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Impact of future obesity trends in the Mexican
population: Development of a computer simulation
model

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Declaration of authorship

I, Luz María Sánchez Romero confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

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Date: _____

Abstract

Introduction. Mexico is one of the top 10 countries with the highest prevalence of obesity worldwide. In 2012, 22 million Mexican adults were classified as obese. As a consequence, the country has seen an increase in morbidity and mortality from obesity-associated diseases that have impacted the country's health and economy.

Objective. To develop a computer simulation model that estimates future obesity prevalence and its impact on four cardiometabolic risk factors in the Mexican adult population aged 20-79y from 2015 to 2030.

Methods. Using the best and most recent available Mexican data, I developed the Mexican Obesity Forecast Model (MexOb-Model), a population-based computer simulation model that is composed of two sub-models: 1) a linear trend model that projects future prevalence of obesity; and a 2) discrete-state Markov model that estimates the impacts of rising levels of obesity on morbidity and mortality from hypertension, type 2 diabetes, hypertriglyceridaemia and hypercholesterolaemia in the adult population. Additionally, I estimated the potential health benefits of three hypothetical obesity prevalence reduction scenarios.

Results. If current trends continue, by 2030 there would be 48million obese adults (20–79y) in Mexico. The prevalence of hypertension, hypertriglyceridaemia and hypercholesterolaemia in the obese population would reach >50%, and 30% for diabetes. Decreasing the projected 2030 obesity prevalence by 3% would reduce the number of disease cases in the obese population by 150,000-500,000 and would reduce the number of deaths by 16,000-30,000. If Mexico achieved a bigger reduction in obesity levels, a 10% reduction in 2015 obesity prevalence by 2030, the number of disease cases avoided could be between 2 million and 7 million and total deaths reduce by nearly 500,000.

Conclusion. The country's prevalence of obesity, and obesity-related cardiometabolic risk factors, are expected to increase. A reduction of as little as 3% in the projected prevalence of obesity could result in a significant reduction in the health burden of obesity in Mexico.

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List of Abbreviations

BMI Body mass index

CONAPO National Population Council *“Consejo Nacional de Población”*

CVD Cardiovascular disease

ENN National Nutrition Survey *“Encuesta Nacional de Nutrición”*

ENSA National Health Survey *“Encuesta Nacional de Salud”*

ENSANUT National Health and Nutrition Survey *“Encuesta Nacional de Salud y Nutrición”*

HT Hypertension

HTG Hypertiglyceridaemia

HCI Hypercholesterolaemia

MxFLS-1 Mexican Family Life Survey-1 *“Encuesta Nacional sobre Niveles de Vida en los Hogares-1”*

MexOb-Model Mexican Obesity Forecast Model

MexOb-HT MexOb-hypertension model

MexOb-T2DM MexOb-type 2 diabetes mellitus model

MexOb-HTG MexOb-hypertriglyceridaemia model

MexOb-HCI MexOb-hypercholesterolaemia model

NCDs Non-communicable diseases

T2DM Type 2 diabetes mellitus

Glossary

Agent-based simulations (ABS): A system is modelled as a collection of autonomous decision-making entities called agents. An ABS simulates the actions and interactions of autonomous agents with a view to assessing their effects on a system as a whole (1).

Autoregressive integrated moving average (ARIMA) model: A mathematical model designed to forecast data within a time series. They are suited for time series data that is stationary in mean and variance. This technique uses moving averages, regression methods and detrending. It models to find the best fit of a time series to past values, in order to make forecast. The three terms to be estimated in the model are: autoregressive (p), integrated (trend- d), and moving average (q) (2, 3).

Auto-regressive terms (p): The number of terms in the model that describe the dependency among successive observations.

Moving Average terms (q): The number of terms that describe the persistence of a random shock from one observation to the next

Trend- terms (d): The terms needed to make a non-stationary time series stationary.

Calibration: It involves the process of estimating the values of the model's unobservable parameters so that the model outputs closely match the external data (4).

Computer simulation model or simulation model: A model adapted for simulation on a computer (5).

Continuous-time model: Treat time as a continuous variable and use differential equations to express instantaneous rates of change. For example; the rate of change of new cases might be a function of the number of susceptible (S), cases (C) and some contact parameter (b) ($dC/dt=SxCxb$) (6).

Deterministic sensitivity analysis: It assesses the sensitivity/uncertainty of the main model outcomes to variations of a parameter value. These new parameter values are

selected manually and they are usually the lower and upper bound of the 95% confidence limit of the selected parameter's mean (7).

Disability-adjusted life year (DALY): Defined as one year lost of "*healthy life*". It is calculated as the sum of years lost to disability (YLD) plus the years of life lost (YLL) due to premature mortality. It is a measure that represents the gap between the ideal health status and the actual health situation of the population (8).

Discrete-event simulations (DES): A modelling method characterized by its ability to represent complex behaviour and interaction between individuals, populations and their environment. The term "discrete" means that it moves forward in time and that the events are mutually exclusive (9). Each event occurs at a particular instant in time and marks a change of state in a system. Between consecutive events, no change in the system is assumed to occur; the simulation can directly jump in time from one event to the next. DES portrays state changes at a precise point in simulated time.

Discrete-time model: This model divides time into units of equal duration and employs the algebra of finite difference equations. For example, the number of susceptible (S) cases in the population at the next time period equals the number of susceptible cases at this time period minus the number of new cases ($S_{t+1} = S_t - C_{t+1}$) (6).

Forecast: Attempt to predict what will happen. The predictions can be compared with actual data (10).

Life-tables (actuarial tables): Tables that are used to describe the pattern of mortality and survival in a population. The survival data are time-specific and show the cumulative probabilities of survival of a group of people subject, throughout life, to the age-specific death rates in question. They include information to calculate health expectancy, and other endpoints such as onset of a disease or occurrence of health complications (11, 12).

Multistate life-tables (MSLF): MSLF are based on transition rates in and out of the different health states. They are frequently used to analyse stochastic processes involving multiple and recurrent events to estimate

expected duration in various states. The process allows individuals to exit and re-entry into the same state (13, 14).

Microsimulation models (MSMs): Model that focus on micro-units (individuals) as the unit of analysis (5).

- a) **Static microsimulation:** A model which does not describe changes in given quantities in the model over time. It assumes that the exogenous change being evaluated by the model do not produce second order changes in variables that are central to the analysis. It is often used to describe models which do not explicitly describe the contact between individuals ,and in which the risk parameters take a fixed value (15).
- b) **Dynamic microsimulation:** A model which describes changes in given quantities over time. (14). The dynamic element into a microsimulation model requires that changes in characteristics or behaviour are applied either to an individual, a group or the model as a whole. This model attempts to incorporate various second order effects of an exogenous change. They include second-order effects by subjecting individual records to a number of transition probabilities (15).

Macro level model: Model focused on high level units such as: groups, populations or subpopulations as its unit of analysis (16).

Mathematical model: A representation of a system or process in mathematical form used to simulate the behaviour of a study or a process.

- a) **Stochastic (random):** The model includes elements of random variation and chance (6).
- b) **Deterministic:** The dependent variables involved do not allow for any play of chance. They give the same results every time they are run (6).

Markov model: Mathematical modelling technique that describes the transitions a cohort or individual make between a number of mutually exclusive health states during a series of cycles (17).

Cycle: It refers to the time period in the Markov process of moving from one health state to another. It is recommended to choose a length of the cycle that represents the frequency of the model event (18).

Markov property (memoryless): The future process is independent from the past. It means that in a Markov process the probability from moving between health states is based solely on the present state (19).

Transition probability: In a Markov chain, it refers to the probability of moving from one health state to another in one cycle.

Transition matrix: It is the group of all the possible transition probabilities that could occur between health states during one cycle

Model: An abstract representation of the relationship between logical, analytical or empirical components of a system (11).

Monte Carlo simulation: It is a probabilistic sensitivity analysis (PSA) in which random probability distributions are created around model parameters that have uncertainty. This method is used to estimate uncertainty values around the simulation model's main outcome by running a large number of trial runs or simulations around different random values drawn from the selected parameter's distribution (20).

Non-parametric statistics: Is a distribution free method whose interpretation do not depend on fitting an underlying distribution (11).

Open cohort (dynamic): Members can leave or be added over time to the original population (21).

Ordinary differential equation model (ODE): A mathematical model used to describe the relations between variables and their derivatives. The derivative of a function provides the rate at which the function is changing with respect to its independent

variable. In this model the variables often represent subpopulations of susceptible, disease, recovered and other (22, 23).

Parametric statistics: Depends on the assumption that the distribution of the data is based on set parameters (11).

Projection: Describes what would happen given a certain hypothesis. It provides information to support plausible hypotheses of interventions (10).

Quality adjusted life year (QALY): A measure of health improvement for cost-effectiveness analysis. This measure has a scale of 0 to 1 (0=death, 1= perfect health). It calculates the years of life remaining for a person after a treatment or diseases onset. It usually is measured by evaluating the ability of the individual to perform daily life activities (24, 25).

Regression model: A mathematical model that is used to study the relationship between variables. Typically it can have two purposes: To estimate the relation of the average value of a dependent variable to other variables (covariates or independent), or to predict the value of the dependent variable based on historic data from the explanatory variables (11, 26).

- a) **Quantile regression:** A method for estimating functional relations between variables for all portions of a probability distribution. It estimates multiple rates of change (slopes) from the minimum to maximum response, providing a more complete picture of the relationship between variables (27).
- b) **Linear regression model (general linear models):** Estimates the coefficient of a linear equation. A model in which the average value of a dependent variable y at a given value of a factor x , is assumed to be equal to $\alpha + \beta x$ where α and β are constants (11, 26).
- c) **Generalized linear model (GLM):** Is a flexible generalization of ordinary linear regression that allows for response variables that have other than a normal distribution. It includes other types of regression models such as: logistic, Poisson and Cox regression in which we model a transformation of the outcome variable rather than the outcome itself. The linear model for the exposure variable is related to the outcome via a link function (26).

- d) Logistic regression:** It is a regression model that is used to performed trend analyses when the target variable is a categorical variable. This method is based on a binomial distribution The link functions for the logistic regression is the logit (log odds) function (26, 28).
- e) Nonlinear regression:** Is a regression analysis which is used to obtain the best-fit values of the data parameters. It is also used to fit a curve that best comes closest to the data. two popular methods are: exponential curves or power curves (29).

Simulation: Is the process of imitating the behaviour of system patterns. Simulation is a tool that helps to generate information about how something will behave without actually testing it in real life. They are useful in creating theories, examining effects of policy options, and support decision making processes (5).

System Dynamics (SD): SD is a modelling method that understands the behaviour of a complex system over time. SD represents a process of accumulation and feedback that effects the behaviour of the entire system (30).

Uncertainty analysis (UA): Provides uncertainty intervals around the mean estimate of one or more outcomes of interest, in order to quantify the uncertainty around the outcome or parameter of interest (7, 31).

Validation: It is the act of comparing model results with observed events. It is used to judge the model's outcomes accuracy and reliability. Methods to assess the validity of a model can include the following (32):

- a) Face validation:** The data sources, structure of the model and outcomes are evaluated by experts in the field. They assess how accurate the model represents the problem of interest
- b) Internal validation:** It assesses if the mathematical calculation for the model are performed correctly. For this type of validation, the model outcomes are compared with the observed data from a source that was also used in the development of the model.

- c) External validation:** It compares the model's components or outcomes with observed data. It is recommended to compare model outcomes with outcomes generated from data sources not included in the model.
- d) Cross-validation:** It compares outputs from the model with results from different models that address the same problem.
- e) Predictive validation:** It compares the projected outcomes with observed data. This involves identifying a similar evaluated intervention or scenario that has been implemented and comparing the results.

Chapter 1. Introduction

1.1 Background

Mexico, official name United Mexican States, is one of the three countries that constitute North America. It is also one of the fifth largest countries in the American continent and according to the World Bank standards it is classified as an upper middle income developing country (33). The latest national population survey in 2010 reported that Mexico had a population of 120 million inhabitants with a median age of 26 years. The average life expectancy at birth of the Mexican population in 2015 was 74.9 years (34). The Mexican population ≥ 15 y has on average 9.1 years of education. 92% of the population are affiliated to a Healthcare Institution (35). Mexico's total expenditure on health in 2012 was 6.2% of the gross domestic product (GDP) (36).

Mexico's principal causes of morbidity and mortality in the adult population are cardiovascular diseases and diabetes (37), and one of the principal risk factors that contribute to the development of these diseases is obesity. Obesity has become one of the greatest public health problems in Mexico. In 2014, Mexico occupied the sixth place in the ranking of countries with the highest obesity prevalence for adult men and women (38). Mexico is also one of the 10 countries with the highest prevalence of childhood obesity (39). In the last three decades, the prevalence of obesity has increased alarmingly (35). In 2012, it was estimated that there was around 26 million individuals with obesity (≥ 5 years and older) in Mexico (35). This problem brings an enormous burden of economic and social cost to a country, and as a consequence alters its development. It was estimated that in 2012 the healthcare cost of diabetes attributed to obesity and overweight was £3.3 billion (82 billion Mexican pesos(MXN)) (40), which corresponded to 73% of the total health expenditure for 2012 (41).

In the near future, the country will encounter an enormous increase in morbidity and mortality associated with non-communicable diseases. This will translate into social and economic costs for both governments and individuals, particularly affecting the

most vulnerable population groups (i.e. the people in the lowest socioeconomic groups and children).

The absence of up-to date evidence for policy makers and the public health community in Mexico regarding the impact of long-term health and economic consequences of chronic diseases is an impediment to planning effective public health programmes for its prevention and control and the proper allocation of resources. This type of information is especially relevant in Mexico, as more than half of the population healthcare costs depend on government programmes (35).

Mexico therefore needs prompt and reliable evidence regarding the potential long-term outcomes of health policies and programmes. This evidence would help sustain the development of national policies or interventions and facilitate their continuation in the long-term. It would be possible to obtain this type of information through longitudinal studies; unfortunately they require a long time and a great amount of resources. In a country like Mexico, where the resources for research are limited and the need for preventive programmes is immediate, this option is unlikely. However, by using computer simulation models, it is possible to obtain this information sooner and at less cost.

Population computer simulation modelling studies have been used to provide information for policy and health (31, 42). They are of great utility in the prediction of disease prevalence and estimation of health parameters. Population computer simulation models are a tool that evaluates the impact of health risk factors and public health policies and their influence on the population's health over time at a national level or in different population subgroups (43).

The aim of this thesis was to develop a mathematical population simulation model to estimate the future trends of obesity in the Mexican population and to evaluate the consequent potential health effects. This information will provide evidence-based data that will be useful for making decisions regarding public health interventions that aim at reducing the obesity prevalence in the population. It will also inform policy-makers about the short and long term health consequences related to this public health problem. Results will increase the capacity of policy makers and public health researchers to make informed decisions about resource allocation and implementation of preventive interventions.

The purpose of this chapter is to give an introduction to the health and economic burden of obesity. This information will help the reader to have an overview of the problem of obesity; what causes it; which are its consequences and which particular characteristics of Mexico have contributed to the increase of this problem. This information is useful to understand the problem of obesity in Mexico and the importance of the increase in obesity prevalence.

The contents of this chapter includes: the aetiology of obesity and how its metabolic aspects influence in the development of cardiometabolic risk factors. It also presents examples of the financial consequences of obesity. This chapter also provides detailed information about the problem of obesity in Mexico: the social and environmental determinants of obesity in Mexico; the historic trends of obesity in the population; and its impact on Mexican's health. At the end of this chapter I present in detail the aims and objectives of my research project, and outline the PhD thesis chapters that follow.

1.2 Obesity as a worldwide problem

Obesity is a worldwide public health problem. It is a leading modifiable risk factor for most of the principal causes of mortality and morbidity. It is associated with many

major non-communicable diseases such as: hypertension, diabetes, dyslipidaemias, musculoskeletal disorders, renal disease, cardiovascular disease, some cancers, and depression (44-47).

The Global Burden of Disease project reported that in 2010, two of every three deaths were from non-communicable diseases, and the leading mortality causes were ischaemic heart disease and stroke (48). They also estimated that obesity contributed to 3,371,323 deaths and accounted for 93,609 disability adjusted life years (DALYS) worldwide (49). Mortality from cardiovascular diseases in the Americas Region in 2008 accounted for 31% of the total mortality, and of this total, 43% was due to ischaemic heart disease and 22% to stroke (50). In 2014, about 266 million men (10%) and 375 million women (14%) were classified as obese (body mass index (BMI) $\geq 30 \text{kg/m}^2$) (38).

1.2.1 Obesity and its health consequences

Obesity occurs as the result of the negative difference between energy expenditure and consumption, and it is defined as having a body mass index (BMI) of $\geq 30 \text{kg/m}^2$. However, it is known that there are a large number of factors that influence an individual to develop obesity (51). These risk factors can be classified in two groups:

- a) *Biological susceptibility*: genetics, hormones, gender, age, ethnicity
- b) *Environmental influences*: physical activity, social influence, food environment, and food consumption.

Pathophysiology

Adipose tissue is recognized as an endocrine organ. Its main metabolically active cell is the adipocyte. The adipocytes are used normally to store free fatty acids as triglycerides to be used as an alternative source of energy in case of prolonged fasting periods, a process that is regulated by insulin and other hormones. The adipocytes and pre-adipocytes mainly secrete cytokines (adipokines) and other factors that have anti-

inflammatory and pro-inflammatory properties that can alter the regular biological processes (e.g. adiponectin and leptin) in individuals with obesity (52-54). In a person with obesity, the adipocytes increase in both size and number as their storage of triglycerides increases. The increase in the rate of lipolysis results in an elevated amount of free fatty acids (FFA) which as a consequence, leads to a chronic release of cytokines. The chronic release of cytokines causes a chronic low-grade inflammatory state that can alter lipid and glucose metabolism, contributing to metabolic dysfunction (44, 52).

Obesity-related cardiometabolic risk factors

All the metabolic alterations caused by adipose tissue contribute to insulin resistance and other obesity related comorbidities such as hypertension, type 2 diabetes and dyslipidaemias which have been found to serve as mediators for the development of cardiovascular diseases (44, 55). The excess mobilization and oxidation of FFA by muscle and liver decrease the utilization of glucose, creating a state of hyperglycaemia, hyperinsulinemia, β -cell dysfunction and hepatic insulin resistance (44, 45, 56). Additionally, this increases exposure of the liver to fatty acids and brings as a consequence a reduction in high density lipoprotein (HDL) cholesterol, an increase in very low density lipoproteins (VLDL), and increases the small low density lipoprotein (LDL) cholesterol levels. LDL-C particles are highly atherogenic because of their ability to penetrate the arterial wall (57).

The risk of hypertension is higher in obese people than in people of normal weight (58). The relationship between hypertension and obesity is through a number of different mechanisms. There is an increase in sodium retention due to an increase in renal tubular reabsorption (59). Furthermore, it has been observed that with obesity there is an alteration of the renin-angiotensin system modifying the secretion of aldosterone and angiotensin II, altering the endothelial vasomotor tone which is central in hypertension (52, 60). Moreover, the hyperinsulinaemic state commonly

found in obese people may alter vascular functionality by promoting vasoconstriction, causing hypertension (61) .

1.3 Obesity in Mexico

1.3.1 Epidemiological and demographic transition

Mexico has experienced a rapid increase in the prevalence of overweight and obesity in its population. These changes are a consequence of a rapid epidemiological and demographic transition that has influenced the environmental characteristics of the country (socio-economic conditions, education, culture and urbanization) as well as the population's life styles.

In the last decades, Mexico has experienced an epidemiological transition characterized by demographic and nutritional changes. Mexico has been in an intense process of urbanization that began with industrialization between 1940 and 1970. The population has been shifting from a rural environment to an urban location (62). The fecundity rate has been steadily decreasing for four decades. The Mexican population has been ageing. In 2010 the average age was 26 years, and the average life expectancy currently is 77 years for women and 72 for men (34, 63).

Infectious diseases are being substituted by non-communicable diseases as the most important causes of mortality. The latest report by the Mexican Ministry of Health in 2010 listed cardiovascular diseases, diabetes mellitus, and cancer as the principal causes of mortality, and non-communicable diseases as one of the leading causes of morbidity (64).

Under-nutrition is no longer the main public health nutrition problem. The prevalence of under-nutrition in children under-five years of age has been decreasing

progressively. The prevalence of stunting decreased from 27% in 1988 to 14% in 2012; and wasting from 6% in 1988 to 2% in 2012 (35). Moreover, the prevalence of anaemia has also been decreasing in the whole population. In under-fives, it changed from 32% in 1999 to 23% in 2012; in children aged 5 to 11 years, it decreased from 15% to 10% in the same period, and in adolescents it decreased from 10% in 2006 to 6% in 2012(35, 65). 18% of pregnant women and 12% of non-pregnant women aged 12-49 years were considered anaemic in 2012, a decrease in 13 years of 13.5 percentage points (pp) in pregnant women and a decrease of 10 pp. in non-pregnant women (35, 65, 66).

1.3.2 Social and environmental determinants of obesity in Mexico

The epidemiological transition shaped by urbanization, economic growth, health improvement and migration has modified the diet and physical activity patterns among the Mexican population (67, 68). Increased consumption of energy dense food and physical inactivity are two of the main risk factors associated with the growth of the obesity epidemic.

Physical activity and sedentary behaviour

Insufficient physical activity is common in the Mexican population. A study showed that Mexican schools only account for 60 minutes of moderate to vigorous physical activity per week, which represents only a fifth of the recommended amount of activity for school-aged children (69). The Mexican National Health and Nutrition Survey (ENSANUT) 2012 showed that 58% of children aged 10 to 14y reported not to have participated in any competitive sport in the last year. For adolescents, 59% were physically active and 23% inactive. The report also showed that only 33% of children (5 to 11 years) had a TV-viewing time of less than two hours daily, while 28% spent more than four and a half hours per day watching TV. Only 36% of adolescents (13 to 19 years) reported watching TV for two hours or less per day. Physical inactivity in Mexican adults increased from 13% in 2006 to 19% in 2012 (35).

The Mexican National Health and Nutrition Survey (ENSANUT 2012) measures physical activity levels using the International Physical Activity Questionnaire (IPAQ). This evaluates total physical activity (i.e. leisure-time, occupational, housework and transport-related activity). Medina et al defined physical inactivity as participating in <150 min/week of moderate-to-vigorous physical activity. The study by Medina et al implies that currently 81% of the Mexican adult population perform at least 150 min/week of moderate-to-vigorous physical activity. The high prevalence could be due to a number of factors, including the emphasis of the IPAQ on total physical activity (i.e. including occupational and transport-related activity) and the well-known tendency of self-report instruments to typically over-report physical activity levels compared to objective assessments using accelerometers and other electronic movement sensing devices (70)

Nutrition profile of the Mexican population

Mexico has experienced changes related to food patterns and dietary intake across all age groups. There was a decrease in exclusive breastfeeding practices of almost 8 pp, from 22% in 2006 to 14% in 2012 (35, 65). The typical diet of adults in the Mexican population now includes foods with high content of energy from fat and sugar. In 1988, fat intake represented 28% of the total energy intake in the Mexican female population; by 1999 it was 30% and carbohydrate intake in that same year was between 55% and 60% (71). In 2006, on average, adults consumed 26% of their calories from fat and 61% from carbohydrates (72). For adolescents, 28% of their daily energy intake came from fat carbohydrate and 62% from carbohydrates (73).

As a consequence of environmental, economic and cultural changes, there has been a change in the products consumed by the population. Between 1984 and 1998 there was a decline in purchase of almost all food groups except for sugars and refined carbohydrates, which increased by 10%, with a particular increase in soda purchase (74). Mexican population has a low consumption of fruit and vegetables. In 2006, the

average fruit and vegetable daily consumption was 103g in school-aged children, 116g in adolescents and 123g for adults (75). This means that Mexicans are consuming 300g less than what is recommended by the World Health Organization (WHO) (at least 400g of fruit and vegetables per day) (76).

There has been a substantial increase in the consumption of caloric beverages and low-cost high energy food. In children the total energy intake from beverage increased from 259kcal/day in 1999 to 304kcal/day in 2012. For adult women, the total energy intake from beverages increases from 250kcal/day in 1999 to 347kcal/day in 2012 (77). In 2012 beverages represented 17.5% and 19% of the total daily energy intake for children and adults, respectively. In that same year, it was observed that soda was the most common beverage consumed by the adult and adolescent population (77).

1.3.3 Obesity trends in Mexico

The changes associated with the epidemiology and demographic transition outlined in the previous section have transformed Mexico into one of the countries with the highest prevalence rates of overweight and obesity in the world.

Children and adolescents

The prevalence of overweight and obesity in Mexican children under five years of age has increased from 7.8% in 1988 to 9.7% in 2012. Among school age children in 2012, the prevalence of overweight and obesity was 34.4% (representing a population of 5.6 million) (19.8% overweight and 14.6% obese) (35). In 2012, 6.3 million adolescents were overweight or obese. This represents that one in five Mexican adolescents was overweight (21.6%), and one in ten was obese (13.3%). The prevalence of overweight and obesity combined for this age group was 36% for girls and 34% for boys (35).

Adults

The nationally representative ENSANUT 2012 survey found that the prevalence of combined overweight and obesity for men and women 20y and older was 71.3% (representing a population of 48.6 million). For women, the combined prevalence was 73% (35.5% overweight and 37.5% obese) and for adult men 69% (42.6% overweight and 26.8% obese). The prevalence of overweight found in urban and rural inhabitants in 2012 was similar (38.9% vs. 39%). However, obesity prevalence was 28.5% higher in the urban than the rural adult population (35).

Abdominal obesity is considered a better indicator for predicting pathological cardiometabolic risk factors and mortality than thresholds based on body mass index (BMI) (78, 79). In Mexico, according to ENSANUT 2012, 74% of the Mexican population aged 20 years and above had abdominal obesity (waist circumference of ≥ 80 cm for women and ≥ 90 cm for men). The prevalence of abdominal obesity was higher for women than for men (83% of women and 64% of men). The age group with the highest prevalence for abdominal obesity was the 50-59 year olds (35).

1.3.4 Burden of disease associated with obesity in Mexico

The increase in the prevalence of obesity has contributed to the increase of the incidence of obesity-related diseases: type 2 diabetes mellitus (T2DM), hypertension, and dyslipidaemias that have led to making cardiovascular events, diabetes and chronic kidney disease the principal causes of mortality in the Mexican population (80). This section presents the crude changes in numbers and prevalence rates, which affects the healthcare provision needed. Some of the increase is due to rising age-specific rates, and some due to the growing numbers of older people.

From 1990 to 2010 the number of deaths among Mexican women from ischaemic heart disease and from diabetes increased in relative terms by 97% and 82%

respectively, and deaths from chronic kidney disease increased by an alarming 410%. In men, the number of ischaemic heart disease and diabetes deaths increased by 104% and 111% respectively, and the number of deaths from chronic kidney disease increased by 429% (80). It was also reported that in 2010, four risk factors - high body mass index (BMI), high blood glucose, high blood pressure and high levels of alcohol consumption - were responsible for 65% of total mortality and 65% of the total population disability adjusted life years (DALYs) (80).

