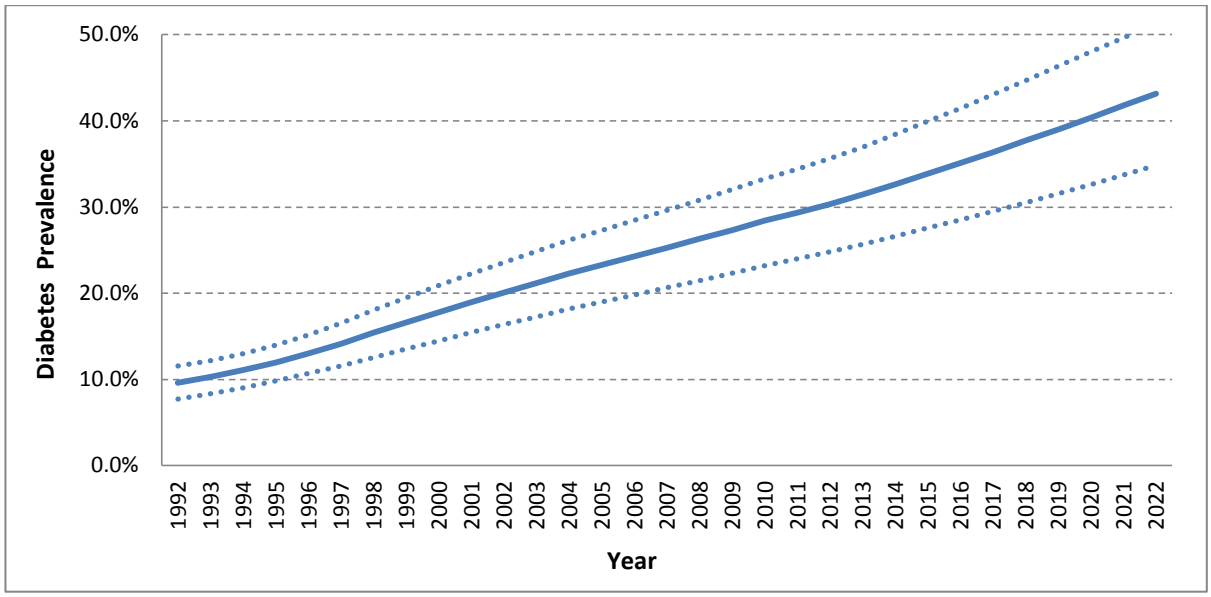


Figure 7.20. *(Scenario 4)* Trends in the estimated diabetes total prevalence (and uncertainty values) for population aged 25-75+ years, without capping of projected obesity prevalence, Saudi Arabia (1992-2022)

[*Solid line:* point (best) estimates; *Dotted lines:* minimum and maximum uncertainty estimates. Diagnostic criteria: WHO 1985]

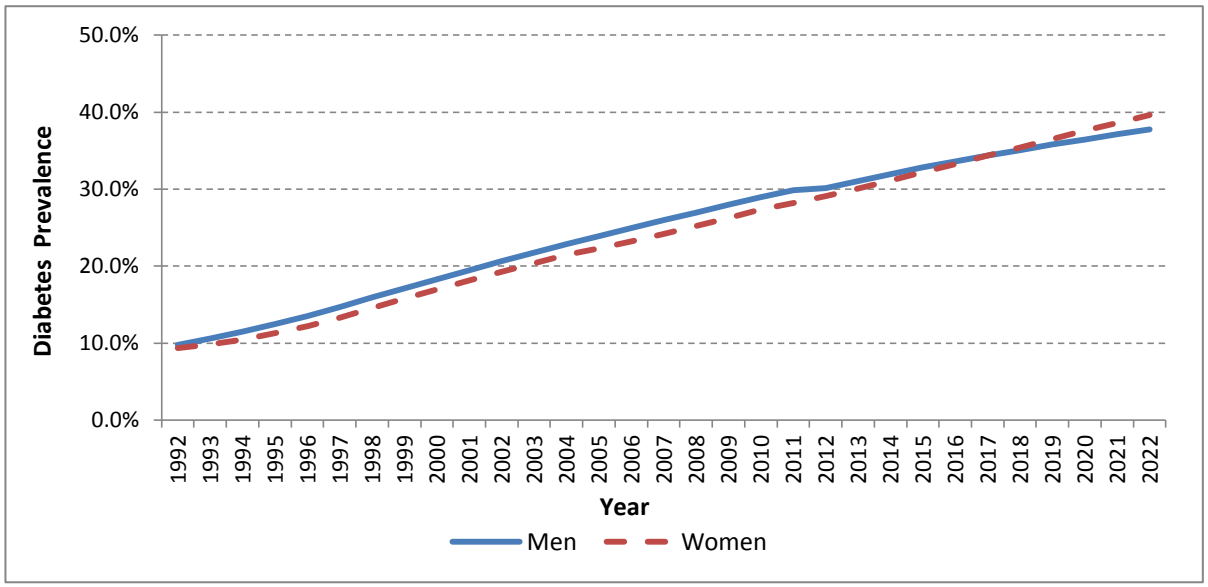


Figure 7.21. *(Scenario 3)* Trends in the estimated diabetes prevalence (and uncertainty values) for men and women aged 25-75+ years, with capping of projected obesity prevalence, Saudi Arabia (1992-2022)

[Diagnostic criteria: WHO 1985]

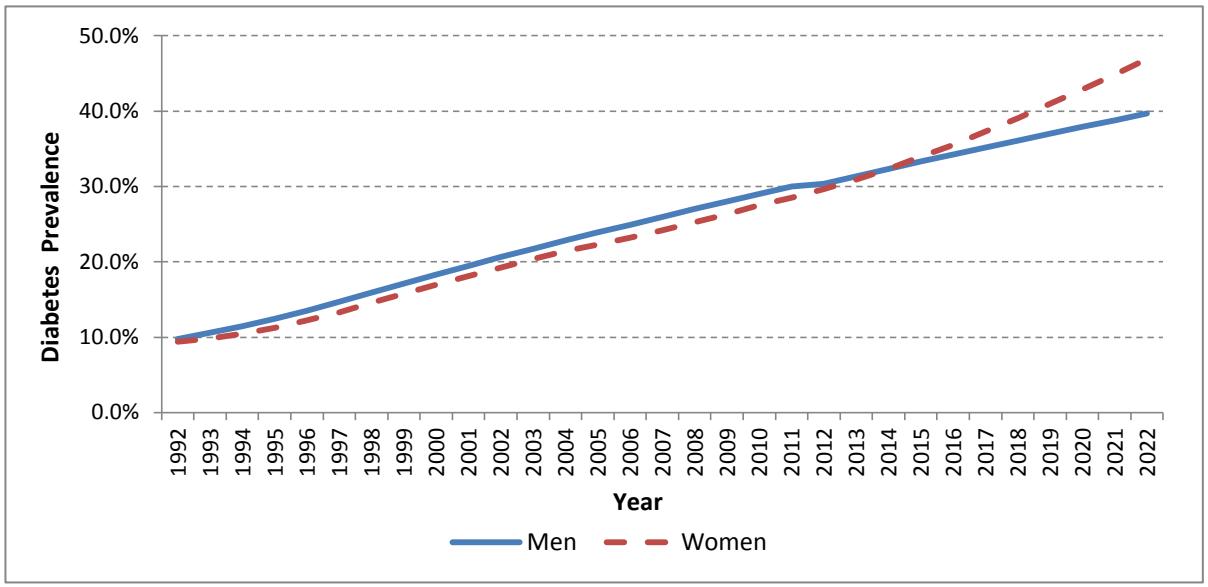


Figure 7.22. *(Scenario 4)* Trends in the estimated diabetes prevalence (and uncertainty values) for men and women aged 25-75+ years, without capping of projected obesity prevalence, Saudi Arabia (1992-2022)

[Diagnostic criteria: WHO 1985]

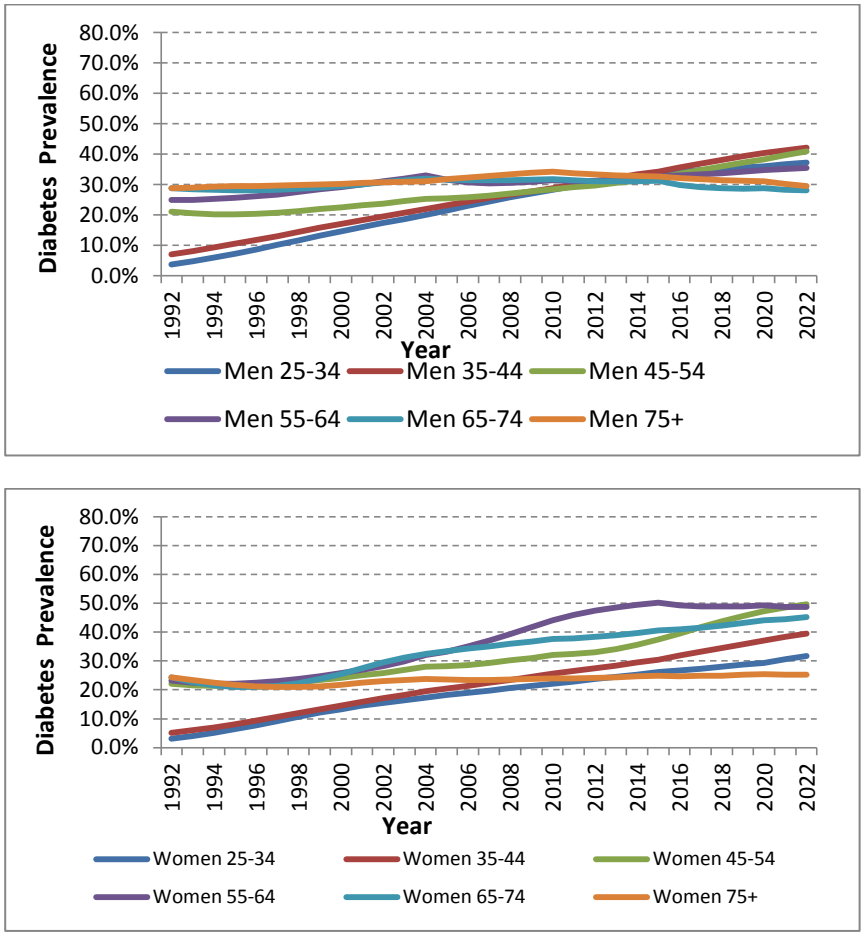


Figure 7.23. *(Scenario 3)* Trends in the estimated prevalence of diabetes per age group (years) in men and women aged 25-75+ years, with capping of projected obesity prevalence, Saudi Arabia (1992-2022) [Diagnostic criteria: WHO 1985]

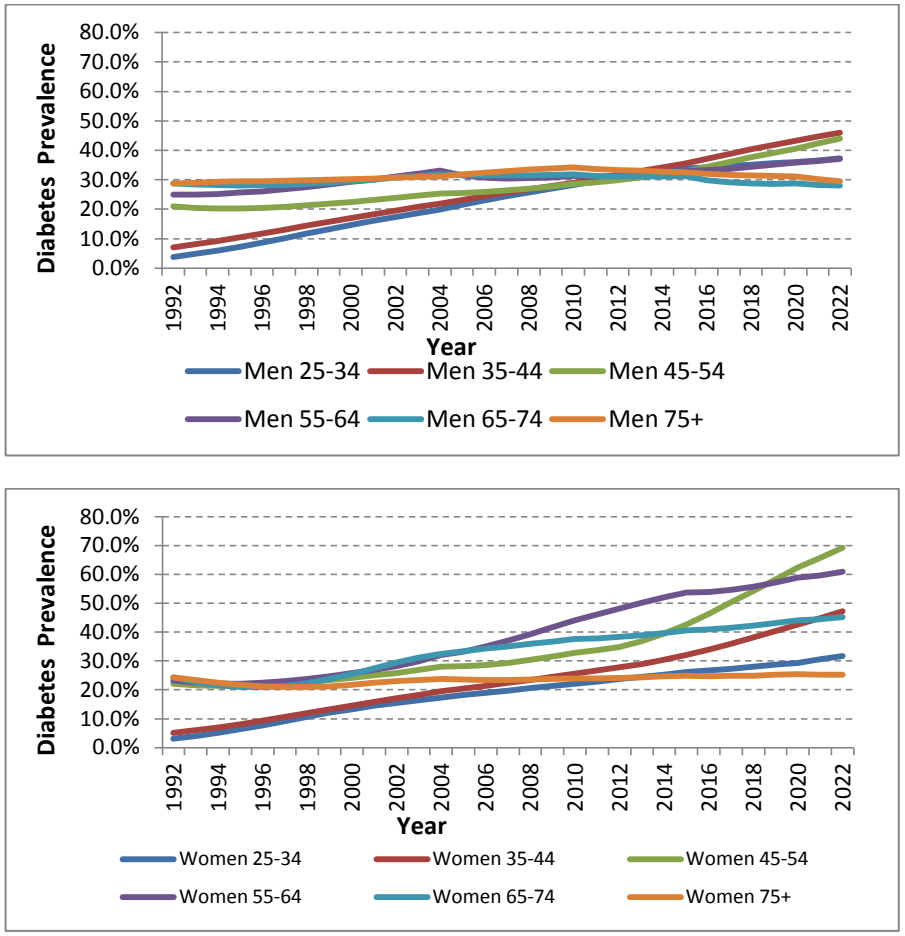


Figure 7.24. *(Scenario 4)* Trends in the estimated prevalence of diabetes per age group (years) in men and women aged 25-75+ years, without capping of projected obesity prevalence, Saudi Arabia (1992-2022) [Diagnostic criteria: WHO 1985]

7.3. Impact of adjusting the modelling results of diabetes prevalence to the more recent diagnostic criteria

7.3.1. Background

The results of predicted diabetes prevalence in Saudi Arabia as estimated by the model were based on the local observed prevalence data in 1992 from the study of Warsy and El-Hazmi.[36] As indicated in chapter 3, that study used the WHO 1985 diagnostic criteria (fasting glucose ≥7.8 mmol/l and/or OGTT glucose ≥11.1 mmol/l) to define diabetes. However, the WHO STEPS survey[19] (2005) and the GBD model[20] (2011), which were used for validation (as discussed in chapter 6) used the more recent ADA criteria (only fasting glucose ≥7.0 mmol/l) to define diabetes. Therefore, the reported results of diabetes prevalence by Warsy and El-Hazmi[36] for 1992 were adjusted to the ADA criteria in order to investigate the impact of such an adjustment on the model's predictions of diabetes prevalence in Saudi Arabia.

When the new diagnostic fasting threshold was first recommended by the ADA in 1997 to be used alone in epidemiological studies, the ADA reported that changing from the WHO threshold (with OGTT) to the new one would lead to a minimal reduction in the overall population prevalence of diabetes.[3] The ADA reported supporting data from the US, where diabetes prevalence fell from 14.3% to 12.3% with shifting from the threshold of WHO to that of ADA.[3] This fall in prevalence was equivalent to an absolute reduction of 2 percentage points and a relative reduction of around 14.0%.

Moreover, Shaw et al.[266] further investigated the impact of such a change in diagnostic thresholds on the prevalence of diabetes in some other populations. They used previously collected data from nine southern hemisphere population-based studies, in which the OGTT was used for diagnosis of diabetes. The settings of these studies include Nauru, Western Samoa, Rodrigues, New Caledonia and Wallis Islands, Cook Islands, Fiji, Kiribati, Mauritius, and Papua New Guinea. These studies covered different ethnic groups such as Micronesian, Polynesian, Melanesian, Asian Indian, Chinese, African, European, and Malagasy ancestry. Diabetes in these surveys was diagnosed as 'known' diabetes mellitus (KDM) if subjects were on oral hypoglycaemic

drugs or insulin. These subjects had only a fasting plasma glucose measured, whereas all other subjects had an OGTT. To compare prevalence estimates according to the ADA (1997) and WHO (1985) diagnostic criteria, diabetes was determined in all non-KDM subjects according to the ADA criteria irrespective of OGTT, and according to WHO criteria, irrespective of fasting plasma glucose.[266] The authors found that changing the diagnostic criteria had variable effects on diabetes prevalence in these different populations. The relative difference in prevalence ranged from +30% to -19%, and the absolute difference ranged from +4.1 percentage points to -2.8 percentage points. Some countries (Fiji and Cook Islands) were found to have a 0% difference in diabetes prevalence with changing the diagnostic criteria. Shaw et al. reported that the logistic regression analysis showed that the interaction term between survey site and diabetes criteria (ADA or WHO) was a highly significant predictor of diabetes status ($p< 0.0001$), which could confirm that the variability in performance of the two sets of criteria between populations was not due to chance.[266]

Nevertheless, Shaw et al. did not include countries from the EMR, in which Saudi Arabia is located. The reported results for the countries included in the study might not be applicable to populations in this region. In the literature, there is a study from Oman (a neighbouring country to Saudi Arabia) which assessed the impact of applying the ADA diagnostic criteria on the reported diabetes prevalence based on the WHO criteria (fasting glucose and OGTT) from the National Diabetes Survey (1991).[267] The authors used the database generated by that survey, which involved 4,682 subjects with no missing data on fasting and 2-hour (OGTT) glucose. To compare the two diagnostic criteria, all individuals were classified on the basis of the ADA's versus WHO's threshold values of venous fasting plasma glucose and OGTT. It was found that applying the ADA criteria on the Omani population resulted in an overall reduction of diabetes prevalence from 10.5% to 8.3%. This is equivalent to a relative reduction of approximately 21%, and an absolute reduction of 2.2 percentage points.

There are no obvious reasons for the large variations in the effects of changing the diagnostic criteria (from the WHO to ADA) between countries. Shaw et al.[266] concluded that such variations are unpredictable and seemed to be related to various factors. To investigate the influence of some potential contributing

factors, they categorised the diabetic individuals from the nine countries in their study based on sex, age and BMI. It has been found that obesity (BMI ≥30 kg/m^2) was the most important factor in determining on which criterion diabetes was diagnosed. Obese diabetic subjects were much less likely than lean diabetic subjects to have low fasting and high OGTT levels, but more likely to have both elevated fasting and OGTT ($p< 0.00001$). Thus, diabetic subjects defined by the ADA criteria were found to be more obese than those identified by the WHO criteria.[266] Among all the studies from the nine countries, the two studies from Nauru and Western Samoa (which had the highest mean population BMI) had the highest proportion of diabetic subjects with FPG ≥7.0 mmol/l. However, this finding was not consistent among all the populations included, which might suggest that there are other important factors. However, the influence of other factors, such as age, was not clear-cut.[266]

7.3.2. Results of adjustment

In this thesis, the results of diabetes prevalence in Saudi Arabia for the starting year of modelling (1992), as obtained from the study of Warsy and El-Hazmi,[36] were adjusted to the ADA diagnostic threshold. Three values were used for this adjustment. First, the diabetes prevalence in Saudi Arabia for 1992 was assumed to vary by the first extreme value found by Shaw et al.[266] (relative difference of +30%) when the diagnostic criteria are changed from WHO threshold to that of ADA. Second, it was assumed that the diabetes prevalence for the starting year of modelling would vary by the second extreme value of Shaw et al. (relative difference of -19%) with a similar change in diagnostic criteria. Third, diabetes prevalence in 1992 was assumed to show a relative reduction of -21% (as that found in Oman[267]) with changing the diagnostic thresholds. Table **7.15** summarises the model results of the predicted diabetes prevalence before and after adjustment for the starting year (1992), in addition to years 2000, 2005 and 2008 (years used for validation against the WHO STEPS survey[19] and the GBD model[20] as discussed in chapter 6).