Diabetes /Impaired fasting glucose

In Mexico, the overall prevalence of T2DM (diagnosed and undiagnosed) increased by 7.4 pp from 1993 to 2006, with a prevalence of 14% in 2006. The proportion of survey-identified diagnosed diabetes in people younger than 40 years of age grew progressively from 2.3% in 2000 to 5.8% in 2006. The prevalence of diagnosed T2DM in the population increased from 5% to 7% between 1993 and 2006. 56% of those diagnosed in 2006 had poor control of the disease (81). In 2012 the survey results reported that the prevalence of diagnosed diabetes had increased to 9.2% (35).

Hypertension

Hypertension is one of the principal risk factors for cardiovascular disease. It accounts for 62% of the total incidence of stroke and 49% of ischaemic heart disease cases worldwide (82). In Mexico, high blood pressure prevalence increased from 24% in 1993 to 31% in 2006 and 31.5% in 2012, with a prevalence of hypertension (diagnosed and undiagnosed) in the obese individuals for that same year of 42% (83, 84). In 2012 the prevalence of undiagnosed hypertension was 47% of the total hypertensive population; of the previously diagnosed individuals, only 74% had received pharmacological treatment. The results showed that the prevalence of hypertension in 2012 was three times higher in the population aged 60 years and older than in the youngest adult age group (20 -29y) (84).

Dyslipidaemias

In Mexico, the most common lipid abnormality in the adult population is low HDL cholesterol (HDL < 40mg/dl or <1.0mmol/L; conversion rate 38.6) (85). The prevalence of low HDL cholesterol was 60.5% in 2006; this prevalence has remained fairly unchanged since the first report in 1993 (86). The second most common lipid abnormality is hypercholesterolaemia (≥ 200 mg/dl or ≥ 5.2 mmol/L conversion rate 38.6 (85)) with a prevalence of 43.6% in 2006. The average mean total cholesterol in the population rose from 4.7mmol/L in 1993 to 5.1mmol/L in 2006. Only 9% of the population with high cholesterol had been previously diagnosed, of whom 72% were receiving drug treatment. Furthermore, the prevalence of high LDL-C (≥ 130 mg/dl or ≥ 3.4 mmol/L) in Mexican adults was 46% for that same year. The least frequent dyslipidaemia was hypertriglyceridaemia (≥ 150 mg/dl or ≥ 1.7 mmol/L; conversion rate 88.7), with a prevalence of 31.5% in 2006 (86).

The obesity-related consequences (e.g. hypertension, diabetes and dyslipidaemias) have also started to be observed in the adolescent population. In 2012, 0.7% and 1.8% of the adolescent population (aged 10 to 19y) were observed to have received a physician-diagnosis of diabetes and hypertension, respectively (35).

1.4 Economic implications of obesity

Obesity and overweight bring as a consequence a decrease in the performance of national economies by decreasing the population's productivity and increasing the health care costs, disability, and mortality (87). Sturm calculated that obesity increases annual healthcare costs by around US\$395 per person (88). Finkelstein et al. reported that obese patients in USA have 46% higher inpatient costs, 37% more physician visits and costs, and 80% higher spending on prescribed medicines than patients of normal weight (89).

It was calculated that in 2006 the obesity prevalence in the USA cost a total of US\$40 billion, of which 17% was attributed to drug costs (89). For that same year, the UK National Health Service (NHS) costs associated with overweight and obesity was £5.1 billion. It was estimated that for 2002, the loss earnings attributed to obesity were estimated to be in the range £2.3 billion-£2.6 billion (90, 91). A simulation projection calculated for the USA and UK populations showed that by 2030, obesity will account in those countries for 26-55 million quality adjusted life years (QALYs) lost (92).

In Mexico, the estimated direct costs attributed to obesity related diseases showed an increase of 61% between 2000 and 2008. The total cost for 2008 represented 33% of the health expenditure for that year. Additionally, the indirect cost attributed to loss of productivity for early mortality attributed to obesity and overweight increased annually by 13.5% between 2000 and 2008 (93).

The economic burden that obesity represents for national health systems, and for households, puts at risk the sustainability of public health programmes. It was estimated that obesity-related diseases, such as cardiovascular diseases, cancer, diabetes, chronic respiratory disease and mental health, will represent a loss of US\$47 trillion worldwide over the next 20 years, which represents 75% of the gross domestic product (GDP) in 2010. Of this total, it will be the middle-income countries such as Mexico the ones which are expected to experience a bigger economic burden in their growth (94).

Analysis of the ENSANUT 2012 data has shown that obesity, diabetes and cardiovascular disease together accounted for 12% of the total consultations in the healthcare services in 2011 in Mexico. They were also the first reason for consultation for the population aged 50 years and older (35). A major report on health expenditure in Mexico in 2006 showed that for obesity, T2DM, and cardiovascular disease the total expenditure was approximately 7% of the total healthcare expenditure, and was

approximately 0.4% of the gross national income for that year. Of this total, 55% was due to cardiovascular diseases, 41% to diabetes mellitus, and 4% directly due to obesity (95). Figueroa-Lara et al. reported that the annual cost per person of hypertension and diabetes for 2014 was approximately US\$200 for both diseases for the Ministry of Health (MoH) and approximately US\$600 for the Mexican Institute of Social Security (IMSS), two of the three principal health care service providers in Mexico. The financial burden to the Mexican health institutions that came from non-communicable chronic diseases (e.g. chronic kidney disease, diabetes, and ischaemic heart disease) in 2014 was estimated to be approximately US\$1.4 billion for the MoH and around US\$4 billion for IMSS. These costs represented 88% and 85% respectively of the total chronic disease healthcare services financial burden for 2014 (96).

There is evidence from the Netherlands and more recently from the USA, that obese persons have lower lifetime costs compared with those of normal weight due to a shorter life expectancy (97, 98). The potential lower lifetime costs for obese persons compared with those of normal weight might imply therefore that prevention efforts targeted at risk factors such as obesity might not result in savings in medical costs as above (97).

1.5 Goals

To develop the Mexican Obesity Forecast Model (MexOb-Model), a population-based simulation model to quantify the future trends of obesity and estimate its health consequences on the Mexican population.

1.6 Aims & objectives

1.6.1 Aim

To project the future prevalence of obesity in the Mexican population and the health impact of these future levels of obesity on four obesity-related cardiometabolic risk factors.

1.6.2 Objectives

1. To develop a population-based forecasting simulation model for the obese Mexican population (MexOb-Model).
2. To project the Mexican population obesity trends to 2030 stratified by age group and sex.
3. To estimate the impact of projected obesity trends on the incidence, prevalence, and mortality of four obesity-related cardiometabolic risk factors (hypertension, type 2 diabetes, hypertriglyceridaemia and hypercholesterolaemia) in the obese adult population in Mexico.
4. To explore the effects of three national level hypothetical scenarios for obesity prevalence reduction on the health of the future obese population in Mexico.

1.7 Outline of the thesis

This chapter is followed by a systematic literature review that examines the modelling methods used by different population simulation models that estimate both the future trends of obesity and its consequences at a population level. Chapters three to five describe the steps taken to build the Mexican Obesity Forecast Model (MexOb-Model). The MexOb-Model is a simulation model developed to estimate the future trends of obesity and its health consequences for four obesity-related cardiometabolic risk factors (hypertension, type 2 diabetes, hypertriglyceridaemia and hypercholesterolaemia) in the Mexican adult population. Chapter three describes the analysis undertaken to project the future trends of obesity in the population to 2030. Chapter four describes in detail the methods used to build the MexOb-Model, including descriptions of the data used as inputs, the steering parameters of the model, and the key outcomes. Chapter five describes the results of validation exercises performed to assess the MexOb-Model's fitness for purpose.

Chapter six examines the results of the baseline simulation that aim to examine the impact of the future obesity rates on the four obesity-related cardiometabolic risk factors in the Mexican adult population if the historical trends of obesity continue in the long-term. Chapter seven presents the results of three hypothetical scenarios for the reduction of obesity prevalence. To finalize my research project thesis, the last chapter discusses the implications of the results from the MexOb-Model, and outlines my overall conclusions and recommendations.

Chapter 2. Population-based health forecasting mathematical simulation models for obesity: Results of a systematic literature review.

2.1 Background

One of the principal components of the decision-making process regarding public health problems is to predict the course of the disease, how it will impact on the population, and the changes that could happen after the implementation of an intervention (99). Health policy decision-making commonly relies on short-term results of interventions or observation studies that usually apply to a subgroup of the population. Rarely are they provided with evidence about the long-term impact of the intended interventions when implemented at a population level. The use of mathematical modelling in population health has the potential to simulate the long term effects of possible preventive and treatment interventions for non-communicable diseases (NCDs), which usually need a long time frame and a large population to observe significant effects (100). A simulation model allows to integrate facts about the disease of interest and creates evidence that synthesize the health consequences and costs of the disease to the policy makers (101).

Mathematical models (MMs) are a substitute for real life study (102). They provide information on how a system works, and help address risk factors and future outcomes. They are used extensively in several areas, including: economics, weather, agriculture, technology, and health. They have a predictive competence for public health. MMs have been used to examine transmission of infectious diseases and to forecast changes in chronic disease risk factor trajectories such as tobacco, nutrition, and obesity (103, 104). They are also used to estimate the impact of healthcare policies, and the cost-effectiveness and distribution of healthcare services.

2.1.1 Characteristics of mathematical models

The use of mathematical models has increased with the availability of large computers, more user-friendly software and greater data (105). They are able to process a large

amount of data and produce information previously inaccessible because experimentation was not possible. In epidemiology, mathematical models have four major aims (10, 106):

- 1) Understanding the expression of concepts and theories.
- 2) Identifying areas that need better epidemiological information to improve the understanding of a theory or make a better prediction.
- 3) Prediction
- 4) Creation of a hypothesis by using provable scenarios that can be simulated.

Population-based health mathematical forecasting models provide useful information about how changes in different variables within a complex system may impact the future health of individuals based on the population's current socio-demographic characteristics. Within these models, it is possible to create hypothetical scenarios that can be used to evaluate different interventions, newly created or already implemented, to help assess where to focus efforts and budget allocation. They are a useful tool for identifying research priorities.

It is possible to classify the type of prediction made by mathematical models in two types: *forecast* and *projection*. A *forecast* intends to predict what will happen and its predictions can be compared with actual data: all assumptions are expected to occur. A *forecast* reflects the conditions that already exist. On the other hand, a *projection* presents the results of a plausible hypothetical intervention by describing what would happen, given a certain hypothesis. In other words, the outcomes of a projection may not occur.

Furthermore, mathematical models can be broadly classified in two groups according to the complexity of the modelling method used to calculate their estimates:

simulations and *mathematical projections*. A *simulation* uses mean values and takes into account the variability and the distribution of these values. In contrast, a *mathematical projection* only uses the average or central values that the variable had in the past (107).

Mathematical models have several distinctive characteristics; these characteristics are based on the scientific question that led to the development of the model. The characteristics vary in their level of complication according to how closely they follow the history of the disease (108). The models can be *static* or *dynamic*. *Static* models consider snapshots at two points in time or two different scenarios at a single time point. *Dynamic* models create longitudinal databases and allow exposures and behaviours to alter over time (109). Models can also use different approaches such as *micro-models* tracking individuals, that generate life histories: by aggregating these individual events, they create population outcomes or *macro-models* separating group of individuals (43, 110). Furthermore, they can be *discrete* or *continuous* in time. *Discrete* models divide the time into units of equal duration; *continuous* models use time as a continuous variable (6). The effect of chance can be *stochastic*, with multiple possible outcome values, including elements of random variation, or *deterministic* in which the outcome is precisely determined through known relationships and there is no room for random variation (6).

The purpose of this literature review was to identify the different population-based health mathematical forecasting models and their methods used to estimate future obesity prevalence in the general population and its health consequences in order to decide which type of method could be the best for the development of a Mexican obesity population-based mathematical forecast model.

At the time of this review, there were no guidelines published on how to report population-based models for non-communicable diseases (111). Therefore for the

purpose of this analysis I used as a guideline the recommendations by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Task Force on Good Research Practices-Modelling Studies which are intended to give advice on how to publish studies that used a health model. They include the following characteristics: conceptualization of the model, modelling methodology, and validation and transparency (112). However, this guideline was developed for models focused on health care decision-making oriented to individual-level health-care decision models and to the use of methods to quantify the cost-effectiveness of health care technologies for their potential use in health care systems. Consequently, some recommendations were not followed as stated.

2.2 Systematic literature review methods

2.2.1 Types of study

For this systematic literature review, I included articles published in peer-reviewed journals or reports that included a simulation modelling statistics design to project future trends of obesity in the general population. The term 'simulation modelling' included computer simulation models (macro- and micro-simulations), and linear regression models. The studies could also combine outcomes on future prevalence of non-communicable diseases (NCDs), health or economic outcomes, and evaluation of interventions.

2.2.2 Type of participants

I included studies that were based on general populations. I classified the studied populations into two groups: children and adults. Additionally, I included studies that took into account transitions from childhood to adulthood. I also included studies that evaluated only overweight or obese populations or those with a particular chronic disease.

2.2.3 Type of interventions

Mathematical models. I included studies that used for their future projection simulation modelling techniques (micro- or macro-simulations) or mathematical projections.

Intervention. If the studies mentioned the evaluation of an intervention, this intervention should be a lifestyle modification intervention or reduction of risk factors applicable at a population level.

Settings. The projection should be made within a country at national or state level or for subgroups within the population.

2.2.4 Type of outcome measures

To be included, the studies had to report one of the following primary outcomes presented at baseline and future trends.

Primary outcomes

- Weight
- BMI classification
- Waist circumference

Secondary outcomes

- Measures of NCDs: prevalence, incidence or mortality of NCDs related to obesity.
- Measures of health outcomes (burden of diseases): for example disability adjusted life years (DALYs), years lived with disability (YLD), years of life lost due to premature mortality (YLL), quality adjusted life years (QALYs), life expectancy, or loss of productivity.
- Measures of economic outcomes: life cost of the disease, cost of treatment, units saved, health care cost.

2.2.5 Studies excluded

I excluded studies if they were not full articles published in peer-reviewed journals or reports (i.e. conference proceedings, non-availability of full text). I also eliminated studies that did not include in their outcomes future projections of obesity or that used obesity only as a risk factor for projections of other diseases.

Search methods for identification of studies

Electronic searches

Articles were included if they were published between 1980 and 2016, and written in English, Spanish, French or Portuguese. The last search was made on April 18th 2016.

Combination of key words in the title or abstract related to forecast outcomes (forecast OR projection OR trends) AND methodology (simulation OR computer simulation), AND outcomes (obesity OR overweight) informed the search.

For this report, the following databases were searched:

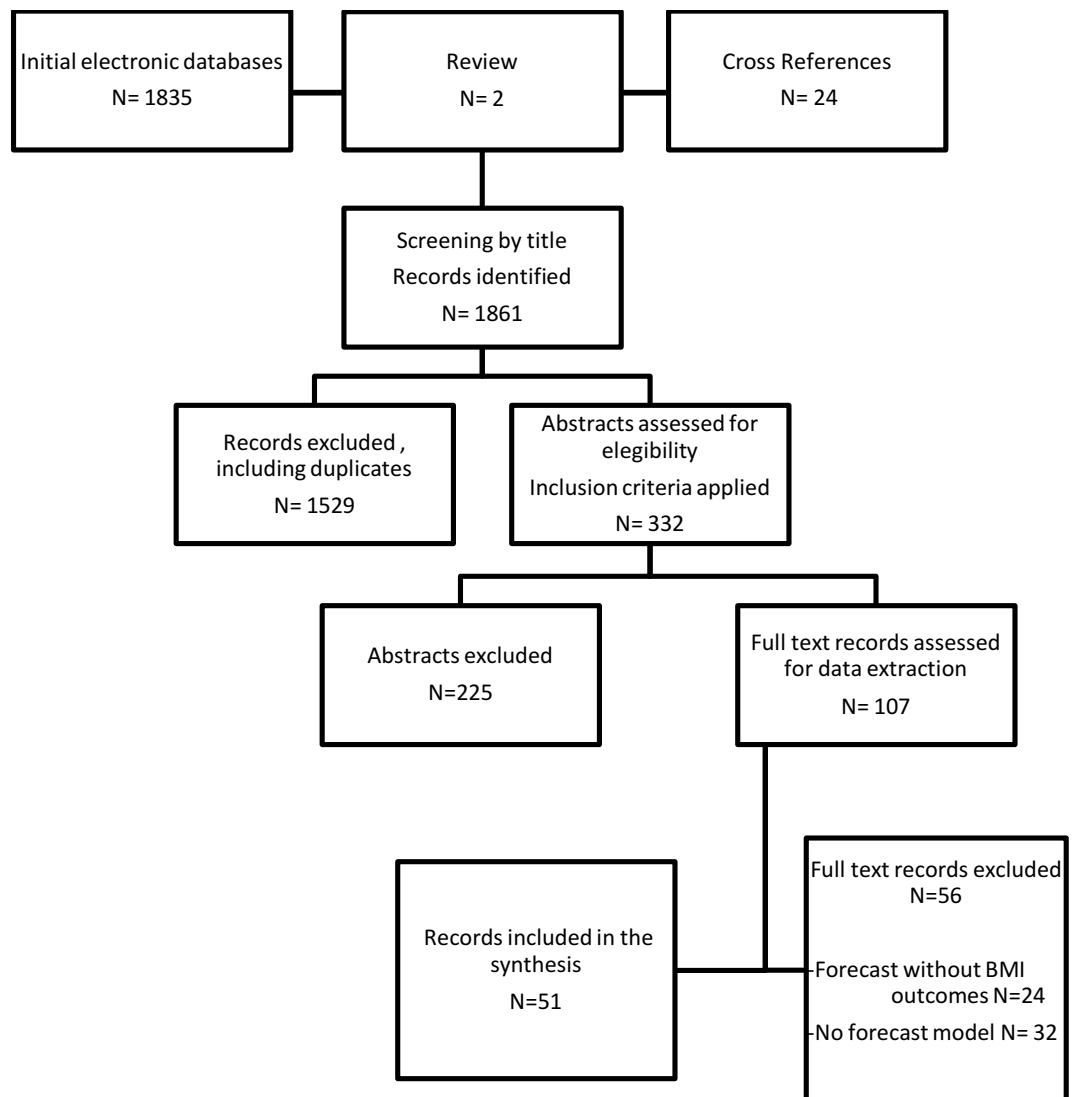
- PubMed
- Embase/Ovid

Reference list checked

I scanned the reference list of the selected full text articles to identify potential additional studies for inclusion in the review.

Figure 2-1 shows the final flowchart of the literature review of obesity forecast simulation models.

Figure 2-1 Flowchart of the literature review of obesity forecast simulation models



2.3 Results

Table 2.1 shows the characteristics of the mathematical population simulation models found in this review. It presents a description of the modelling methods used to estimate the projections, the population and the aim of the study. It also includes technical information about the development of the model: if the authors performed any validation analysis, calibration of any of the model parameters; if they describe in

detail the formulas used for the model and data extractions, and the software they used for their analyses.

A total of 51 articles were selected for review (Figure 2-1). The selected articles were published between 2007 and 2015, with the highest number of publications being in 2014 (n=10). In the articles reviewed, the Foresight model, originally developed for the UK, was the simulation model most frequently used and adapted to other countries, with a total of 10 articles presenting projections estimates using it (92, 113-119).

2.3.1 Study populations

The articles were classified by continent according to the population that was analysed. One third of the studies were from Europe (n= 17, 33%), half from America (n=24, 47%), and four articles were from Australia. The USA (n=17) was the country with the most obesity population-based simulation studies. Recently, more studies presenting projected results from Asia (120) and Latin America (115, 121) and the Middle East (122, 123) have been published. Additionally, there has been recently an increase in the number of articles that forecast outcomes from several countries (n=3) with the aim of assessing the differences in future obesity and NCDs prevalence between countries, or to estimate future regional trends (113, 114, 123, 124).

The population subgroups studied also varied among the articles. The majority of the studies (71%, n=36) focused only on the adult general population. I also found modelling studies that calculated estimates for a specific subgroup of the population (n=8). For example, Cardone et al. (107) focused only on the obese population, and Dall et al. (125) focused on the overweight and obese population. Other modelling studies such as Jodar et al. (126) and Bibbins-Domingo et al. (127) followed a cohort of children and evaluated the health impact of risk factors in adult life.

2.3.2 Modelling methods

The studies reviewed showed a great diversity of modelling methods used to estimate future population obesity prevalence and its associated outcomes. The forecasting methods varied in the complexity of the mathematical techniques and the number of models used for calculating the outcomes. According to their modelling methods, I broadly classified the models in two groups: mathematical projections and simulation models.

Mathematical projections

I classified as mathematical projections those studies that used the estimation of the projections based only on the historic trends of the outcome of interest. I included in this category all the studies that used as the only forecast method a statistical regression analysis or analysis of trends.

A total of 20 articles were included within this category. The simplest method used to estimate future obesity trends was linear regression analysis, as used by Zaninotto et al. (128) and Huffman et al. (129). Other authors used more complex forms of regression analysis: Wang C et al. (130) used a parametric polynomial regression model, and ordinary least square regression (OLS) was used by Nepal and Brown (131).

Simulation models

A simulation characteristic is that it uses mean values of the risk factors and also considers the variability in the distribution that values may have. Simulation models have started to be used more frequently as the method of choice for forecasting models. I included a total of n=28 studies from the articles reviewed in this group. Within the models using this approach, I observed that some researchers used only one modelling technique as their simulation method to estimate their projections (n=14). However, there were also “hybrid models” (n=14), models built by two or more

projection methods that were combined in order to obtain their estimates of the outcomes of interest.

Simulation models utilized a diverse variety of complex methods for their modelling techniques. The most frequent technique I found in these type of models was state-transition (n=21). State-transition models are characterized by representing a disease or health problem in a set of health states. Some of the models have the characteristic of having no memory of the history of previous events when moving between those health states (known as the Markov assumption) (132). Some examples of this modelling method were used by Neovius et al. (133), Dall et al. (125) and Al-Quwaidhi et al. (122). One characteristic commonly found in the state-transition models reviewed was the use of Monte Carlo simulation (MCS) methods. MCS are commonly used to estimate uncertainty around the key parameters in the model. Monte Carlo simulation is a probabilistic sensitivity analysis (PSA). A MCS incorporates random variability into the model by selecting at random different values within the specified distribution of the selected model steering parameter to estimate uncertainty around the outcomes (134).

Furthermore, there was also an important use of dynamic simulation models (n=7). These models are characterized by taking into account the transition probabilities between variables of interest and the influence of external factors on the probabilities of transition between states (135); in other words, they include a feedback process (126, 136). Some of the studies included in this review used as a modelling technique ordinary differential equations (ODE) (22, 137).

As mentioned above, some simulation models used a combination of two different modelling techniques (“hybrid models”). The hybrid models found in this review (n=14) like the Foresight Model (116, 117) and the University of California Los Angeles (UCLA) Health Forecasting Tool (138), were models formed by combining two different type of

modelling techniques. Firstly, a regression analysis was used to estimate projections of obesity or other risk factors. Secondly, the results from the first model were used as input data for a more complex model to calculate projections of obesity-related complications.

Other types of models

Other mathematical models that had characteristics that made them difficult to include in either the mathematical projection or simulation model groups were: autoregressive integrated moving average (ARIMA) models (139), life-table analysis (140, 141) and functional data analysis (142).

2.3.3 Unit of analysis

Another difference between modelling methods was the unit of analysis used. According to the unit of analysis, mathematical models can be classified into micro- or macro-level simulations (110). A total of 21 (41%) used a micro-simulation analysis. Microsimulation models (MSM) are characterized by focusing on micro-units or individuals as their unit of analysis. MSMs simulate individual life-histories associated with the characteristic components of a disease process (e.g. from health to illness, from illness to death). Outputs from individual life-histories are usually summed to estimate outcomes at the population level.

In contrast, macro-level models focus on higher level units such as populations or subpopulations as their unit of analysis. The review of models presented two main options for modelling their population: 1) following the entire population of a country; or 2) following a subgroup. Of the studies that chose to follow a subgroup, some (e.g. Goldman et al. (143)) followed a closed cohort, i.e. they observed the same population over time until they left the original population through terminating events such as death or left the model due to age of termination. Other studies used an open

cohort. An open cohort is one in which the members of the original population can leave or new members can be added over time to the original population. For example the study by Santoja et al. (144) considered newly recruited individuals aged 24y in the normal weight, overweight and obese population groups for every year of the simulation. These newly recruited individuals were distributed between the BMI subgroups according to the BMI distribution of the population aged 23y (i.e. the BMI subgroup they belong to before turning to 24y), and the individuals left the system when they reached 65 years old.

2.3.4 Transparency and validation

Different guidelines for health computer modelling have remarked on the importance of computer transparency when publishing academic papers that present modelling results (42, 112). Important parts of the model, such as input data, equations, algorithms, assumptions, data sources, calibration and validation, should be mentioned in the main paper or in a document available to the reader (112). Documentation is important in order to enable other scientists the possibility replicate the model results.

Following the recommendations by the ISPOR report (32, 112), I created four main themes to describe the content of the models found in the papers to observe the feasibility to replicate the model results. These themes are: (1) computer implementation transparency, (2) calibration, (3) validation, and (4) software used. I briefly describe these in turn.

Transparency

One important part of the modelling process is to describe in detail the model's structure, calculations or provide a description of any changes that have been made to

a previously used model that was also used for that particular paper, and make a clear reference of where to find any previous detailed description of the model if necessary.

I used the articles by Bennet and Manuel (42), Weinstein et al. (108) and Eddy et al. (32) to define transparency. Transparency was outlined as follows: *“The description of the modelling methods should be sufficiently detailed so that the model can be replicated mathematically”*. This document could either be in the paper reviewed or in another document (e.g. web-based supplementary information) used as a reference.

Of the 51 studies included in this review, a total of 34 (66%) articles were identified as having computer implementation transparency. It was common to observe that the studies that used an already known model referred the reader to another document for a detailed description, like the Foresight Model (145), CHD Policy Model (127) and the Population Health Model (POHEM) (146).

Validation

Model validation is of great relevance, because it is important to assess the fitness for purpose of the model. (32). ISPOR-Task Force recommends that modelling studies should provide a clear description in the document of how the validity of the model was checked (32).

As recommended, I classified the type of validation into three principal categories: *internal validation, cross-validation, and external validation*. The guidelines recommend two additional forms of validation: *face-validity and predictive validation*. However, none of the articles reviewed made reference to these two validation methods. Below I describe the three principal categories.

a) Internal validation: Ensures that the calculations are performed correctly and are consistent with the model specifications. Validation is considered internal when the model outcomes were compared to the observed data of a source used in the development of the model.

b) Cross-validation: These methods compare the estimates of the studied model with other models that estimate similar results.

c) External validation: The results of the model are compared with actual data and evaluate the similarity of their results. Validation is considered external when the model outcomes were compared with observed data for years or data sources not used in the development of the model.

In my analysis, fewer than half of the 51 studies (n=18, 35%) included information about the validation of the model. The most frequent type of validation was external validation (n=10). Most of the studies that used external validation compared the results with data not used as input in the model. Other authors applied another technique of external validation: they estimated projections of current years by using as baseline a previous year than the one used for the original model from the same data source and compared the projected outcomes with the already published results from that input data source. Authors that used this technique were Neovious et al. (133) as well as Finkelstein et al. (147) and Kopec et al. (148).

The studies that used cross-validation as their method of validation used two main approaches. Cardone et al. (107) and Huffman et al. (129) compared their forecasted outcomes with the results obtained by other modelling methods but using the same input data. Al-Quwaidhi et al. (122) compared their results with other published models that estimated similar outcomes. On the other hand, there were authors, such as Dall et al. (125) and Wang C et al. (130), that applied both internal and external validation techniques.

Calibration

Calibration is used in the context of mathematical modelling to describe the process of comparing model estimates with empirical data in order to detect variations between these parameters and make potential adjustments to produce a better fit to the expected values (149). A range of values for multiple parameters can be used to identify which set of parameter values are consistent with the observed data (7). It is possible that most mathematical modellers calibrate their model at the time of its development. However it is common for this information not to be included in the main papers. In the review I was able to identify only six articles that made explicit reference to calibration. However little detail was given about the techniques they used to perform this analysis.

Software used

Reporting information about the type of software used for modelling in the paper is an important characteristic for other researchers if they are interested in replicating the model. Nowadays, different computer simulation software packages and programming languages exist that can be used to calculate the model's projections, and their use requires different levels of skill. Stating this model's characteristic also gives a greater transparency and improves its credibility. 65% (n=33) of the studies in this review provided information about the software used for the analysis. The most common software used was C++ (25%, n=13) and Stata (n=4). C++ software requires good programming skills but allows more flexibility in the type of calculations it can perform. Other software packages reported were: Maple, Mathematica, Matlab, Excel, STELLA, SPSS, SAS, R, Sudaan and TreeAge.

Table 2.1 Characteristics of the population-based obesity forecasting models.

Study	City, country	Population	Model Name	Modelling Method	Study description	Tran ^a	Validation ^b	Calibration	Software
Europe									
Gonzalez Parra et al. 2010 (22)	Valencia, Spain	All. OW/OB (0-65y)	NO	Age-structure system of ordinary differential equations (OED) model	Described the future dynamic of obesity prevalence for different ages.	YES	NO	NO	Maple
Jodar et al. 2008 (126)	Valencia, Spain	Children (3-5y)	NO	Dynamic, state transition, macro model	Studied the evolution of obesity in the next years including the influence of high consumption of BFS (bakery, fried meals and soft drinks).	YES	NO	NO	Not stated
Keaver et al. 2013 (117)	Ireland	Adults (≥20y)	Foresight Model	A) Multivariate categorical regression model. B) Discrete time, Markov, Monte Carlo simulation, micro model	Projected disease burden and direct healthcare costs for obesity-related conditions in Ireland by 2030.	YES	NO	NO	C++
Majer et al. 2013 (139)	Netherlands	Adults (20-70y)	Lee-Carter Model	Auto-Regressive Integrated Moving Average (ARIMA) model	Projected parameters of future BMI distributions.	YES	<i>External:</i> Compared projected data with observed data not fitted in the model	NO	Not stated

Study	City, country	Population	Model Name	Modelling Method	Study description	Tran ^a	Validation ^b	Calibration	Software
McPherson et al. 2007 (116)	England	All (6-80y)	Foresight model	A) Multivariate categorical regression model. B) Discrete time, Markov, Monte Carlo simulation, micro model	Predicted future levels of obesity in English population to 2050.	YES	<i>Internal:</i> Compared to observed data	NO	C++
Mills 2009 (150)	England	All (≥16y)	NO	Linear trend models for the log-ratio transformations	Forecasted obesity trends in English population.	YES	NO	NO	Not stated
Neovius et al. 2010 (133)	Sweden	Adults (19-56y)	NO	Markov, Monte Carlo simulation, macro model	Estimated the net effect on future premature deaths due to trends in obesity and smoking in adolescent Swedish men.	NO	<i>Internal:</i> Using smoking and obesity prevalence in 1969-1970 compared with observed data	NO	Stata 10.0. Microsoft Excel 2003
Santonja et al. 2012 (151)	Valencia, Spain	Adults. OB (24-65y)	NO	Dynamic, state-transition, open cohort, Monte Carlo simulation, micro model	Showed the evolution of overweight and obesity over the next few years and the effect of public health strategies to reduce them.	YES	NO	NO	Not stated
Santonja et al. 2010 (144)	Valencia, Spain	Adults (24-65y)	NO	Dynamic, state-transition, open cohort, Monte Carlo simulation, micro model	Predicted the incidence of excess weight in the population in the coming years and proposed strategies to reduce it.	YES	NO	YES	Mathematica

Study	City, country	Population	Model Name	Modelling Method	Study description	Tran ^a	Validation ^b	Calibration	Software
Stamatakis et al. 2010 (152)	England	Children (2-18y)	NO	Linear regression. Power and exponential curves	Provided time trends of childhood and adolescent obesity prevalence in England 95-07 and projected obesity trends to 2015.	NO	NO	NO	SPSS 13
Von Ruesten et al. 2011 (153)	Europe	Adults (40-65y)	NO	Linear and Log-regression model, cohort	Predicted obesity prevalence to 2015 in European population.	NO	<i>External:</i> Compared simulation results to the reported by another study (EPIC Potsdam cohort)	YES	Not stated
Wang, C et al. 2011 (92)	England and USA	NS	Foresight Model	A) Multivariate categorical regression model. B) Discrete time, Markov, Monte Carlo simulation, micro model	Updated projections for obesity trends and increases in health-care expenditure consequent of an increase in obesity-related diseases.	YES*	NO	NO	C++ 12.0
Webber et al. 2012 (114)	10 Eastern Europe Countries	Adults (≥20y)	Foresight Model	A) Linear regression analysis. B) Discrete time, Markov, Monte Carlo Simulation, micro model	Projected obesity trends and its related disease in 10 Eastern Europe countries.	YES	NO	NO	C++ 12.0

Study	City, country	Population	Model Name	Modelling Method	Study description	Tran ^a	Validation ^b	Calibration	Software
Webber et al. 2014 (119)	Poland	All (All)	Foresight Model	A) Multivariate categorical regression model. B) Discrete time, Markov, Monte Carlo simulation, micro model	Projected BMI trends and related diseases to 2030.	NO	NO	NO	C++
Westphal et al. 2014 (154)	Germany	Adults (≥50y)	NO	Multinomial logistic regression model	Projected the number of pre-obese and obese men and women in Germany until 2030.	YES	NO	NO	Not stated
Zainal et al. 2014 (136)	UK	Children (2-15y)	Intervention Childhood Obesity Dynamics (ICOD)	System Dynamics (SD) model	Evaluated how eating behaviour modifications in the British child population might lead to reverse the prevalence of obesity to 2000 levels by 2020.	NO	<i>Internal:</i> Compared the simulation trends for both average weight and average BMI with real data	YES	Vensim software
Zaninotto et al. 2009 (128)	England	Adults (≥19y)	NO	Linear regression. Power and exponential curves	Updated the current state and time trends of obesity prevalence in England between 93-04 by age group and social class, and projected the extent problem to 2012.	NO	NO	NO	SPSS 13

Study	City, country	Population	Model Name	Modelling Method	Study description	Tran ^a	Validation ^b	Calibration	Software
America									
Bancej et al. 2015 (146)	Canada	All (6-79y)	Population Health Model (POHEM-BMI)	Continuous time, Markov, Monte Carlo simulation micro model	Estimated the future prevalence of obesity in Canada.	NO	NO	NO	Not stated
Basu et al. 2010 (155)	USA	All (6-85y)	NO	Discrete-time, cell-based, open cohort macro model	Forecasted BMI distribution to 2014 capturing the transition across BMI categories.	NO	<i>External:</i> Compared the predictions in 2005 for different age groups to estimates from 2005-2006 NHANES	NO	Stata 10.0. Simulations code using MATA language
Basu et al. 2014 (156)	USA	All (≥10y)	NO	Linear regression model	Combined an epidemiological-metabolic model to estimate what changes in calorie intake and physical activity are necessary to achieve "Healthy People 2020 objectives".	YES	NO	NO	POWER version 3 (National Cancer Institute, Bethesda, MD)
Bibbins-Domingo et al. 2007 (127)	USA	Children. OW/OB (12-19y)	CHD Policy Model	a) Linear trend (regression) b) State-transition (Markov), open cohort, Monte Carlo simulation, macro model	Estimated the potential effects of adolescent overweight on future adult CHD.	YES*	NO	NO	C++

Study	City, country	Population	Model Name	Modelling Method	Study description	Tran ^a	Validation ^b	Calibration	Software
Cardone et al. 2010 (107)	Argentina	Adults. OB (NS)	NO	Stochastic, dynamic simulation cohort, macro model	Estimated the prevalence of obesity based on past trends.	YES	<i>Cross:</i> Compared outcomes with three classic statistical techniques: linear, exponential and logarithmic with the same data.	NO	STELLA 5.1.1
Dall et al. 2011 (125)	USA	Adults. OW/OB or smokers (18-65y)	The Health Promotion Microsimulation Model (HPMM)	Markov cohort, Monte Carlo simulation, micro model	Quantified the health and medical cost implications of excess weight loss, analysing the potential cost avoidance from reduce or delay disease onset and additional expenditures from increased longevity	YES	<i>External</i> validation compares with published statistics and modelling studies <i>Internal:</i> Projected data compared to observed historical data involved in the model development	NO	Not stated

Study	City, country	Population	Model Name	Modelling Method	Study description	Tran ^a	Validation ^b	Calibration	Software
Finkelstein et al. 2012 (147)	USA	Adults (≥18y)	NO	Log-time trends and state-specific linear time trends	Forecasted future obesity and severe obesity prevalence over the next 20 years. Simulated the savings through obesity prevention efforts.	NO	<i>External:</i> Assessed by dropping the last 5 years of data and comparing the predicted obesity prevalence for those 5 years with the actual prevalence	NO	Not stated
Goldman et al. 2009 (143)	USA	Adults (≥51y)	The Future Elderly Model (FEM)	Dynamic, Markov cohort, micro model	Simulated the potential health benefits and medical cost savings of successfully treating cardiovascular risk factors (obesity, DM, HTA and smoking) among middle-age and older Americans.	NO	NO	NO	Not stated
Hoque et al. 2010 (157)	Texas, USA	Adults. OB (≥18y)	NO	Linear trend	Projected the number of population by BMI categories through 2040, and the direct and indirect costs associated with overweight and obesity.	NO	NO	NO	Not stated
Huang et al. 2009 (158)	USA	Adults.DM (24-85y)	Diabetes Population Cost Model (DPCM)	A) Discrete-time, probabilistic, Markov cohort B) State-transition, Monte Carlo simulation, micro model	Used data for obesity, and diabetes incidence and complications to forecast the future size of the diabetic population and their health care costs.	YES*	NO*	NO	Not stated

Study	City, country	Population	Model Name	Modelling Method	Study description	Tran ^a	Validation ^b	Calibration	Software
Huffman et al. 2012 (129)	USA	Adults (≥20y)	NO	Linear regression model	Calculated prevalence of cardiovascular health behaviours and health factors.	NO	<i>Cross:</i> Compared with results from log-linear and logit models	NO	SAS 9.1
Kopec et al. 2015 (148)	Canada	Adults (≥20y)	Population Health Model (POHEM-OA)	Continuous time, Markov, Monte Carlo simulation micro model	Projected the effect of a change in the distribution of body mass index on osteoarthritis burden in men and women.	NO	<i>External:</i> Simulation results prior to 2011 compared to published estimates of observed trends	YES	Not stated
Kristensen et al. 2014 (159)	USA	Children (6-18y)	NO	Markov, micro model	Estimated the impact of three federal policies on childhood obesity prevalence in 2032.	YES*	NO	YES	TreeAge
Lo et al. 2014 (160)	Quebec, Canada	Adults (≥18y)	NO	Weighted compositional regression	Projected the prevalence and numbers of individuals by BMI category for adult men and women	YES	NO	NO	Not stated
Rtveladze et al. 2013 (121)	Brazil	Adults (≥20y)	Foresight Model	A) Multivariate categorical regression model. B) Discrete time, Markov, Monte Carlo simulation, micro model	Mapped a trajectory of future obesity trends in Brazil to 2050, consequences of these trends in incidence of disease and health care costs, and the impact of reducing obesity rates.	YES	NO	NO	C++

Study	City, country	Population	Model Name	Modelling Method	Study description	Tran ^a	Validation ^b	Calibration	Software
Rtveladze et al. 2013 (115)	Mexico	Adults (≥20y)	Foresight Model	A) Multivariate categorical regression model. B) Discrete time, Markov, Monte Carlo simulation, micro model	Mapped a trajectory of future obesity trends in Mexico to 2050, consequences of these trends in incidence of disease and health care costs, and the impact of reducing obesity rates.	YES*	NO	NO	C++ 6.0+
Ruhm 2007 (161)	USA	Adults. OB (20-74y)	NO	Quantile regression	Examined past patterns and projected future prevalence of rates of obesity and severe obesity.	YES	<i>Internal</i> Projected estimates for 2011 were similar to actual 1999-2004 rates	NO	Stata
Shi et al. 2011 (138)	California, USA	Adults (NS)	UCLA Health Forecasting Tool	A) Linear trend (regression). B) Dynamic, continuous-time, open cohort, micro model	Forecasted the prevalence of type 2 DM in California and examined the potential effect of risk factor modifications.	YES*	NO	NO	Not stated
Stewart et al. 2009 (162)	USA	Adults (≥18y)	NO	Linear trends	Forecasted the effect of trends in obesity and smoking on future USA life expectancy and quality-adjusted life expectancy.	NO	NO	NO	Not stated

Study	City, country	Population	Model Name	Modelling Method	Study description	Tran ^a	Validation ^b	Calibration	Software
Thomas et al. 2014 (137)	USA and England	All, (NS)	NO	Differential equation system	Modelled known multiple population parameters associated with change in BMI classes and established conditions under which obesity prevalence will plateau.	YES	<i>External:</i> Compared projected data with observed data from the same source for years not used for the model	YES	MATLAB
Van Mejjgaard et al. 2009 (163)	California, USA	Adults (≥18y)	UCLA Health Forecasting Tool	A) Linear trend (regression). B) Dynamic, continuous -time, open cohort, micro model	Examined the effects of physical activity and BMI on mortality rates and medical expenditures in the population of California.	YES*	<i>External:</i> Compared with observed data.	YES	C++ (microsimulations) SAS 9.1(stats)

Study	City, country	Population	Model Name	Modelling Method	Study description	Tran ^a	Validation ^b	Calibration	Software
Wang, C et al. 2007 (130)	USA	Adults (20-74y)	NO	Parametric polynomial regression model	Forecasted BMI distribution in the USA population along with demographic changes based on past race, sex and birth cohort specific secular trends.	YES	<i>Internal:</i> Multiplied baseline BMI values of a defined population by annual proportional changes derived from means <i>External:</i> Compared the proportional changes in mean BMI in 2 large-scale follow up studies with the ones obtained from the model	NO	SAS 9.1 and SUDAAN 9.0.1
Wang, Y et al. 2008 (164)	USA	All (≥6y)	NO	Linear regression model	Estimated potential future trends in obesity and the related health-care costs.	NO	NO	NO	Stata 9.0
Webber et al. 2012 (113)	Latin America	Adults (≥20y)	Foresight Model	A) Regression analysis B) Discrete time, Markov , Monte Carlo simulation, micro model	Projected obesity trends and related burden of disease in Latin America to 2050.	YES	NO	NO	C++
Australia									

Study	City, country	Population	Model Name	Modelling Method	Study description	Tran ^a	Validation ^b	Calibration	Software
Backholer et al. 2012 (140)	Australia	Adults (≥25y)	NO	Dynamic, multistate life-tables, open cohort, macro model	Projected the prevalence of BMI categories according to educational attainment.	NO	NO	NO	Microsoft Excel 2007
Hendrie et al. 2015 (142)	South Australia	Adults (≥18y)	NO	Functional data analysis (FDA)	Projected overweight and obesity prevalence in South Australia.	YES	<i>Internal:</i> Compared simulation results for 2011-2012 to actual data through averaging of the Integrated Squared Forecast Error (ISPE)	NO	R software
Nepal and Brown, 2013 (131)	Australia	Adults (50y)	NO	Ordinary least-square (OLS) regression	Projected the possible number of older Australians who are likely to have a history of midlife obesity. Follows a cohort of 50 year old individuals.	YES	NO	NO	Not stated
Walls et al. 2012 (141)	Australia	Adults (≥25y)	NO	Dynamic, multistate life-tables, macro model	Estimated the future burden of obesity and the lifetime risk of overweight and obesity in a 25 to 29y cohort.	NO	NO	NO	Microsoft Excel 2007

Study	City, country	Population	Model Name	Modelling Method	Study description	Tran ^a	Validation ^b	Calibration	Software
Other									
Kelly et al. 2008 (124)	106 countries, grouped into world regions	Adults (≥20y)	NO	Log-time trend	Estimated the overall prevalence and absolute burden of overweight and obesity in the world and various regions in 2005 and projected the global burden in 2030.	NO	NO	NO	Not stated
Al-Quwaidhi et al. 2014 (122)	Saudi Arabia	Adults. OB or smoker (≥25y)	IMPACT Diabetes Forecast Model	Discrete-state, Markov model	Compared estimates and projections of T2DM in Saudi Arabia from a Markov model, IDF Diabetes Atlas and GBD project.	YES	<i>Cross:</i> Compared estimates with IDF diabetes Atlas and the GBD study <i>External:</i> Compared against local observed data from STEPS 2005	NO	Microsoft Excel

Study	City, country	Population	Model Name	Modelling Method	Study description	Tran ^a	Validation ^b	Calibration	Software
Basu et al. 2014 (120)	India	Adults (25-65y)	NO	Discrete-time, micro model	Estimates the potential health effect on overweight, obesity and type 2 diabetes of a tax on SSB in India.	YES	<i>External:</i> Compared historical projections of 2000-2010 obesity and type 2 diabetes prevalence in India using 2000 inputs against WHO survey-based estimates	NO	MATLAB
Kilpi et al. 2014 (123)	9 Middle East Countries	Adults (≥20y)	Foresight model	A) Multivariate categorical regression model. B) Discrete time, Markov, Monte Carlo simulation, micro model.	Predicted future levels of obesity in population of 9 Middle East Countries to 2050.	YES	NO	NO	C++
Rtveladze et al. 2012 (145)	Russia	Adults (≥20y)	Foresight Model	A) Multivariate categorical regression model. B) Discrete time, Markov, Monte Carlo simulation, micro model.	Examined the consequences of body weight on Russia and the impact of BMI change on the health profile of the country.	YES	NO	NO	C++

Study	City, country	Population	Model Name	Modelling Method	Study description	Tran ^a	Validation ^b	Calibration	Software
Saidi, et al. 2015 (165)	Tunisia	Adults. OB or smoker (≥25y)	IMPACT Diabetes Forecast Model	Discrete-state, Markov model	Projected the future prevalence of T2DM according to demographic changes and trends in: obesity and smoking. Estimated the impact of policies to improve tobacco control and reduce obesity.	YES	<i>External:</i> Compared simulation T2DM results for 2005 estimated based on prevalence data in 1997 to observed prevalence estimates for that year	NO	Microsoft Excel

UW: Underweight, **NW:** normal weight. **OW:** overweight, **OB:** obese.

^a**Tran (Transparency)** : The article or a referred paper had a detailed description of the data manipulation and simulation methods used for the analysis to be replicated mathematically.

^b**Validation:** The article mentioned how the model was validated.

Calibration: The article described if any calibration was made to model inputs

Software used: The article mentioned which type of simulation software was used for the analysis

NS: Not specified. *The paper referred to another article for Tran details

Table 2.2 shows a more detailed description of the outcomes from the obesity models: data sources, length of the projection period, outcomes from the model, and scenarios evaluated. These are discussed in turn below.

Data sources

The model's objectives and complexity, and knowledge about the disease are some of the most influential characteristics when choosing the quantity of data needed to feed the model, a difference that I observed between the two main types of model: simulation models, and mathematical projection models.

Mathematical projection models normally used less complex modelling techniques and commonly the quantity of estimated outcomes was less than for simulation models. Therefore, the models required fewer amounts of data. Of the articles reviewed that fall into this category of models, I observed that they usually used data from different years but from only one source: health examination surveys, or censuses of the population. For example, Stamatakis et al. (152) used several years' data only from the Health Survey of England. Similarly, Basu et al. (156) used several years' data only from NHANES.

In contrast, I observed that simulation models used a larger number of data sources such as: population censuses, national health examination surveys, and possible values for input parameters were informed by literature reviews from clinical or observation studies. Simulation models had a more complex structure than mathematical projection models and consequently they required more data inputs from wider sources.

2.3.5 Length of projection period

The length of the estimated projection period varied substantially across the studies. Models calculated future results from as short as a projection period of five years

(Mills et al. (150)), or until all the members of a cohort / population died (Gonzalez Parra et al. (22)). The most frequent length of projection I observed was from 20 to 40 years (n=21) followed by projections of less than 20 years (n=16). The number of years forecasted did not vary in a systematic way across modelling types.

2.3.6 Obesity model outcomes

Body Mass Index (BMI)

Reporting a forecast of BMI outcomes was the principal criterion for inclusion of the studies in this literature review. In a number of studies, the objective was exclusively to estimate future projections of obesity; others used obesity as a risk factor for assessing related conditions. The studies differed on the BMI classification used for presenting their results. The most common forecast reported was the future prevalence of BMI divided into three categories (n=17): normal weight (BMI: ≥ 18.5 to < 25 kg/m²), overweight (BMI: ≥ 25 to < 30 kg/m²), and obese (BMI: ≥ 30 kg/m²), and the second most frequent was only obesity (BMI ≥ 30 kg/m²) (n=14). Of the papers reviewed, a total of eight stratified the obese category into subgroups: BMI (> 30 to ≤ 35 , > 35 to ≤ 40 & > 40 kg/m²) (155, 163); BMI (≥ 30 to < 35 & ≥ 35 kg/m²) (125, 130), and BMI (≥ 30 & ≥ 40 kg/m²) (137, 147). However, the study by Huffman et al. (129) was an exception, as they presented their outcomes not as BMI classes but as poor, intermediate and ideal body weight for cardiovascular health.

Non-Communicable Diseases (NCDs)

A total of 25 studies included in this review reported the projected health impact of obesity on related non-communicable diseases or general mortality; most of these studies were simulation models. I observed two studies that used a mathematical projection model to estimate these outcomes: Huffmann, et al. (129) and Kristensen et al. (159). The most common presentation of these estimates was the number of incident cases, followed by the prevalence, and the incidence and mortality of the forecasted obesity-related disease. Of all the outcomes reported, the most frequent

NCD found was type 2 diabetes mellitus (T2DM) (n=20); CHD (ischaemic heart disease) (n=13); and cancer (n=11).

The total number of NCDs outcomes estimated varied between one and six. The highest number of outcomes reported was in Keaver et al. (117), Wang C. et al. (92), and in Rtveladze et al. (115, 121, 145). These studies reported a total of six outcomes. Each model used the Foresight model as the simulation model of choice for estimating obesity-related projections.

Health and economic outcomes

Population simulation mathematical models share similar methodologies with health economic models. Some of the models reviewed included as part of their estimation burden of disease and a range of economic outcomes (n=17). Reporting economic outcomes (n=14) was more frequently found than reporting health outcomes (n=6). Usually economic outcomes were reported in combination with health outcomes or by themselves. Only two of the reviewed articles presented exclusively reported health outcomes, Shi et al. (138) and Stewart et al. (162).

The most frequent types of economic outcomes reported were annual expenditure and costs associated with obesity. However there were other authors, such as Finkelstein et al. (147) and Dall et al. (125), who reported future cash savings due to reducing obesity prevalence, or Goldman et al. (143) who calculated lifetime expenditure. The health outcomes reported in the studies reviewed were life expectancy (n=5), quality adjusted life years (QALYs) (n=3), and loss of productivity (n=1).

2.3.7 Scenarios evaluated

A distinctive characteristic of simulation models is their capacity to create hypothetical scenarios to evaluate how a possible intervention or range of interventions could influence the predicted outcomes. These scenarios are usually influenced by the precise nature of the research question used to build the model.

More than half the models reviewed included an evaluation of a hypothetical scenario (n=32). The most frequent type of scenario evaluated was a direct reduction of BMI levels (n=18). Other authors assessed the effect of a specific intervention (n=9). For example, Jodar et al. (126) evaluated a reduction in levels of baked, fried meals and soft drinks consumption, and Shi et al. (138) an increase in physical activity levels. Furthermore, a number of models evaluated a modification in the wider environmental characteristics: Backholer et al. (140), for example, examined the impact of a reduction in educational inequalities using a model applied to the population of Texas, USA. Hoque et al. (157) evaluated a possible change in the levels of migration and how this could influence obesity rates.