In general, the variations in the estimated diabetes prevalence in Saudi Arabia were small, assuming that the 'observed' diabetes prevalence in 1992 would change by any of the three adjustment values mentioned above. For instance, with scenario 1, using the adjustment value of Shaw et al.[266] (relative difference

of +30%), the ‘adjusted’ prevalence of diabetes was estimated to increase by 2.5 percentage points in 1992, 1.2 percentage points in 2000, 0.7 percentage points in 2005, and 0.5 percentage points in 2008. Similarly, using the adjustment value of Al-Lawati et al.[267] (relative difference of -21%), the ‘adjusted’ prevalence showed an estimated reduction by 1.8 percentage points in 1992, 0.8 percentage points in 2000, 0.5 percentage points in 2005, and 0.3 percentage points in 2008.

Overall, this chapter reports the model predictions of T2DM prevalence in Saudi Arabia during 2014-2022, and discusses the potential impact of adjusting the older diabetes diagnostic criteria (used for measuring T2DM prevalence in 1992) to the more recent criteria on the modelling outputs. The next chapter presents the methods and results of the ‘what if’ policy analyses, using local and international policy reduction targets of adult obesity and smoking.

Table 7.15. Summary of the model results for selected years after applying assumed adjustments of the starting year diabetes prevalence

Modelling scenario	Year	Baseline predicted diabetes prevalence (%)	Predicted diabetes prevalence (%) after adjustment of the starting year results (using assumed values of relative difference)		
			+30% *(Shaw et al.)* [266]	**-19%** *(Shaw et al.)* [266]	**-21%** *(Al-Lawati et al.)* [267]
Scenario 1	1992	8.5	11.0	6.9	6.7
	2000*	17.2	18.4	16.4	16.4
	2005*	22.8	23.5	22.3	22.3
	2008*	25.9	26.4	25.6	25.5
Scenario 2	1992	8.5	11.0	6.9	6.7
	2000*	17.2	18.4	16.4	16.4
	2005*	22.8	23.5	22.3	22.3
	2008*	25.9	26.4	25.6	25.6
Scenario 3	1992	9.6	12.5	7.8	7.6
	2000*	17.8	19.1	17.0	16.9
	2005*	23.3	24.0	22.8	22.7
	2008*	26.3	26.8	25.9	25.9
Scenario 4	1992	9.6	12.5	7.8	7.6
	2000*	17.8	19.1	17.0	16.9
	2005*	23.3	24.0	22.8	22.7
	2008*	26.3	26.8	26.0	25.9

* years used for validation of the model [as discussed in chapter 6]

Chapter 8. Using the Saudi IMPACT Diabetes Forecast Model for "What if" analyses: quantifying the impact of the targeted reduction of obesity and smoking prevalence in Saudi Arabia

In chapters 6 and 7, results for past, current and predicted future prevalence rates of diabetes in Saudi Arabia have been presented. In this chapter, local and international population targets to reduce the prevalence of adult obesity and smoking are discussed. Also, this chapter presents the impact of applying such targets on the prevalence of T2DM in Saudi Arabia, as predicted by the Saudi IMPACT Diabetes Forecast Model.

8.1. Background

The available evidence (discussed in chapter 2) showed that the diabetes incidence among adults can be reduced through some lifestyle interventions, including weight reduction[82] and/ or smoking cessation.[140] However, at the overall population (e.g. national) level, no evidence is available to investigate the impact of reducing the prevalence of adult obesity and smoking on the population diabetes burden.

The structure of the Saudi IMPACT Diabetes Forecast Model (discussed in detail in chapter 5) cannot adapt to directly simulate the lifestyle interventions reported in literature. Alternatively, the model structure can adapt to simulate specific 'reduction targets' for the prevalence of adult obesity and smoking in Saudi Arabia over a specific period, and then estimate the impact of applying such targets on the overall diabetes prevalence. Setting up such policy targets to reduce adult obesity and smoking prevalence has been supported and used by some international authorities, as discussed in detail in the next section.

8.2. Local and international policy targets for adult obesity and smoking prevalence

In 2007, the Ministries of Health in the GCC countries have set an action plan (for the period 2008-2018) for prevention and control of diabetes[198], as a response from these countries to the massive and growing burden of the disease on their populations and health care systems. The first objective in this

action plan was to apply “primary prevention” measures to reduce the prevalence of T2DM. To achieve this objective, policy targets were set to reduce obesity prevalence by 10% and current smoking prevalence by 5% in each individual member country during 2008-2018.[198] However, currently, there are no available data on monitoring the progress toward achieving such reduction targets.

Internationally, there are some few examples of setting national targets for adult obesity and smoking. A first example is from England, where the Department of Health (in 1992) set specific targets to reduce obesity prevalence rates in England for men from 7% in 1986-1987 to 6% by 2005 and for women for the same period from 12% to 8%.[268] However, those specific targets were not attained, and the obesity prevalence in England increased substantially in men and women over time, and reached more than 20% for each sex in 2005.[255]

A second example is the objectives set by “Healthy People 2020” in the United States. Healthy People (HP) is a national health strategy, where the national public health objectives in the United States are set 10 years into the future and published as health objectives for the nation. These objectives define specific numerical targets for reductions in most major health problems as well as for increases in the prevalence of health-promoting behaviours.[269] So far, three HPs have been published: HP 2000, HP 2010 and HP 2020. In HP 2020, one of the objectives was “to reduce the proportion of adults (aged ≥20 years) who are obese”. The target obesity prevalence was set at 30.6%, which is equivalent to a 10% reduction of the prevalence in 2005-2008 (34.0%).[270] However, it is important to note that the target in HP 2020 is relatively conservative, since the previous targets set for HP 2000 and HP 2010 were not attainable. For instance, the objective in HP 2000 was to reduce the overweight prevalence in adults (20-74 years) from 26% in 1987 to 20% by 2000.[271] The observed prevalence in 2000 moved around 150% away from the target, and the adult overweight prevalence exceeded 30% by 2000.[272] Similarly, the target in HP 2010 was to reduce the proportion of adults (aged ≥20 years) who are obese from 23% in 1988-1994 to 15% by 2010.[273] The reported prevalence of adult obesity in the US adults in 2010 was 35.7%, which was more than double the target.[274]

A third example is the targets recommended by a “WHO Technical Working Group on Non-communicable Disease Targets” in July 2011.[275] This working group, composed of international experts in NCD surveillance and WHO staff members, recommended, through several technical meetings, a number of proposed targets to monitor progress in reducing the burden of NCDs. These targets have been set to achieve major reductions in NCDs and their risk factors by 2025, and the baseline for all targets is 2010. According to the WHO, targets were established following scientific review of the current situation and trends, combined with a critical assessment of feasibility based upon demonstrated country achievement. For obesity, the target was “to halt the rise in obesity prevalence among persons aged 25+ years”.[275] Interim targets for 2015 and 2020 will be set at a later date to assess progress and achievement towards the target. However, there are no available data so far on such progress assessment.

Moreover, there are four examples of recent national policy targets for adult smoking. First, HP 2020 set a target to reduce the prevalence of cigarette smoking in adults aged ≥18 years from 20.6% in 2008 to 12.0% in 2020, which is equivalent to a 41.7% relative reduction.[276] Second, the WHO technical working group (2011) set a target of a 40% relative reduction in the prevalence of current daily tobacco smoking among persons aged ≥15 years by 2025, using 2010 as a baseline.[275] Third, the “Healthy Lives, Healthy People”, which is a strategy setting out the Government's long-term vision for the future of public health in England, set a target to reduce adult (aged ≥18 years) smoking prevalence in England from 21.2% in 2009-2010 to 18.5% in 2015,[277] and this is equivalent to approximately 12.7% relative reduction. Fourth, the Australian Government set a target to reduce the rate of daily smoking in those aged ≥14 years from 16.6% in 2010 to 10% in 2018,[278] which is equal to around 40% relative reduction.

8.3. Impact of reducing the prevalence of obesity and smoking on the burden of type 2 diabetes in Saudi Arabia

8.3.1. Methods

The targets used in this thesis for the 'What if' policy assumptions are those of the GCC Action Plan, in addition to the international targets (HP 2020 and WHO), which have been mentioned in the previous section. However, the final year of modelling in the Saudi IMPACT Diabetes Forecast Model is 2022, whereas the target years for the GCC Action Plan, HP 2020 and WHO are 2018, 2020 and 2025 respectively. Therefore, these international targets were incorporated into the model assuming that they will be achieved by 2022. The baseline year was set at 2008 for targets of the GCC Action Plan, and at 2010 for the targets of HP 2020 and WHO.

The 'What if' policy assumptions quantified the impact of reducing the prevalence of adult obesity *alone* (as the major and powerful risk factor in this thesis) on the burden of T2DM in Saudi Arabia. In addition, the impact of reducing the prevalence of *both* risk factors in this thesis (obesity and smoking) was also investigated. Hence, in total, six 'What if' policy assumptions/ questions were studied in this thesis, as summarised in Table **8.1**.

All six assumptions were applied to each of the four modelling scenarios discussed in chapters 6 and 7. For the targets of HP 2020 and WHO, for example, the trends in the prevalence of obesity (presented in chapter 5) were kept unchanged, as estimated by each scenario, till 2010 (baseline). Then, from 2011 onwards, the 'what if' targets were incorporated into the model. For example, to apply the target of HP 2020 for obesity, the obesity prevalence rates were assumed to start an annual relative reduction by approximately 0.83% from 2011 onwards. So, after 12 years from the baseline, the obesity prevalence was assumed to decrease by 10% (0.83 X 12) from that in 2010. Similarly, to apply the target of HP 2020 for smoking, an annual relative reduction of the estimated smoking prevalence by around 3.33% was assumed to start from 2011 onwards, so that by 2022, a 40% relative reduction of smoking prevalence (3.33 X 12) was assumed to be achieved. Furthermore, the WHO target for obesity (halt the rise in obesity prevalence with 2010 as a

baseline) was applied to the model by assuming that the estimated obesity prevalence for 2011-2022 would be the same as that in 2010.

Table 8.1. The 'What if' policy questions investigated in this chapter

	'What if' policy question	Reference
1	What will be the impact of a **10% relative reduction in obesity prevalence** by 2022 (baseline 2008) on diabetes burden in Saudi Arabia?	GCC Action Plan [198]
2	What will be the impact of a **10% relative reduction in obesity prevalence and a 5% reduction in smoking prevalence** by 2022 (baseline 2008) on diabetes burden in Saudi Arabia?	GCC Action Plan [198]
3	What will be the impact of a **10% relative reduction in obesity prevalence** by 2022 (baseline 2010) on diabetes burden in Saudi Arabia?	HP 2020 [270]
4	What will be the impact of a **10% relative reduction in obesity prevalence and a 40% reduction in smoking prevalence** by 2022 (baseline 2010) on diabetes burden in Saudi Arabia?	HP 2020 [270]
5	What will be the impact of **halting the rise in obesity prevalence** by 2022 (baseline 2010) on diabetes burden in Saudi Arabia?	WHO [275]
6	What will be the impact of **halting the rise in obesity prevalence and a 40% reduction in smoking prevalence** by 2022 (baseline 2010) on diabetes burden in Saudi Arabia?	WHO [275]

After incorporating each target into each of the four modelling scenarios, the model was run to obtain the results of 'what if' trends in the predicted diabetes prevalence and the number of diabetic individuals.

8.3.2. Results

8.3.2.1. Results for the total population

Table **8.2** summarises the results of impact of applying the different 'what if' assumptions on the diabetes burden in the total Saudi population, as estimated by the Saudi IMPACT Diabetes Forecast Model.

A. Modelling scenario 1 – population aged 25-64 years with capped obesity trends

The model estimated that the diabetes prevalence in Saudi Arabia in 2022 can show a 6.0% relative reduction (equivalent to a reduction of 383,399 individuals) if the obesity target of the GCC Action Plan (10% relative reduction in obesity prevalence from that in 2008) would be achieved. The reduction in diabetes prevalence by 2022 is estimated to show a minimal improvement if the GCC Action Plan's smoking target (5% relative reduction in smoking prevalence from that in 2008) is added to the obesity target.

Diabetes prevalence could be reduced by 4.8% (312,765 individuals), assuming that the target of HP 2020 (10% relative reduction in obesity prevalence from that in 2010) could be applied in Saudi Arabia. The reduction in diabetes prevalence by 2022 is estimated to show a minimal improvement if the HP 2020 smoking target (40% relative reduction in smoking prevalence from that in 2010) is added to the obesity target. Such a relative reduction is estimated to be 5% (331,627 individuals).

With applying the WHO target for adult obesity (halt the rise in obesity prevalence from 2011 onwards), the relative reduction in diabetes prevalence in 2022 is estimated at 1.6% (107,394 individuals). If the WHO smoking target (40% relative reduction in smoking prevalence from that in 2010) is added, the diabetes prevalence in 2022 is estimated to be reduced by 1.9% (125,507 individuals).

B. Modelling scenario 2 – population aged 25-64 years without capping of obesity trends

With scenario 2, the 'what if' values for reduction in diabetes prevalence and the number of diabetic individuals would be higher than that estimated with scenario 1. The estimated relative reductions of diabetes prevalence in 2022 are 14.9% (1,098,449 individuals) using the obesity target of the GCC Action Plan, and 15.1% (1,107,027 individuals) using both obesity and smoking targets of the GCC Action Plan.

Relative reductions of diabetes prevalence are estimated at 12.7% (935,741 individuals) using the HP 2020 target for obesity, and 13.0% (954,239 individuals) using the HP 2020 target for obesity and smoking combined.

If the WHO target for obesity is applied, a 9.8% reduction in diabetes prevalence in 2022 (718,855 individuals) is estimated to be achieved. This estimated reduction would show a minimal improvement to reach 10.0% (736,586 individuals) if the WHO targets for both obesity and smoking are applied.

On the other hand, if the assumed 'conservative' target for obesity is used, a reduction of 11.3% in diabetes prevalence (829,431 individuals) in 2022 is

estimated. If both ‘conservative’ targets for obesity and smoking are used, the reduction is predicted to be 11.6% (841,354 individuals).

C. Modelling scenario 3 – population aged 25-75+ years with capped obesity trends

If the obesity target of the GCC Action Plan is used, a 6.3% reduction in diabetes prevalence (448,760 individuals) could be achieved by 2022. However, if the smoking target is added, the reduction could increase to 6.5% (457,567 individuals).

Using the HP 2020 target for obesity could result in a 5.2% reduction of diabetes prevalence (369,701 individuals) in 2022. In comparison, using the HP 2020 targets for both obesity and smoking would show an estimated reduction of 5.5% in diabetes prevalence (389,183 individuals) in 2022.

Applying the WHO target of obesity could produce an estimated reduction in diabetes prevalence of 2.1% (149,929 individuals) by 2022. Using a combination of the WHO targets for obesity and smoking could result in a 2.4% reduction in prevalence (168,646 individuals).

D. Modelling scenario 4 – population aged 25-75+ years without capping of obesity trends

The model estimated that a 14.8% reduction in diabetes prevalence (1,163,810 individuals) could be achieved by 2022 if the obesity target of the GCC Action Plan is used. Adding the smoking target could result in a 14.9% reduction of diabetes prevalence (1,172,546 individuals) in 2022.

The estimated reductions in diabetes prevalence by 2022 could reach 12.7% (992,677 individuals) if the HP 2020 target for obesity is used. If the HP 2020 target for smoking is added, a 12.9% reduction of diabetes prevalence (1,011,795 individuals) in 2022 could be attained.

Using the WHO target for obesity could produce a reduction of 9.7% in diabetes prevalence (761,389 individuals) in 2022. This estimated reduction could increase to 9.9% (779,725 individuals) if the WHO targets for both obesity and smoking are used.

Figures **8.1**- **8**.**4** present graphical illustrations of the ‘what if’ policy assumptions applied to the total Saudi population in each of the four modelling scenarios. However, since the addition of smoking targets produced only minimal effects on the reduction of diabetes burden (as discussed in the previous sections), these figures show the results of applying the obesity targets only.

Table 8.2. Results of the impact of reducing obesity (or obesity and smoking) on the diabetes burden in Saudi Arabia (total population) using different targets

	Baseline burden of T2DM (2022)		Burden of T2DM (2022) with the "What if" policy assumption		Reduction of burden of T2DM (2022)		Target (What if assumption)*
	Prevalence (%)	Number (T2DM cases)	Prevalence (%)	Number (T2DM cases)	Prevalence (%)	Number (T2DM cases)	
Scenario 1	39.5	6,581,511	37.2	6,198,112	-6.0	-383,399	10% O (Baseline 2008)
			37.1	6,189,463	-6.0	-392,049	10% O + 5% S (Baseline 2008)
			37.6	6,268,746	-4.8	-312,765	10% O (Baseline 2010)
			37.5	6,249,884	-5.0	-331,627	10% O + 40% S (Baseline 2010)
			38.8	6,474,117	-1.6	-107,394	Halt O (Baseline 2010)
			38.7	6,456,004	-1.9	-125,507	Halt O + 40% S (Baseline 2010)
Scenario 2	44.1	7,353,447	37.5	6,254,998	-14.9	-1,098,449	10% O (Baseline 2008)
			37.4	6,246,420	-15.1	-1,107,027	10% O + 5% S (Baseline 2008)
			38.5	6,417,706	-12.7	-935,741	10% O (Baseline 2010)
			38.4	6,399,208	-13.0	-954,239	10% O + 40% S (Baseline 2010)
			39.8	6,634,593	-9.8	-718,855	Halt O (Baseline 2010)
			39.7	6,616,861	-10.0	-736,586	Halt O + 40% S (Baseline 2010)
Scenario 3	38.9	7,072,814	36.5	6,624,054	-6.3	-448,760	10% O (Baseline 2008)
			36.4	6,615,247	-6.5	-457,567	10% O + 5% S (Baseline 2008)
			36.9	6,703,114	-5.2	-369,701	10% O (Baseline 2010)
			36.8	6,683,632	-5.5	-389,183	10% O + 40% S (Baseline 2010)
			38.1	6,922,885	-2.1	-149,929	Halt O (Baseline 2010)
			38.0	6,904,168	-2.4	-168,646	Halt O + 40% S (Baseline 2010)
Scenario 4	43.2	7,844,750	36.8	6,680,941	-14.8	-1,163,810	10% O (Baseline 2008)
			36.7	6,672,205	-14.9	-1,172,546	10% O + 5% S (Baseline 2008)
			37.7	6,852,074	-12.7	-992,677	10% O (Baseline 2010)
			37.6	6,832,956	-12.9	-1,011,795	10% O + 40% S (Baseline 2010)
			39.0	7,083,361	-9.7	-761,389	Halt O (Baseline 2010)
			38.9	7,065,025	-9.9	-779,725	Halt O + 40% S (Baseline 2010)

(*)***10% O:*** 10% relative reduction of *Obesity* prevalence by 2022; ***10% O + 5% S:*** 10% relative reduction of *Obesity* prevalence & 5% relative reduction of *Smoking* prevalence by 2022;
10% O + 40% S: 10% relative reduction of *Obesity* prevalence & 40% relative reduction of *Smoking* prevalence by 2022;
Halt O: halt the rise in *Obesity* prevalence by 2022; ***Halt O + 40% S:*** halt the rise in *Obesity* prevalence & 40% relative reduction of *Smoking* prevalence by 2022

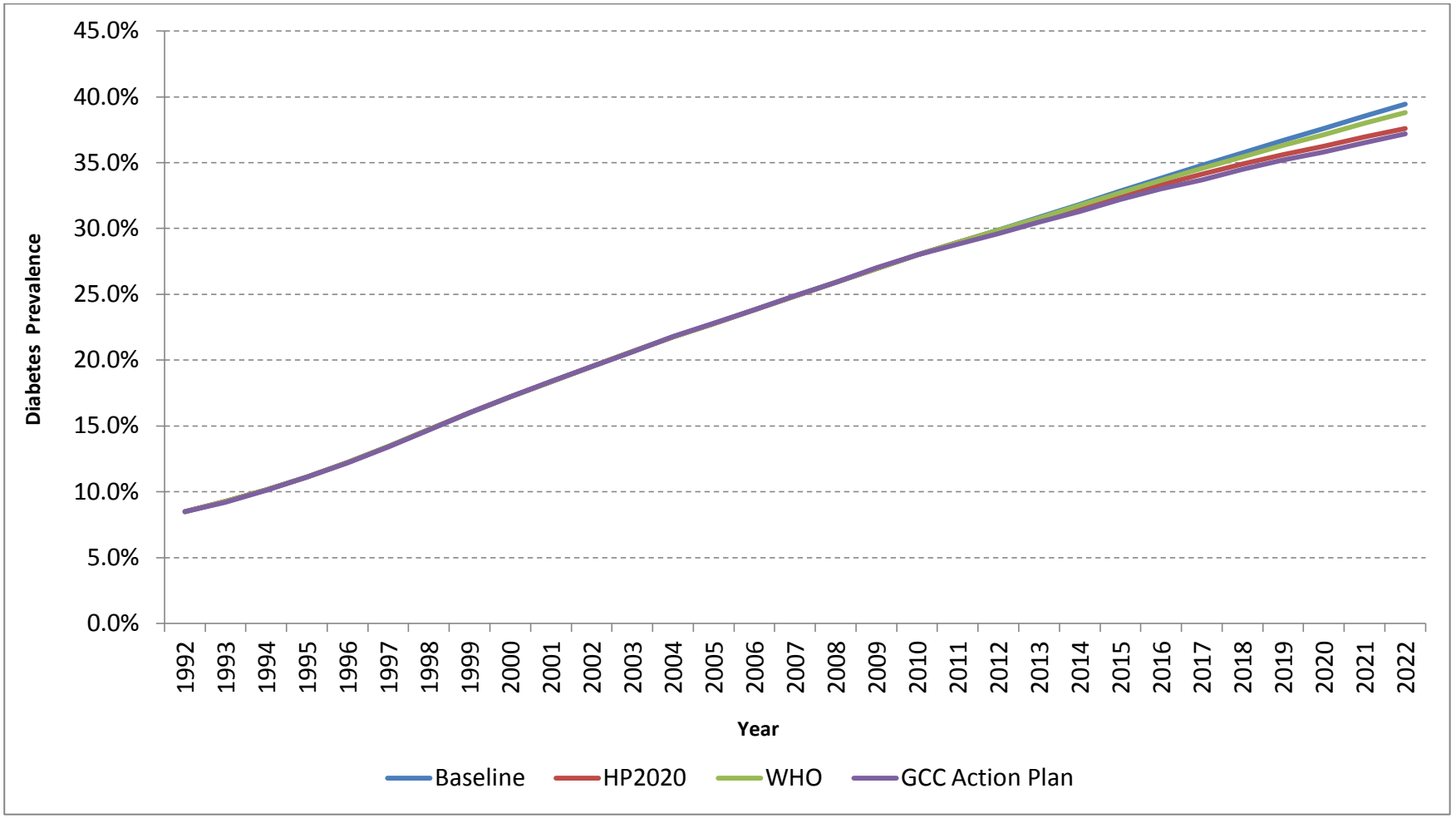


Figure 8.1. *(Scenario 1)* Results of the impact of reducing obesity on the diabetes burden in Saudi Arabia (total population) using different targets

(Scenario 1: population aged 25-64 years with capped obesity trends)

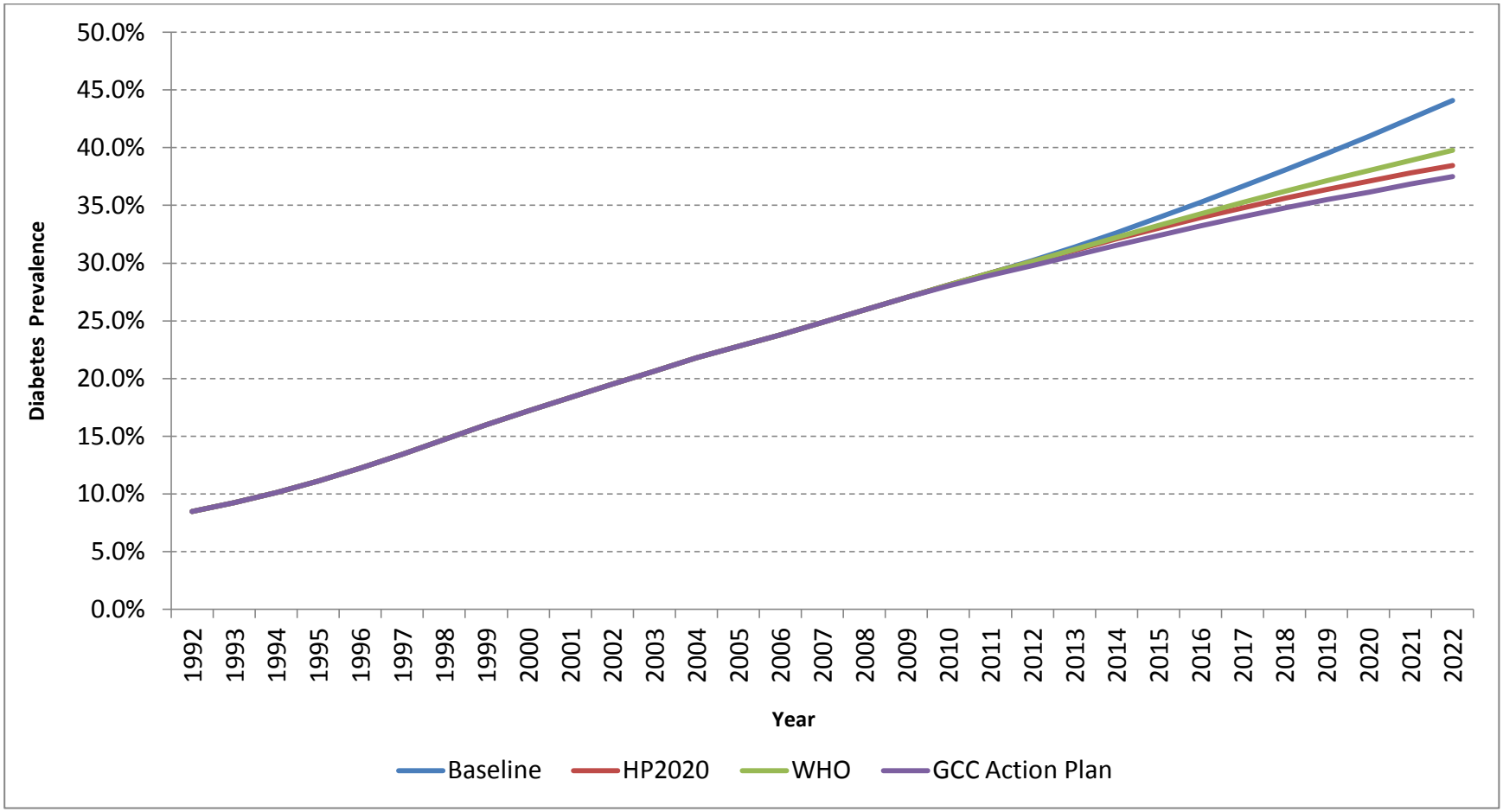


Figure 8.2. *(Scenario 2)* Results of the impact of reducing obesity on the diabetes burden in Saudi Arabia (total population) using different targets

(Scenario 2: population aged 25-64 years without capped obesity trends)

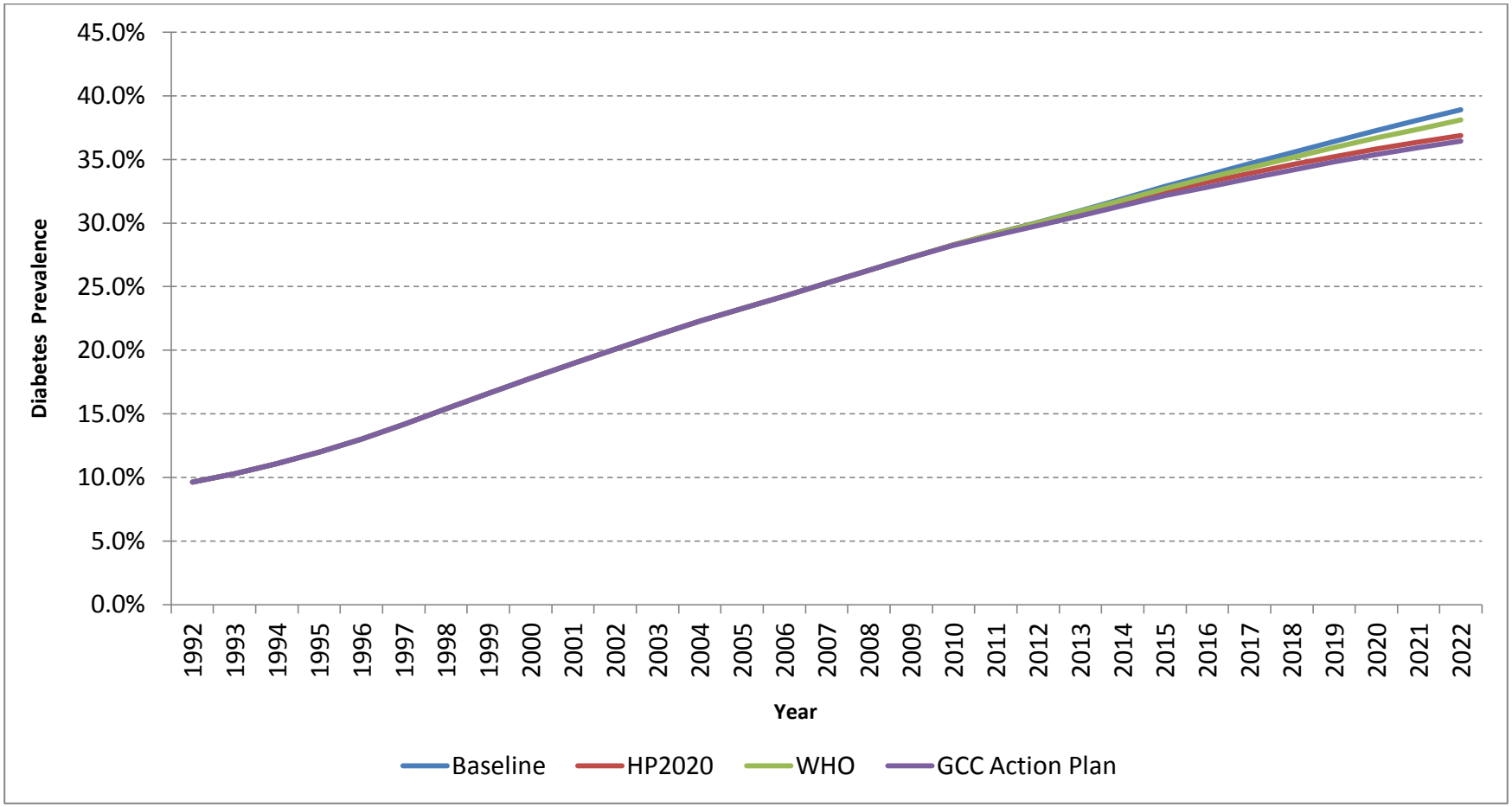


Figure 8.3. *(Scenario 3)* Results of the impact of reducing obesity on the diabetes burden in Saudi Arabia (total population) using different targets

(Scenario 3: population aged 25-75+ years with capped obesity trends)

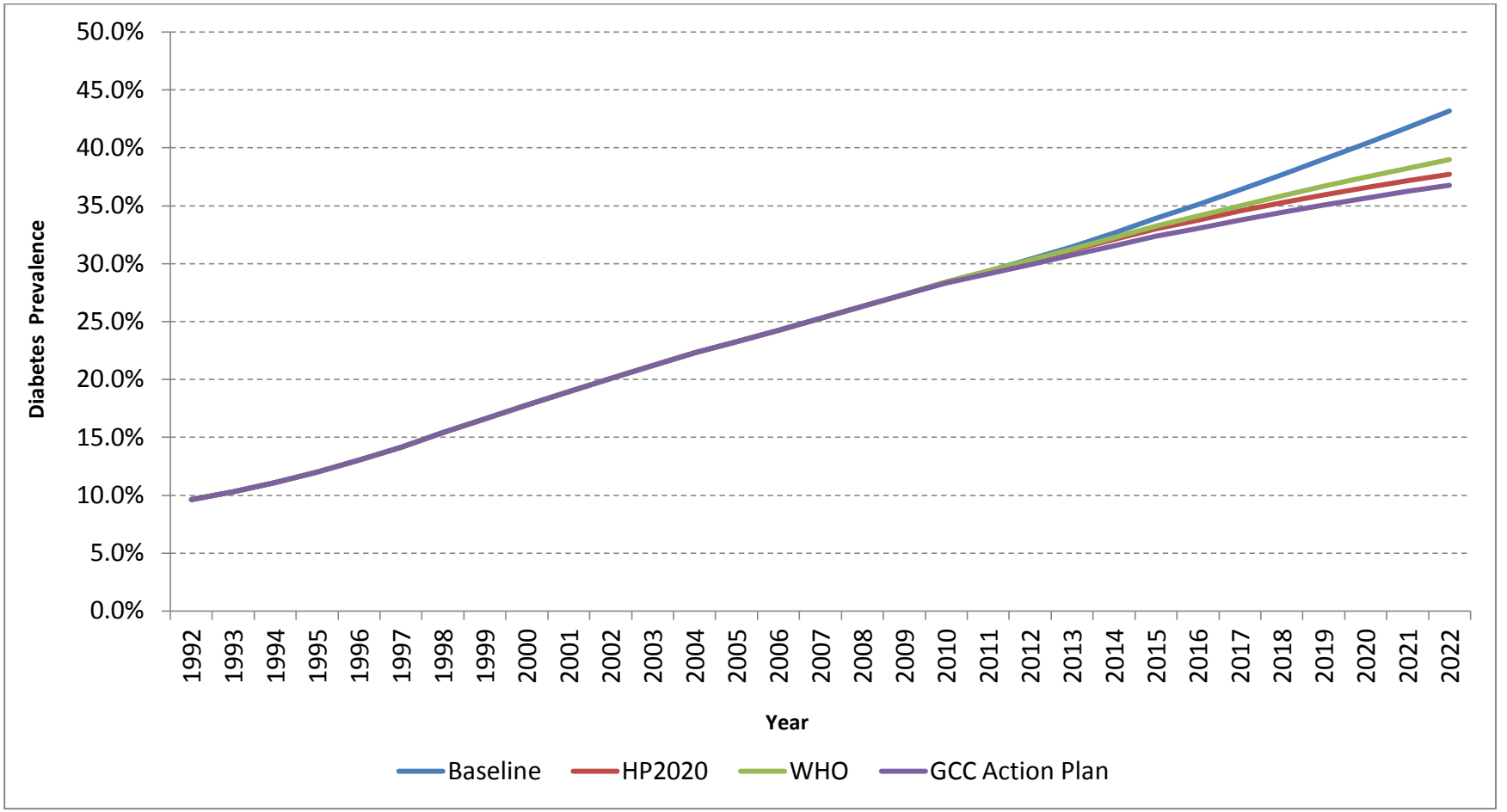


Figure 8.4. *(Scenario 4)* Results of the impact of reducing obesity on the diabetes burden in Saudi Arabia (total population) using different targets

(Scenario 4: population aged 25-75+ years without capped obesity trends)

8.3.2.2. Results for men and women

In this section, the results of applying the 'what if' targets are compared in men and women of the Saudi population, as estimated by each of the four modelling scenarios. Table **8.3** provides a summary of the results for the 'what if' policy assumptions/ targets in men, while Table **8.4** summarises the results in women.

A. Modelling scenario 1 – population aged 25-64 years with capped obesity trends

By scenario 1, the GCC Action Plan's target for obesity could result in an estimated reduction in diabetes prevalence in 2022 by 4.1% (148,532 individuals) and 8.1% (234,868 individuals) in men and women respectively. Applying both targets for obesity and smoking could produce a small improvement in such a reduction among men [4.3% (157,141 individuals)], with almost no effect on the results for women.

The estimated diabetes prevalence in 2022 could be reduced by 3.3% (120,925 individuals) and 6.8% (191,840 individuals) in men and women respectively, if the HP 2020 target for obesity is used. If both HP 2020 targets for obesity and smoking are used, such reductions are estimated to slightly improve in men to reach 3.8% (139,567 individuals), with almost no change in the results for women.

If the WHO target for obesity is used, the estimated reduction in diabetes prevalence would be 1.0% (42,487 individuals) in men and 2.3% (64,908 individuals) in women. With using the WHO targets for both obesity and smoking, this reduction is again estimated to show a minimal improvement in men only [1.5% (60,401 individuals)].

B. Modelling scenario 2 – population aged 25-64 years without capping of obesity trends

If the GCC Action Plan's target for obesity is used, the estimated reductions in diabetes prevalence in 2022 would be 8.4% (323,458 individuals) in men and 22.2 % (774,991 individuals) in women. Moreover, if both targets for obesity and smoking are applied, the reduction in men is estimated to minimally improve to 8.6% (331,998 individuals), with nearly no effect on the results for women.

Using the HP 2020 target for obesity could result in an estimated reduction of 7.0% (271,324 individuals) and 19.1% (664,416 individuals) in diabetes prevalence in men and women respectively by 2022. Adding the HP 2020 target for smoking could increase such an estimated reduction in men to 7.5% (289,624 individuals) with almost no change in women.

Applying the WHO target for obesity, the reduction in diabetes prevalence in 2022 is estimated at 5.1% (189,822 individuals) in men and 15.1% (529,032 individuals) in women. If the WHO target for smoking is also added, the reduction is estimated to improve to 5.6% (207,378 individuals) in men and 15.3% (529,208 individuals) in women.

C. Modelling scenario 3 – population aged 25-75+ years with capped obesity trends

By scenario 3, if the GCC Action Plan's target for obesity is used, the estimated potential reduction in diabetes prevalence would be 2.7% (161,511 individuals) in men and 9.0% (287,249 individuals) in women. Applying both assumed targets for obesity and smoking could result in an inconsiderable improvement of reduction results [3.0% (170,274 individuals)] in men, and nearly no effect on the results for women.

The model estimated that the reduction in diabetes prevalence in 2022 respectively in men and women could reach 2.1% (132,065 individuals) and 7.6% (237,636 individuals) with using the HP 2020 target for obesity. If both obesity and smoking targets of HP 2020 are used, the reduction in diabetes prevalence in men is estimated to be 2.4% (151,300 individuals), with almost no change among women.

Using the WHO targets for obesity and smoking would not produce any significant reduction in diabetes prevalence in 2022 among men. However, using such targets among women could result in an estimated reduction of 3.3% (100,212 individuals) by 2022.