Table 2.2 Outcome characteristics of the population-based obesity forecasting models

Study	Length of projection period	Data source	BMI outcomes (kg/m ²)	NCDs outcomes	Health outcomes	Economic Outcomes	Scenario Evaluated
Europe							
Gonzalez Parra et al. 2010 (22)	200y	Health reports from 1992 to 2006	OB (≥30) by age				Reduction of overweight and obesity
Jodar et al. 2008 (126)	2002-2010	Health Survey of Region of Valencia 2000-2001; Technical report on obesity of Valencia 99-05; Nutritional Observatory (Comp. Nutricia); Report from Abbot laboratories on success in obtaining normal weight; Survey to the members of the Valencian Society of Endocrinology and Nutrition	NW 3 to 4 y OW or OB if BMI >7.5. 5y OW or OB BMI >18. Percentiles cut-off not specified. Total population				Decrease consumption of BFS (baked, fried meals and soft drink) and continued BFS consumption
Keaver et al. 2013 (117)	2010-2030	National Adult Survey 2001, Survey of Lifestyle; Attitudes & Nutrition in Ireland (SLAN) 1998, 2002, 2007; The Irish Longitudinal study on Aging 2011; Literature Review	OW (≥25-<30), OB (≥30) by gender	DM2, CHD, Stroke, Cancer, Arth, HT. (I,P)		Total direct annual healthcare costs	BMI reduction of 1% and 5%
Majer et al. 2013 (139)	2008-2020	Dutch Health Survey (POLSGezond) 1981-2008	BMI continuous distribution by age group and gender				

Study	Length of projection period	Data source	BMI outcomes (kg/m ²)	NCDs outcomes	Health outcomes	Economic Outcomes	Scenario Evaluated
McPherson et al. 2007 (116)	2007-2050	Health Survey for England (HSE) 1993-2004	UW (<18.5), NW (≥18.5-<25), OW (≥25-<30), OB (≥30-<35, ≥35-<40 & ≥40) by age group and gender. <20y IOTF cut-off points	DM2, CHD, Stroke, Cancer, Arth. (I)	LE	Total NHS cost for the disease	BMI reduction in general population and overweight/obese
Mills, 2009 (150)	2005-2010	HSE 1993-05	NW (<25), OW (≥25-<30), OB (≥30) by age group and gender				
Neovius et al. 2010 (133)	2004-2035	Swedish Military Service Conscription Register 1969-1970 cohort; Population and Housing Census 1970; Register of the Total Population	UW (<18.5), NW (≥18.5-<25), OW (≥25-<30), OB (≥30). Total population	General Mortality			
Santonja et al. 2012(151)	2000-2030	Health survey for Valencia 2000 & 2005; Valencia Department of Health two technical reports for reduction strategies BMI	NW (≥18.5-<25), OW (≥25-<30), OB (≥30). Total population				Seven different prevention and treatment interventions targeting different groups: normal weight, overweight or obese population

Study	Length of projection period	Data source	BMI outcomes (kg/m ²)	NCDs outcomes	Health outcomes	Economic Outcomes	Scenario Evaluated
Santonja et al. 2010 (144)	2005-2011	Health Survey of Valencia 2000 and 2005	NW (≥ 18.5 - < 25), OW (≥ 25 - < 30), OB (≥ 30). Total population			The economic (direct and indirect) cost of obesity annually in Valencia in 2011	Increase physical activity in obese only and overweight only and decrease in social transmission parameter
Stamatakis et al. 2010 (152)	2007-2015	HSE 1997-2005	OB (≥ 30) by age group and gender. IOTF cut-off points				
Von Ruesten et al. 2011 (153)	2011-2015	Data from five European countries participating in the Diet, obesity and Genes (DiOGenes) project	OB (≥ 30) by age group				
Wang, C et al. 2011 (92)	2008-2030	NHANES (1988-2008) and HSE (1993-2008); US & UK census population; British Heart Foundation statistics, heart disease and stroke US statistics; National Health and Wellness Survey (NHWS) US 2008. National Cancer Institute data US	NW (≥ 18.5 - < 25), OW (≥ 25 - < 30), OB (≥ 30), by age group and gender	DM2, CHD, Stroke, Cancer, Arth, HT. (I, M)	QALYs, Loss of productivity	Annual medical cost for treating obesity-related disorders in population	BMI trends continue, 1% reduction of BMI, and obesity rates similar to 1990

Study	Length of projection period	Data source	BMI outcomes (kg/m ²)	NCDs outcomes	Health outcomes	Economic Outcomes	Scenario Evaluated
Webber et al. 2012(114)	2010-2050	Pubmed, google scholar, WHO and personal communication; Dynamo HIA (relative risks); National statistics; US National Diabetes Statistic; Heartstats, and The British Heart Foundation data	NW (≥ 18.5 - < 25), OW (≥ 25 - < 30), OB (≥ 30) by gender	DM2, CHD, Stroke, Cancer. (I)			1% and 5% reduction of mean BMI
Webber et al. 2014 (119)	2010-2030	WHO, CINDI 2003; Eurostat: National Health Interview Survey for Poland 1996; Household food consumption and anthropometric survey 2001; Statistical Office Poland 2004, 2009. Globocan 2008	OW (≥ 25 - < 30), OB (≥ 30) by gender	DM2, CHD, Stroke, Cancer. (I)			Mean BMI reduction of 1% and 5%
Westphal et al. 2014 (154)	2009-2030	Scientific Use File (SUF) of the Germany Microcensus 1999, 2003, 2005, 2009; 12th Population Projection of the Federal Statistical Office	UW (< 18.5), NW (≥ 18.5 - < 25), OW (≥ 25 - < 30), OB (≥ 30). Total population				Six scenarios based upon the time trends. Acceleration and deceleration scenarios of weight change

Study	Length of projection period	Data source	BMI outcomes (kg/m ²)	NCDs outcomes	Health outcomes	Economic Outcomes	Scenario Evaluated
Zainal et al. 2014 (136)	2013-2030	Health Survey for England (HSE) and literature review data	OB (≥30). Total population. Average weight and average BMI				Achieve the desired average weight target in 2020 by a modification of eating behaviours
Zaninotto et al. 2009 (128)	1993-2012	HSE 1994-2004	OB (≥30) by gender				
America							
Bancej et al. 2015 (146)	2001-2031	Canadian Health Survey 1978/1979. Canadian Fitness Survey 1981; Campbell's Survey on Well-being 1988; Canadian Community Health Survey (CCHS); Cycle 2.2 Nutrition 2004; Canadian Health Measures Survey 2007-2009, 2009-2011 and 2012-2013	OB (≥30) by age group, children (6 to 17y) and adults (18-79y)				

Study	Length of projection period	Data source	BMI outcomes (kg/m ²)	NCDs outcomes	Health outcomes	Economic Outcomes	Scenario Evaluated
Basu, et al. 2010 (155)	2004-2014	Medical Expenditure Panel Survey (MEPS) 2000-2001 & 2004-2005 and NHANES 2003-2004	NW (≤ 25), OW ($>25-\leq 30$), OB ($>30-\leq 35$, $>35-\leq 40$ & >40). Children at risk of overweight (≥ 85 th & <95 th, ≥ 95 th - <99 th & ≥ 99), by age groups				
Basu et al. 2014 (156)	2010-2020	NHANES 1999-2010	OB (≥ 30) by age group, gender, ethnicity and income				Reduction of % of calorie intake and increase % of physical activity separate and combined
Bibbins-Domingo et al. 2007 (127)	2000-2035	NHANES I, II, III & IV (1999-2000); National Centre for Health Statistics mortality data, Framingham Heart Study; Olmstead County Data; US census; National Hospital Discharge Survey; Medicare; National Health Interview Survey	OB (≥ 30) by gender	CHD (I,M)			Eliminating obesity-related increases in diastolic blood pressure, LDL cholesterol and reversing HDL cholesterol decrease

Study	Length of projection period	Data source	BMI outcomes (kg/m ²)	NCDs outcomes	Health outcomes	Economic Outcomes	Scenario Evaluated
Cardone et al. 2010 (107)	2007-2027	Coronary Risk Factor in America (FRICAS) 1991-94; National Risk Factors Survey (ENFR) 2005; and Relevamiento de Distritos de Cardiología de Argentina de factores de Riesgo Coronarios (REDIFA) 2001	OB (≥30) Total population				
Dall et al. 2011 (125)	2008-Death	Military Health Systems' TRICARE Prime & NHANES 1999-2008 & CDC mortality Data 2005. Defense Enrollment Eligibility Reporting System 2008 (DEERS); IARC=international Agency for Research on Cancer; Pharmacy Data Transaction Service. MEPS (2002-2007); CDM=TRICARE Clinical Data Mart (2008)	OW (≥25-<30), OB (≥30-<35 & ≥35) by age group	DM2, CHD, HT. HDL. (I, M)		Average lifetime medical expenditures by obesity or overweight reduction. Expenses from prolonged life by BMI class and age range	Weight reduction (1%, 5%)
Finkelstein et al. 2012 (147)	2010-2030	1990-2008 Behavioural Risk Factor Surveillance System (BRFSS); NHANES 1999-2000. US Census Population; US Bureau of Labour Statistics (BLS); Prices from the American Chamber of Commerce Research Association (ACCRA); Census of Retail Trade	OB (≥30) OB (≥30 & ≥40). Total population			Obesity-attributable annual savings in medical costs due to lower obesity prevalence in 2020 and 2030 in the country	1pp reduction in future forecasted obesity prevalence. No growth in obesity after 2010. Healthy People 2010 goal obesity prevalence of 15%

Study	Length of projection period	Data source	BMI outcomes (kg/m ²)	NCDs outcomes	Health outcomes	Economic Outcomes	Scenario Evaluated
Goldman et al. 2009 (143)	2004-Death	Health and Retirement Study (HRS); Medicare beneficiary survey 2002-2004; MEPS 2001	OB (≥30) by age	Smoke, DM2, HT. (I)	QALYs, LE	Lifetime medical spending per person	Treatment for (prevention) DM2, HTA, obesity and smoking. Success of 10%, 25% 50% and 100% of the at-risk population
Hoque et al. 2010 (157)	2000-2040	Texas Behavioral Risk Factor Surveillance System 1999-2002; Texas Department of State Health Services 1999-2001; US Census Bureau	OW (≥25-<30), OB (≥30) by age group and ethnicity			Total annual (direct and indirect) cost associated with overweight and obesity prevalence in Texas	Different sets of migration assumptions
Huang et al. 2009 (158)	2008-2034	NHANES 2005-2006 & MEPS 2004-2005; US life tables 2004; National Health Interview survey; Heart Outcome Prevention Evaluation Study (HOPE)	NW (≥18.5-<25), OW (≥25-<30), OB (≥30). Total population	DM (I)		Average annual cost of living with diabetes by age, sex, racial group and major duration of diabetes	Intensification of the treatment of people with diabetes
Huffman, et al. 2012 (129)	2006-2020	NHANES III and 1999 to 2008	Poor, intermediate and ideal body weight for cardiovascular disease	Smoke, DM2.HT, HLD (I)			

Study	Length of projection period	Data source	BMI outcomes (kg/m ²)	NCDs outcomes	Health outcomes	Economic Outcomes	Scenario Evaluated
Kopec et al. 2015 (148)	2010-2030	Canadian National Population Health survey (NPHS) 2000 and 2002, Canadian Community Health Survey 2001, Statistics Canada's projections	OB (≥30). Total population		Arth		BMI increased or decreased by a different fixed amounts, ranging from -2 to +2 BMI units per year, in 0.1 increments and an specific intervention targeting obese population ≥50
Kristensen et al. 2014 (159)	2012-2032	US Census 2010; NHANES 2001-2010; Literature Review.	CDC definitions of obesity (BMI ≥ 95th percentile for age and sex) and overweight (BMI ≥ 85th - < 95th percentile for age and sex) , by age group and ethnicity		DM2, CHD, Stroke, Cancer. (I)		Physical activity programme; SSB excise Tax; Ban on Fast Food Television Advertising targeting children.
Lo et al. 2014 (160)	2013-2030	Quebec Health Survey (ESQ) 1987; Quebec Health and Social Survey (ESS) 1992-1993, 1998; The National Population Health Survey (NPHS) 1994-1995, 1996-1997, 1998-1999; The Canadian Community Health Survey (CCHS) 200-2012.	UW(<18.5), NW (≥18.5-<25), OW (≥25-<30), OB (≥30) by gender		DM2 (P)		Obesity prevalence constant 2013. 2% reduction in 2013 obesity prevalence. 2% reduction in obesity prevalence relative to 2020 projected values

Study	Length of projection period	Data source	BMI outcomes (kg/m ²)	NCDs outcomes	Health outcomes	Economic Outcomes	Scenario Evaluated
Rtveladze, et al. 2013 (121)	2010-2050	Literature Review; National Survey of Health and Nutrition 1989; World Health Survey 2003; VIGITEL 2006-2010; GLOBOCAN 2008	NW (≥18.5- <25), OW (≥25- <30), OB (≥30) by age group and gender	DM2, CHD, Stroke, Cancer, MSK, HT. (I)		Total cost of hospitalization for the disease	BMI reduction of 1% and 5%
Rtveladze, et al., 2013 (115)	2010-2050	National Health and Nutrition Survey (ENSANUT) 2000-2006 ;National Nutrition Survey (ENN) 1993-1999; GLOBOCAN 2008	NW (≥18.5- <25), OW (≥25- <30), OB (≥30) by age group and gender	DM2, CHD, Stroke, Cancer, MSK, HT. (I)		Total annual cost for health care of obesity-related diseases in the country	BMI reduction of 1% and 5%
Ruhm, 2007 (161)	2004-2020	National Health Examination Survey (NHES) 1960-1962, and NHANES I,II, III and 1999-2004	OW (≥25), OB (≥30), OB class II (≥35) III (≥40) and IV (≥45) by sex				
Shi et al. 2011 (138)	2003-2020	NHANES and California health information; US census; National Health Interview Survey	OB (≥30) total population	DM2 (I)	LE		No further BMI increase for the cohort entering adolescence, childhood rates of overweight and obesity decrease. Childhood and adult BMI decrease. BMI decrease in the population with an increase in PA levels

Study	Length of projection period	Data source	BMI outcomes (kg/m ²)	NCDs outcomes	Health outcomes	Economic Outcomes	Scenario Evaluated
Stewart et al. 2009 (162)	2005-2020	MEPS 2003; NHANES I,II,III, 1999-2002 and 2003-2006, and National Health Interview Survey (NHIS) 1978,1991,1999,2004-2006; Life Tables from the National Centre for Health Statistics and the Social Security Administration	NW (≥18.5-<25), OW (≥25-<30), OB (≥30-<35, & ≥35). Total population	Smoke (I)	QALYs, LE		Eliminating obesity and smoking
Thomas et al. 2014 (137)	1998-2040	Prevalence trends of obesity among the US 1988-1998; Health Survey for England 1993-1997	OW (≥25-<30), OB (≥30-≥40 & >40). Total population				
Van Meji garrrd et al. 2009 (163)	2005-2025	NHANES and California health survey information, Data from California Department of finance; US Census Bureau; National Health Interview Survey/ Behavioural Risk Factor Surveillance System. Literature Review	UW(18.5),NW (≥18.5-<25), OW (≥25-<30), OB (≥30-<35, ≥35-<40 & ≥40)	CHD (I,M)		Direct personal future lifetime medical expenditures	
Wang, C et al. 2007 (130)	2000-2010	NHANES I,II & III, 1999-2004 (4 waves)	NW (≥18.5-<25), OW (≥25-<30), OB (≥30<35 & ≥35) by ethnicity				

Study	Length of projection period	Data source	BMI outcomes (kg/m ²)	NCDs outcomes	Health outcomes	Economic Outcomes	Scenario Evaluated
Wang, Y et al. 2008 (164)	2004-2030	NHANES 1970-2004; MEPS; National Health Expenditure Account (NHEA)	Children 6-11y and adolescents 12-19y OW (≥95th percentile). Adults OB (≥25) OB (≥30) by gender and ethnicity			Annual total health-care direct costs attributable to obesity and overweight for all US adults.	
Webber et al. 2012 (113)	2010-2050	Literature review on BMI data; personal communication; The WHO BMI database; National Surveys; Globocan 2008	OW (≥25-<30), OB (≥30) by gender	DM2, CHD, Stroke, Cancer. (I, M)			Unrestricted BMI growth, and BMI reduction of 1% and 5%
Australia							
Backholer et al. 2012 (140)	2000-2025	Australian Diabetes Obesity and Lifestyle (AusDiab) 2000-follow up at 2005	NW (≥18.5-<25), OW (≥25-<30), OB (≥30) by age group and education				Elimination of educational inequalities
Hendrie et al. 2015 (142)	2013-2019	South Australian Monitoring and Surveillance system (SAMSS) 2003-2012	OW (≥25-<30), OB (≥30), mean BMI, change in BMI by age group and gender				

Study	Length of projection period	Data source	BMI outcomes (kg/m ²)	NCDs outcomes	Health outcomes	Economic Outcomes	Scenario Evaluated
Nepal and Brown, 2013 (131)	2010-2050	Risk Factor Prevalence Surveys 1980, 1983 & 1989. National Health Surveys 1995 & 2007; Australian Diabetes, Obesity and Lifestyle study 1999	NW (≥ 18.5 - < 25), OW (≥ 25 - < 30), OB (≥ 30) by gender. Total population				
Walls et al. 2012 (141)	2000-2025	Australian Diabetes, Obesity and Lifestyle (AusDiab) 2000-follow up at 2005	NW (≥ 18.5 - < 25), OW (≥ 25 - < 30), OB (≥ 30) by age group and gender		LE		
Other							
Kelly et al. 2008 (124)	2005-2030	Internet search on national data; regional or multi-site; US census bureau; WHO Global Cardiovascular and Non communicable Disease Infobases	OW (≥ 25 - < 30), OB (≥ 30) by world region				
Al-Quwaidhi et al. 2014 (122)	1992-2022	Nationwide population bases study (Warsy and El-Hazim 1999); Estimations from DISMOD-2	OB (≥ 30) by gender	Smoke, DM2 (I)			1) BMI trends to continue to increase. 2) Projected obesity trends capped at 35% for men and 60% for women
Basu et al. 2014 (120)	2014-2023	Indian National Sample Survey; Indian Migration Study (IMS) 2007-2010; UN Food and Agricultural Organization estimates	OW (≥ 25 - < 30), OB (≥ 30). Total population	DM2 (I)			20% excise tax on SSBs

Study	Length of projection period	Data source	BMI outcomes (kg/m ²)	NCDs outcomes	Health outcomes	Economic Outcomes	Scenario Evaluated
Kilpi et al. 2014 (123)	2010-2050	Literature review on sub-national and national data on BMI in the Middle Eastern region (1990-2010); GLOBOCAN; DYNAMO-HIA	OW (≥ 25) by gender	DM2, CHD, Stroke, Cancer (I)			BMI reduction of 1% and 5%
Rtveladze et al. 2012 (145)	2010-2050	RLMS-HSE 1995-2009; United Nations Population database; Literature Review	NW (< 25), OW (≥ 25 - < 30), OB (≥ 30) by age group and gender	DM2, CHD, Stroke, Cancer, MSK, HT. (I, P)		Annual treatment costs	BMI reduction of 1% and 5%
Saidi et al. 2015 (165)	2005-2027	National Institute of Statistics Census data. Tunisian National Nutrition Survey 1996/97; Smoking data from the National Institute of Public Health Survey of Transition Epidemiological and Health Impact in the North Africa project (TAHINA); Cardiovascular Epidemiology and Prevention Research Laboratory	OB (≥ 30) by gender	DM2			Reduce smoking and obesity prevalence by 20% each in a 10 year period

UW: Underweight, **NW:** normal weight. **OB:** obese. **OW:** overweight.

BMI: Body Mass Index. **NCDs:** Non-communicable disease. **I:** incidence. **M:** mortality

1. ACCRA: Prices from the American Chamber of Commerce Research Association. **AusDiab:** Australian Diabetes Obesity and Lifestyle/ **BRFSS:** Behavioural Risk Factor Surveillance System. **DEERS:** Defense Enrollment Eligibility Reporting System. **ENFR:** National Risk Factors Survey "Encuesta Nacional de Factores de Riesgo". **ENN:** National Nutrition Survey. "Encuesta Nacional de Nutrición". **ENSANUT:** National Health and Nutrition Survey "Encuesta Nacional de Nutrición y Salud". **FRICAS:** Coronary Risk Factor in America. **GLOBOCAN:** WHO's data base of estimated cancer incidence, mortality, prevalence and disability-adjusted life years (DALYs) from major type of cancers for 184 countries. **HSE:** Health Survey for England. **MEPS:** Medical Expenditure Panel Survey. **NHANES:** National Health and Nutrition Examination Survey. **NHEA:** National Health Expenditure Account. **NHIS:** National Health Interview Survey. **REDIFA:** Coronary Risk Factors Survey in Argentina "Relevamiento de Distritos de Cardiología de Argentina de Factores de Riesgo Coronario".

2. DM2: Type 2 diabetes mellitus. **CHD:** coronary heart disease. **HT:** hypertension. **HDL:** Hyperlipidaemia. **MSK:** musculoskeletal disease. **Smoke:** smoking. **Arth:** arthritis

3. LE: life expectancy. **Loss of productivity:** absenteeism or disability. **QALYs:** quality adjusted life years

2.4 Discussion

My systematic review of the literature identified a great variety of distinct population-based obesity forecasting models that differ in the characteristics of the modelling methods used, their structure, and the health and economic outcomes produced. However this diversity in modelling methods is not exclusive for obesity models.

The variability in methods has also been reported in other systematic reviews of health forecast models (166, 167). The selection of the methods for development of population based models depends on several factors of equal importance. Traditionally, forecasting models are built to answer a particular research or policy question. Therefore, the methods chosen for modelling future estimates have to be the ones that best answer the particular question or objective (168). Model choices are also influenced by how much knowledge exists about the disease, and which methods according to current knowledge is the best to replicate the story of that disease (102, 105, 169). Additionally, according to Fielding and Kominski, the choice of forecasting method depends on: the levels of forecast accuracy needed; the complexity of the relationship between variables; constraints in time for the analysis; and the balance of forecasting costs relative to benefit (170). One other important aspect to consider is the availability and quality of the data, as this has a substantial impact on the modelling methods that could be used, and the interpretation of the results. Lastly, the modellers need to consider the target population (the entire population or specific subpopulations) and the progress of the disease in that study group, as well as their modelling skills, and the economic resources available to conduct the study (100, 105, 169).

All the aforementioned aspects that need to be carefully considered when developing a population based health model explain the large amount of variability in the modelling techniques that I found during this systematic review of the literature. They

justify the difficulty of trying to classify all the selected articles into groups, as each particular model has its own unique set of characteristics.

It is of great importance for end-users such as policy-makers and the research community to have as much information as possible about the model in order to have a clear understanding of the model, and the connection between inputs and outputs, to enable a proper interpretation of the results (108). In order to achieve that, the authors have to include as much detailed information as possible about data sources, data transformation analyses, detailed description of the modelling techniques, as well as the set of assumptions made during the development of the model, and acknowledgement of the limitations of the modelling techniques they have used. Additionally, the guidelines for describing population models put emphasis on authors giving a detailed description of the calibration process, if performed, and on the validation of the outcomes, as these later characteristics can confer a higher strength to the overall model results. During my review of the literature, I observed that not all the models included a detailed description of the development of the methods. Many of the published articles included in this review did not make reference to any attempt to calibrate their model parameters, or any validation (internal or external) of their results. A number of studies did not even mention the statistical software used for their analyses. This could be due in part to the word count restrictions of the journal that published the paper. However, many authors, in order to overcome that limitation, presented a detailed description of their methods as Supplementary information. Another possible reason is a lack of clear guidelines of how mathematical modellers should report this type of research study. As I mentioned previously, there are some guidelines that can be used, but these are not specific for population simulation models, even though some authors used those guidelines for reporting how their model was developed and their results. I have also used those guidelines to review the models for my systematic review, but there is no consensus on how to report them. The lack of detailed description of methodologies from a number of the articles included in this systematic review acted to constrain my choice of modelling methods as I was not able to accurately assess if I was going to be able to successfully

replicate the modelling techniques that on paper at least looked promising for my PhD project as I did not have all the information needed to do that.

2.4.1 Advantages and disadvantages of modelling methods

During this review, to simplify the analysis of the modelling methods used in the previous obesity modelling work, I classified the methods used in the studies into two broad groups: mathematical projections, and simulation models. Each of them possesses different characteristics that give them some advantages and disadvantages, which I took into account later on to choose the structure and methods for development of my Mexican Obesity Forecast Model (MexOb-Model).

Mathematical projections

Mathematical projections estimate future prevalence of obesity by extrapolating data from past trends (139, 152). Mathematical projection methods are usually less complex, more transparent, and easier to implement than simulation models, as I also observed from my literature review (170). As a consequence, the modelling skills required are less specialized. Another advantage of using this type of modelling technique is the low amount of data needed to feed the model. Therefore, the resources and time needed to calculate model outcomes is much less than for complex forecasting models such as simulation models.

However, extrapolation models have some disadvantages. Even though they can be used to calculate long-term results, their accuracy is better for short-term forecasts. They do not take into account transitions between BMI categories, or interactions between other risk factor variables that could influence the outcome. They assume that the distribution of the data will remain the same through the projected time period. Mathematical projections can calculate only a limited number of possible outcomes, and they have limited flexibility for evaluating possible scenarios (166, 170).

For example; Kelly et al. reported as the only outcome the prevalence of overweight and obesity (124). Wang.Y et al. presented just the future trends of obesity and its associated health care costs (164).

Simulation models

Simulation modelling techniques like the ones used for the Foresight model (116), the Future Elderly model (143), and the UCLA Health Forecasting tool (138), are the preferred models for forecasting the trends of obesity, and the effect of those trends on its associated diseases. They are also the method of choice for the evaluation of the future effect of possible policies or interventions.

Simulation models take into account the variability of the explanatory variables, as well as simultaneous interaction between them and their influence on the outcome. Consequently, they can make a more accurate representation of the impact on real life (107, 171). Simulation models use more complex forecasting methods than mathematical projections, and the variability of the chosen modelling methods used within these models is high. However, they present several advantages. It is possible to perform analysis at an individual level or among an entire population. It is possible to estimate a larger number of outcomes than projection models. Simulation models also have the facility to evaluate the impact of different hypothetical scenarios. The Foresight model by McPherson et al. evaluated the impact of two possible reductions in the mean BMI levels of the general population (116), in contrast with the model of Mills et al. that used a mathematical projection model for forecasting, which presented only the future prevalence of obesity (150).

However, simulation models have some disadvantages: they are more complex to implement and could appear to be less transparent. They need extensive data to feed the model in order to take into account the influence of risk factors. Therefore, they are more prone to make assumptions about the behaviour of a risk factor on the outcome. Implementing a simulation model requires more advanced modelling and

programming skills as they frequently use more complicated modelling techniques (e.g. algorithms), requiring specialist software for programmers such as: C++ and MATLAB (92, 137, 144). Due to the complexity of these types of models, they are usually developed by a group of experts, in consequence, they require more economic resources and time to develop and refine (172).

In my review, the most frequent type of simulation model used was microsimulation, which was used as a modelling method in 21 of the reviewed articles.

Microsimulations share the characteristics mentioned above for simulation models in general, with the distinction that they use individuals as the unit of analysis. Their objective is to create individual life-histories, so that when combined, the results can be translated into estimates of health outcomes at the population level (173). Taking individuals as the unit of analysis gives microsimulations the advantage of creating a more heterogeneous population. They simulate the behavioural reactions of the individual following the changes brought about by the implementation of that policy (19). Microsimulations can be *static* if they assume that the change being evaluated by the model produces no second order of changes in the variable of analysis, or *dynamic* allowing changes in the characteristic of the individual in response to the accumulated experience in the process (174-176).

The most common modelling techniques found in the simulation models were Markov process (Markov chain) and Monte Carlo simulations. The Markov process was mentioned as a component of the modelling methods used in 20 of the reviewed articles. A Markov process is a stochastic mathematical modelling technique that is used to describe the course of a disease, for a fixed period of time or until death, experienced by a patient or group in terms of “health states”, and the probability of transition among them (17, 177). The principal characteristic of a Markov process is that the states should be mutually exclusive and the patient has to be in one of the health states at each time (178). Markov processes characteristically have one limitation called the “*Markovian assumption or property*”, meaning that the prediction

of the future of the process depends only on the description of the present state. They do not keep any memory of the history of the past states. This means that all the people in the same state at the same time will have the same prognosis regardless of their previous history (17).

A Monte Carlo simulation (MCS) is a modelling technique in which an individual/population in the model is followed over time. A random number generator is used together with the transition probabilities to determine in which of the “health states” the person will be in next, allowing his/her individual characteristic(s) to modify the magnitude of the transition probabilities; each repetition of the model generates potentially different results by using different sets of transition probabilities. MCS allows the model to incorporate more complexity. After repeating the process for a large number of trials, the mean value of the distribution of the outcomes will represent a more realistic picture of the population’s health outcomes, and the spread of the distribution can give an estimate of the of the likely variance (uncertainty) associated with the parameters estimated (177-179). MCS has been used by modellers to estimate uncertainty (credible) intervals around the mean of the outcomes estimated from their models.

During my review I found that a number of models could be classified as “*hybrid models*”. These forecasting models used as their modelling method a combination of a mathematical projection and a simulation model in order to obtain the most accurate results. One of the examples of a hybrid model is the Foresight model used by McPherson et al.(116), in which first they used a multivariate categorical regression model to calculate the future cases of obesity, and then combined the results in a microsimulation model to calculate the number of new cases, and the subsequent mortality related to the diseases associated with obesity. The combination of methods gives models more flexibility to allow for projections of risk factors, and use those projections as input data to calculate the projected health impact.

In summary, results from this literature review showed that as with all statistical models, the population simulation models have strengths and limitations that the modelers and the users have to always consider.