D. Modelling scenario 4 – population aged 25-75+ years without capping of obesity trends

By using the GCC Action Plan's target for obesity, the reduction in diabetes prevalence in 2022 among men and women is estimated respectively at 6.9%

(336,437 individuals) and 22.0% (827,372 individuals). However, again, using both targets for obesity and smoking could produce a slight increase in the reduction results among men [7.2% (345,131 individuals)], with nearly no impact on women.

The estimated reductions in diabetes prevalence in 2022 which could be achieved as a result of applying the HP 2020 target for obesity are 5.5% (282,464 individuals) in men and 19.0% (710,213 individuals) in women. This estimated reduction could increase to 6.0% (301,357 individuals) among men only with using both HP 2020 targets for obesity and smoking.

Using the WHO target for obesity could result in an estimated reduction of 3.5% (197,276 individuals) in men and 14.9% (564,113 individuals) in women. Adding the WHO target for smoking could slightly increase the estimated reduction in men to 4.0% (215,411 individuals), with, again, almost no effect on the results for women.

Figures **8.5**-**8**.**12** illustrate the results of impact of using the 'what if' policy targets on the diabetes prevalence among men and women, based on each of the four modelling scenarios. Because of the minimal impact of smoking targets on the results (as discussed in the previous sections), these figures show only the 'what if' results of the obesity targets.

In sum, this chapter presents extensive analyses of the potential impacts of reducing the adult obesity and smoking in Saudi Arabia (using local and international policy targets) on the predicted T2DM prevalence. The next chapter provides detailed comparisons of the model outputs against other existing modelling estimates, such as those produced recently by the IDF[9] and the GBD project.[20]

Table 8.3. Results of the impact of reducing obesity (or obesity and smoking) on the diabetes burden in Saudi Arabia (men) using different targets

	Baseline burden of T2DM (2022)		Burden of T2DM (2022) with the "What if" policy assumption		Reduction of burden of T2DM (2022)		Target (What if policy assumption)*
	Prevalence (%)	Number (T2DM cases)	Prevalence (%)	Number (T2DM cases)	Prevalence (%)	Number (T2DM cases)	
Scenario 1	39.2	3,666,613	37.6	3,518,081	-4.1	-148,532	10% O (Baseline 2008)
			37.5	3,509,472	-4.3	-157,141	10% O + 5% S (Baseline 2008)
			37.9	3,545,688	-3.3	-120,925	10% O (Baseline 2010)
			37.7	3,527,046	-3.8	-139,567	10% O + 40% S (Baseline 2010)
			38.8	3,624,126	-1.0	-42,487	Halt O (Baseline 2010)
			38.6	3,606,212	-1.5	-60,401	Halt O + 40% S (Baseline 2010)
Scenario 2	41.3	3,859,003	37.8	3,535,545	-8.4	-323,458	10% O (Baseline 2008)
			37.7	3,527,005	-8.6	-331,998	10% O + 5% S (Baseline 2008)
			38.4	3,587,679	-7.0	-271,324	10% O (Baseline 2010)
			38.2	3,569,379	-7.5	-289,624	10% O + 40% S (Baseline 2010)
			39.2	3,669,181	-5.1	-189,822	Halt O (Baseline 2010)
			39.0	3,651,625	-5.6	-207,378	Halt O + 40% S (Baseline 2010)
Scenario 3	37.8	3,897,879	36.8	3,736,368	-2.7	-161,511	10% O (Baseline 2008)
			36.7	3,727,605	-3.0	-170,274	10% O + 5% S (Baseline 2008)
			37.0	3,765,814	-2.1	-132,065	10% O (Baseline 2010)
			36.9	3,746,579	-2.4	-151,300	10% O + 40% S (Baseline 2010)
			37.9	3,847,939	-0.0	-49,940	Halt O (Baseline 2010)
			37.7	3,829,445	-0.3	-68,434	Halt O + 40% S (Baseline 2010)
Scenario 4	39.7	4,090,269	36.9	3,753,832	-6.9	-336,437	10% O (Baseline 2008)
			36.8	3,745,138	-7.2	-345,131	10% O + 5% S (Baseline 2008)
			37.5	3,807,805	-5.5	-282,464	10% O (Baseline 2010)
			37.3	3,788,912	-6.0	-301,357	10% O + 40% S (Baseline 2010)
			38.3	3,892,993	-3.5	-197,276	Halt O (Baseline 2010)
			38.1	3,874,858	-4.0	-215,411	Halt O + 40% S (Baseline 2010)

(*)***10% O:*** 10% relative reduction of *Obesity* prevalence by 2022; ***10% O + 5% S:*** 10% relative reduction of *Obesity* prevalence & 5% relative reduction of *Smoking* prevalence by 2022;
10% O + 40% S: 10% relative reduction of *Obesity* prevalence & 40% relative reduction of *Smoking* prevalence by 2022;
Halt O: halt the rise in *Obesity* prevalence by 2022; ***Halt O + 40% S:*** halt the rise in *Obesity* prevalence & 40% relative reduction of *Smoking* prevalence by 2022

Table 8.4. Results of the impact of reducing obesity (or obesity and smoking) on the diabetes burden in Saudi Arabia (women) using different targets

	Baseline burden of T2DM (2022)		Burden of T2DM (2022) with the "What if" policy assumption		Reduction of burden of T2DM (2022)		Target (What if policy assumption)*
	Prevalence (%)	Number (T2DM cases)	Prevalence (%)	Number (T2DM cases)	Prevalence (%)	Number (T2DM cases)	
Scenario 1	39.8	2,914,899	36.6	2,680,031	-8.1	-234,868	10% O (Baseline 2008)
			36.6	2,679,991	-8.1	-234,907	10% O + 5% S (Baseline 2008)
			37.1	2,723,059	-6.8	-191,840	10% O (Baseline 2010)
			37.1	2,722,838	-6.8	-192,061	10% O + 40% S (Baseline 2010)
			38.9	2,849,991	-2.3	-64,908	Halt O (Baseline 2010)
			38.9	2,849,792	-2.3	-65,107	Halt O + 40% S (Baseline 2010)
Scenario 2	47.7	3,494,444	37.1	2,719,453	-22.2	-774,991	10% O (Baseline 2008)
			37.1	2,719,415	-22.2	-775,029	10% O + 5% S (Baseline 2008)
			38.6	2,830,028	-19.1	-664,416	10% O (Baseline 2010)
			38.6	2,829,829	-19.1	-664,615	10% O + 40% S (Baseline 2010)
			40.5	2,965,412	-15.1	-529,032	Halt O (Baseline 2010)
			40.4	2,965,236	-15.3	-529,208	Halt O + 40% S (Baseline 2010)
Scenario 3	39.7	3,174,935	36.1	2,887,686	-9.0	-287,249	10% O (Baseline 2008)
			36.1	2,887,642	-9.0	-287,293	10% O + 5% S (Baseline 2008)
			36.7	2,937,299	-7.6	-237,636	10% O (Baseline 2010)
			36.7	2,937,053	-7.6	-237,882	10% O + 40% S (Baseline 2010)
			38.4	3,074,947	-3.3	-99,988	Halt O (Baseline 2010)
			38.4	3,074,723	-3.3	-100,212	Halt O + 40% S (Baseline 2010)
Scenario 4	46.9	3,754,481	36.6	2,927,109	-22.0	-827,372	10% O (Baseline 2008)
			36.6	2,927,067	-22.0	-827,414	10% O + 5% S (Baseline 2008)
			38.0	3,044,268	-19.0	-710,213	10% O (Baseline 2010)
			38.0	3,044,044	-19.0	-710,437	10% O + 40% S (Baseline 2010)
			39.9	3,190,368	-14.9	-564,113	Halt O (Baseline 2010)
			39.9	3,190,167	-14.9	-564,314	Halt O + 40% S (Baseline 2010)

(*)***10% O:*** 10% relative reduction of *Obesity* prevalence by 2022; ***10% O + 5% S:*** 10% relative reduction of *Obesity* prevalence & 5% relative reduction of *Smoking* prevalence by 2022;
10% O + 40% S: 10% relative reduction of *Obesity* prevalence & 40% relative reduction of *Smoking* prevalence by 2022;
Halt O: halt the rise in *Obesity* prevalence by 2022; ***Halt O + 40% S:*** halt the rise in *Obesity* prevalence & 40% relative reduction of *Smoking* prevalence by 2022

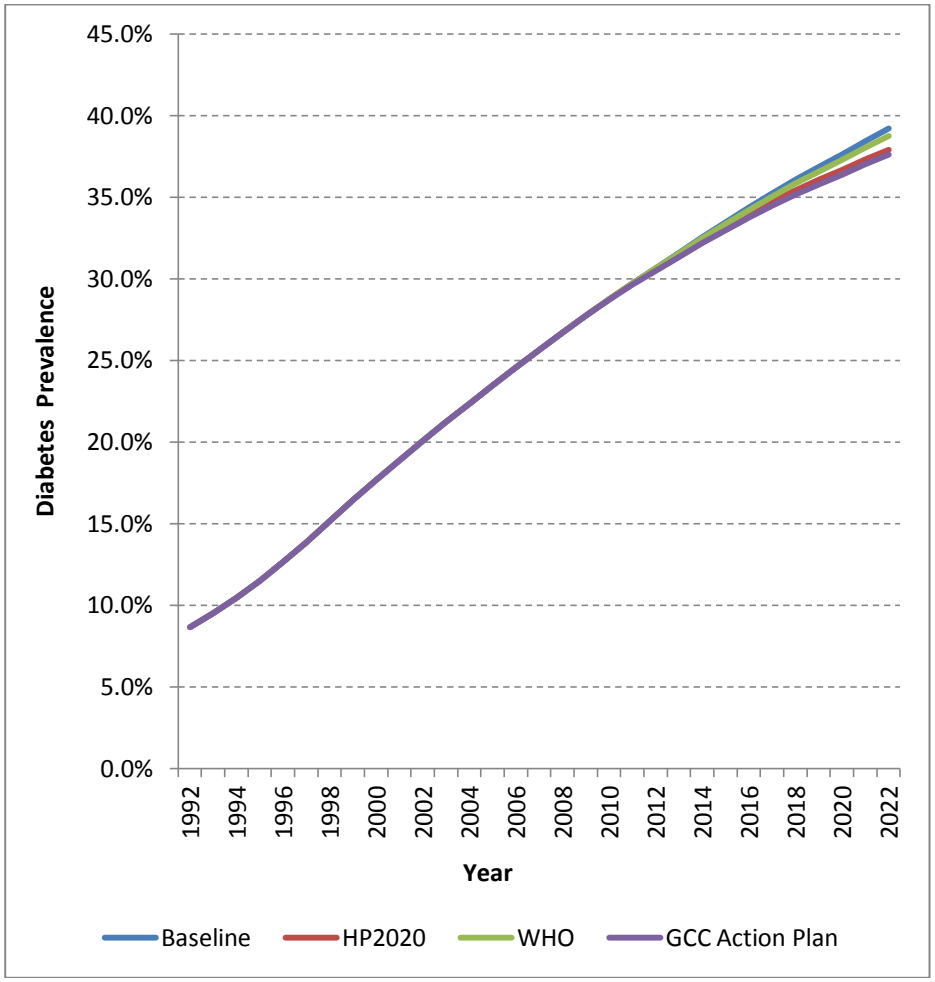


Figure 8.5. *(Scenario 1)* Results of the impact of reducing obesity on the diabetes burden in Saudi Arabia (Men) using different targets

(Scenario 1: population aged 25-64 years with capped obesity trends)

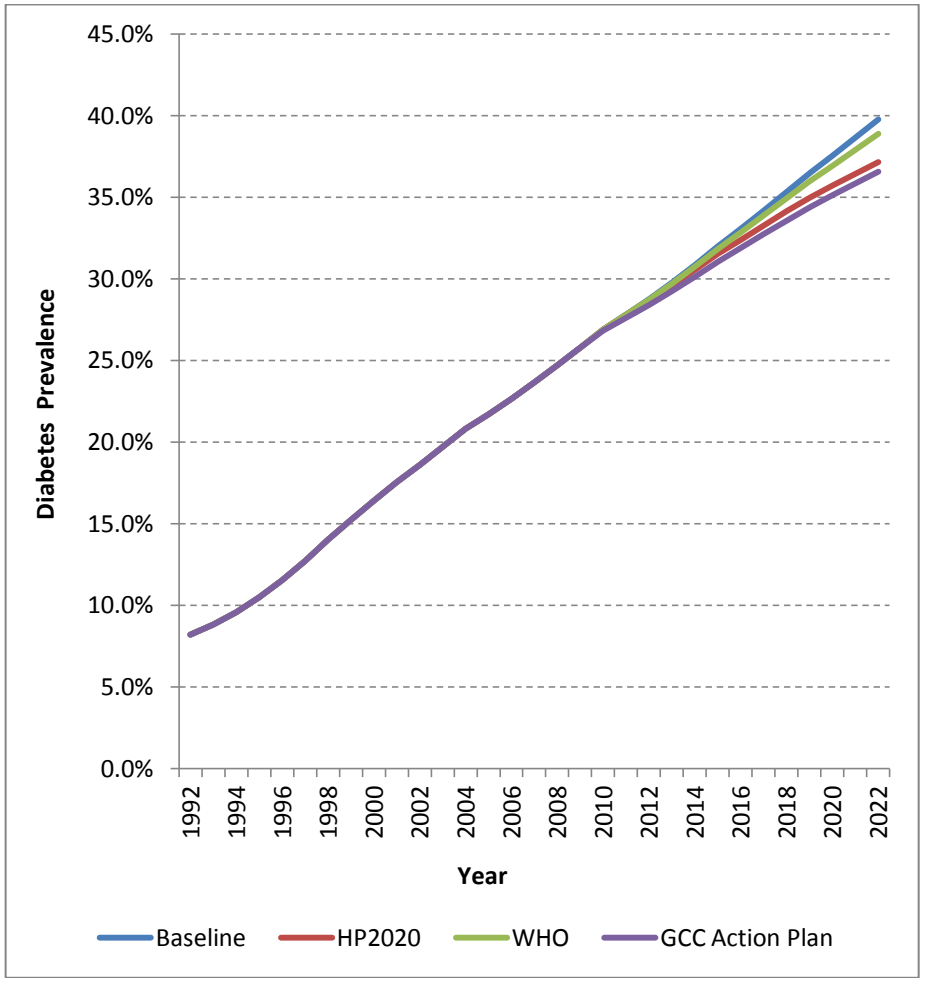


Figure 8.6. *(Scenario 1)* Results of the impact of reducing obesity on the diabetes burden in Saudi Arabia (Women) using different targets

(Scenario 1: population aged 25-64 years with capped obesity trends)

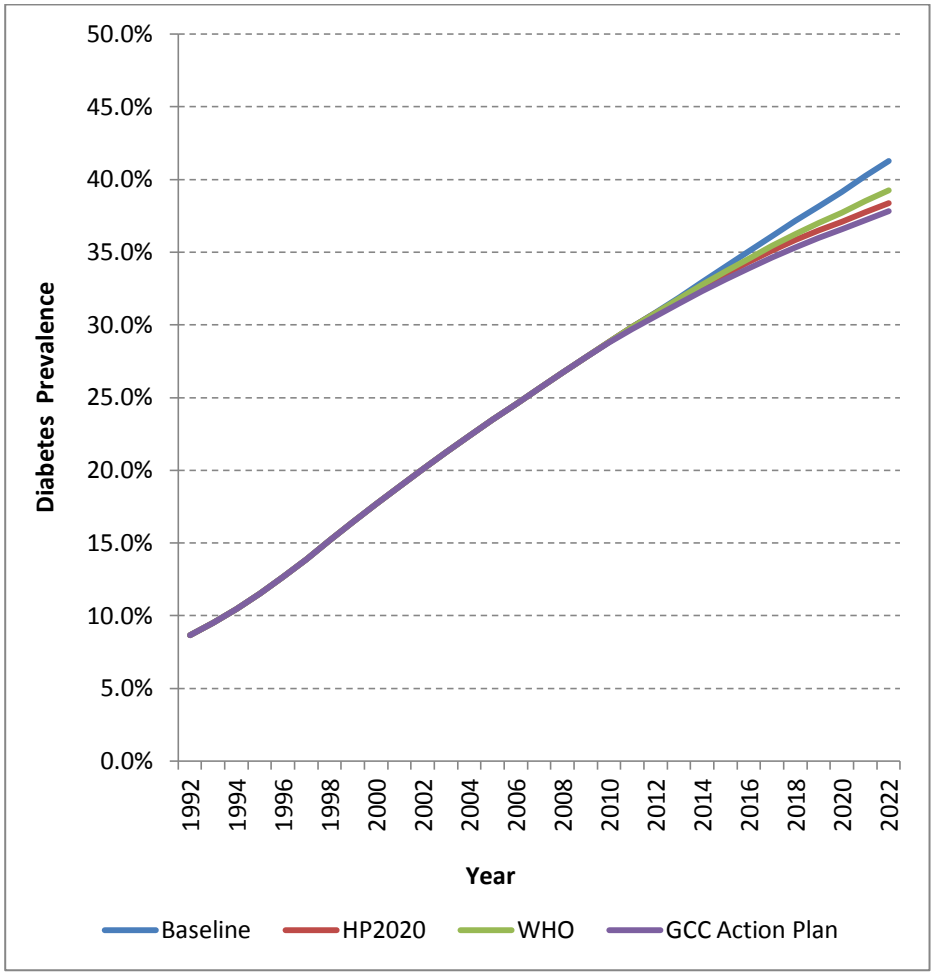


Figure 8.7. *(Scenario 2)* Results of the impact of reducing obesity on the diabetes burden in Saudi Arabia (Men) using different targets

(Scenario 2: population aged 25-64 years without capped obesity trends)

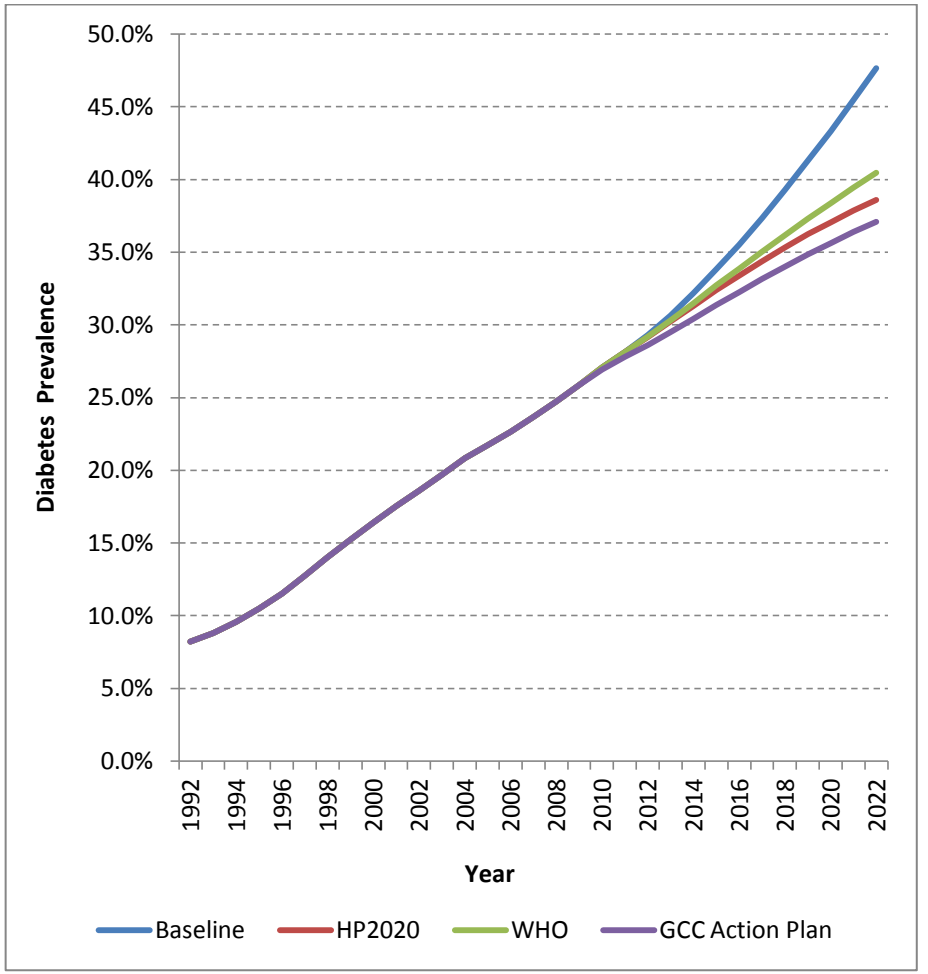


Figure 8.8. *(Scenario 2)* Results of the impact of reducing obesity on the diabetes burden in Saudi Arabia (Women) using different targets

(Scenario 2: population aged 25-64 years without capped obesity trends)

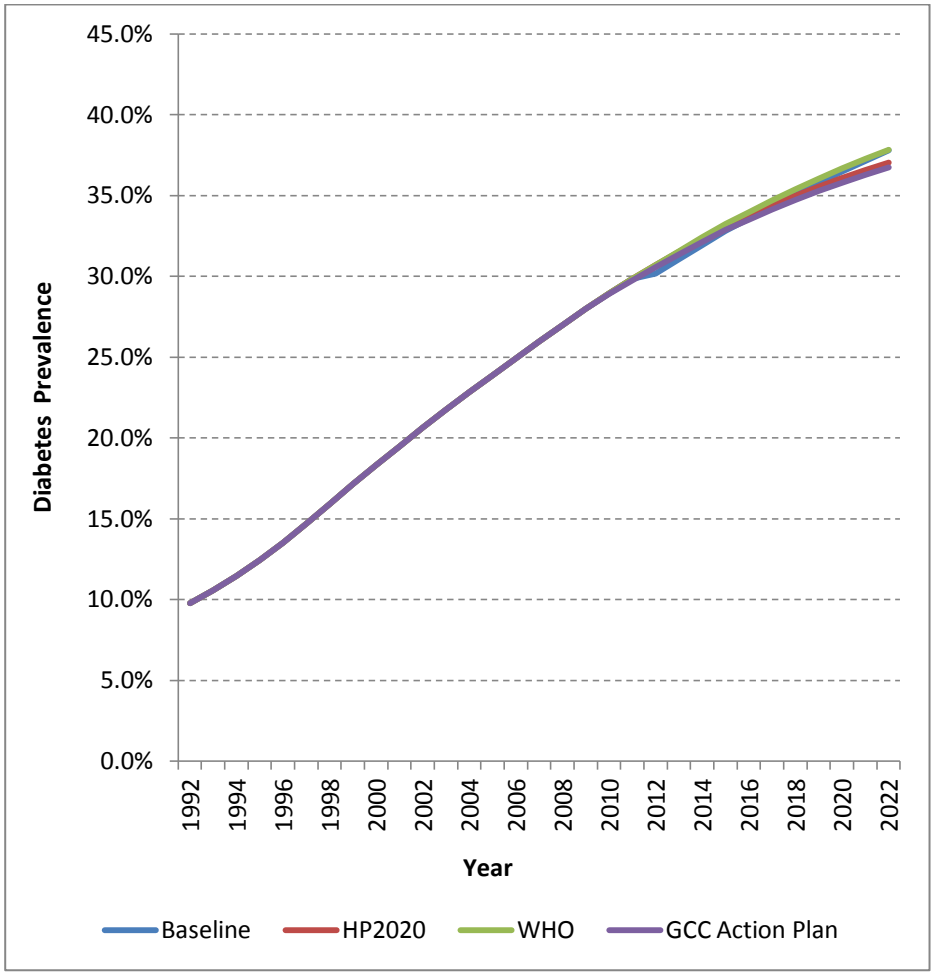


Figure 8.9. *(Scenario 3)* Results of the impact of reducing obesity on the diabetes burden in Saudi Arabia (Men) using different targets

(Scenario 3: population aged 25-75+ years with capped obesity trends)

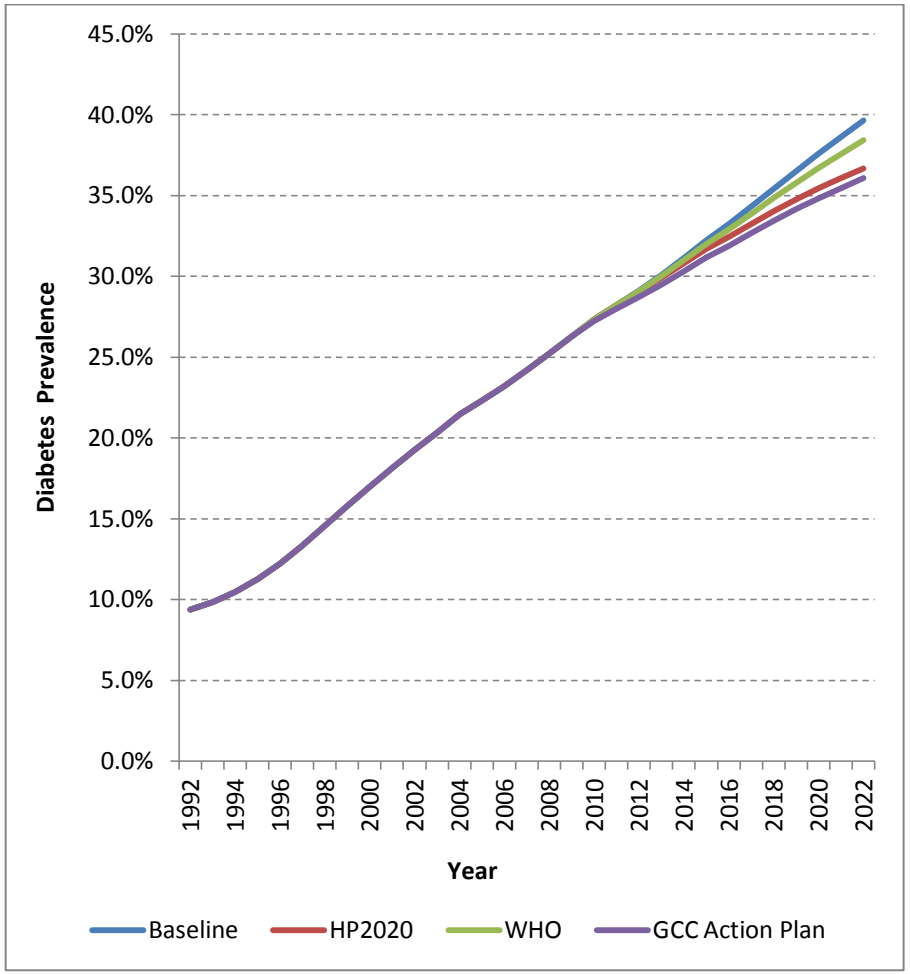


Figure 8.10. *(Scenario 3)* Results of the impact of reducing obesity on the diabetes burden in Saudi Arabia (Women) using different targets

(Scenario 3: population aged 25-75+ years with capped obesity trends)

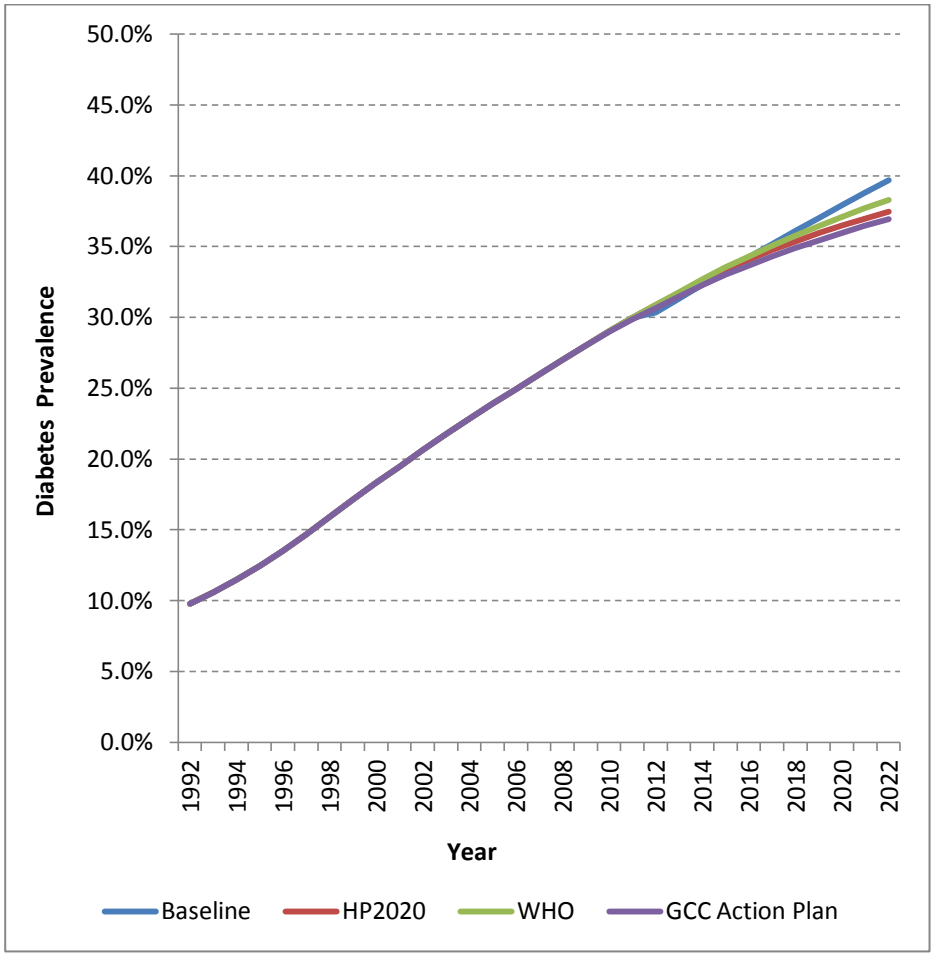


Figure 8.11. *(Scenario 4)* Results of the impact of reducing obesity on the diabetes burden in Saudi Arabia (Men) using different targets

(Scenario 4: population aged 25-75+ years without capped obesity trends)

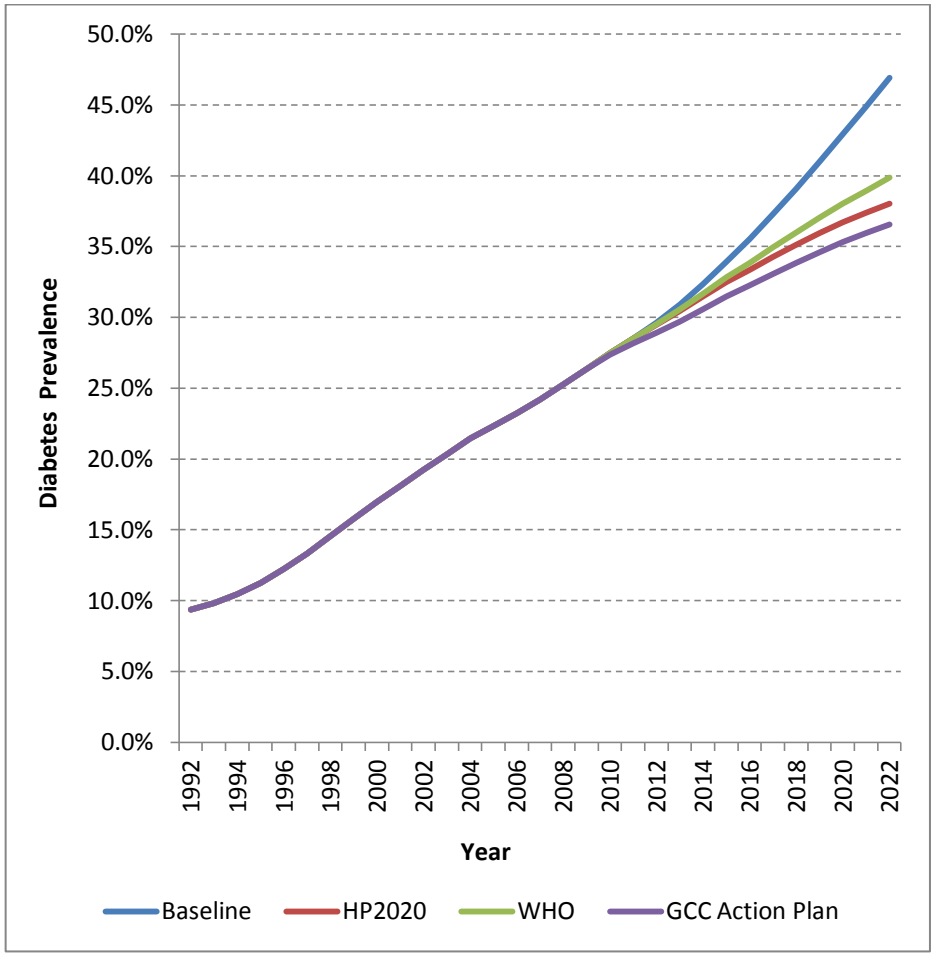


Figure 8.12. *(Scenario 4)* Results of the impact of reducing obesity on the diabetes burden in Saudi Arabia (Women) using different targets

(Scenario 4: population aged 25-75+ years without capped obesity trends)

Chapter 9. Comparison of the main results of the Saudi IMPACT Diabetes Forecast Model against other studies of diabetes prevalence estimates

9.1. Background

In the last few decades, several estimates and projections of the global diabetes prevalence have been produced. Examples of such studies have been discussed in chapter 3.[9, 14-17, 20] These studies resulted in substantial variations of diabetes prevalence and its projections between the world regions as well as between countries. As discussed in previous chapters, several factors were suggested to explain such variations.[16] These factors include, for example, variations in the prevalence of some diabetes risk factors (e.g. obesity), lifestyle and types of foods, and ethnic and genetic susceptibility.

The pioneer statistician George E. Box wrote *"essentially, all models are wrong, but some are useful"*.[279] The reliability and accuracy of diabetes prevalence estimates are highly dependent on the data sources used in modelling process, model structure and methodology.[280] Thus, comparing the results of different diabetes prevalence estimates may be difficult because different studies often utilise different data sources, apply different methodologies for estimation and projection, and use different assumptions. Furthermore, Danaei et al.[20] reviewed the available global diabetes estimates and reported some other potential reasons for variations in their results. For instance, the definition of diabetes varied in different studies, as diagnostic criteria have been repeatedly changed over time. In addition, studies were different in their populations of interest, and some of them used data sources with subnational samples, regarding them as equally representative of national populations. This could lead to biased results, as those specific subnational groups might differ from the general populations in many aspects, such as the prevalence of some risk factors for diabetes.

As discussed in chapter 4, the modelling process is primarily a logical connection between inputs (data and assumptions) and outputs in the form of valued consequences (e.g. prevalence estimates) that are of interest to the

health care decision makers.[22] It has been discussed in chapter 4 that the model results should never be presented as point estimates, or as unconditional claims of estimates and projections but, rather, the outputs should be represented as conditional upon the input data and assumptions. Thus, a model should not be a “black box” for the end-user, but be as transparent as possible, so that the logic behind its results can be grasped at an intuitive level.[22]

This thesis used the Saudi IMPACT Diabetes Forecast Model, which integrates nationally representative data on the prevalence of diabetes, obesity and smoking in Saudi Arabia from different sources, along with various assumptions and literature-derived data in order to model trends of diabetes and its future projections during a time period of 30 years (1992–2022). Methodology and data sources have been described earlier in detail with their strengths and limitations. Also, all assumptions used in modelling have been explicitly discussed in chapter 5.

Sections 9.2 and 9.3 compare the main results of diabetes prevalence in Saudi Arabia as estimated and projected by the Saudi IMPACT Diabetes Forecast Model against two of the *most recent* global diabetes estimates. The first is that of the IDF Diabetes Atlas, 2011[9, 280] and the second is that of the WHO Global Burden of Disease (GBD) project, 2011.[20] These two sections discuss briefly the differences between these studies in terms of several aspects, such as study populations, data sources, methods of estimation and some assumptions used in modelling (summarised in Table **9.1**). In addition, section 9.4 presents briefly a similar comparison of the model in this thesis against the *relatively older* modelling studies[14-17] (summarised in Table **9.2**).

Table 9.1. Comparison of the Saudi IMPACT Diabetes Forecast Model against the IDF (2011) model and the GBD (2011) model

	IDF (2011)[9, 280]	GBD (2011) [20]	Saudi IMPACT Diabetes Forecast Model
Estimated DM prevalence in Saudi Arabia (%)	2011 Total: **16.2** *	2000 Males: **17.5**** Females: **17.7**	2000 Males: **17.7**† Females:**16.4** Total: **17.2**
	2030 Total: **20.8**	2008 Males: **22.0** Females: **21.7**	2008 Males: **26.7** Females: **24.7** Total: **25.9**
	2012 update[281] ***Total: 23.4***††		2011 Males: **29.8** Females: **28.1** Total: **29.2**
			2022 Males: **41.3** Females: **47.7** Total: **44.1**
Age of study population (years)	20 - 79	25+	25 – 64†
Main data sources for DM prevalence in Saudi Arabia	Al-Nuaim et al. [202] El-Hazmi et al. [282] Warsy & El-Hazmi [36] Al-Nozha et al. [18] WHO STEPS [19]	Warsy & El-Hazmi [36] Al-Nozha et al. [18] WHO STEPS [19]	Warsy & El-Hazmi [36] (for starting year prevalence) WHO STEPS [19] (for validation)
Estimation methodology	Logistic regression modelling	Complex multi-level Bayesian hierarchical modelling	Markov modelling
Covariates used for estimating DM prevalence	▪ Urbanisation ▪ Ageing	▪ National income ▪ Urbanisation ▪ National availability of multiple food types ▪ Age-standardised mean BMI	▪ Trends in population structure ▪ Trends in obesity prevalence ▪ Trends in smoking prevalence ▪ Estimated incidence of diabetes ▪ Estimated case-fatality rate ▪ Evidence-based estimates of RRs for transition probabilities

* IDF estimates: prevalence adjusted to national population

** GBD estimates: age-standardised to the WHO reference population

† Results of the Saudi IMPACT are based on the modelling scenario 2

†† IDF's update for 2012 was obtained from a local study with subnational sample

Table 9.2. Comparison of the Saudi IMPACT Diabetes Forecast Model against four (relatively old) modelling studies

	Shaw et al. [14]	Wild et al. [15]	King et al. [16]	Amos et al. [17]	Saudi IMPACT Diabetes Forecast Model
Estimated DM prevalence in Saudi Arabia (%)	2010 Total: **13.6** 2030 Total: **17.0**	2000 Total: **6.2** 2030 Total: **8.1**	1995 Total: **8.7** 2000 Total: **9.1** 2025 Total: **10.1**	1995 Total: **10.0** 2000 Total: **12.0** 2010 Total: **13.8**	1995 Total: **11.1** 2000 Total: **17.2** 2010 Total: **28.1** 2022 Total: **44.1**
Age of study population (years)	20 – 79	20+	20+	20+	25 – 64*
Main data sources for DM prevalence in Saudi Arabia	Al-Nuaim et al. [202] El-Hazmi et al. [282] Al-Nozha et al. [18]	El-Hazmi et al. [282]	Asfour et al. [178] *(Study from Oman)*	El-Hazmi et al. [283] Asfour et al. [178] *(study from Oman)*	Warsy & El-Hazmi [36] (for starting year prevalence) WHO STEPS [19] (for validation)
Estimation methodology	Logistic regression modelling	DISMOD II	Age-specific diabetes prevalence estimates were applied to UN population estimates and projections	Country-specific diabetes prevalence data were applied to the corresponding national age distribution	Markov modelling
Covariates used for estimating DM prevalence	▪ Demographic changes ▪ Urbanisation	▪ Demographic changes ▪ Urbanisation	▪ Trends in population size and age structure ▪ Urbanisation	▪ Level of economic development (GNP per capita) ▪ Urbanisation	▪ Trends in population structure ▪ Trends in obesity prevalence ▪ Trends in smoking prevalence ▪ Estimated incidence of diabetes ▪ Estimated case-fatality rate ▪ Evidence-based estimates of RRs for transition probabilities

*Results of the Saudi IMPACT are based on the modelling scenario 2

9.2. The IDF Diabetes Atlas (Fifth edition), 2011[9,280]

9.2.1. Methods

The IDF has routinely produced global estimates of diabetes prevalence every three years since 2000. The most recent estimates are that of the Diabetes Atlas 2011 *(there is a recent update for only 2012, discussed in section 9.2.3)*. In the Diabetes Atlas 2011, the IDF used a simple approach to estimate and project diabetes prevalence in adults aged 20-79 years in different world regions and countries for the years 2011 and 2030.