Strengths

The development of new mathematical models has been in accordance with the availability of large computers, and are adapted to more user-friendly software, and are now able to accommodate greater data which is often freely available online. The use of population simulation models has increased in popularity and it is possible to observe different methods used to estimate the future outcomes of different diseases in different populations. As a consequence, there has been an increase in the number and range of methods used to manipulate data to feed into the models.

Limitations

The reporting of the obesity models in academic publications such as journals often lacks sufficient detail in the description of the methods used. Researchers in the modelling community should strive to reach a consensus on the type of quality and quantity of information that should be provided to enable their model to be considered as “transparent”.

Specifically in relation to the statistical models of obesity themselves, the weaknesses or limitations of the existing evidence base include the following.

Firstly, the majority of modelling studies have been conducted in the United States and European countries. It is important that researchers in Mexico have a population simulation model that is their own, and which can be easily adapted to Mexico’s specific circumstances and the epidemiologic data available.

Secondly, the majority of modelling studies have been conducted on general populations. A model focusing specifically on the obese population enables me to demonstrate the potential health effects of the rise in obesity prevalence, and to estimate the potential benefits of reducing the obese population.

Thirdly, it is true to say that all modelling studies involve simplifying assumptions: but those assumptions can be important limitations of the existing evidence base (even though they are often acknowledged in the limitations sections of the published articles). For example, a number of modelling studies by design assume a closed cohort: i.e. a model which observes the same population over time until members leave the original population through the terminating event of death. For populations such as Mexico, modelling studies need to accommodate incoming members to populations through events such as migration and change in BMI category (i.e. overweight to obese).

Modelling studies also often assume that key parameters such as transition probabilities will remain stable over time through the projected time period. There is increasing epidemiological evidence from the US which suggest a reduction of the effect of obesity on mortality over time. Markov studies also often have the *Markovian assumption or property*: meaning that the prediction of the future of the process depends only on the description of the present state.

Fourthly, as is commonly stated, all models are simplifications of reality. Markov modelling studies for example can only sensibly handle a limited number of possible outcomes and transitions. My results from the literature review showed that modelling studies of obesity have often not taken into account transitions between BMI categories (e.g. from obese to non-obese), or interactions between other risk

factor variables (i.e. modelling individual diseases separately rather than a combined comorbidity such as the Metabolic Syndrome) that could influence the outcome.

2.4.2 Implications of the literature review for my research project

After a systematic review of the different types of modelling methods used for forecasting obesity, and an appreciation of their range of methods and objectives, I concluded that my decision regarding which specific modelling method(s) to apply to the Mexican adult population depended heavily on the research questions that I wanted to answer. As mentioned in the previous chapter, the research questions that I wanted to answer with my final model were as follows:

- What will the obesity prevalence in Mexico be in 2030?
- How does it vary between different age groups and gender?
- How will the future prevalence of obesity contribute to the incidence and mortality of NCDs (hypertension, type 2 diabetes, hypertriglyceridaemia and hypercholesterolaemia) in the obese adult population?
- How will the size of the health burden associated with obesity differ if I reduce, in different degrees, the projected increase in the prevalence of obesity in the population?

Any mathematical model should be seen as a simplification of the reality of a system. In real life, a system is influenced by a number of different external characteristics that impact on the outcome, and this makes it difficult to know exactly how the system will behave in different scenarios (102). Obesity is a clear example of this: there exist multiple causes that influence body weight and that increase the likelihood of becoming obese. From a simplistic point of view, obesity is the difference between energy intake and expenditure. In reality, obesity is influenced by more complex causal linkages such as: psychological, genetic, environmental, economic, and infrastructure risk factors (51).

Therefore an ideal forecasting model for obesity will have to be very complex to include all the parameters that operate to influence the development of the disease. It will need to be *dynamic and continuous-in time* to be able to take into account the impact of the large number of explanatory variables on obesity and how this will affect obesity-related health outcomes throughout life such as: health complications, psychological, economic and productivity. The model should be able to capture the influence of modifications at different levels, e.g. environment, government, household and individual, to try to capture as much influence of the explanatory variables at different levels as possible. This model should account for heterogeneity of the population, and provide flexibility so that it could be adapted to the evaluation of different scenarios or proposed interventions (167, 180).

A modelling technique that could incorporate these characteristics would be an agent-based model. This type of model considers the interaction between individuals and their environment. It incorporates complex dynamics that allow modelling simultaneously multiple mechanisms. Moreover, it has great flexibility that could encourage the evaluation of a diversity of policies for obesity reduction or prevention (1, 181, 182). Unfortunately, building this type of model, even though not impossible, would represent a huge task that I was not going to be able to complete during my PhD research period. First of all this "*ideal model*" would need a huge amount of data to account for all the determinants of health and the interactions between variables in the model. This represents an obstacle because the range of available data for the Mexican adult population is limited. It does not compare to the availability of data in countries such as the USA or UK. This "*ideal model*" would need to combine different complex modelling methods which would need a range of specialised mathematical and statistical skills, some of which have only recently been developed. Therefore, the amount of resources and time needed to build such an ideal model would surpass the budget and time allocated for my PhD.

Furthermore, simulation models are originally developed by taking into account the availability of data for the country for which the model is being built. Unfortunately, this could have a downside when trying to adapt those models for other countries, e.g. the inclusion of many variables in the model for which there is no data available. This is particularly relevant for low- and middle-income countries for which the range of epidemiological data is not vast.

This characteristic could bring as a consequence the need to use data from other countries to feed the model, and this could impact on the results by showing a different future scenario that does not fit the particular country well. Therefore, I decided to create a model that could be fed exclusively from Mexican data. Furthermore, it is also important that Mexican researchers have a population simulation model that they could call their own. Mexican researchers will be certain that they have the epidemiological data to correctly feed into the model. Using Mexican data enables us to set out projections to policymakers that clearly represents the reality in Mexico as accurately as possible..

The creation of simulation models requires the use of many resources, including data and personnel. Therefore, it is understandable that once a model is created, the modelling group charges a fee for its use. This is a constraint for low- and middle-income countries that could greatly benefit from the estimation of future results to evaluate the impact of different health interventions but that have limited resources.

Based on the results and knowledge obtained from my literature review, and taking into account the research questions I wanted to answer, my data resources, my modelling skills and time, I decided to build the Mexican Obesity Model (MexOb-Model) as a less complex hybrid model based on the structure of the two following models:

- 1) The Foresight model, which is a combined model which used first a non-linear regression analysis to calculate future trends of obesity, and then a stochastic microsimulation to calculate the changes in ten different obesity-related diseases, and the effects of obesity reduction. This model also includes a cost module to calculate total health expenditure and burden of disease (116).
- 2) The IMPACT model: A discrete state Markov model that uses obesity as a risk factor to estimate the impact of risk factor reduction on population trends in NCDs such as diabetes and CHD (122, 165).

Recently I performed an update of my literature review from April 18th to July 17th 2016. Only five articles were selected for abstract and three had the inclusion criteria to be selected for data extraction (183-185). These recent result are not included in the content of this chapter as none of the articles recently found changed the approach I had until now for the development of the model.

As we will see, the MexOb-Model was composed of two sub-models. The first sub-model was a mathematical projection (linear regression) to project the future prevalence of obesity in the population stratified by age and sex. The second sub-model was a discrete-state Markov model that estimated the health impact of changes in the prevalence of obesity on the prevalence, incidence and mortality of four related cardiometabolic risk factors (hypertension, type 2 diabetes mellitus, hypertriglyceridaemia and hypercholesterolaemia). The health states for possible transition were: obese without the risk factor of interest, obese with the risk factor of interest (e.g. obese with hypertension), and dead (Figure 2-2).

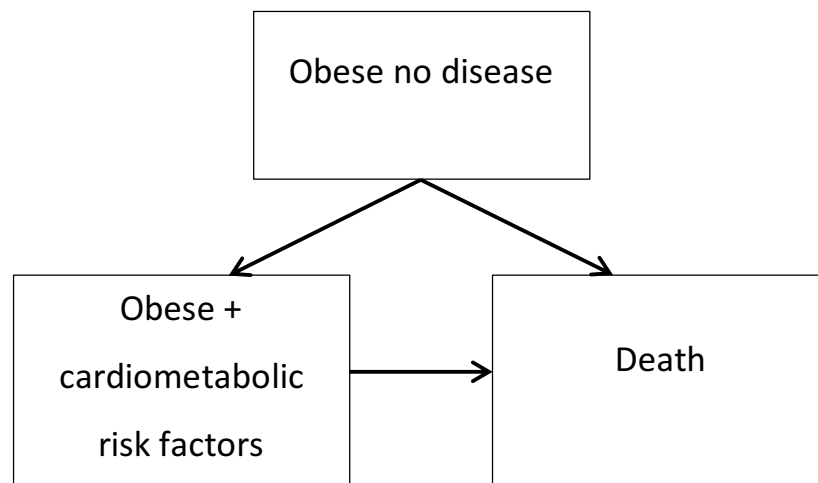
Even though obese individuals have a higher risk than non-obese individuals of having more than one chronic disease, I decided to model each of the four diseases separately instead of grouping them as a syndrome such as the “metabolic syndrome”.

First, the definition of the metabolic syndrome often involves abdominal obesity as one of the diseases rather than obesity based on the body mass index, which is the main outcome of the MexOB-Model

Second, the groups of combinations of diseases for metabolic syndrome diagnosis could be large. Evidence from Mexico in a study that I was involved in showed that there could be up to 16 possible metabolic syndrome combinations out of just five conditions(186). Therefore, modelling the effect of a combination of comorbidities would require developing a substantially more complex simulation model, which would go beyond the scope of this thesis. However future research could extend the simulation models to include co-morbidities.

In reality, individuals with obesity are more frequently targeted for disease diagnosis during primary care consultations in Mexico. It will be easier to diagnose and prevent further diseases in those individuals by controlling their weight. Information on potential reductions in specific diseases among the obese population may therefore be more useful for health care planners.

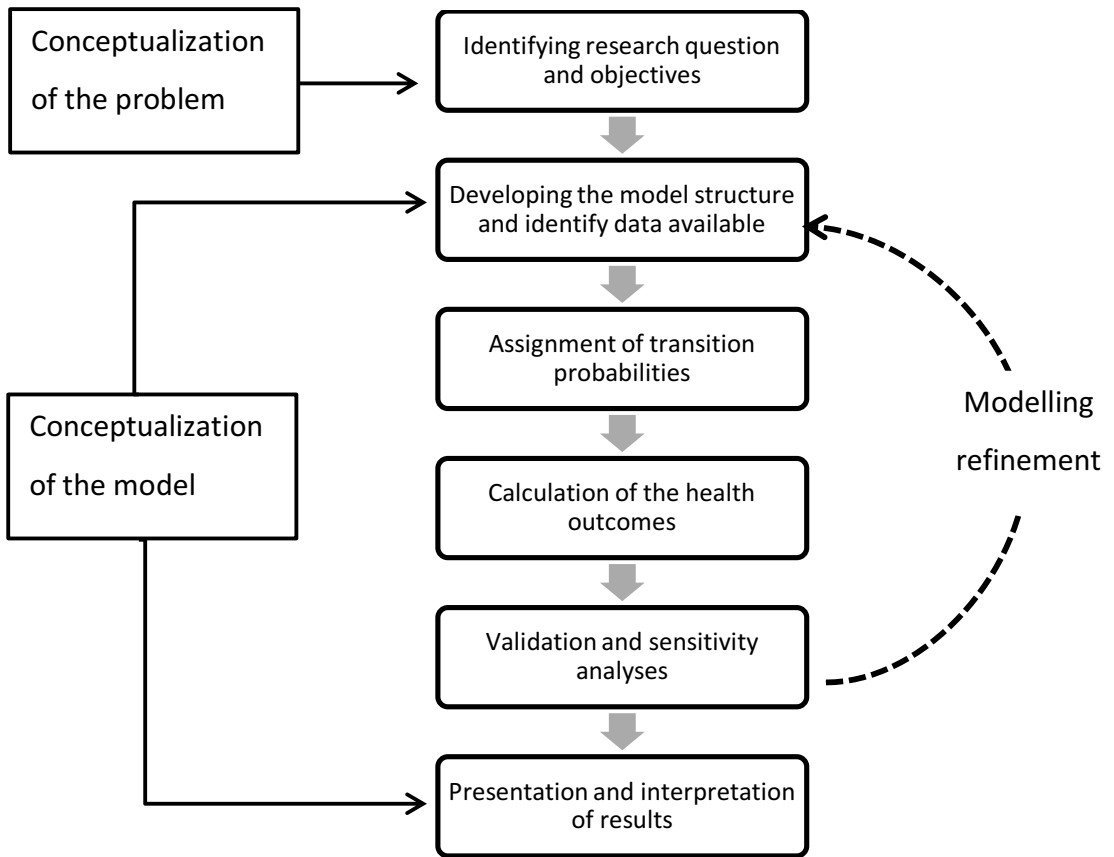
Figure 2-2 Example of the proposed state-transition model for the Mexican Obesity Forecasting Model (MexOb-Model).



A summary of the steps I took for the conceptualization and development of the MexOb-Model can be observed in Figure 2-3. These steps were based on the recommendations for model conceptualization of the ISPOR-SMDM task Force (187, 188). They stated that the process of developing a model can be divided in two principal components: 1) *conceptualization of the problem*, which for the MexOb-Model included knowledge about Mexico's obesity problem and the specification of the objectives I wanted to achieved. It also included specifying the MexOb-Model target population and identifying the main health outcomes for the model; 2) *conceptualization of the model*, this refers to the acto of choosing a model that could adequately address the problem of interst and reflects the knowledge of the disease. In the case of the MexOb-Model, I decided that the best representation of my research problem would be to model obesity using a hybrid model; a combination of a linear regression and state-transition Markov model.

The next chapters of this thesis will describe in detail the methods used for the second component of the development of the MexOb-Model, *conceptualizing the model*. They include the statistical analyses performed to manipulate the data, the validation of the model and the outcomes generated.

Figure 2-3 Flowchart for developing the MexOb-Model



Flow chart adapted from Sun Xi (189).

Chapter 3. Future obesity prevalence in Mexican population

3.1 Introduction

The Mexican Obesity Forecast Model (MexOb-Model) aim was to forecast the future prevalence of obesity in the Mexican adult population (20-79y) and estimate its impact on four obesity-related cardiometabolic risk factors: hypertension, type 2 diabetes, hypertriglyceridaemia and hypercholesterolaemia.

The MexOb-Model is a computer simulation model composed of two sub-models: 1) a linear trend model that projected future prevalence of obese population; 2) a discrete-state Markov model that estimated the health impacts of obesity on the prevalence, incidence and mortality of four obesity-related cardiometabolic risk factors.

This chapter contains the description of the methods used for the first sub-model of the MexOb-Model, linear trends. It presents the projected obesity prevalence trends from 2015 to 2030 based on historic trends during 1999 to 2012, stratified by age group and sex. The estimates describe here were used as baseline data for the second component of the MexOb-Model to calculate the future health impact on the four obesity-related cardiometabolic risk factors (see: Chapter 4).

3.2 Methods

3.2.1 Population

The target population for the first sub-model of the MexOb-Model was the obese population, male and female aged 2 to 80 years and older. I estimated the size of the target population by estimating the prevalence of obesity among the general population. The data used were extracted from five Mexican nationally representative health examination surveys: Encuesta Nacional de Nutrición (ENN) 1999 “*National Nutrition Survey*”; Encuesta Nacional de Salud (ENSA) 2000 “*National Health Survey*”;

Encuesta Nacional sobre Niveles de Vida en los Hogares-1 (MxFLS-1) 2002 “*Mexican Family Life Survey*”; and Encuesta Nacional de Nutrición y Salud (ENSANUT) 2006 and 2012 “*National Health and Nutrition Survey*”. Summarised information about these five surveys is described in Table 3.1. Detailed information about each of the Mexican nationally representative health surveys can be seen in Appendix A.

The ENN-99, ENSA-00, and ENSANUT-06 and 12 have a probabilistic, multistage, stratified, clustered sample design and were designed to be nationally representative. These surveys distinguish between four geographical Mexican regions (north, central, Mexico City and south), and between urban (defined as population $\geq 2,500$) and rural areas. Information regarding socio-economic and health characteristics were gathered through questionnaires administered in face-to face interviews. The surveys also included anthropometric measurements and biological samples from a subsample that were obtained by trained personnel using standardised protocols.

In ENN-99, the sample included all children aged 0 to 11 years old in each selected household, and one woman aged 12 to 49 years was randomly selected from every selected household (190). In ENSA-00 and ENSANUT 06 and 12, one individual from each of the three age group; (children ($<10y$), adolescents (10-19y) and adults ($\geq 20y$) was selected from every household using a randomized design (35, 65, 191).

MxFLS-1 had a probabilistic multi-thematic stratified clustered design. It was designed to be a nationally representative longitudinal database and to distinguish between urban and rural areas and Mexican regions. Its units of analysis are community, households and individuals. It provides socio-demographic and economic information about the Mexican population. Questionnaire and anthropometric measures were also obtained by trained personnel (192).

For my analysis, it was necessary to construct the data for the year 1999 by combining two surveys, ENN-99 and ENSA 2000, in order to compile a complete sample across all ages for that year. The data for 1999 was built by combining BMI information from children 2 to 9 years of age from ENN-99 and BMI for population ≥ 10 years from ENSA-00. This was because ENN-99 had adult anthropometric data only for women 12 to 49 years of age and ENSA-00 did not collect anthropometric information from the population younger than 10 years (190, 193).

Table 3.1 Characteristics of five Mexican national representative surveys.

Survey	ENN 1999	ENSA 2000	Mx-FLS-1 2002	ENSANUT 2006	ENSANUT 2012
Date of data collection	Oct 98- Mar 99	Nov 99-Jun 00	2002	Oct 05-May 06	Oct 11-Mar 12
Age groups (years)	Children (0-4 & 5-11)	Children (0-9)	Children (<15)	Children (0-9)	Children (0- 4 & 5-9)
	Adult women (12-49)	Adolescents (10-19)		Adolescents (10-19)	Adolescents (10-19)
		Adults (≥20)	Adults (≥15)	Adults (≥20)	Adults (≥20)
Calculated household sample	21,000	47,040	10,000	48,600	55,008
Achieved household sample (%) [†]	17,944(85.4%)	45,726(97.2%)	8,440(84.4%)	47,152(97%)	50,528(91.8%)
Achieved individual sample	37,737	190,214	35,677	94,710	96, 031
Individuals with anthropometry data	37,737	66,684*	32,169	71,469	75,406

ENN, (National Nutrition Survey); ENSA (National Health Survey), MxFLS-1-(Mexican Family Life Survey); ENSANUT (National Health and Nutrition Survey)

* Survey sample with anthropometric data only included population ≥10 years old

[†] Total household sample as percentage of the calculated household sample

3.2.2 Obesity cut-off points

Body mass index (BMI) was calculated as weight (kg) divided by height in meters squared (m^2). Obesity was defined for children, adolescents and adults according to BMI categories using international cut-off points, as specified below.

Children and adolescents

BMI categories for the population 2 to 19 years of age were classified using the age- and sex-specific classification of the International Obesity Task Force (IOTF) body mass index cut-off reference (194). In addition, for the purpose of comparison, BMI categories for children and adolescents were also classified using WHO 2007 BMI standards (195, 196).

IOTF cut-off references were estimated from six nationally representative surveys from different countries and they were extrapolated from the adult BMI overweight ($\geq 25\text{kg}/m^2$) and obesity ($\geq 30\text{kg}/m^2$) cut-offs (194). In contrast, WHO 2007 standards were formed by combining the results of the WHO Multicentre Growth Reference Study (MGRS) which took place in six cities in USA, Oman, Norway, Brazil, Ghana and India from 1997 to 2003 for children 0 to 71 months (197). The cut-offs for children aged 5 to 19 years old was constructed by pooling data from three data sets: two data sets from the Health Survey of England (HSE), Cycle II (children aged 6–11y) and Cycle III (adolescents aged 12–17y), and the third data set Health and Nutrition Examination Survey (HANES) Cycle I (population aged 1-24y) (198).

Adults

For the adult population (≥ 20 years), I used WHO cut off points, that classified BMI into four categories: underweight ($< 18.5\text{ kg}/m^2$), normal weight (18.5 to $< 25\text{kg}/m^2$), overweight (25 to $< 30\text{kg}/m^2$) and obese ($\geq 30\text{ kg}/m^2$) (199).

In order to make my results as similar as possible to the results already published, I decided to apply the same exclusion criteria used in the ENSANUT 2012 report to exclude individuals with the following extreme BMI data:

- Children 2 to 5: BMI <10.0 kg/m² and BMI >38.0 kg/m²
- Population 5 to 19: BMI <10.0 kg/m² and BMI >58.0 kg/m²
- Adults 20 to 80: BMI <10.0 kg/m² and BMI >58.0 kg/m² or height <1.30m.
- Pregnant or breastfeeding women ≥12 years of age.

Removing individuals with these values eliminated about 0.5% of the total sample (35,200).

3.3 Statistical Analysis

Obesity prevalence was calculated separately for each year (1999/2000, 2002, 2006, 2012) stratified by 17 age groups and by sex. The age groups were defined as follows: children (2-4y and 5-9y); adolescents (10-14y and 15-19y); and adults (5-year age groups from 20-24y to 75-79y and 80+y). The separate estimates from the 1999 and 2000 surveys were combined to calculate the national prevalence for 1999 using direct standardisation for the 1999 population. Additionally, to facilitate the comparison across surveys, the total population obesity prevalence for each of the four data points was age-standardised to the 2012 population. The total analytical sample for the linear analysis with valid BMI was 283,465 individuals (Table 3.1). The study population, of males and females aged 2 to 80y and older classified as obese (BMI≥30kg/m²) was a total of 39,586 individuals.

The projections of future obesity rates were calculated by fitting a linear regression model to extrapolate the prevalence data from 1999/2000, 2002, 2006 and 2012, assuming that the past trends will remain unchanged. The linear model used obesity prevalence as the dependent variable and year as the predictor. The β -coefficients (β) obtained represent the annual percentage point increase in obesity prevalence.

The estimated prevalence of obesity for each year was given by:

$$y = const + (\beta \text{eta} * \text{year})$$

The year 1999 was taken as the baseline year and the results were extrapolated to 2030 (a total of 18 years beyond the measured data); predicted 95% confidence intervals were also calculated for each prevalence. All the analyses were stratified by age group and by sex. In addition, I ran separate projections for broader age groups: 2-9y, 10-19y and 20+y to examine differences in obesity trends between genders. The results for children and adolescents in the main analyses were estimated using the IOTF classification cut-off points. WHO BMI categories were only used in the comparison between BMI cut-off points analyses.

All analyses were conducted using Stata software version 13.0. The SVY module was used in all descriptive and linear regression analysis to account for the complex sampling design of the health surveys.

Individual data linear regression was selected as the regression method of choice as it showed a better fit for the data. Other methods for estimating the future prevalence were tested (i.e. linear regression with aggregated data and nonlinear (i.e. squared). The difference in estimated percentage points (pp) from 2030 estimated obesity prevalence were in general <1 pp between individual data linear regression and aggregated data linear regression. However, I observed differences between 10 pp and 70 pp for both male and female individual data linear estimates and non-linear estimation. The results obtained from the non-linear method, squared estimation showed a large uncertainty. This outcomes showed that the number of available data points was not sufficient to produce reliable prediction intervals to 2030. De Onis et al. reported that (see: Appendix B) using a squared term for analysis could result in wide CIs particularly due from too few data points (201). As recommended by Rokholm, graphically showing the confidence intervals around each measurement point from the linear trend estimates will allow to visually inspect the trend without solely relying on

the authors' choice of statistical test (202). However, as more years of obesity data from Mexican becomes available, it will be possible to check the assumption of linear trend again.

3.4 Results

3.4.1 Historic prevalence of obesity in Mexico

Table 3.2 and Table 3.3 show the descriptive statistics of the prevalence of obesity among the male and female population ≥ 2 years of age from 1999 to 2012. The results showed that obesity prevalence is still increasing over this time period in both males and females.

In males, the total population prevalence of obesity increased from 13.2% (95%CI: 12.8, 13.6) to 19.9% (95%CI: 19.2, 20.7) in 2012, an absolute increase of 6.7 percentage points (pp). This represents an annual increase of 0.5 pp. Overall there was a steady increase in obesity prevalence among adult males in most age groups. The highest prevalence of obesity from all the age groups was found in most surveys in the population aged 35-54y. The highest growth in obesity prevalence was in males 40 to 44 years old that showed an increase in prevalence from 21.7% (95%CI: 18.9, 24.7) in 1999 to 35.9% (95%CI: 32.6, 39.3) in 2012, an absolute increase of 14.2 pp in 13 years. The infant male age group (2-4y) showed a contrasting trend, with a point prevalence that decreased slightly from 4.8% (95%CI: 3.9, 6.0) in 1999 to 3.5% (95%CI: 2.7, 4.4) in 2012. Prevalence of obesity was steady between 2006 (9.1%; 95%CI: 8.1, 10.2) and 2012 (8.9%; 95%CI: 7.8, 10.5) among boys 5-9y (Table 3.2).

The prevalence of obesity among the total female population increased by 0.6 pp each year from 19.2% (95%CI: 18.8, 19.5) in 1999 to 27.4% (95%CI: 26.6, 28.2) in 2012. The highest prevalence of obesity for females in each of the surveys was found in the population aged 45-59y. In the majority of the female adult age groups, the increase in

prevalence between 1999 and 2012 varied annually from 0.6 to 0.8 pp. I found that girls aged 5-9y had no apparent change in obesity prevalence from 2006 (9.2%; 95% CI 8.1, 10.5) to 2012 (9.0%; 95%CI: 8.0, 10.1) (Table 3.3).