Data used in the IDF study were obtained from country-level data sources, including peer-reviewed studies, national health statistics reports, commissioned studies on diabetes prevalence, and unpublished data obtained through personal communication. The data search was performed through a systematic literature review of PubMed and Google Scholar, in addition to relevant citations from within papers, and gathered information from the IDF network beginning in November 2010 and ending in April 2011. Moreover, other sources were used such as relevant government websites, WHO STEPS surveillance projects and contacts with diabetes researchers in all regions. Data search yielded a total of 565 studies containing prevalence data for either diabetes, impaired glucose tolerance, or both from the year 1980 onwards. These studies were reviewed and exclusion criteria were applied. Exclusion criteria were the following: insufficient data for characterisation or modelling, duplicate data, an update of a previous study, inadequate description of the methodology, clinic-based or hospital-based studies. Then, data sources were ranked by a panel of experts from each of the IDF regions using a validated qualification system called the *Analytic Hierarchy Process* (AHP). Studies were classified by 6 criteria (sample representation, study design, sample size, diagnostic criteria, study date, and type of data). AHP allows criteria from different domains to be compared, e.g. study size versus age of the study. Scores for each criterion were determined by the panel of experts. In general, nationally representative, population-based sources, using oral glucose tolerance test as the primary diagnostic criteria, that were conducted in the last five years received the highest score. Then, a frequency plot of the final scores of all the sources was generated and two thresholds, lower and upper, were

determined. It was found that the scores followed a bimodal distribution, with nearly half of all data sources scoring 0.3 and more. The data sources scoring above and below were examined, and the minimum threshold was then set at 0.3, where all sources with scores below this threshold were automatically discarded. The upper threshold was set at 0.52, corresponding to a gap in the distribution, above which data sources were all of high quality and, accordingly, were automatically included. For each country, where there were no studies above the upper threshold, the top-scoring study between the lower and upper threshold along with any other studies with a score that was within 10 percentage points of the top-scoring study were selected. In countries where more than one study was selected, a weighted average, based on the score, was calculated for each age-specific prevalence. In general, a total of 170 studies from 110 countries were selected for modelling.

If sources were selected for a particular country, these were the only studies used to generate prevalence estimates for that country. However, if no studies were selected for a country, data from countries within a 'data region' were used as a proxy. A data region was defined from a combination of IDF region, World Bank country income group and most common ethnicity. Estimates of the IDF were made for the total diabetes population, including those who were newly diagnosed in surveys, and those with type 1 diabetes.

For Saudi Arabia, the IDF used five data sources for modelling. These sources were four published national surveys[18, 36, 202, 282] (discussed in chapter 3) and the WHO STEPS survey in Saudi Arabia.[19]

In the IDF study, prevalence was modelled for each data source using logistic regression, and rates were estimated separately for men and women, and for urban and rural populations. Where data were not available for one setting or for one sex, these were estimated from prevalence ratios from other sources within the data region. The smoothed age- and sex-specific prevalences for urban and rural settings were then applied to each national population distribution for the years 2011 and 2030 (using the UN Population estimates, as that used in the Saudi IMPACT Diabetes Forecast Model) to estimate national prevalence and numbers of adults with diabetes. The age- and sex-adjusted prevalences for each country were also estimated by applying the age-specific

prevalences to the world population distribution. The IDF methodology used changes in *age*, *sex* and *urbanisation* as covariates for estimating diabetes prevalence.

9.2.2. Relevant results and comparison with the Saudi IMPACT Diabetes Forecast Model

The IDF estimated the total prevalence of diabetes in Saudi Arabia at 16.2% in 2011 and 20.8% in 2030 (both were adjusted to the Saudi population using the UN population estimates). According to the IDF, these estimates place Saudi Arabia to be the 6th country with highest prevalence of diabetes globally in 2011 and 2030.

In comparison, the Saudi IMPACT Diabetes Forecast Model estimated the total diabetes prevalence in the Kingdom in 2011 to be 28.9% (by scenario 1), 29.2% (by scenario 2 and scenario 3), and 29.4% (by scenario 4). In 2022, the Saudi IMPACT model estimated the diabetes prevalence at 39.5% (by scenario 1), 44.1% (by scenario 2), 38.9% (by scenario 3), and 43.2% (by scenario 4).

The substantial differences between the two studies could be attributed mainly to the different methods of modelling of diabetes prevalence and the covariates used for that purpose. According to the IDF, the estimation approach was deliberately kept simple and conservative.[9] The model used logistic regression method and based its predictions for 2030 on predicted demographic changes (urbanisation and ageing). Moreover, the IDF model did not attempt to account for the effects of changes in diabetes risk factors (e.g. obesity), because the estimates and projections were generated for almost all countries in the world and not specifically for a single country. Indeed, assessing the relationship between risk factors and diabetes is difficult across such a very diverse global population. Consequently, the IDF reported this as a main limitation which was likely to result in underestimation of diabetes prevalence if the levels of obesity and other risk factors continue to rise.[9]

On the other hand, as discussed in chapter 5, the Saudi IMPACT Diabetes Forecast Model utilised a different estimation approach (Markov modelling). It used only the prevalence of diabetes for the starting year (1992) along with demographic trends of the Saudi population (1992-2022) and the trends in

prevalence of two risk factors (obesity and smoking) over the same 30-year-period. In addition, the model used a number of transition parameters in the process of modelling, such as the estimated incidence of diabetes, case fatality rate, general mortality and evidence-based RRs. The Saudi IMPACT Diabetes Forecast Model used published nationally representative, population-based studies to obtain data on the prevalence of obesity and smoking in Saudi Arabia, and assumed a linear increase of the prevalence of these two risk factors over time (1992–2022) with assuming capped versus uncapped linear obesity trends.

As mentioned in chapter 2, urbanisation has been implicated in the aetiology of T2DM, because it is mostly associated with several risk factors for the disease. These risk factors include, for example, obesity, physical inactivity and increased consumption of high caloric foods.[8] Therefore, urbanisation has been used by the IDF model as a proxy for these lifestyle risk factors in order to estimate and project the levels of T2DM, rather than the direct modelling of risk factors. However, quantification of the effects of urbanisation on health is difficult, due to difficulty in defining 'urban' versus 'rural' settings. The definitions of urban and rural populations are mostly made individually by each country. Because of national differences in the characteristics that distinguish urban from rural areas, the distinction between urban and rural populations is not yet amenable to a single definition that would be applicable to all countries, or even to the countries within a region.[284] The majority of definitions across the world rely on the size of population in an area. For example, in Saudi Arabia, an urban area is defined as that with a population of ≥5000 inhabitants.[284] Accordingly, the Food and Agriculture Organisation (FAO) of the UN estimated the urban population in Saudi Arabia to be 86.2% in 2000 and 91.8% in 2020.[285] Importantly, relying only on the population size of an area does not take into account the levels of infrastructures and socio-economic status of the population. Some low-populated areas may have as good infrastructures and socio-economic status as highly-populated big cities, particularly in high income developing countries. Therefore, significant differences in the levels of lifestyle risk factors (e.g. physical inactivity and obesity) become less likely to be informed by such a definition. However, some few countries use other criteria for definition, such as population density, predominant type of economic activity,

availability of some specific services and facilities, etc.[284] A systematic review has revealed that the majority of studies relied mainly on these pre-existing measures of urbanisation using an 'urban - rural dichotomy'.[286] The IDF model obtained the data on the proportion of urban population for all countries from the UN estimates.[280]

These measures of urbanisation are crude and may mask many variations in the levels of some important risk factors (e.g. obesity) within a country and between countries. In other words, using the crude dichotomy of (urban–rural) is likely to make it difficult to identify and track components of the urbanisation process that may affect diabetes risk.[286] Alternatively, some studies directly use the levels and trends of important diabetes risk factors, such as obesity (as in the Saudi IMPACT Diabetes Forecast Model), or, in addition, some individual measures that might serve as 'surrogates' for the levels of urbanisation,[286] such as national income and national availability of multiple food types (as in the GBD model discussed in the next sections). Therefore, again, using different modelling covariates might explain the discrepancy between the IDF estimates (which used the level of urbanisation in Saudi Arabia as a main covariate in modelling) and the higher IMPACT estimates (which directly used the trends in prevalence of obesity and smoking, assuming a linear increase over time).

The Saudi IMPACT Diabetes Forecast Model and the IDF model were similar in the data sources used to obtain diabetes prevalence in Saudi Arabia. The IDF used five published national studies that were also covered through the literature review in chapter 3 of this thesis. One of these studies (Warsy and El-Hazmi)[36] was used by the IMPACT Model to obtain diabetes prevalence for the starting year of modelling (1992), and another study (the WHO STEPS survey)[19] was used for validation. Also, the age of population covered by the two models was comparable (20-79 years in the IDF model and 25-75+ years in this thesis). Furthermore, both models used the UN population estimates for obtaining the Saudi population structure trends. However, population data in this thesis were obtained from local sources (national censuses) for 1992 and 2004, and filled in the gaps within this period range by linear interpolation. It used the UN population estimates to obtain data for 2005–2022.

9.2.3. The IDF update for 2012

The IDF has recently released on its website an update of its diabetes prevalence estimates for 2012, using new studies that became available in 2011. The new studies that were reviewed came from Saudi Arabia, Japan, and some other countries.[281] The updated estimates were reported for 2012 only, and there were no updated future projections of diabetes prevalence. The studies used for the 2012 updates were not cited on the IDF website.

For Saudi Arabia, the IDF has updated the prevalence of diabetes in 2012 at 23.4%. The IDF used for this update a recent local study,[287] published in 2011 *(personal communication, D. Whiting and L. Guariguata, IDF)*. However, this study covered a subnational sample of population (aged 7-80 years) from the Riyadh Region only. The sample size was 9,149 individuals (58.6% men and 41.4% women). Diagnosis of T2DM was based on the ADA 1997/ WHO 1999 criteria (fasting plasma glucose ≥7.0 mmol/l). The reported overall crude prevalence of T2DM in the study was 23.1% (95% CI: 20.5-22.2%).

As that study included a subnational sample from only one region of the Kingdom, it might be difficult to generalise its findings to the population of other regions. However, generally, the 2012 update has supported the suggestion (mentioned in the previous section) that the previous IDF's estimates and projections of diabetes prevalence in Saudi Arabia were most likely underestimated.

9.3. The GBD Model, 2011 - the Global Burden of Metabolic Risk Factors of Chronic Diseases Collaborating Group (Blood Glucose)[20]

9.3.1. Methods

In this WHO project, trends and uncertainties in mean fasting plasma glucose (FPG) and diabetes prevalence were estimated for the period 1980-2008 in adults aged 25 years and older in 199 countries and territories of the world. Diabetes was defined by the ADA criteria (FPG ≥7.0 mmol/l), previous diagnosis, or use of a glucose lowering drug. Data sources were obtained from health examination surveys and epidemiologic studies, review of published articles, in addition to unpublished data sources identified through the WHO

Global InfoBase. More than 3000 published articles were identified through searching Medline and Embase databases. After review of all articles and applying the exclusion criteria, a total of 128 published studies were retained. In brief, studies were included if they were from a representative sample, including from a national, subnational, or community population, and if the data were based on measured (vs. self reported) glucose and diabetes. On the other hand, studies were excluded if they contained only diagnosed diabetes, and self-reported diabetes status and diagnosis history with no data on measured glucose; had used capillary blood for postprandial glucose; used a sampling method that may be related to diabetes (e.g. studies on hypertensive, diabetic, or obese patients and populations); were not population-based or used non-representative samples (e.g. convenience or non-random sampling); reported data only on children or those who were 25 of years of age or younger; or did not report the sampling method.

For Saudi Arabia, the GBD used three data sources for modelling. These sources were two published national surveys[18, 36] (discussed in chapter 3) and the WHO STEPS survey in Saudi Arabia.[19]

The GBD model used more complicated statistical methods than that used in the IDF model. The model converted systematically different glycaemic metrics reported in studies to one metric (FPG). Although mean FPG was the most common metric in data, some sources reported mean postprandial glucose or HbA_{1c}. The model used data sources that had mean FPG and other metrics to develop regression models to estimate mean FPG. The dependent variable in these regressions was mean FPG; while the independent variables were mean postprandial glucose, mean HbA_{1c}, or diabetes prevalence, and age, sex, year of survey, and whether the country was high income. A similar approach was used to estimate diabetes prevalence, from the estimated mean FPG. The dependent variable of this regression was the logit of prevalence (based on the ADA definition), and the independent variables were the natural logarithm (Ln) of mean FPG, age, sex, as well as whether the country was high income (as classified by the Institute for Health Metrics and Evaluation).

The GBD model estimated mean FPG by age group, country, and year, separately for men and women. The statistical methods were sophisticated, but

in brief, a multi-level statistical approach (Bayesian hierarchical modelling) was used. The FPG trends over time were modelled as a linear trend plus a smooth non-linear trend. The estimates were informed by several country-level covariates. These covariates were national income (Ln per-head gross domestic product), urbanisation (proportion of population that lived in urban areas), age-standardised mean BMI (from a previous GBD systematic analysis of country data), and national availability of multiple food types for human consumption (from the food balance sheets of the Food and Agriculture Organization (FAO) of the United Nations).

Mean FPG and diabetes prevalence were estimated from the model for 5-10 year age groups for adults aged ≥25 years. Estimates for subregions, regions, and the world were calculated as population-weighted averages of the constituent country estimates by age group and sex. The presented estimates for each country or region and year were age-standardised to the WHO reference population.

9.3.2. Relevant results and comparison with the Saudi IMPACT Diabetes Forecast Model

The GBD model estimated the prevalence of diabetes in Saudi Arabia among men and women (≥25 year-old) respectively as follows: 17.5% and 17.7% in 2000, and 22.0% and 21.7% in 2008. On the other hand, the estimates of the Saudi IMPACT Diabetes Forecast Model for men and women in 2000 were respectively as follows: 17.7% and 16.4% (by scenario 1 and scenario 2), and 18.3% and 17.0% (by scenario 3 and scenario 4). In 2008, the results of the Saudi IMPACT for men and women were respectively as follows: 26.7% and 24.7% (by scenario 1 and scenario 2), and 27.0% and 25.2% (by scenario 3 and scenario 4).

Clearly, the results of the GBD model and the Saudi IMPACT Diabetes Forecast Model are very comparable, in spite of differences in the general methods of estimation. This similarity in results of the two models could be attributed primarily to the several covariates used in both models to estimate diabetes prevalence. In contrast to the IDF model that was conservative and used only ageing and level of urbanisation as covariates, the GBD model incorporated more covariates to inform its estimates. However, among all these covariates,

mean BMI is likely to have the most important contribution to the higher estimates of the GBD model than that of the IDF model; because mean BMI could serve as a 'direct' informant of the trends in obesity levels. Another GBD modelling study for trends in the global BMI[13] showed that the estimated mean BMI in Saudi Arabia followed a linear increase between 1980 and 2008. The estimates of mean BMI (kg/m^2) in men and women in Saudi Arabia were respectively as follows: 25.0 (UI: 23.8-26.3) and 26.3 (UI: 24.8-27.8) in 1980, 25.9 (UI: 25.6-26.2) and 27.3 (UI: 26.9-27.8) in 1990, 27.0 (UI: 26.6-27.4) and 28.5 (UI: 28.0-29.0) in 2000, and 27.9 (UI: 27.2-28.6) and 29.6 (UI: 28.7-30.5) in 2008. Furthermore, the WHO's GBD estimates showed that the region of 'North Africa and Middle East' witnessed the largest increase in mean BMI in men and women between 1980 and 2008 after the region of 'Oceania'. Saudi Arabia was among the countries with the highest increase in mean BMI within its region.[13] Unfortunately, country-specific estimates of the prevalence of obesity (BMI ≥30 kg/m^2) were not reported. However, the region of 'North Africa and Middle East' had the seventh (among the 21 GBD regions of the world) highest prevalence of obesity in men, and the second highest in women between 1980 and 2008. In men, the estimated prevalence of obesity in that region increased substantially from <10% in 1980 to 20-30% in 2008. On the other hand, obesity prevalence in women increased from 10-20% in 1980 to 30-40% in 2008.[13]

As discussed earlier, the Saudi IMPACT Diabetes Forecast Model assumed a linear increase in obesity prevalence during the period of 1992-2022 based on the estimated annual rate of increase, as informed by the available national studies (with assuming capped versus uncapped trends).

One of the advantages of the GBD model is its use of a single definition of diabetes across all studies included in modelling process. The three Saudi studies used in the GBD model had different definitions of diabetes. For instance, Warsy and El-Hazmi[36] used the WHO 1985 diagnostic criteria with the OGTT, while the WHO STEPS study[19] and the study of Al-Nozha et al.[18] used the ADA 1997 criteria with measuring only the fasting plasma glucose (FPG). As mentioned earlier, the GBD model systematically converted all data that were reported in other glucose metrics (e.g. mean postprandial glucose or HbA_{1c}) to mean FPG, and then estimated the diabetes prevalence from mean FPG. This use of a single definition for diabetes could be a good solution to

improve the comparability of results. As discussed in detail in chapter 7, using different diagnostic criteria for diabetes was reported to have an impact on the results of diabetes prevalence.

The GBD study modelled only the available local data on diabetes prevalence, and did not make future projections. In comparison, the Saudi IMPACT Diabetes Forecast Model estimated the past trends in diabetes prevalence from 1992 and also projected the estimates up to 2022, based on the predicted trends in obesity and smoking. This 'logical' prediction of future might be more useful to the health care planners and decision makers for proper allocation of resources. In addition, the model in this thesis could also serve as a helpful tool for decision makers, through conducting a series of "what if" analyses in order to quantify the impact of reducing the prevalence of obesity and/ or smoking on the levels of diabetes in Saudi Arabia.