Table 3.2 Male obesity prevalence rates in Mexico from 1999 to 2012 by age group in five National Health Examination Surveys*

Age group	ENN 1999/ENSA 2000 [†]		MxFLS-1 2002		ENSANUT 2006		ENSANUT 2012	
	N(n)	%(95%CI)	N(n)	%(95%CI)	N(n)	%(95%CI)	N(n)	%(95%CI)
2-4	3,487,562(2597)	4.8(3.9, 6.0)	2,608,057(858)	3.3(2.0, 2.5)	2,362,308(2658)	4.9(3.9, 6.1)	3,372,261(3410)	3.5(2.7, 4.4)
5-9	5,585,711(4152)	5.9(4.8, 7.1)	5,053,124(1659)	4.6(2.6, 7.9)	4,307,222(5264)	9.1(8.1, 10.2)	5,875,793(6008)	9(7.8, 10.5)
10-14	5,413,653(5443)	6.5(5.5, 7.7)	5,132,380(1730)	6.4(4.6, 8.8)	5,092,009(5589)	9.2(8.1, 10.3)	5,877,197(5066)	11.5(10.0, 13.0)
15-19	4,824,060(3670)	6.3(5.2, 7.5)	4,189,188(1379)	8.5(7.0, 10.4)	3,628,077(3765)	9.3(8.0, 10.7)	5,805,428(4161)	10.6(9.2, 12.2)
20-24	4,301,246(1773)	9.7(7.9, 12.0)	2,833,548(894)	10.3(6.9, 15.0)	2,355,022(1464)	14.7(12.3, 17.5)	5,140,166(1842)	17.5(15.0, 20.4)
25-29	3,570,452(1678)	14.1(12.0, 16.6)	2,782,809(862)	15.9(12.7, 19.7)	1,983,643(1345)	19.5(16.4, 23.1)	3,617,546(1507)	24.4(21.4, 27.7)
30-34	3,070,230(1554)	18.7(16.0, 21.7)	2,814,105(810)	17.5(15.4, 19.8)	2,077,114(1645)	23.2(20.2, 26.5)	3,666,170(1674)	28.1(24.8, 31.6)
35-39	2,729,437(1559)	23.1(20.1, 26.4)	2,397,764(785)	27.2(21.8, 33.4)	2,011,216(1684)	27.7(24.5, 31.2)	3,482,866(1873)	34.2(30.3, 38.3)
40-44	2,132,585(1324)	21.7(18.9, 24.7)	2,012,144(681)	28.1(22.1, 35.1)	1,840,984(1532)	30.0(26.6, 33.6)	3,258,833(1759)	35.9(32.6, 39.3)
45-49	1,720,770(1104)	26.4(22.8, 30.4)	1,947,565(615)	34.4(27.8, 41.7)	1,698,287(1212)	26.3(22.8, 30.1)	3,167,222(1517)	32.6(29.1, 36.3)
50-54	1,406,126(951)	27.8(23.6, 32.4)	1,520,281(505)	32.9(24.8, 42.1)	1,371,305(991)	30.1(26.2, 34.3)	2,664,938(1344)	31.4(27.4, 35.6)
55-59	1,058,842(860)	22.4(18.4, 26.9)	1,228,015(416)	24.9(18.8, 32.3)	1,210,960(800)	30.6(25.2, 36.6)	2,240,191(1119)	25.6(21.5, 30.1)
60-64	916,737(728)	22.2(18.2, 26.7)	965,005(353)	26.2(21.2, 31.9)	1,011,057(708)	25.0(20.8, 29.9)	1,607,408(934)	25.2(21.1, 29.7)
65-69	672,137(656)	25.7(21.3, 30.6)	793,198(307)	20.7(13.5, 30.3)	830,536(602)	21.5(16.8, 27.2)	1,244,429(787)	21.7(17.7, 26.3)
70-74	510,255(494)	18.6(13.0, 25.8)	684,545(240)	20.2(15.8, 25.4)	664,059(493)	16.2(12.4, 20.9)	951,363(674)	23.6(19.0, 28.8)
75-79	307,988(352)	10.2(6.1, 16.7)	527,849(176)	21.6(10.1, 40.3)	422,427(355)	16.0(11.1, 22.6)	669,781(447)	16.1(11.1, 22.6)
80+	317,305(322)	10.3(6.4, 16.1)	467,260(180)	8.4(5.1, 13.6)	407,955(395)	9.0(5.9, 13.3)	681,180(485)	9.3(5.5, 15.2)
Total	42,025,096(29217) [‡]	13.2(12.8, 13.6)	37,956,837(12450)	14.8(8.1, 25.6)	33,274,181(30502)	16.6(15.9, 17.2)	53,322,773(34607)	19.9(19.2, 20.7)
All SD[§]		13.8(13.5, 14.2)		16.0(15.4, 16.7)		17.9(17.5, 18.3)		20.2(19.8, 20.6)

* ENN, (National Nutrition Survey); ENSA (National Health Survey), ENNVIIH-1 (Mexican Family Life Survey); ENSANUT (Health and Nutrition National Survey)

*BMI Cut-off points for 2 to 18 years from IOTF, ≥19 years from WHO.

† ENN 1999/ENSANUT 2000 combined data for population 2 to 9 years of age from ENN 1999, and 10+ from ENSA 2000

‡ Age –standardised total obesity prevalence to the Mexican population for 1999.

§SD Age standardised total obesity prevalence of the Mexican population for 2012

Table 3.3 Female obesity prevalence rates in Mexico from 1999 to 2012 by age group in five National Health Examination Surveys*.

Age group	ENN 1999/ENSA 2000 [†]		MxFLS-1 2002		ENSANUT 2006		ENSANUT 2012	
	N(n)	%(95%CI)	N(n)	%(95%CI)	N(n)	%(95%CI)	N(n)	%(95%CI)
2-4	3,354,329(2473)	5.3(4.3, 6.6)	2,714,208(890)	2.8(1.8, 4.2)	2,293,692(2536)	4.4(3.3, 5.7)	3,392,441(3394)	5.9(4.6, 7.5)
5-9	5,824,584(4231)	6.3(5.4, 7.4)	5,399,231(1692)	5.1(3.8, 6.9)	4,308,151(5225)	9.2(8.1, 10.5)	5,709,803(6000)	9.0(8.0, 10.1)
10-14	5,347,106(5878)	6.0(5.2, 7.1)	5,823,794(1871)	5.5(4.5, 6.6)	4,815,757(5408)	8.3(7.3, 9.4)	5,711,459(4948)	9.2(7.9, 10.8)
15-19	4,791,482(4683)	6.6(5.6, 7.8)	4,704,987(1459)	5.6(3.9, 7.9)	3,836,107(4133)	10.0(8.5, 11.7)	5,273,182(3914)	10.9(9.6, 12.4)
20-24	3,672,841(3652)	13.0(11.4, 14.8)	3,440,202(1090)	13.3(10.4, 16.8)	2,868,500(1875)	14.7(12.6, 17.1)	4,054,882(1818)	20.3(17.6, 23.3)
25-29	3,672,841(3882)	19.6(18.0, 21.3)	3,480,415(1044)	23.1(20.5, 25.9)	2,803,995(2187)	26.5(23.8, 29.4)	3,802,341(1969)	27.9(24.9, 31.1)
30-34	3,232,118(3743)	26.7(24.8, 28.8)	3,630,672(1033)	26.5(23.7, 29.4)	3,021,507(2760)	30.8(28.3, 33.4)	4,423,774(2432)	35.1(32.3, 38.1)
35-39	2,969,45(3581)	32.5(30.2, 35.0)	3,299,960(922)	34.3(31.0, 37.7)	3,079,416(2810)	38.2(35.4, 41.0)	3,936,562(2853)	41.2(38.5, 44.0)
40-44	2,288,960(2993)	38.2(35.7, 40.9)	3,006,803(776)	39.5(36.0, 43.2)	2,851,307(2277)	42.2(39.0, 45.4)	3,633,956(2510)	43.0(40.2, 45.8)
45-49	1,871,905(2265)	42.0(38.9, 45.1)	2,430,886(608)	41.0(33.4, 49.1)	2,266,140(1697)	44.5(41.0, 48.0)	3,390,011(2164)	49.8(46.2, 53.4)
50-54	1,500,396(1985)	41.0(37.9, 44.1)	1,992,697(465)	37.1(33.9, 40.3)	1,911,310(1368)	45.3(41.3, 49.3)	2,829,126(1714)	47.7(43.8, 51.5)
55-59	1,149,524(1673)	39.5(35.0, 44.2)	1,459,664(423)	45.4(39.6, 51.3)	1,406,797(1026)	44.1(39.2, 49.1)	2,538,818(1484)	47.9(43.6, 52.3)
60-64	1,024,911(1369)	36.6(33.0, 40.4)	1,181,761(423)	43.0(34.6, 51.8)	1,255,672(964)	46.6(41.9, 51.3)	1,838,848(1157)	44.5(39.8, 49.2)
65-69	752,719(1089)	34.9(30.9, 39.0)	1,119,457(342)	34.5(27.7, 42.1)	1,004,354(769)	38.4(33.4, 43.7)	1,442,930(916)	42.8(37.6, 48.2)
70-74	559,029(777)	29.5(24.6, 35.1)	807,063(250)	27.8(19.2, 38.4)	774,385(687)	36.3(30.9, 42.0)	1,062,335(722)	39.0(33.0, 45.3)
75-79	339,272(529)	24.0(19.3, 29.5)	511,230(165)	28.7(22.8, 35.4)	546,251(477)	26.6(20.6, 33.6)	792,290(541)	29.8(23.6, 36.9)
80+	353,157(443)	15.9(11.0, 22.5)	474,746(175)	21.2(15.8, 27.9)	579,483(470)	14.7(10.8, 19.6)	759,178(513)	20.9(15.6, 27.4)
Total	42,704,419(45246 [‡])	19.2(18.8, 19.5)	45,477,776(13628)	20.3(12.0, 32.3)	39,622,824(36669)	24.6(23.8, 25.3)	54,591,937(39049)	27.4(26.6, 28.2)
All SD[§]		20.6(20.2, 21.0)		22.0(21.3, 22.7)		25.6(25.2, 26.1)		28.0(27.8, 28.5)

* ENN, (National Nutrition Survey); ENSA (National Health Survey), ENNVIH-1 (Mexican Family Life Survey); ENSANUT (Health and Nutrition National Survey)

*BMI Cut-off points for 2 to 18 years from IOTF, ≥19 years from WHO.

† ENN 1999/ENSANUT 2000 combined data for population 2 to 9 years of age from ENN 1999, and 10+ from ENSA 2000

‡ Age –standardised total obesity prevalence to the Mexican population for 1999.

§SD Age standardised total obesity prevalence of the Mexican population for 2012

3.4.2 Linear regression analyses for projecting obesity prevalence

The constant (representing the obesity prevalence in the base year, 1999) and β -coefficients (representing the annual percentage points increase) obtained from the linear regression model are shown in Table 3.4. The highest annual average increase in male obesity prevalence was in the population 40 to 44 years of age ($\beta= 1.009$; SE= 0.182). Among females, the age group 30 to 34 years had one of the highest annual increases ($\beta= 0.707$; SE= 0.125), together with the 70 to 74 years age group ($\beta= 0.863$; SE= 0.283). Most of the coefficients indicated an annual increase except the coefficient for males 2 to 4 years of age, 65 to 69y; and 80+y where I found signs of stability ($\beta= -0.056$; SE= 0.099; $\beta= -0.215$; SE= 0.238; and $\beta= -0.042$; SE= 0.099, respectively). Adult females in general presented a higher constant (higher prevalence of obesity in base year) and higher slope coefficients (higher annual increase) than adult males.

Table 3.4 β -coefficients and constants obtained by a linear regression model stratified by sex and age group.

Age group	Males		Females	
	β -Coef(SE) [*]	Const(SE)	β -Coef(SE)	Const(SE)
2-4	-0.056(0.099)	4.435(0.742)	0.107(0.152)	3.945(1.147)
5-9	0.326(0.173)	5.267(1.307)	0.276(0.161)	5.846(1.212)
10-14	0.416(0.076)	5.979(0.575)	0.290(0.093)	5.595(0.697)
15-19	0.307(0.073)	6.894(0.549)	0.406(0.154)	5.946(1.158)
20-24	0.647(0.102)	9.340(0.766)	0.575(0.139)	12.023(1.046)
25-29	0.808(0.034)	13.836(0.255)	0.624(0.151)	20.698(1.136)
30-34	0.816(0.193)	17.181(1.455)	0.707(0.125)	25.707(0.945)
35-39	0.792(0.140)	23.508(1.051)	0.689(0.065)	32.589(0.493)
40-44	1.009(0.182)	23.130(1.367)	0.379(0.083)	38.562(0.622)
45-49	0.237(0.499)	28.566(3.759)	0.658(0.165)	40.542(1.243)
50-54	0.158(0.248)	29.644(1.868)	0.682(0.340)	38.822(2.564)
55-59	0.278(0.388)	24.282(2.919)	0.534(0.233)	41.162(1.756)
60-64	0.146(0.191)	23.82(1.439)	0.548(0.377)	39.502(2.840)
65-69	-0.215(0.238)	23.619(1.793)	0.665(0.122)	33.830(0.917)
70-74	0.302(0.326)	17.883(2.453)	0.863(0.283)	28.189(2.134)
75-79	0.193(0.571)	14.875(4.303)	0.343(0.213)	25.323(1.602)
80+	-0.042(0.094)	9.480(0.706)	0.209(0.396)	16.974(2.984)

*SE: standard error. β -coef: β -coefficient
Baseline year for this analysis, 1999.

3.4.3 Projected obesity prevalence to 2030

Table 3.5 and Table 3.6 show the projected trajectories of obesity prevalence in the male and female Mexican population every five years until 2030 assuming the observed trends from 1999 to 2012 continue.

Among males, those aged 40-44y showed the highest projected obesity prevalence; reaching over one in two males by the year 2030 (54.4%; 95%CI: 45.3, 63.5). The lowest prevalence rates would belong to the youngest (2-4y) and oldest (≥ 80 y) age groups: 2.7% (95%CI: 0.0, 7.7) and 8.2% (95%CI: 3.4, 12.9) respectively (Table 3.5). Estimated obesity prevalence $\geq 50\%$ by 2030 was observed only in males 35 to 44 years old.

The results for the projected obesity prevalence in the female population showed that by 2030, obesity prevalence would reach 50% or higher for females aged between 35 and 74 years. The highest prevalence rate of obesity in females by 2030 would be found in the population aged 45-49y: (61.0%; 95%CI: 52.6, 69.3) (Table 3.6).

Table 3.5 Predicted male obesity prevalence from 2015 to 2030 by age group.

Age group	2015		2020		2025		2030	
	%	(95% CI)	%	(95% CI)	%	(95% CI)	%	(95% CI)
2-4	3.5	1.3, 5.7	3.3	0.2, 6.4	3.0	0.0*, 7.0	2.7	0.0*, 7.7
5-9	10.5	6.6, 14.3	12.1	6.7, 17.6	13.7	6.7, 20.8	15.4	6.6, 24.1
10-14	12.6	10.9, 14.3	14.7	12.3, 17.1	16.8	13.7, 19.9	18.9	15.0, 22.7
15-19	11.8	10.2, 13.4	13.3	11.1, 15.6	14.9	11.9, 17.9	16.4	12.7, 20.1
20-24	19.7	17.4, 22.0	22.9	19.7, 26.1	26.2	22, 30.3	29.4	24.3, 34.5
25-29	26.8	26.0, 27.5	30.8	29.7, 31.9	34.8	33.5, 36.2	38.9	37.2, 40.6
30-34	30.2	25.9, 34.5	34.3	28.2, 40.4	38.4	30.5, 46.3	42.5	32.7, 52.2
35-39	36.2	33.1, 39.3	40.1	35.8, 44.5	48.0	41.0, 55.1	52.0	43.6, 60.4
40-44	39.3	35.2, 43.3	44.3	38.6, 50.0	49.4	41.9, 56.8	54.4	45.3, 63.5
45-49	32.4	21.3, 43.5	33.5	17.9, 49.2	34.7	14.4, 55.1	35.9	10.8, 61.1
50-54	32.2	26.7, 37.7	33.0	25.2, 40.7	33.8	23.6, 43.9	34.5	22.0, 47.0
55-59	28.7	20.1, 37.3	30.1	18.0, 42.3	31.5	15.7, 47.3	32.9	13.4, 52.4
60-64	26.2	21.9, 30.4	26.9	20.9, 32.9	27.6	19.8, 35.4	28.3	18.7, 38
65-69	20.2	14.9, 25.5	19.1	11.6, 26.6	18.0	8.3, 27.7	17.0	5.0, 29.0
70-74	22.7	15.5, 30.0	24.2	14.0, 34.4	25.7	12.4, 39.0	27.2	10.8, 43.7
75-79	18.0	5.3, 30.7	18.9	1.0, 36.8	19.9	0.0*, 43.2	20.8	0.0*, 49.6
80+	8.8	6.7, 10.9	8.6	5.7, 11.5	8.4	4.6, 12.2	8.2	3.4, 12.9

*Estimates of projected obesity prevalence below "<0"

CI: confidence interval

Table 3.6 Predicted female obesity prevalence from 2015 to 2030 by age group.

Age Group	2015		2020		2025		2030	
	%	(95% CI)	%	(95% CI)	%	(95% CI)	%	(95% CI)
2-4	5.7	2.3, 9.0	6.2	1.4, 11.0	6.7	0.5, 13.0	7.3	0.0*, 14.9
5-9	10.3	6.7, 13.8	11.6	6.6, 16.7	13.0	6.4, 19.6	14.4	6.3, 22.5
10-14	10.2	8.2, 12.3	11.7	8.8, 14.6	13.1	9.4, 16.9	14.6	9.9, 19.2
15-19	12.4	9.0, 15.9	14.5	9.6, 19.3	16.5	10.2, 22.8	18.5	10.8, 26.3
20-24	21.2	18.1, 24.3	24.1	19.7, 28.4	27.0	21.3, 32.6	29.8	22.8, 36.8
25-29	30.7	27.3, 34.0	33.8	29.1, 38.5	36.9	30.8, 43.1	40.0	32.4, 47.6
30-34	37.0	34.2, 39.8	40.6	36.6, 44.5	44.1	39.0, 49.2	47.6	41.3, 53.9
35-39	43.6	42.2, 45.1	47.1	45.0, 49.1	53.9	50.6, 57.2	57.4	53.5, 61.3
40-44	44.6	42.8, 46.5	46.5	43.9, 49.1	48.4	45.1, 51.8	50.3	46.2, 54.5
45-49	51.1	47.4, 54.7	54.4	49.2, 59.5	57.7	50.9, 64.4	61.0	52.6, 69.3
50-54	49.7	42.2, 57.3	53.1	42.5, 63.8	56.5	42.6, 70.4	59.9	42.8, 77.1
55-59	49.7	44.5, 54.9	52.4	45.1, 59.7	55.0	45.5, 64.6	57.7	46.0, 69.5
60-64	48.3	39.9, 56.6	51.0	39.2, 62.8	53.7	38.3, 69.1	56.5	37.5, 75.5
65-69	44.5	41.8, 47.2	47.8	44.0, 51.6	51.1	46.2, 56.1	54.5	48.3, 60.6
70-74	42.0	35.7, 48.3	46.3	37.4, 55.2	50.6	39.1, 62.2	54.9	40.7, 69.2
75-79	30.8	26.1, 35.5	32.5	25.9, 39.2	34.2	25.6, 42.9	36.0	25.2, 46.7
80+	20.3	11.5, 29.1	21.4	8.9, 33.8	22.4	6.2, 38.6	23.5	3.5, 43.4

*Estimates of projected obesity prevalence below “<0”

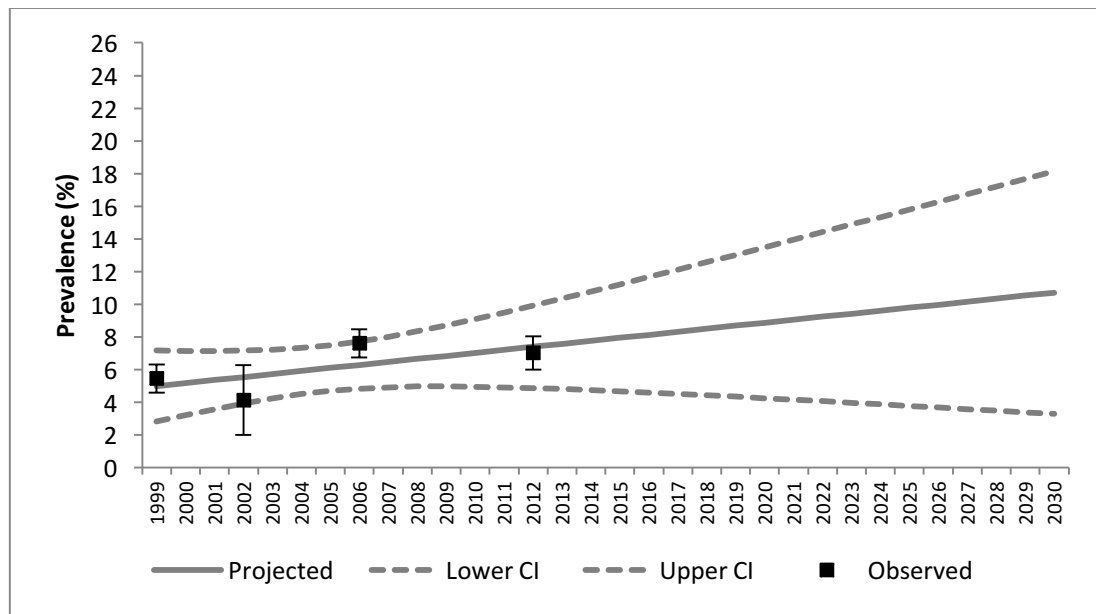
CI: confidence interval

Children and adolescents obesity future trends

Using the IOTF classification, my projections based on a linear trend suggested that by the year 2030, obesity prevalence in boys aged 2 to 9y would be 10.7% (95%CI: 3.3, 18.1) and 11.8% (95%CI: 4.9, 18.6) for girls (Figure 3-1 and Figure 3-2)

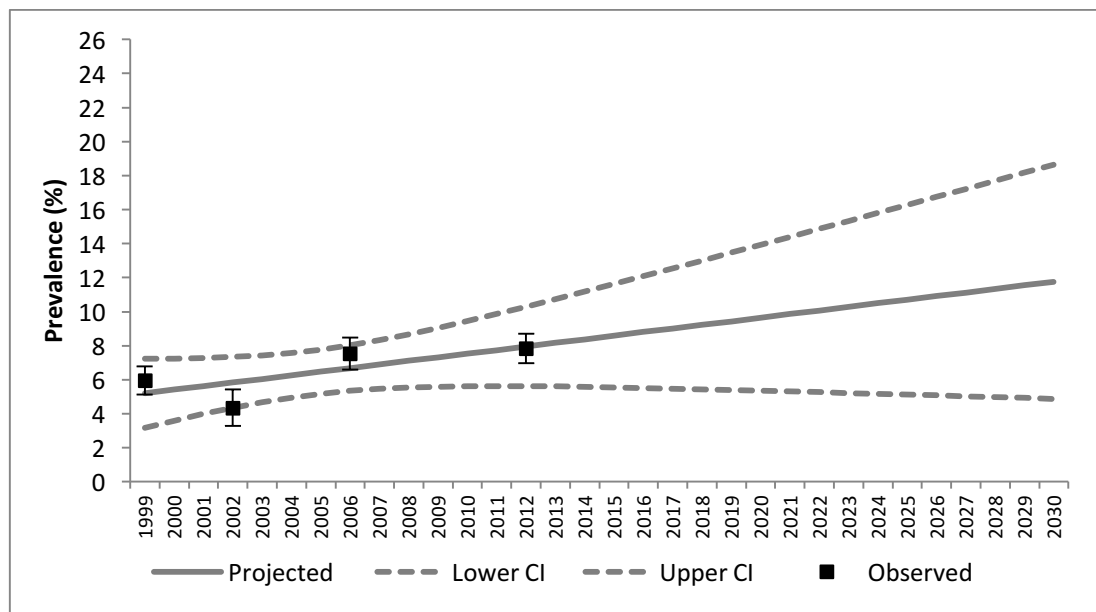
The male adolescent population (10-19y) is projected to have an obesity prevalence of 14.1% (95%CI: 13.3, 14.7) in 2020, with an increase of around 0.4 pp every year to reach 17.7% (95%CI: 9.6, 23.6) in 2030. Among female adolescents, the obese population would be 13.6% (95%CI: 10.0, 17.3) in 2020, and would increase by 3.8 pp to reach a level of 17.4% (95%CI: 11.6, 23.3) in 2030 (Figure 3-3 and Figure 3-4).

Figure 3-1 Observed and projected obesity prevalence in boys 2 to 9 years of age to 2030. Results from a linear regression analysis.



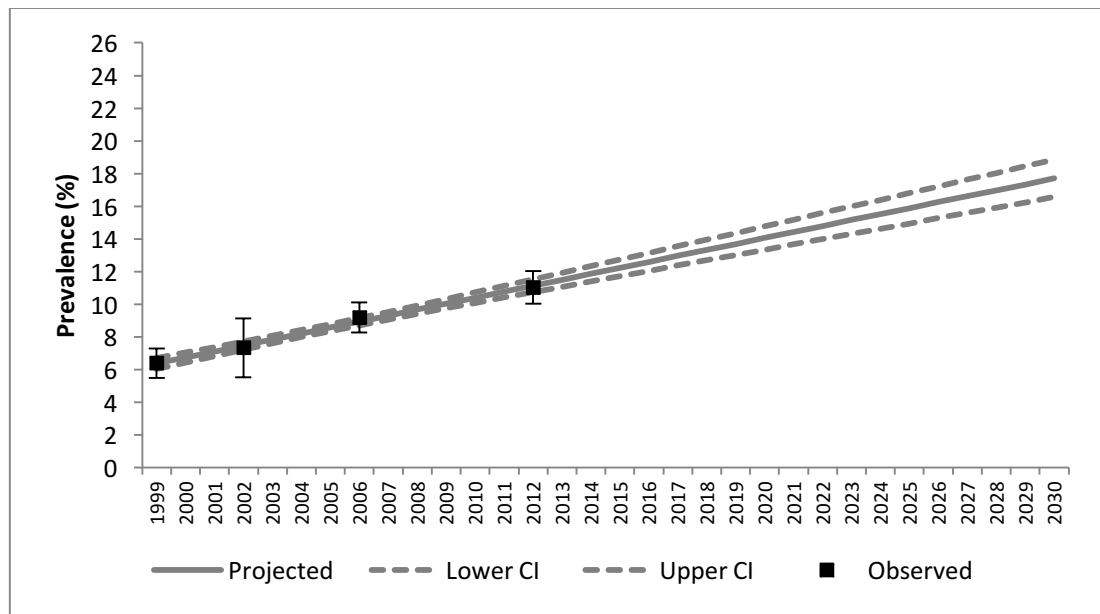
Dotted lines represent the upper and lower 95% CI of the forecast obesity rates. The observed data shows the reported prevalence from Mexico's national surveys; each dot represents one data point.

Figure 3-2 Observed and projected obesity prevalence in girls 2 to 9 years of age to 2030. Results from a linear regression analysis.



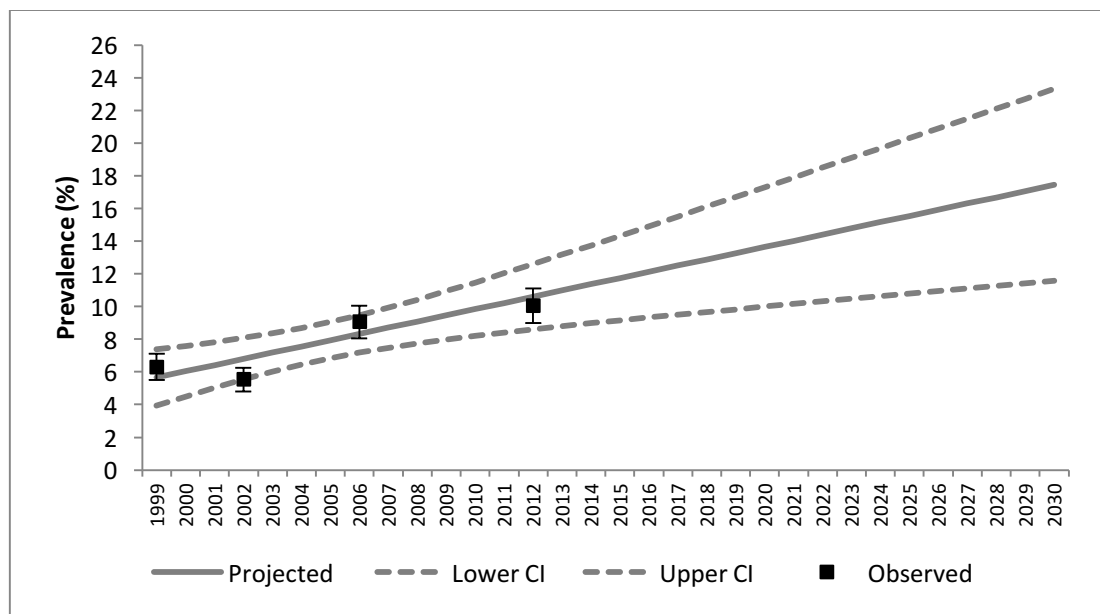
Dotted lines represent the upper and lower 95% CI of the forecast obesity rates. The observed data shows the reported prevalence from Mexico's national surveys; each dot represents one data point.

Figure 3-3 Observed and projected obesity prevalence in male adolescents 10 to 19 years of age to 2030. Results from a linear regression analysis.



Dotted lines represent the upper and lower 95% CI of the forecast obesity rates. The observed data shows the reported prevalence from Mexico's national surveys; each dot represents one data point.

Figure 3-4 Observed and projected obesity prevalence in female adolescents 10 to 19 years of age to 2030. Results from a linear regression analysis.



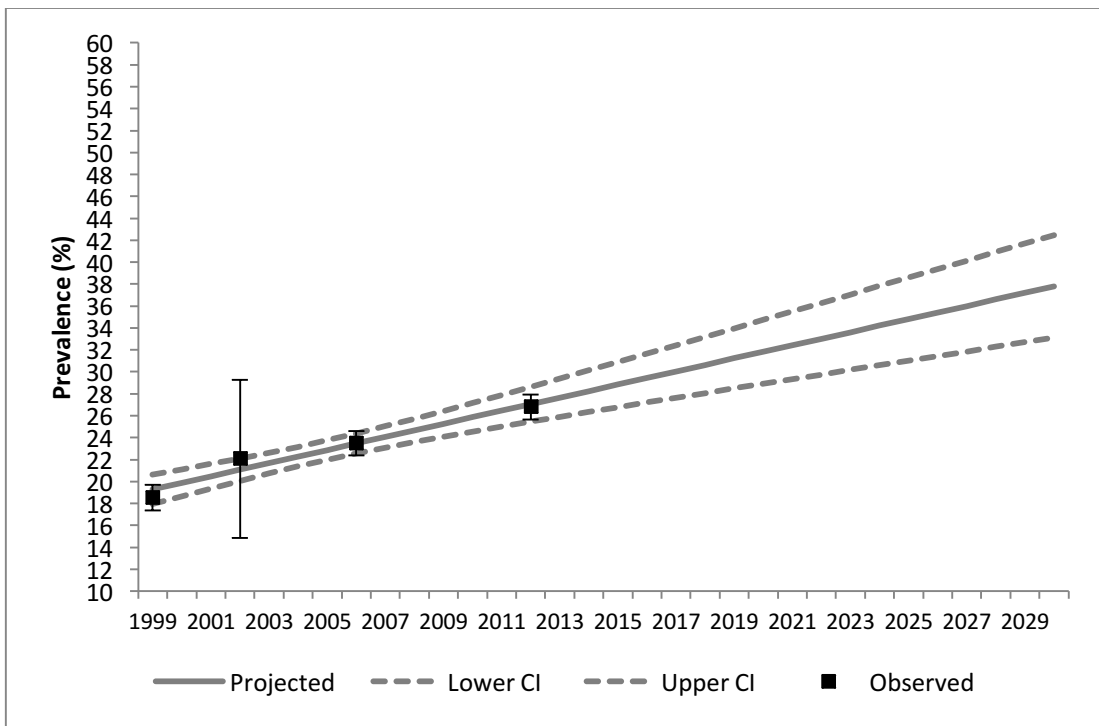
Dotted lines represent the upper and lower 95% CI of the forecast obesity rates. The observed data shows the reported prevalence from Mexico's national surveys; each dot represents one data point.

Adult obesity future trends.

The linear regression analysis for the adult population showed that the obesity prevalence for males would increase by 0.6 pp annually. For males, the obesity prevalence would be expected to reach 30% (95%CI: 27.6, 32.4) by 2017, 35% (95%CI: 31.0, 38.6) by 2025, and increase to almost 40% by 2030 (37.8%; 95%CI: 31.1, 42.5) (Figure 3-5)

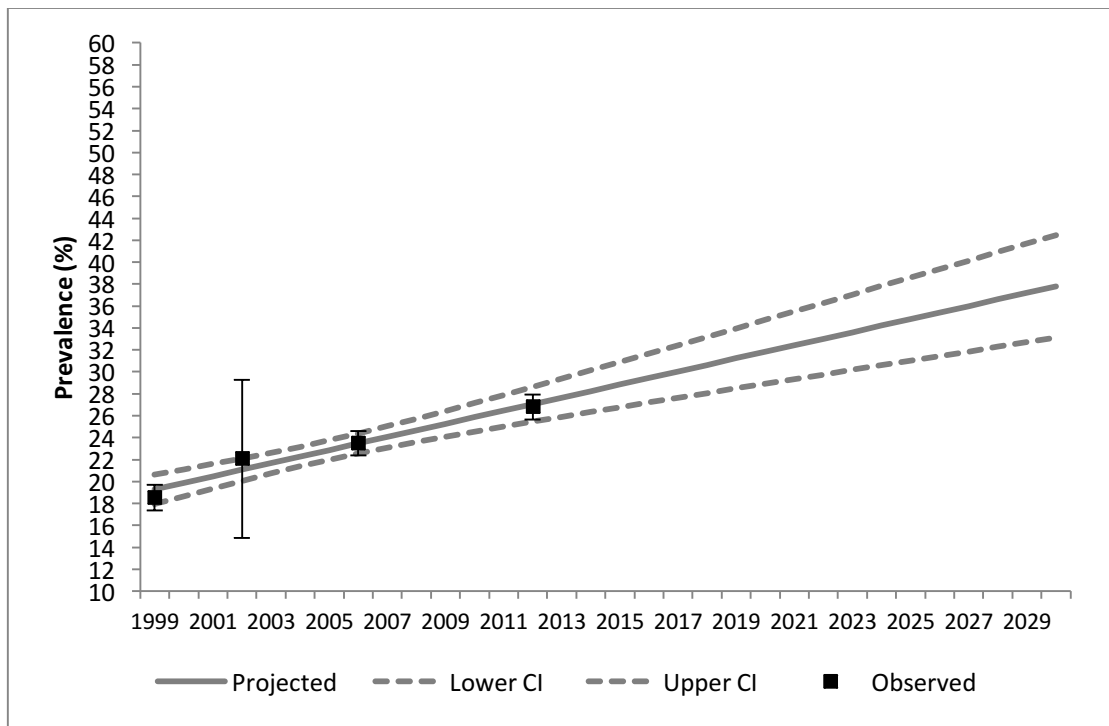
The rates of projected obesity for Mexican females ≥ 20 years of age were higher than for males. My analysis projected a prevalence of 40.7% (95%CI: 39.2, 42.3) in 2015; 48.3% (95%CI: 45.5, 51.2) by 2025; by 2030, over 50% of the adult female population would be obese (52.1%; 95%CI: 48.6, 55.7) (Figure 3.6). This represented an increase every year since 1999 of almost 0.8 pp.

Figure 3-5 Observed and projected obesity prevalence in male adults 20+ years of age to 2030. Results from a linear regression analysis.



Dotted lines represent the upper and lower 95% CI of the forecast obesity rates. The observed data shows the reported prevalence from Mexico's national surveys; each dot represents one data point.*The graph Y axis starts at 10%

Figure 3-6 Observed and projected obesity prevalence in female adults 20+ years of age to 2030. Results from a linear regression analysis.



Dotted lines represent the upper and lower 95% CI of the forecast obesity rates. The observed data shows the reported prevalence from Mexico's national surveys; each dot represents one data point.*The graph Y axis starts at 10%

3.4.4 Difference in projected obesity rates between the IOTF and the WHO body mass index classification for children and adolescents.

Children 2 to 9 years old

My findings for comparing projected obesity trends between the IOTF and the WHO 2007 body mass index cut-off points for children showed that obesity prevalence estimates using the IOTF classification thresholds were between 5 pp and 10 pp lower than when using the WHO cut-off points.

For boys aged 2 to 9 years, obesity prevalence by 2020 was projected to be 8.9% (95%CI: 4.3, 13.5) using the IOTF thresholds and 16.8% (95%CI: 11.8, 21.8) using the WHO cut-off points. This represents an absolute difference of 8 pp between the two classifications. This difference increased to 9.3 pp by 2030 (IOTF: 10.7%; 95%CI: 3.3, 18.1; WHO: 20.0%; 95%CI: 12.0, 28.0) (Figure 3-7).

Differences between the two cut-off points for girls were not as marked as for boys. The difference in estimated obesity prevalence varied around 3 pp in all the projected years, with the WHO estimates being higher than the IOTF. By 2030, the IOTF obesity prevalence for girls aged 2-9y was projected to be 11.8% (95%CI: 4.9, 18.6) compared with 15.0% (95%CI: 8.9, 21.0) for the WHO thresholds (Figure 3-8).

Adolescents 10 to 19 years old

Among the total adolescent population (10-19y), the difference between the projected obesity prevalence for 2030 using the IOTF and the WHO cut-off points were smaller than for children aged 2-9y.

For adolescent males, the IOTF obesity projection was estimated to be 17.7% (95%CI: 16.6, 18.9) in 2030. Using the WHO BMI classification, the future projected obesity rate

was 24.3% (95%CI: 21.5, 27.1) in 2030, a prevalence estimated to be 6.6 pp higher than the IOTF figure (Figure 3-9).

In female adolescents, the observed differences between the IOTF and the WHO thresholds were smaller than for males. IOTF projected obesity estimates for 2020 were 2 pp lower than WHO estimates (IOTF: 13.6%; 95%CI: 10.0, 17.3; WHO: 15.5%; 95%CI: 11.2, 19.9). By 2030, projected obesity prevalence was 17.4% (95%CI: 11.6, 23.3) using the IOTF cut-off points and 19.2% (95%CI: 12.2, 26.2) with the WHO thresholds representing an absolute difference of 1.7 pp higher in the projected prevalence of obesity using the WHO 2007 BMI cut-off points than the IOTF (Figure 3-10).

Figure 3-7 Comparison between future trends of obesity prevalence using the IOTF and the WHO cut-off points in boys 2 to 9 years of age.

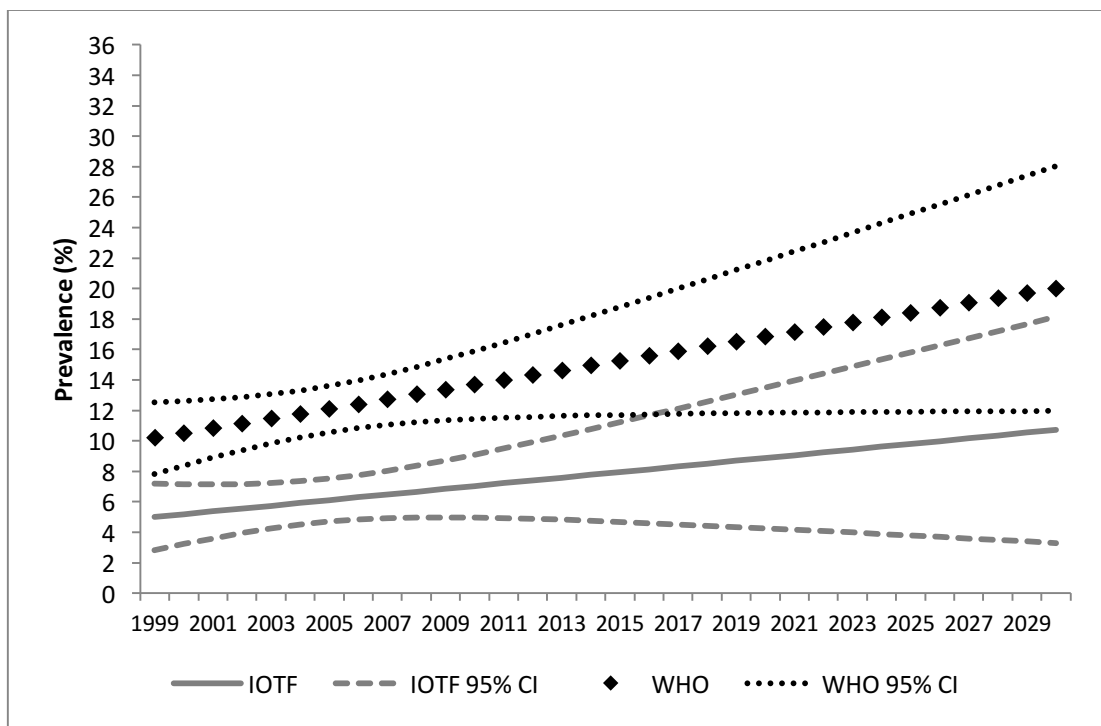


Figure 3-8 Comparison between future trends of obesity prevalence using the IOTF and the WHO cut-off points in girls 2 to 9 years of age.

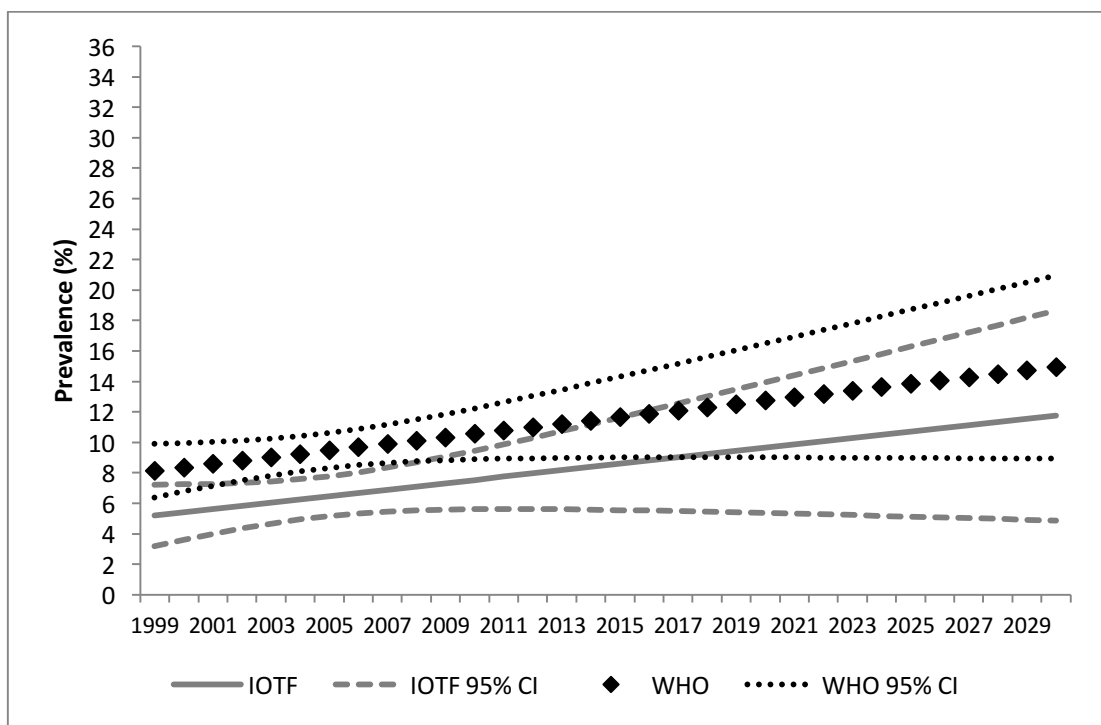


Figure 3-9 Comparison between future trends of obesity prevalence using the IOTF and the WHO cut-off points in male adolescents 10 to 19 years of age.

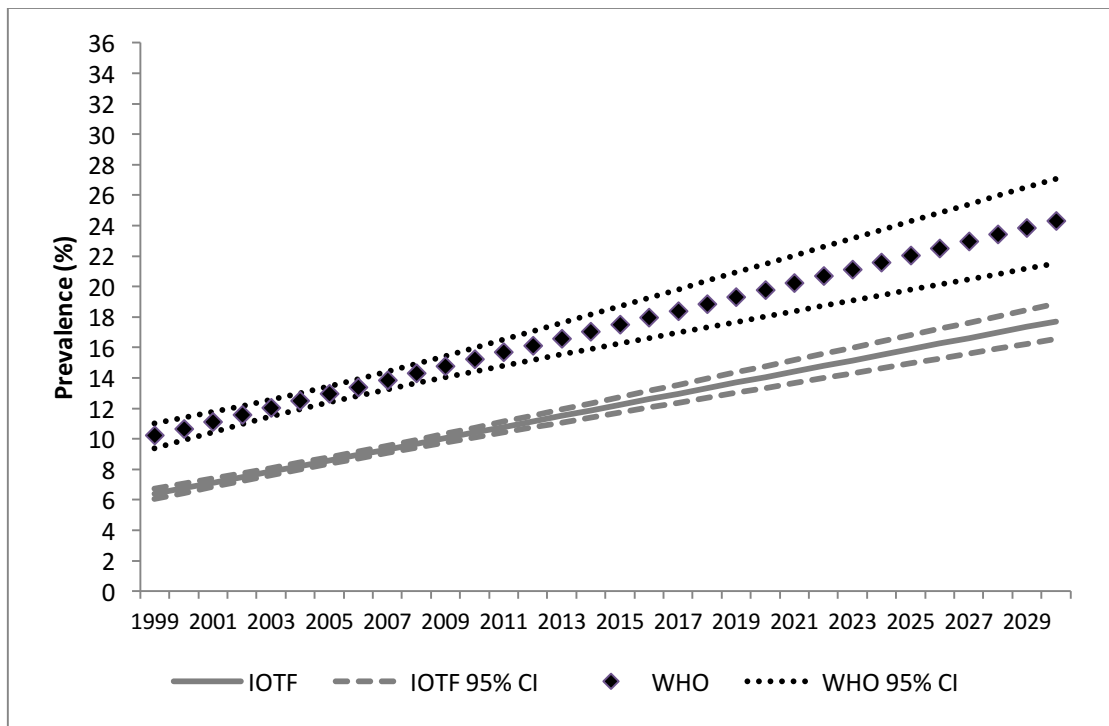
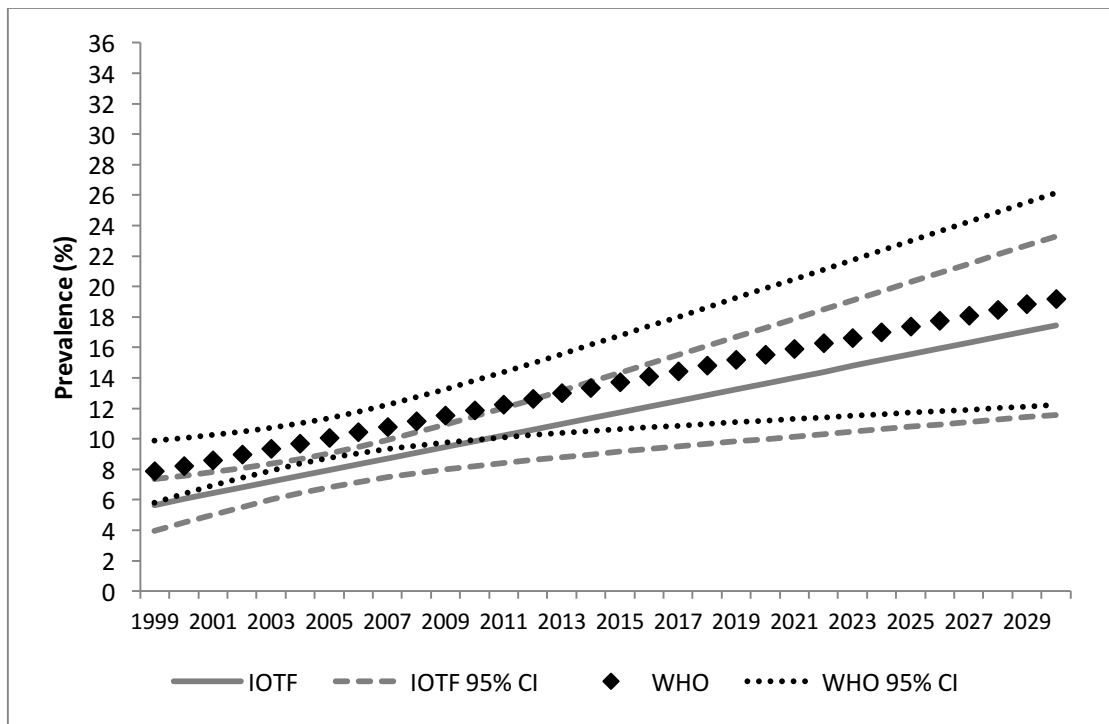


Figure 3-10 Comparison between future trends of obesity prevalence using the IOTF and the WHO cut-off points in female adolescents 10 to 19 years of age.



3.5 Discussion

According to my analysis, the overall male observed obesity prevalence increased by almost 7 pp from 1999 to 2012 and for females by about 8 pp. The biggest growth in obesity prevalence from 1999 to 2012 was seen in the adult population aged 25 to 44y. My analysis projected that if these trends continue to increase at the same pace, by the year 2030 there will be about 48 million individuals (≥ 2 years) classed as being obese in Mexico. Among the total projected obese population, the highest prevalence would be observed in females ≥ 20 years with an estimated obesity prevalence of around 52%, which could represent that by 2030, one of every two adult females will be obese (approximate 26 million females with a BMI $\geq 30\text{kg/m}^2$).

Even though most age groups in both sexes showed an increase in obesity rates, my results showed that the growth of obesity in both children and adolescents has been levelling off in both genders, and in one age group for boys obesity has started to decrease. The observed obesity prevalence in 1999 for male children (2-9y) was 5.5% and increased by 1.5 pp by 2012 (7.0%). In male adolescents the increase from 1999 (6.4%) to 2012 (11.0%) was 4.6 pp. However, the prevalence over the last six years (2006 and 2012) increased only slightly (9.2% to 11.0%, respectively). Similar results were found in females 2 to 19 years of age. From 1999 (6.0%) to 2012 (7.8%) the obesity rates among girls 2 to 9 years increased by only 2 pp, and in female adolescents rates increased by 4.2 pp between those same years (6.3% to 10.5%, respectively). The increase slowed down in the last six years where in both age groups, I observed an increase of around 1 pp between 2006 and 2012 (Table 3.1 and Table 3.2).

My results are corroborated by the ones reported in the latest Mexican Health and Nutrition survey 2012, using the same database but with children and adolescents BMI categorised using the WHO 2007, cut-off points, which showed that children aged 5 to 11y did not show an increase in the combined prevalence of overweight and obesity

between 2006 and 2012. It also showed that from 1999 to 2006 the yearly increase was 1.1 pp for adolescents (12-19y), and that the increase between 2006 and 2012 was only 0.3 pp/year (203).

Data quality, as mentioned before, has an important influence on the projected estimates. A clear example of this can be observed on the influence that values from the MxFLS-1 had on the projected estimates. MxFLS-1 was designed to be a national representative survey, however, the size of the analytical sample was smaller than the samples from the other surveys used. As a consequence, the obesity prevalence estimates from this data point showed wider 95% CI than the corresponding estimates from other surveys. These values were taken into account when calculating the projections and therefore had an effect on the width of the 95% confidence intervals of the mean.

This is not the first attempt to forecast Mexican obesity trends. "The Foresight model" previously estimated future obesity rates in the Mexican population. The authors reported that by 2030, obesity prevalence in the Mexican population aged $\geq 20y$ will be 43% for men and 49% for women. In contrast, my study showed prevalence of 37.8% for men and 52.1% for women. This represents that my analysis projected obesity prevalence was 5.2 pp lower for males and 3.1 pp higher for females than the forecasted prevalence from the Foresight model (115). There are two possible reasons for these differences: Firstly, the Foresight model used ENSANUT 2006 as the final data point for the projections, therefore not taking into account the latest prevalence from the most recent survey, ENSANUT 2012. Secondly, due to the Foresight model obesity projections taking into account the transition rates between normal, overweight and obesity when modelling the future trends, an aspect that my analysis did not include.

There are different BMI classifications available for children and adolescent populations; the majority of studies that previously reported obesity prevalence in the

Mexican population used the WHO 2007 BMI classification. However, I decided to calculate projections using also the IOTF cut off points in my analyses to ensure comparability with other studies conducted worldwide (152). It is important to take into account that there is clearly a difference in the prevalence of childhood and adolescent obesity according to which threshold is used. My outcomes based on the WHO cut off points showed a higher prevalence of obesity than the IOTF thresholds. The classification effect was more pronounced in boys than in girls; and in younger age groups. The most affected age group was boys 2 to 9 years of age, with the difference in the projected obesity prevalence being 10 pp higher when using WHO cut-offs; by 2030, obesity projections were estimated to be 10.7% (95%CI 3.3, 18.1) with IOTF vs. 20.0% (95%CI 12.0, 28.0%) with WHO cut-off points. My results concur well with other studies. For example, results from the Canadian Health Measures survey 2009-2011 reported that the difference in prevalence between the WHO and the IOTF cut-offs was more pronounced in the population aged 5-11y than 12-17y (204, 205). Their results showed that only 72% of the children classified as obese using the WHO BMI classification would be classified as obese with the IOTF classification. Similar results were also found in other populations, including China, Russia and USA (206).

The MexOb-Model first sub-model has some limitations that are necessary to take into account when interpreting the results. By using a linear regression method to forecast obesity, I am assuming that the historic trends of obesity prevalence will continue at the same pace of change until 2030. However, it is highly probable that these outcomes may be influenced by external variables that could modify the rate of change in obesity prevalence, such as: education, socio-economic status, diet, implementation of preventive policies and interventions, etc.

Using linear trends for forecasting have been shown to produce unrealistic scenarios of overestimations, when calculating long term projections (207). This method does not consider, as other methods (non-linear) do, the potential effect of circumstances such as levelling off of the prevalence, could have on the future projections (137, 153). Von

Ruesten et al. (153) compared two methods for forecasting: linear and log-transformed (non-linear) methods to observe the differences between their estimated projections. Their results showed that a linear trend fitted more accurately a scenario in which obesity prevalence increases in a relative linear way, compared to a log transformed method which fitted better a population in which the increase in prevalence started to slow down or reach a saturation point. To overcome the limitations of the use of linear trends to estimate my projected obesity prevalence, I decided to estimate only a medium-term forecast (15 years) to avoid the possibility of unrealistic projections, as part of the overall model. I also performed a sensitivity analysis to illustrate uncertainty around the model parameters that increase the size of the obese population (β -coefficients from the estimated linear trends and growth ratio), to take into account the possibility of lower or higher estimates of the rate of increase in obesity prevalence (see: Chapter 6).

However, it is possible that the future Mexican Health and Nutrition survey planned for 2018 could show a levelling-off of obesity prevalence in the adult population, like the levelling-off that has been recently observed in Mexican children and in other populations (152, 208-210). Therefore, I will have to consider for future possible modifications to the model to incorporate non-linear trends of obesity prevalence into the design of the MexOb-Model.

Furthermore, the data used to feed the model is based on repeated cross-sectional surveys and each of the five surveys contained independent probability samples at each measurement occasion, and this does not allow taking into account the dynamic there is with respect to age (153). However, this effect can only be observed using longitudinal studies and unfortunately, results from a Mexican longitudinal study were not available.