9.4. Comparison of results in this thesis against other modelling studies

Table **9.2** summarises a comparison of the results of the Saudi IMPACT Diabetes Forecast Model against four modelling studies[14-17] that provided global and a large number of country-specific estimates and projections of diabetes prevalence. These modelling studies are older than the IDF and GBD models, and have been discussed in detail in chapter 3.

For Saudi Arabia, Shaw et al.[14] and Wild et al.[15] used for estimation local population-based surveys (also used by the IDF and GBD models). On the other hand, the oldest two studies (King et al.[16] and Amos et al.[17]) used old data from Oman[178] and extrapolated such data to Saudi Arabia.

In general, all these four models produced much lower estimates and projections of diabetes prevalence than the Saudi IMPACT Diabetes Forecast Model. Again, as with the IDF model, the most likely reason for such large discrepancies is the use of *only* demographic changes and/ or urbanisation in these models as covariates to inform the future projections.

Overall, this chapter discusses in detail the variations and similarities of the model outputs in this thesis and the estimates of the IDF, GBD project, and other existing modelling studies. The next final chapter presents the overall

discussion and conclusions. It presents a summary of the main findings, strengths and limitations of the thesis, implications of the results, recommendations for policy action and further research, and conclusion.

Chapter 10. Discussion

10.1. Summary of the main findings

This thesis developed and validated the Saudi IMPACT Diabetes Forecast Model to estimate the prevalence of T2DM in Saudi Arabia during the period 1992-2022. The model used, as a baseline, local data on the prevalence of T2DM in 1992, and combined several other types of data to inform its estimates and projections. These data include the prevalence of obesity (BMI ≥30 kg/m^2) and smoking, assuming linear increasing trends, population structure trends, and a number of parameters of the disease epidemiology (incidence, case fatality, RRs of T2DM if obese or smoker, and total mortality). The results of model validation against local observed data and another model (the GBD model 2011) were generally consistent.

The thesis used data for 1992 as a baseline for modelling (rather than using the more recent WHO STEPS in 2005) in order to provide an overall picture of the disease trends in Saudi Arabia since the earliest time point at which diabetes data were available. In addition, the model was capable of reproducing the prevalence of T2DM at a time point 'forward' (i.e. WHO STEPS, 2005), and this could result in gaining the acceptance of policy makers that the model forecasts for the 'more forward' time points (till 2022) are most likely reliable.

Based on the projections in this thesis, T2DM prevalence in Saudi Arabia is set to rise substantially in the next decade, even considering more 'optimistic' future obesity trends. In those aged 25-64 years, the T2DM prevalence is estimated to increase from 8.5% (UI: 6.8–10.2%) in 1992 to 39.5% (UI: 32.5–45.9%) in 2022, assuming capped obesity trends, and 44.1% (UI: 35.4–52.5%), assuming uncapped increasing obesity trends. As discussed in chapter 5, the assumed capping points of the projected obesity prevalence were 35% in men and 60% in women.

The huge and accelerated elevation in the estimated T2DM prevalence in Saudi Arabia was found to be driven mainly by high and steep estimated increases of the disease prevalence among the young adult men aged 25-44 years, and women aged 25-64 years. This can be attributed primarily to the markedly high

observed and projected relative increases in the prevalence of obesity (the main driver of T2DM projections in the model) in these particular age groups. In addition, the estimated incidence of T2DM (by DISMOD) in these age groups was relatively high, with low estimated case fatality and total mortality rates. Hence, the 'pool' of cases of T2DM in these age groups increases progressively over time, as it receives a large inflow of incident cases with a relatively smaller outflow of disease-specific deaths and other mortality competing risks.

Generally, the higher estimated incidence and rapid increases in prevalence of T2DM among young/ middle-aged adults in Saudi Arabia is consistent with the findings of other studies regarding the T2DM projections in developing countries.[15, 16, 57] As discussed in chapters 2 and 3, evidence has revealed that the disease in developing countries has been found to start at relatively younger age groups,[57] and the majority of people with T2DM in these countries are aged 45-64 years (compared to ≥65 years in developed countries).[15, 16]

The overall prevalence of T2DM during 1992-2022 was estimated in this thesis to show higher relative increases in women than men. In men, the estimated relative increase was around 351% (assuming capped obesity trends) and 375% (assuming uncapped obesity trends). On the other hand, in women, the estimated relative increase was approximately 385% (assuming capped obesity trends) and 481% (assuming uncapped obesity trends). It is important to note that the DISMOD-derived incidence rates of T2DM in this thesis for men were higher than that for women in almost all age groups. However, the higher predicted relative increases in T2DM prevalence in women could be explained primarily by the substantially higher trends in obesity prevalence than that in men. This is generally consistent with data from the WHO's Regional Office for the Eastern Mediterranean[114, 288], which clearly showed a much higher prevalence of obesity in adult women across almost all countries of the region.

The large sex differences in the prevalence of obesity in Saudi Arabia (and other EMR countries) have been attributed mainly to the greater sedentary lifestyle patterns among women than men. For instance, Mabry et al.[289] reviewed the studies on prevalence and sex differences in adults' physical activity participation in the GCC countries. They reported that the prevalence of 'sufficient' physical activity (at least 150 minutes per week) in the GCC countries

is significantly lower among adult women (prevalence ranges from 26.3-28.4%) than men (prevalence ranges from 39.0-42.1%). According to the reviewers, these prevalence rates of sufficient physical activity are much lower than that reported in developed countries, such as Australia (60% for men and 54% for women) and the US (49.7% for men and 46.7% for women). Moreover, the prevalence rates of sufficient physical activity in the GCC countries are even lower than that reported in other neighbouring countries of the EMR. For example, in Egypt, the reported prevalence was 54.9% for men and 42.6% in women.[289] This can be explained by the unique socioeconomic and cultural context of the GCC countries, which poses special constraints on the physical activity of women. Most women have restricted movement outside home, limited opportunities to attend gyms and health clubs, as well as high dependency on automobiles and domestic maids.[289]

The obesity prevalence rates in the two oldest age groups of the Saudi population (65-74 and 75+ years) were extrapolated using data from Oman, as discussed in chapter 5. If such a method of extrapolation was valid, these two age groups would have almost a stable/ flat pattern of trends in the estimated T2DM prevalence in men during 1992-2022. In women, the age group (65-74 years) would have a relative increase of around 85%, while the age group (75+ years) would also have flat trends in T2DM prevalence. This finding is in agreement with that reported by Wild et al.,[15] who used DISMOD 2 models to estimate the global prevalence of diabetes (all ages) for 2000 and 2030. They reported a flattened trend pattern or modest reduction of diabetes prevalence in the oldest ages.

However, in this thesis, the starting year prevalence of T2DM and the trends in obesity prevalence over time were based on cross-sectional data. These cross-sectional data reflect only the situation at a specific time across the age groups. Importantly, however, age plays an important role in the aetiology of T2DM. If a group of individuals was followed from birth, their risk for the disease would vary as the birth cohort aged. So, different birth cohorts may have different levels of exposure to a particular risk factor, which might be expected to produce a change in disease incidence and prevalence for individuals born at a particular time.[290] These effects are known as the 'age and birth cohort effects', which are recognised as potential limitations in all prevalence forecasting models that

mostly utilise cross-sectional data for prevalence predictions. In this thesis, obesity trends suggest that obesity prevalence peaks between the ages of 35-64 years in men and women, and then, a drop of the prevalence rates is projected in the oldest age groups (65-74 and 75+ years). However, this drop in the prevalence does not necessarily mean that elderly people lose weight. Instead, it could be the result of age and birth cohort effects and reflect the fact that older birth cohorts had not gained similar weight with age as birth cohorts being born in a later time period.[291] Moreover, beside age and birth cohort effects, prevalence forecasting models can also be constrained by potential 'period effects'. A period effect specifies that time trend patterns of a disease could be influenced by some specific circumstances at the date (period) the disease was diagnosed (e.g. war famines, changes to some diagnostic technologies/ tests, etc), so that there might be unique effects that are produced by inducing a similar change in the disease risk for all individuals alive at a particular point in calendar time, regardless of age.[290]

These age-period-cohort effects have been suggested to probably explain the plateau or declining trends in obesity prevalence[292] and lung cancer mortality[293] in the oldest age groups over time, as projected by two prediction models. Such age-period-cohort effects might also have some influence on the findings in this thesis regarding the projected flat trends in T2DM prevalence for the oldest age groups versus increasing trends in younger age groups, which converge at some point in time and then invert. However, it is difficult to disentangle these potential effects with cross sectional data. Therefore, longitudinal data (such as multiple sequential cross-sectional surveys with several birth cohorts and several specific ages or preferably prospective cohort studies) are better sources of data for prevalence forecasting models. However, longitudinal data on T2DM and obesity trends are very rarely found in the literature compared to cross-sectional data.[291]

The assumed capping of the projected obesity prevalence trends (at 35% in men and 60% in women) was found to have some impact on the future projections of T2DM prevalence. As a result of capping, the overall prevalence of T2DM by 2022 is predicted to reduce by around 10.4% (from 44.1% to 39.5%) in population aged 25-64 years, and by approximately 10.0% (from 43.2% to 38.9%) in population aged 25-75+ years. Such an impact of capped

obesity was found to be more prominent in women than men. For instance, in population aged 25-64 years, the prevalence of T2DM is predicted to reduce by 16.6% in women (from 47.7% to 39.8%), compared to 5.1% in men (from 41.3% to 39.2%). These prominent differences in the predicted diabetes prevalence for women with and without capping of obesity trends are expected, since the uncapped projected obesity prevalence in most age groups of women are substantially higher than the assumed level of capping (60%). However, it is important to note that the "extrapolated" prevalence rates of obesity in the two oldest age groups of men and women were relatively low, and did not reach the assumed levels of capping. Hence, there was no effect of capping on the results of these two age groups in both sexes.

Comparison of the results of the Saudi IMPACT Diabetes Forecast Model against other modelling studies has been extensively discussed in chapter 9, as such a comparison requires a detailed and long discussion of the estimation methodology, study population, data inputs, assumptions, and covariates used to generate the projections. In general, the large differences between the results in this thesis and the other modelling studies are primarily attributed to the different variables used to inform T2DM prevalence trends and projections. The majority of models[9, 14-17] have relied only on demographic trends and urbanisation, and produced much lower projected prevalence rates of T2DM in Saudi Arabia than the local 'observed' data and those predicted in this thesis. In contrast, the model in this thesis was validated against the observed data and it produced consistent results. In the literature, the APHO Diabetes Prevalence Model[30] is a recent consistent example that reported similar variations in the estimated prevalence of diabetes when compared to other models. As discussed in chapter 4, the APHO Diabetes Prevalence Model used the trends in overweight and obesity in England to estimate diabetes prevalence, which was approximately one third higher than that estimated by the IDF. For Saudi Arabia, the only modelling study (GBD model 2011)[20] that used the BMI trends in the Kingdom as an informant of projections has produced very comparable results to the model in this thesis, in spite of the different modelling methodology. However, the Saudi IMPACT Diabetes Forecast Model has the advantage of providing future projections of T2DM prevalence (the GBD model

has only reported the results for 1980, 2000, and 2008), in addition to presenting several 'what if' policy scenarios.

10.2. Strengths and limitations of the Saudi IMPACT Diabetes Forecast Model

The Saudi IMPACT Diabetes Forecast Model has several strengths. First, as previously discussed in chapter 5, the model was originally designed to use a relatively limited number of data inputs that should be obtainable from a developing country. This is an advantage over the other diabetes models (reviewed in chapter 4), which require more types of data inputs that may not be available from Saudi Arabia.

Second, the model is based in a very common spreadsheet package (MS Excel), and is user-friendly.

Third, modelling data were obtained from the best available sources, and the strengths and limitations of such sources were explicitly documented. Missing and incomplete data were handled by appropriate inter- and extrapolation, as well as explicit assumptions.

Fourth, different types of extensive sensitivity analyses (e.g. scenario analysis and analysis of extremes) were conducted to test the potential uncertainties around data inputs and assumptions. All modelling results were presented in different scenarios and with uncertainty intervals.

Fifth, the model was well validated against both local observed data and an external model.

Sixth, the model directly incorporated data on trends in adult obesity and smoking to inform the projections of future T2DM prevalence in Saudi Arabia. This is a big advantage over other models, and is the most likely reason for the large differences in the estimates and projections of T2DM.

Seventh, the section of 'what if policy analyses' in the Saudi IMPACT Diabetes Forecast Model involved several useful and comprehensive policy scenarios. A number of reduction targets were incorporated, as set by local and leading international authorities. The 'what if' analyses in this thesis can form a useful platform for policy planning and decision making.

However, the model has some limitations. First, as discussed in chapter 4, modelling studies mostly require data inputs from several sources, which may differ in the data quantity and/or quality. In this thesis, as mentioned earlier, these issues were managed through applying a number of appropriate explicit assumptions, inter-/ extrapolation, and rigorous sensitivity analyses.

Second, the DISMOD-derived transition parameters (incidence, case fatality, and total mortality) were assumed to be constant over the whole modelling period (1992-2022). Globally, data on the trends in diabetes-related mortality are inconsistent. Evidence from many developed countries has showed decreasing trends over the past 4-6 decades.[294-299] However, the most recent IDF Diabetes Atlas reported that the number of deaths attributable to diabetes in 2011 shows a 13.3% increase over the estimates for 2010, which has been attributed to increases in the number of diabetes-related deaths in the South and Central America, Western Pacific, North America and Caribbean, and Middle East and North Africa Regions.[10] In Saudi Arabia (and most other developing countries), such trend data are not available, and, therefore, if the true incidence of T2DM in Saudi Arabia has increased (or the diabetes-related mortality decreased) since 1992, the future projections of T2DM prevalence in this thesis would most likely underestimate the true burden.

Third, the Saudi IMPACT Diabetes Forecast Model used the trends in only obesity (BMI ≥30 kg/m^2) and current smoking as risk factors to inform the projections of T2DM prevalence. The model did not include other risk factors for T2DM (e.g. physical inactivity and diet). As discussed in chapter 1, the available local data on the prevalence of other risk factors are not sufficient to predict the likely trends, as there is only one national study[19] measuring the prevalence of physical inactivity and dietary patterns. In addition, the model did not include overweight as a risk factor, mainly because lack of data to inform the required transitions. Also, it would be difficult to predict the linear future trends in both overweight and obesity simultaneously, as the obesity trends are increasing mainly at the expense of overweight trends. This might complicate the interpretation of the 'what if' policy options, making them confusing to the policy makers and other potential users. The model also did not include ex-smokers in the smoking pool, but this does not appear to have a significant impact on the model predictions, as the recent evidence (discussed in chapter 2) showed that

the risk of developing T2DM among ex-smokers is considerably lower than that among current smokers.[140] However, the model validation results were reassuring and the model appears to capture well the trends in the most important determinant of T2DM (obesity).

Fourth, the model covered the adult population (aged 25-75+ years) only, and did not include the younger age groups of children and adolescents, in whom the incidence and prevalence of T2DM are increasing worldwide.[10]

Fifth, the model used only BMI ≥30 kg/m^2 for definition of obesity, and did not use other measures of central/ abdominal obesity (such as waist circumference) as those data were not available from national surveys. It has been mentioned in chapter 3 that a considerable proportion of population in Saudi Arabia is composed of expatriates from different ethnic origins, with South and Southeast Asians comprising the majority of foreign population. As discussed in chapter 2, evidence revealed that Asians are more prone to abdominal obesity, and they mostly develop adverse health consequences (such as T2DM) at lower BMI than other ethnicities.[89] Therefore, the modelled projections of obesity prevalence might be underestimated, which could result in underestimation of diabetes prevalence in Saudi Arabia. However, such potential uncertainties could be handled by the extensive sensitivity analyses, which provide higher and lower uncertainty limits of obesity and diabetes prevalence rates.

Sixth, the 'what if' policy scenarios presented in this thesis did not consider a lag time between reducing the prevalence of obesity/ smoking and the subsequent potential reduction of T2DM prevalence. In addition, the achievability of the targeted reductions during a relatively short period of 12 years (2010-2022) is not known. Evidence is not clear in this regard, particularly at the population-wide level. However, data from Norway[300] and Cuba[301] revealed that rapid and short-term declines in diabetes burden occurred as a result of significant reductions of the lifestyle risk factors (particularly obesity) during the critical periods of World War II (6-years long) and an economic crisis (25-years long).

10.3. Implications

The modelling work in this thesis offers very useful information to the health policy makers in Saudi Arabia, which has been constantly classified by the IDF to be among the top 10 countries with the highest diabetes prevalence globally.[10] Policy makers need not only data on the current magnitude of T2DM, but also credible data on the likely future projections in order to make proper policy planning and allocation of resources. Currently, there are no local data on the future projections of T2DM in Saudi Arabia, and the available relevant international studies clearly underestimated the disease trends.[9, 14-17] This thesis demonstrates for the health policy planners that T2DM prevalence in the Kingdom is predicted to increase substantially during the period 1992-2022. The major factors contributing to such a huge elevation in T2DM levels are the rapid population ageing and the increasing trends in the disease's risk factors (particularly obesity). This thesis also revealed that the largest part of the growing problem of T2DM in Saudi Arabia is predicted to affect women and young adults of the productive age.

Furthermore, as extensively discussed in chapter 8, this thesis quantifies for the health policy makers in Saudi Arabia the potential impact of achieving the local reduction targets set for obesity and smoking prevalence (the GCC Action Plan[198]) on T2DM prevalence trends. Also, the thesis provides additional future policy options and intervention scenarios (which are in line with current international recommendations) to reduce the burden of T2DM. It has been found that T2DM prevalence could be reduced if effective primary preventive measures are applied to reduce the prevalence of adult obesity and/or smoking. If the local Saudi target for obesity prevalence (10% reduction of that in 2008) would be achieved, a relative reduction of approximately 15% (1.1 million individuals) in T2DM prevalence could be attained by 2022. Furthermore, a relative reduction of around 10% in T2DM prevalence (around 740,000 individuals) could be attained by 2022 if the rise in adult obesity prevalence is halted at 2010 levels (as recommended by the WHO[275]). Such a reduction in T2DM prevalence could increase to 13% (around 960,000 individuals) if the adult obesity prevalence is reduced by 10% of that in 2010 (HP 2020 target[270]). Additional reduction of smoking prevalence was estimated to yield some small improvements of the reduction of T2DM prevalence. However, in terms of

absolute numbers, this additional reduction of smoking could prevent T2DM in a considerable additional number of individuals.

It is unknown if any of the additional international policy targets is effectively applicable to the Saudi context. However, at least for the WHO targets, they were established after analysing the current situation and trends of the targeted conditions in the member states. In addition, the WHO undertook a critical assessment of feasibility of such policy targets based on demonstrated country achievement.[275] Still, the probably 'ambitious' nature of these policy targets should be taken into consideration. Generally, policy makers in Saudi Arabia could compare between the different policy targets offered by this thesis and determine the most suitable/ feasible one, based upon their experience of the local situation and the existing financial and other resources. The progress toward achieving the applied policy target should be monitored periodically through representative population-based surveys.

10.4. Recommendations for policy actions

Based on the findings from this thesis, several recommendations can be suggested to reduce the prevalence of T2DM in Saudi Arabia and to improve the availability and quality of relevant national data. These recommendations are generally compatible with the prevention guidelines of the WHO[302], the WHO's Regional Office for the Eastern Mediterranean[162, 288], the IDF's office in MENA[303], and the GCC Action Plan for prevention and control of diabetes.[198] Relevant recommendations are briefly summarised in this section.

The comprehensive review undertaken in this thesis (chapter 3) showed that the local data on prevalence of T2DM, obesity and smoking are most likely credible and representative of the Saudi population. However, such data are limited in terms of the number of available surveys and the variations in reporting the results. Thus, it would be important to conduct periodic/ regular nationwide epidemiological studies to measure the prevalence of T2DM and its risk factors (e.g. obesity, physical inactivity, dietary patterns, and smoking). These studies should include all age groups of population, preferably measure the prevalence of all conditions simultaneously, and report the results in consistent age-group-intervals to facilitate future comparison and analysis.

Furthermore, the availability and quality of sex- and age-specific data on population structure and mortality should be improved by the Saudi CDSI.

This thesis illustrates the enormous challenge and urgency of addressing the epidemics of obesity and diabetes in the Kingdom. The political commitment to the prevention of diabetes should be urgently increased if the proposed reduction targets are to be attained. Such a political commitment can be achieved through making diabetes one of the top priorities within the national health care framework. Also, the strength of the national Saudi economy should be exploited by allocating a considerable budget for the prevention and monitoring of T2DM. Furthermore, governmental support should be gained for the approval of some legislation that may help in reducing some of the risk factors for T2DM (discussed below).

A multi-sectoral collaboration of the relevant parties should be increased and maintained. There is urgent need for action at all levels, including regulatory/ policy changes in sectors beyond health. The Saudi Ministry of Health (MOH) should actively involve in the prevention strategy the relevant governmental authorities, in addition to some non-governmental organisations (NGOs). Examples of relevant governmental authorities include the ministries of Education, Information, Transport, Commerce and Industry. NGOs can play several roles, such as providing financial support and helping in producing public educational programmes and materials regarding T2DM and its risk factors.

Appropriate preventive measures at the community level, which aim to reduce the prevalence of obesity, should be an urgent action. These preventive measures should focus mainly on promoting healthy diet and physical activity. There should be an adequate budget and resources allocated for the recently established 'Diet and Physical Activity Programme'[199] (discussed in chapter 3). However, as the Programme is still relatively recent, there are no currently available data on the levels of patterns of diet and physical activity to monitor the progress in implementing the national strategy on physical activity and diet. Therefore, it is strongly recommended that such a progress should be carefully monitored and maintained. Examples of some urgent recommended measures include the following:

a) *Promoting healthy diet*. This can be achieved through intensifying health education to public, in order to increase the population knowledge of the health risks of diet-related NCDs including diabetes, and the benefits of healthy and diverse diets. The public should be educated to restrict consumption of fats and sugar and increase consumption of fruit and vegetables. Attractive concentrated information should be delivered to the whole population via different channels, such as primary health care centres, schools, media (e.g. television, internet, magazines), and field public campaigns. Importantly, a special focus should be directed on women, who have prominently higher rates of obesity than men. In addition, the government should be encouraged to establish strict legislation to enforce the food industry to develop healthier products and to make clear product labelling. Moreover, the relative price and taxes of unhealthy food choices can be increased in favour of healthy and less energy-dense foods.

b) *Promoting physical activity*. This can be achieved through increasing and improving the outdoor sport and recreational spaces. However, the weather in Saudi Arabia is extremely hot for around six months a year, and this has been documented as a major barrier to the outdoor physical activity at that period.[304] So, alternative measures could be establishment of convenient public (non-private) indoor exercise venues or encouraging the use of indoor walking trails.

   Physical activity programmes should be implemented and monitored in schools and universities. In addition, the community awareness of the importance of physical activity should be increased through the different channels indicated above, with a special focus on women. Furthermore, there should be changes in the transport system and urban planning policy toward implementation of a widespread and efficient public transport. This could help in promoting physical activity and reducing the currently high dependency on private automobiles.

Appropriate preventive measures at the community level, which aim to reduce the prevalence of smoking, should be an urgent action. The awareness of the hazards of smoking should be continually increased through the various ways indicated above. The recently approved legislations to prohibit smoking at public spaces and workplaces[201] should be monitored and strictly applied.

Governmental support is also required to restrict tobacco imports and advertisement, raise its prices, and strictly ban its selling to children and adolescents. The existing 'Tobacco Control Clinics', which offer free help and advice to people who want to quit tobacco smoking,[201] should be strongly supported by allocating a sufficient financial budget and manpower.

Nevertheless, policy makers should take into consideration some potential barriers/ challenges that might have an influence on the prevention strategies. These challenges could be cultural, political, economic, etc. Generally, it is difficult to change a population's behaviours and dietary beliefs and practices, which are mostly traditional and deeply-rooted. In Saudi Arabia, for example, preventive strategies should consider the unique cultural and religious nature of population, particularly regarding the social restrictions on women's work and physical activity patterns. In addition to establishment of 'females only' gyms and health clubs, another important starting point could be incorporating physical education into the school curriculum for females. Moreover, as mentioned in chapter 3, little is known about the regional disparities/ inequalities in Saudi Arabia, which probably is a politically sensitive issue. It is recommended to make some policy changes in order to provide more detailed information on any regional inequalities for proper planning of prevention strategies and resource allocation.

It is important to indicate that the recommendations above focus only on primary preventive measures (to reduce the prevalence of T2DM, obesity and smoking) as one of the main initial objectives of this thesis, as mentioned in chapter 1. However, the findings are also important for the healthcare planning in Saudi Arabia. It is strongly recommended to plan the diabetes healthcare services properly for the currently large number of 'patients' and the further projected increase of cases in the next decade. These services should include effective and large-scale screening tests for early detection of T2DM in both high-risk groups and those with undiagnosed (occult) disease. Regular screening of high risk individuals should be implemented in primary health care centres and out-patient departments in hospitals. In addition, mass screening campaigns should be conducted periodically in other public places, such as universities, shopping centres/ malls, etc. It is important to offer the early and appropriate treatment to those diagnosed with T2DM by screening tests in order

to delay or prevent progression of the disease. In patients with existing T2DM, screening programmes for the early detection of complications such as retinopathy, nephropathy, coronary heart disease and foot problems are needed to reduce resulting morbidity and mortality. In addition to screening, it is recommended to ensure the adequate financial and manpower resources needed for effective treatment and rehabilitation healthcare services. Diabetes healthcare teams should be multidisciplinary comprising physicians, nurses, pharmacists, and other diabetes specialists such as dieticians and podiatrists. The national treatment guidelines of diabetes, along with an effective referral and feedback system should be strictly implemented. Furthermore, sufficient supplies of insulin and hypoglycaemic drugs should be continuously maintained in primary health care centres and hospitals.

However, it is crucial for the health policy makers in Saudi Arabia to balance action based on the cost effectiveness of different intervention approaches for prevention and treatment of T2DM. There is considerable evidence investigating the cost effectiveness of different diabetes interventions (mainly in developed countries).[26, 210, 231, 233, 305, 306] Li et al.[307] have conducted a recent comprehensive systematic review of 56 studies to synthesise the cost-effectiveness of interventions to prevent and control diabetes, its complications, and comorbidities from 20 countries. They have concluded that many interventions intended to prevent and/or treat diabetes are ‘cost saving’ (more health benefit at a lower cost) or ‘very cost-effective’ (US$ 25,000 per life per LYG or QALY) and supported by ‘strong’ evidence. However, overall, studies suggest that prevention (e.g. lifestyle modifications ‘diet, physical activity and smoking cessation’ and metformin) is more cost-effective than intensive treatment of diabetes.[308-310] On the other hand, the higher intervention costs of intensive therapy are offset by measured reductions in hospitalisation and treatment costs.[26, 306]

In terms of diabetes screening, studies showed different findings in different countries. For example, the IDF has reported that identifying each case of undiagnosed diabetes in Taiwan costs just US$ 17,800 per QALY gained, which compares favourably to the US where the cost is US$ 56,000 per QALY gained. This comparison between Taiwan and the US highlights that the cost-

effectiveness of population screening is sensitive to the prevalence of undiagnosed diabetes.[306]

Information on the cost effectiveness of diabetes interventions is limited from developing countries. In Saudi Arabia, for example, a recent interest in diabetes health economics research has emerged revealing the massive economic burden of diabetes on the healthcare system in the Kingdom. A recent study has estimated that diabetic people have medical healthcare expenditures that are 10 times higher (US$3,686 vs. US$380) than what expenditures would be in the absence of diabetes.[311] However, there are no national studies evaluating the cost effectiveness of the different approaches of prevention and treatment/ control of diabetes in Saudi Arabia. Hence, it is strongly recommended to conduct and support such research in order to obtain evidence from the local context, which is required for proper healthcare planning and resource allocation. A starting point could be, for instance, piloting different preventive approaches (primary, secondary and tertiary) in different regions of the country and assessing the cost effectiveness accordingly. Also, using the approach of modelling for studying the health economics of diabetes should be supported, and collaboration between MOH and academic/ research institutions should be established for this purpose.

10.5. Potential future developments of the Saudi IMPACT Diabetes Forecast Model

A number of prospective developments can be undertaken to the model in this thesis, provided that the availability of relevant local data will improve in the future.

The model can be improved to involve more risk factors for T2DM in Saudi Arabia (e.g. physical inactivity and diet). Incorporation of such risk factors may produce more accurate predictions of T2DM prevalence, and provide the decision makers with more policy intervention options.

The model can also be developed to involve ‘dynamic’ transition parameters (incidence, case fatality, and total mortality), that change over the modelling period. This may also result in more accurate predictions, as these parameters

are important to describe the disease epidemiology, and are most likely variable over time.

The population covered by the model can be expanded to include younger age groups, which, as previously mentioned, have growing trends of obesity and T2DM. This could result in providing more comprehensive policy options in terms of prevention of obesity in children (not only adults). Evidence shows that obese children are likely to stay obese into adulthood and are more likely to develop diabetes at a younger age.[312]

The model can be developed to be broader in terms of the modelling outcomes. In addition to the predicted prevalence of T2DM, it may be worthwhile to study parameters that consider the quality of life of diabetic individuals, such as the Quality Adjusted Life Years (QALYs).

More health states can be added to model the disease epidemiology (e.g. involving some common complications of T2DM, such as cardiovascular disease, retinopathy, and nephropathy).

10.6. Potential areas of future research

Currently, there are no nationwide data on the prevalence of T2DM by socioeconomic status (SES). It has been discussed in chapter 2 that the prevalence of T2DM is known to vary across different SES strata in developed and developing countries. Therefore, it may be useful to include SES as a main variable in future national surveys, in order to examine if the local distribution of T2DM would be compatible with what has been found in other developing countries.[135] Furthermore, the current national censuses and surveys do not account for ethnicity. As discussed in chapter 3, the Saudi population has a large proportion of expatriates of different ethnicities (particularly South and Southeast Asians), who probably have higher risk of developing abdominal obesity and T2DM at lower ages and BMIs. So, it would be important to include ethnicity in censuses and surveys, and to use additional measures of obesity (WC and WHR).

In this thesis, the incidence of diabetes was estimated by DISMOD, and the RRs of the disease in obese and in smokers were obtained from literature. It

may be important to conduct well designed and monitored prospective studies to produce reliable country-specific values for such parameters.

Moreover, it may be very useful to establish collaboration with the concerned departments in the neighbouring GCC countries, in order to test the suitability of using the model to predict the trends in T2DM prevalence in these countries. These countries are similar to Saudi Arabia in having marked prevalence rates (and limited data) of T2DM and its risk factors. This potential collaboration, of course, requires the permission of and ongoing coordination with the principal developers of the model.

10.7. Conclusion

T2DM is a major public health challenge in Saudi Arabia, imposing a massive burden on individuals and the health care system. Information on the prevalence rates and trends in T2DM and its risk factors in Saudi Arabia are currently scarce and patchy. Thus, the availability and quality of population-based data on the disease and its risk factors should be effectively improved. It would be essential to conduct regular nationally-representative studies with standardised methods in order to evaluate and monitor the trends in prevalence of T2DM and its risk factors.

The Saudi IMPACT Diabetes Forecast Model is a very useful and validated tool to forecast the prevalence of T2DM in Saudi Arabia. In contrast to other models that underestimated the true prevalence trends of T2DM in the Kingdom, the model in this thesis uses relatively few data requirements, explicitly incorporates trends in obesity and smoking prevalence as risk factors, and provides health policy makers with a number of useful policy options for prevention.

The trends and future levels of T2DM in Saudi Arabia are projected in this thesis to be substantially high in both sexes, if the current alarming levels of obesity and smoking continue to increase, or even are capped at the observed prevalence rates. Compared to around 555,000 diabetic people aged 25-64 years (8.5%) in 1992, there would be nearly 7.4 million diabetic people (44.1%) in 2022, assuming a continuing increase of obesity levels, and approximately 6.6 million (39.5%), assuming capped obesity levels.

If the current local policy target for obesity prevalence (10% relative reduction from that in 2008) and smoking prevalence (5% relative reduction from that in 2008) would be successfully achieved, the T2DM prevalence in 2022 could be reduced by around 15% (1.1 million individuals). In addition, reducing the prevalence of obesity by 10% of that in 2010, or at least halting its rise, can result in considerable relative reduction of T2DM prevalence of around 10-13% by 2022. This is equivalent to preventing the disease in approximately 740,000 - 970,000 individuals. Additional reduction of smoking prevalence by 40% of that in 2010 can lead to preventing the disease in a reasonable additional number of people.

Overall, this thesis highlights the need for an urgent action to ensure the effective implementation, monitoring and maintaining of the existing national strategy of prevention of T2DM in Saudi Arabia. Appropriate and effective preventive measures should be aggressively implemented at the population level to promote physical activity, healthy diet, and smoking cessation.

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Appendices

Appendix 1. Search strategy results for studies on prevalence of type 2 diabetes, obesity and active smoking in the GCC countries and Saudi Arabia

Table. Search strategy - prevalence studies on type 2 diabetes in the GCC countries

MEDLINE (Search Dates: 1950-week 45, 2011)

Search history	Results
1. Diabetes mellitus.mp. or diabetes mellitus/	237,483
2. hypergly$.mp.	37,708
3. 1 or 2	256,480
4. Prevalence.mp. or prevalence/	317,992
5. Exp Kuwait/ or Kuwait.mp.	2,405
6. Exp Qatar/ or Qatar.mp.	418
7. Exp Bahrain/ or Bahrain.mp.	473
8. Exp United Arab Emirates/ or United Arab Emirates.mp.	1,126
9. UAE.mp.	1,440
10. Exp Oman/ or Oman.mp.	951
11. 5 or 6 or 7 or 8 or 9 or 10	6,131
12. 3 and 4 and 11	184
13. After title review, keep	26
14. After abstract/article review, keep	5
plus 2 studies through cross referencing	

Table. Search strategy - prevalence studies on obesity in the GCC countries

MEDLINE (Search Dates: 1950-week 45, 2011)

Search history	Results
1. obesity.mp. or obesity/	132,344
2. fatness.mp.	2,443
3. Overweight.mp. or overweight/	23,447
4. Body weight.mp. or body weight/	228,976
5. Central obesity.mp.	1,794
6. Abdominal obesity.mp. or abdominal obesity/	2,460
7. Body mass index.mp. or body mass index/	89,092
8. BMI.mp.	42,669
9. Waist circumference.mp. or waist circumference/	7,056
10. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9	398,049
11. Prevalence.mp. or prevalence/	317,537
12. Exp Kuwait/ or Kuwait.mp.	2,404
13. Exp Qatar/ or Qatar.mp.	418
14. Exp Bahrain/ or Bahrain.mp.	473
15. Exp United Arab Emirates/ or United Arab Emirates.mp.	1,122
16. UAE.mp.	1,438
17. Exp Oman/ or Oman.mp.	951
18. 12 or 13 or 14 or 15 or 16 or 17	6,125
19. 10 and 11 and 18	170
20. After title review, keep	34
21. After abstract/article review, keep	5
plus 2 studies through cross referencing	

Table. Search strategy - prevalence studies on active smoking in the GCC countries

MEDLINE (Search Dates: 1950-week 45, 2011)

Search history	Results
1. smoking.mp. or smoking/	157,746
2. cigarette.mp.	33,117
3. cigarette smoking.mp.	19,692
4. tobacco.mp. or tobacco/	68,156
5. tobacco smoking.mp.	4,260
6. active smoking.mp.	660
7. 1 or 2 or 3 or 4 or 5 or 6	195,114
8. Prevalence.mp. or prevalence/	317,992
9. Exp Kuwait/ or Kuwait.mp.	2,405
10. Exp Qatar/ or Qatar.mp.	418
11. Exp Bahrain/ or Bahrain.mp.	473
12. Exp United Arab Emirates/ or United Arab Emirates.mp.	1,126
13. UAE.mp.	1,440
14. Exp Oman/ or Oman.mp.	951
15. 9 or 10 or 11 or 12 or 13 or 14	6,131
16. 7 and 8 and 15	83
17. After title review, keep	29
18. After abstract/article review, keep	3

Table. Search strategy - prevalence studies on type 2 diabetes in Saudi Arabia

MEDLINE (Search Dates: 1950-week 36, 2011)

Search history	Results
1. Diabetes mellitus.mp. or diabetes mellitus/	236,149
2. hypergly$.mp.	37,428
3. 1 or 2	255,008
4. Prevalence.mp. or prevalence/	289,714
5. Exp Saudi Arabia/ or Saudi Arabia.mp.	7,254
6. 3 and 4 and 5	98
7. After title review, keep	13
8. After abstract/article review, keep	4
plus 1 study obtained from the Saudi MOH	

Table. Search strategy - prevalence studies on obesity in Saudi Arabia

MEDLINE (Search Dates: 1950-week 36, 2011)

Search history	Results
1. obesity.mp. or obesity/	131,492
2. fatness.mp.	2,438
3. Overweight.mp. or overweight/	23,275
4. Body weight.mp. or body weight/	227,238
5. Central obesity.mp. or central obesity/	1,775
6. Abdominal obesity.mp. or abdominal obesity/	2,437
7. Body mass index.mp. or body mass index/	88,440
8. BMI.mp.	42,332
9. Waist circumference.mp. or waist circumference/	6,977
10. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9	395,143
11. Prevalence.mp. or prevalence/	314,928
12. Exp Saudi Arabia/ or Saudi Arabia.mp.	7,254
13. 10 and 11 and 12	141
14. After title review, keep	22
15. After abstract/article review, keep	4
plus 1 study obtained from the Saudi MOH	

Table. Search strategy - prevalence studies on active smoking in Saudi Arabia

MEDLINE (Search Dates: 1950-week 36, 2011)

Search history	Results
1. smoking.mp. or smoking/	156,258
2. cigarette.mp.	32,670
3. cigarette smoking.mp.	19,459
4. tobacco.mp. or tobacco/	65,437
5. tobacco smoking.mp.	4,196
6. active smoking.mp.	646
7. 1 or 2 or 3 or 4 or 5 or 6	191,248
8. Prevalence.mp. or prevalence/	314,928
9. Exp Saudi Arabia/ or Saudi Arabia.mp.	7,254
10. 7 and 8 and 9	97
11. After title review, keep	10
12. After abstract/article review, keep	2
plus 1 study obtained from the Saudi MOH	

Appendix 2. Papers submitted to scientific journals

	Title of the submitted paper	Journal
1	Comparison of diabetes prevalence estimates in Saudi Arabia from a validated Markov model against the International Diabetes Federation Diabetes Atlas and other modelling studies	Diabetes Research and Clinical Practice
2	Trends and future projections of diabetes prevalence in Saudi Arabia during 1992 – 2022 using a validated epidemiological Markov model	Bulletin of the World Health Organisation
3	Obesity and type 2 diabetes: a complex association	Journal of Family and Community Medicine