Finally, the MexOb-Model did not consider for the estimations of the projected obesity prevalence the effect of the rates of transition between BMI groups (normal, overweight and obese) that could occur during this 15 year period as was done for the Foresight model projections. However, as a cross-validation exercise, I compared the MexOb-Model obesity estimates with those from the Foresight model to observe if there was a noticeable difference between the two methods. The results of this exercise are described in Chapter 5.

3.6 Conclusions

Mexico's future regarding obesity prevalence does not look promising. Even though the growth in prevalence has been slowing in younger age groups, the obesity prevalence for adults continues to increase, and by 2030 more than 35% of the adult population, around 17% of adolescents, and 10% of children will be classed as obese, if the past trends continue to 2030 at the same pace. These future trends will, as a consequence, have a great impact on Mexico's health and health care services and impact negatively on the productivity of the population.

Chapter 4. Mexican Obesity Forecast Model (MexOb-Model). Data sources, methods for parameter derivation and model structure

4.1 Introduction

The Mexican Obesity Forecast Model (MexOb-Model) is formed by two sub-models. The first sub-model estimates trends of the future prevalence of obesity in the Mexican population. This model was described previously, in Chapter 3. This chapter describes the structure of the second sub-model. The MexOb-Model, is a computer simulation model composed of two sub-models that were developed to estimate future obesity prevalence and its health consequences in the Mexican adult population (20 to 79 years old) from 2015 to 2030.

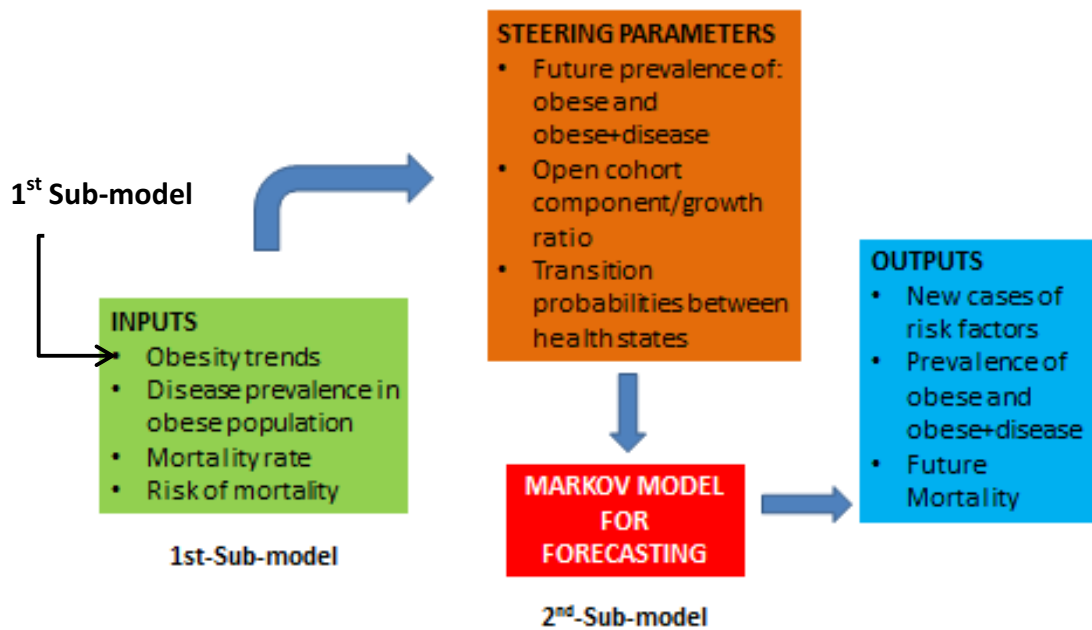
The MexOb-Model purpose was to answer the following research questions: 1) what will the obesity prevalence in Mexico be in 2030?; 2) how does it vary between different age groups and gender?; 3) how will the future prevalence of obesity contribute to the incidence and mortality of hypertension, type 2 diabetes mellitus, hypertriglyceridaemia and hypercholesterolaemia in the obese adult population?; and 4) how will the size of the health burden associated with obesity differ if I reduce, in different degrees, the projected increase in the prevalence of obesity in the population? This model has the capacity to be adapted to estimate the future health effects of possible obesity preventive interventions, policies or programmes implemented at a national level. The MexOb-Model is a hybrid model that was developed using the Foresight model (118) and the Impact model (122, 211, 212) as guides, as both these population simulation models aim to forecast the future trends of non-communicable diseases.

The inputs for the MexOb-Model were: prevalence of obesity, and of being obese with a cardiometabolic risk factor (obese-disease) for the adult Mexican population, mortality data, and disease-specific mortality risk (expressed as risk ratios and hazard ratios). The model's steering parameters were: the future prevalence of obesity with

and without a cardiometabolic risk factor in Mexican adults (obese-disease and obese, respectively), an open cohort component, a growth ratio, and a set of transition probabilities for moving between health states: obese, obese-disease, obese-death, and obese-disease-death. The MexOb-Model's outputs were: prevalence and number of new cases of obesity associated cardiometabolic risk factors in the obese population, and the number of deaths in the obese with and without disease population (Figure 4-1). All of these parameters were stratified by age group and sex. Analyses were performed in three five-year period cycles to represent the 15 year time-period from 2015 to 2030.

This chapter describes the process of development for the second sub-model of the MexOb-Model: the data sources, and the methods used to estimate the input data to feed the model, calculate the transition probabilities between the health states (obese, disease and death), and produce the MexOb-Model specific outcomes for the four diseases.

Figure 4-1 MexOb-Model diagram of data use



4.2 The MexOb-Model second sub-model

The second sub-model integrates the information from the first sub-model (linear regression analysis) to estimate the future prevalence, incidence, and mortality of four obesity-related cardiometabolic risk factors: hypertension (HT), type 2 diabetes mellitus (T2DM), hypertriglyceridaemia (HTG), and hypercholesterolaemia (HCl). The target population of the MexOb-Model is Mexican obese adults (20 to 79 years old), and the forecasting period was 15 years, over the time period 2015 to 2030. Disease-specific components of the second sub-model were created for each of the four cardiometabolic risk factors, separately for each gender:

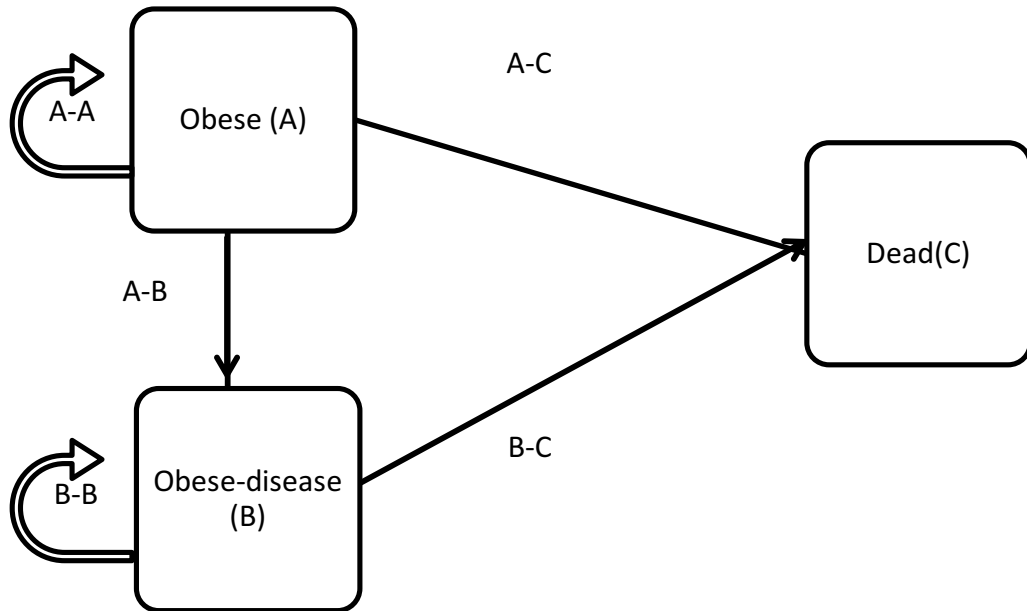
- MexOb-hypertension (MexOb-HT model)
- MexOb-type 2 diabetes mellitus (MexOb-T2DM model)
- MexOb-hypertriglyceridaemia (MexOb-HTG model)
- MexOb-hypercholesterolaemia (MexOb-HCl model)

The MexOb-Model second sub-model is an open cohort, discrete-state, Markov, model for the Mexican obese adult population, implemented in TreeAge Pro version 2015 software (213). I developed this model following the SIR (susceptible, infected and recovered) model framework that has been very useful to study the incidence and mortality rates of a disease. The SIR model framework was originally used for infectious diseases but has also been applied to non-communicable diseases. This framework describes the interaction between health states. It distributes the population into mutually exclusive health compartments or health states and then terms are constructed to describe the flow of individuals between each of the compartments / health states (214).

The second sub-model of the MexOb-Model runs three five-year cycles and distributes the population among four health states. The initial population of the model corresponds to obese adults (20 to 79 years) stratified in two groups: obese without disease (obese), and obese with disease (obese-disease). A graphic representation of the MexOb-Model transitions between health states is shown in Figure 4-2. The **obese** state (A) refers to the obese population without the risk factor of interest for the module (e.g. obese without hypertension). The **obese-disease** state (B) refers to the subset of the obese population with the cardiometabolic risk factor of interest (e.g. obese with hypertension). The **obese-disease-dead** state (C) refers to the flow of obese persons with the risk factor of interest to death; the obese-dead state refers to the flow of obese persons without disease to death (**obese-dead**; C).

In each cycle, individuals can remain in the main state (obese) (A-A) or transition to the obese-disease state (A-B) or to the death state (A-C). If individuals reach the obese-disease state (B), they will either remain in that state (B-B) or transition to the death state (B-C). The model assumes that individuals who enter the obese-disease state cannot make a transition back to the obese without disease state, nor can obese individuals go back to pre-obesity or normal weight.

Figure 4-2: Mexican Obesity Forecast Model for adult obese population. Diagram of the possible transitions between health states.



4.3 Data Sources

The best available data sources for the Mexican population were used to feed the model. However, when Mexican data was not available, I used international data of populations that share similar characteristics with the Mexican population. Data sources are described in Table 4.1.

Table 4.1 Data sources to feed the Mexican Obesity Forecast Model

Value	Source
Obesity prevalence	National Nutrition Survey (ENN) 1999 National Health Survey (ENSA) 2000 Mexican Family Life Survey (MxFLS-1) 2002 National Health and Nutrition Survey (ENSANUT) 2006 and 2012
Population projections	National Population Council (CONAPO)
All-cause mortality	Ministry of Health 2012
Disease prevalence in obese individuals	National Health and Nutrition Survey (ENSANUT) 2006
Mortality Risk ratios and Hazard ratios	Literature review

4.3.1 Initial population

The MexOb-Model initial population consisted of the expected Mexican obese adult population (20 to 79 years old) for 2015 distributed into two groups: obese with and without the cardiometabolic risk factor of interest.

Total obese population in 2015

The total obese population prevalence for 2015 was obtained from the projected obesity trends calculated from five different nationally representative Mexican health

surveys (ENN 1999, ENSA 2000, MxFLS-1, and ENSANUT 2006 and 2012) (35, 65, 192, 193). A detailed description of these datasets and the methods used to estimate those trends can be found in Chapter 3 and Appendix A.

The number of obese individuals by 2015 was obtained from the product of the projected obesity prevalence from the linear trend calculation and the estimated population for that same year taken from the Mexican population projections 2010-2050 obtained from the National Population Council, “*Consejo Nacional de la Población*” (CONAPO) stratified by age-group and sex (63) (Table 4.2).

Table 4.2 Total projected obesity prevalence for 2015 stratified by age group and sex. Results from a linear trend analyses

Age group	Males		Females	
	Total projected population 2015*	% obese (95%CI)	Total projected population 2015*	% obese (95%CI)
20-24	5,278,771	19.7(17.4, 22.0)	5,406,098	21.2(18.1, 24.3)
25-29	4,713,860	26.8(26.0, 27.5)	5,058,416	30.7(27.3, 34.0)
30-34	4,319,749	30.2(25.9, 34.5)	4,790,990	37.0(34.2, 39.8)
35-39	4,098,711	36.2(33.1, 39.3)	4,596,828	43.6(42.2, 45.1)
40-44	3,820,465	39.3(35.2, 43.3)	4,260,132	44.6(42.8, 46.5)
45-49	3,375,572	32.4(21.3, 43.5)	3,748,360	51.1(47.4, 54.7)
50-54	2,817,100	32.2(26.7, 37.7)	3,141,512	49.7(42.2, 57.3)
55-59	2,308,076	28.7(20.1, 37.3)	2,583,112	49.7(44.5, 54.9)
60-64	1,807,535	26.2(21.9, 30.4)	2,021,971	48.3(39.9, 56.6)
65-69	1,341,979	20.2(14.9, 25.5)	1,518,568	44.5(41.8, 47.2)
70-74	974,242	22.7(15.5, 30.0)	1,129,794	42.0(35.7, 48.3)
75-79	671,906	18.0 (5.3, 30.7)	802,002	30.8(26.1, 35.5)
80+	790,273	8.8 (6.7, 10.9)	1,027,528	20.3(11.5, 29.1)

*Total projected population for 2015 obtained from National Population Council of Mexico “*Consejo Nacional de la Población*” (CONAPO)

Prevalence of the four obesity-related cardiometabolic risk factors

The prevalence of hypertension, type 2 diabetes mellitus, hypertriglyceridaemia, and hypercholesterolaemia for the adult obese population was calculated from the Mexican Health and Nutrition Survey (ENSANUT) 2006 database (215). These rates

were held at the same value (2006) for the distribution of the MexOb-Model initial obese population into the non-disease and the disease groups for the first year of the simulation period (2015). At the time of this analysis, it was not possible to use data from the most recent survey (ENSANUT 2012), as the biochemical results needed for this analysis was not yet available.

National Health and Nutrition Survey (ENSANUT) 2006 methods for cardiometabolic risk factors examination

ENSANUT 2006 was a nationally representative survey that collected health and nutritional data from the Mexican population, and additional information about the quality and response of the health services (65). Blood pressure and anthropometric measurements were obtained from all participants. Blood samples from a fasting sub-sample were obtained in randomly selected individuals from the adult survey. A detailed description of the design of the surveys is provided in Appendix A.

The methods used in ENSANUT 2006 for metabolic examinations were: measurement of blood pressure for hypertension, and collection of fasting blood samples for diabetes, hypertriglyceridaemia, and hypercholesterolaemia.

Blood pressure measurements: Systolic and diastolic blood pressure measurements were obtained from all surveyed individuals. A trained nurse used a mercury sphygmomanometer to measure blood pressure in the dominant arm. The nurse performed two measurements. The first reading was made after five minutes of seated rest, and the second measurement was carried out five minutes after the first one. The blood pressure value used for the analysis was the average of the two measurements (83).

Blood samples: A sub-sample of 6,613 individuals from the adult survey was randomly selected, with a statistical power to detect $\geq 8\%$ prevalence of T2DM and dyslipidaemias. 91% of the selected sample (n=6,021) was in the fasting state for more than 8 hours. Antecubital vein blood samples were collected in tubes without anticoagulant. A second sample was collected in heparinized tubes from subjects who reported a medical diagnosis of T2DM (216).

Methods to estimate obesity-related cardiometabolic risk factors

I performed a descriptive analysis of the overall prevalence of the four obesity-related cardiometabolic risk factors (HT, T2DM, HTG, and HCl) from the ENSANUT 2006 database. First, I compared the results with the ones published by Mexican researchers using the same database and the same risk factor definitions (Table 4.3). The purpose of this analysis was to assess that I was using the same risk factor population for my analyses as the used in the published reports, in order to eliminate any noise in my results that could come from using different databases.

Table 4.3 Definition of obesity-related cardiometabolic risk factor used for database comparison analysis.

Cardiometabolic risk factor	Definition
Hypertension	Systolic blood pressure (SBP): ≥ 140 mmHg or Diastolic blood pressure (DBP): ≥ 90 mmHg or previously diagnosed by a physician
Type 2 diabetes mellitus	Glucose: ≥ 126 mg/dl (≥ 7.0 mmol/L)* or previously diagnosed by a physician
Hypertriglyceridaemia	Total triglycerides: ≥ 150 mg/dl (≥ 1.7 mmol/L)*
Hypercholesterolaemia	Total cholesterol: ≥ 200 mg/dl (≥ 5.2 mmol/L)*

* Conversion factor for glucose from mg/dl to mmol/L=18. Conversion factor for triglycerides from mg/dl to mmol/L= 88.57. Conversion factor for cholesterol from mg/dl to mmol/L= 38.6

Additionally, I used the same set of exclusion criteria as the ones published in the ENSANUT 2006 reports to obtain similar estimates of prevalence for the obesity-related cardiometabolic risk factors. These were as follows:

- Pregnant or breastfeeding*
- Glucose: <40mg/dl (<2.22mmol/l)
- High Density Lipoprotein (HDL-cholesterol): < 10mg/dl (<0.26mmol/l)
- Triglycerides (TG): <10mg/dl (<0.11mmol/l)
- Insulin >197 mIU/L
- Total Cholesterol (TC): <50mg/dl (<1.29mmol/l)
- Systolic Blood Pressure (SBP): <80mmHg
- Diastolic Blood Pressure (DBP): <50mmHg
- Waist circumference: <50cm
- Body mass index (BMI) <10kg/m² or >58kg/m²

* The exclusion criteria of pregnant or breastfeeding was used for all the conditions except for hypertension.

Table 4.4 shows the prevalence of the four cardiometabolic risk factors in the total adult population that I estimated from the ENSANUT 2006 database using the same definitions as the ones used in previously published reports. The prevalence I obtained for the four cardiometabolic risk factors showed an absolute difference of <1% between my estimates and those presented in the published reports.

Table 4.4 Prevalence of cardiometabolic risk factors (%) in the adult population used for my analyses and the ENSANUT 2006 report, by sex

Cardiometabolic risk factor ^α	This analysis			ENSANUT 2006			Reference
	Male (%)	Female (%)	Total (%)	Male (%)	Female (%)	Total (%)	
Hypertension	32.6	31.2	31.8	32.4	31.1	31.6	Barquera, et al.(83)
Type 2 diabetes mellitus	15.8	13.8	14.8	15.8	13.2	14.4	Villalpando et al.(217)
Hypertriglyceridaemia	36.1	26.6	31.0	36.9	26.9	31.5	Aguilar Salinas et al.(86)
Hypercholesterolaemia	39.5	45.9	42.9	39.3	47.2	43.6	Aguilar Salinas et al.(86)

^α Definitions used to estimate prevalence:

Hypertension: SBP≥140 or DBP≥90mmHg or previously diagnosed hypertension

T2DM: ≥126mg/dl (7.0mmol/L) or previously diagnosed by a physician

Hypertriglyceridaemia: TG ≥150mg/dl (1.7mmol/L)

Hypercholesterolaemia: TC: ≥200mg//dl (5.2mmol/L)

Table 4.5 describes the definitions used in my analyses to obtain the prevalence of the four obesity-related cardiometabolic risk factors for the obese adult population used as input for the MexOb-Model: with the exception of T2DM, they are slightly different from the ones described above for the previously published reports.

Hypertension

For the purposes of the MexOb-Model, I defined hypertension using the American Eighth Joint National Committee (JNC8) guidelines, which make reference to a different SBP cut-off point for adults ≥ 60 years old (SBP ≥ 150 mmHg rather than ≥ 140 mmHg) and included "*or being previously diagnosed by a physician*" following the definition of Barquera et al. (83).

Hypertriglyceridaemia and hypercholesterolaemia

Hypertriglyceridaemia and hypercholesterolaemia were defined as TG: ≥ 150 mg/dl (≥ 1.7 mmol/L) and TC: ≥ 200 mg/dl (≥ 5.2 mmol/L) respectively plus "*or being previously diagnosed by a physician*" for both dyslipidaemias. The cut-off points are the same as used by Aguilar-Salinas et al. in their ENSANUT 2006 report (86), which are also similar to the ones recommended by the cholesterol classification outlined in the Adult Treatment Panel (ATP) III guidelines (218) and the American Association of Clinical Endocrinologist (219). I decided for my analyses to add "*or being previously diagnosed by a physician*", following the format of the definitions used for T2DM and HT, and also to capture the subset of the population that had been previously diagnosed and could at the time of the survey be on pharmacological or lifestyle treatment, and could have a higher risk of presenting higher values of triglycerides and cholesterol in the future.

Table 4.5 Definitions used for the disease variables in the MexOb-Model

Cardiometabolic risk factors	Definition	Reference
Hypertension	A) SBP ≥ 150 or DBP ≥ 90 mmHg in ≥ 60 y B) SBP ≥ 140 or DBP ≥ 90 mmHg in < 60 y A or B or previously diagnosed by a physician	James et al. Eighth Joint National Committee (JNC8) (220) Barquera et al. (83)
Type 2 diabetes mellitus	Serum glucose ≥ 126 mg/dl (≥ 7.0 mmol/L) or previously diagnosed by a physician	World Health Organization (WHO) (221)
Hypertriglyceridaemia	Serum TG ≥ 150 mg/dl (≥ 1.7 mmol/L) or previously diagnosed by a physician	Aguilar Salinas et al. (86)
Hypercholesterolaemia	Serum cholesterol ≥ 200 mg/dl (≥ 5.2 mmol/L) or previously diagnosed by a physician	Aguilar Salinas et al. (86)

* Conversion factor for glucose from mg/dl to mmol/L=18. Conversion factor for triglycerides from mg/dl to mmol/L= 88.57. Conversion factor for cholesterol from mg/dl to mmol/L= 38.6

Statistical analysis

A descriptive statistical analysis was performed to obtain the four sets of cardiometabolic risk factor prevalence and 95% confidence intervals in the obese population. The data were stratified by sex and age group (≥ 20 y in five-year age groups until 75-79y). For the HT analysis, I used the main adult sample ENSANUT 2006 database survey weights at household and individual level. Additionally, for T2DM, HTG, and HCL analyses, I used the ENSANUT 2006 published weights for the subsample of participants with fasting blood samples. The ENSANUT 2006 main database contains weight factors that were calculated to adjust the distribution of the analytical samples to match the distribution of the 2005 Mexican population. Compared with the Mexican population, the ENSANUT subsamples included a higher number of younger people and were more likely to be female (216). All weights were adjusted for survey non-response. The analyses were adjusted for the complex multistage survey design using the relevant survey design information in the ENSANUT 2006 database. Statistical analysis was carried out using Stata/SE 13.1 (StataCorp, College Station, Texas, US), and the "SVY" module was used to account for the complex survey design.

The size of the ENSANUT analytical samples used for the analyses is shown in Table 4.6. The table shows the number of ENSANUT participants who had plausible cardiometabolic examination values, the number of individuals who were classified as obese ($BMI \geq 30 \text{ kg/m}^2$), and the number of obese individuals classified as having the specific cardiometabolic risk factor (the group described as obese-disease in the MexOb-Model). As aforementioned, hypertension was evaluated among all adult participants of the survey, but the fasting blood samples were taken only in a subsample (roughly a third of the total surveyed population). The MexOb-Model focuses on the disease prevalence exclusively among the obese population.

Table 4.6 Total number of individuals with plausible cardiometabolic risk factor values in the Mexican adult population ≥ 20 years old. Results from ENSANUT 2006.

Cardiometabolic risk factor	Total analytical sample	Total obese analytical sample	Obese+risk factor analytical sample
Hypertension	31,780	9,817	4,270
Type 2 diabetes mellitus	5,754	1,814	345
Hypertriglyceridaemia	5,726	1,786	738
Hypercholesterolaemia	5,683	1,743	924

Table 4.7 shows the prevalence of the four obesity-related cardiometabolic risk factors in the obese population from ENSANUT 2006, stratified by age group and sex. Overall, the prevalence of risk factors in the obese population was higher for males than for females. For hypertension, I observed a clear direct relationship with age in women, with risk factor prevalence exceeding 50% in the population aged 50 years and older. Diabetes prevalence also showed an increase with age, reaching its highest prevalence (50%) in men and in women aged 55-59y: 50% (95%CI: 29%, 71%) and 40% (95%CI:

26%, 56%) respectively. The prevalence of hypertriglyceridaemia in the obese population in 2006 was >40% in males and >30% in females for most of the age groups, and was the second most prevalent cardiometabolic risk factor in the obese population. Finally, hypercholesterolaemia showed on average the highest prevalence of all the four risk factors in all the age groups. For men, the highest prevalence was in the 65 to 69 year old age group (75%; 95%CI: 47%, 91%) and for women the highest prevalence was in the 75 to 79 year old age group (75%; 95%CI: 49%, 91%).

The differences in the definition of the cardiometabolic risk factors for my analysis compared with the ones from the previously published reports described above could impact on the prevalence estimates obtained. For hypertension, my estimates for the population ≥ 60 years old would be expected to be lower because of the higher threshold of SBP for that age group (≥ 150 mmHg rather than ≥ 140 mmHg). My estimated prevalence of HTG and HCl would be expected to be higher as I am also including the subset of the obese population with biochemical values in the normal range but who were previously diagnosed by a physician.

Table 4.7 Prevalence of obesity-related cardiometabolic risk factors in the Mexican adult obese population stratified by age group and sex.

Results from ENSANUT 2006

Age group	Hypertension		Type 2 diabetes mellitus		Hypertriglyceridaemia		Hypercholesterolaemia	
	Male % (95%CI)	Female % (95%CI)	Male % (95%CI)	Female % (95%CI)	Male % (95%CI)	Female % (95%CI)	Male % (95%CI)	Female % (95%CI)
20-24	31.0(23.1, 40.2)	16.2(11.3, 22.6)	0(0)	7.9 (2.4, 22.8)	42.7(23.2, 64.8)	20.6 (7.5, 45.4)	43.4(24.2, 64.8)	33.6(20.2, 50.4)
25-29	33.3(25.4, 42.2)	22.9(18.6, 27.9)	10.4 (1.5, 46.9)	3.8 (1.8, 7.9)	49.8(26.9, 72.8)	31.0(19.7, 45.2)	46.0(23.3, 70.5)	40.2(28.3, 53.3)
30-34	42.5(34.7, 50.7)	25.2(21.0, 29.8)	14.2 (5.0, 34.1)	7.7 (4.0, 14.6)	41.0(27.1, 56.5)	34.3(24.4, 45.9)	44.5(29.6, 60.4)	44.5(34.1, 55.4)
35-39	34.8(28.8, 41.2)	29.5(25.7, 33.6)	21.2 (9.7, 40.2)	9.3 (5.0, 16.8)	55.8(38.4, 71.9)	39.7(29.7, 50.6)	45.4(28.3, 63.7)	47.0(36.8, 57.4)
40-44	43.4(36.3, 50.8)	39.1(34.4, 44.1)	15.9 (8.1, 28.8)	12.1 (5.6, 24.2)	48.6(33.3, 64.1)	40.7(29.5, 53.0)	55.9(40.4, 70.3)	47.3(36.7, 58.2)
45-49	48.5(41.3, 55.8)	41.3(36.3, 46.5)	22.1 (8.8, 45.5)	25.7(11.8, 47.2)	38.8(23.9, 56.2)	32.9(19.1, 50.4)	54.9(37.5, 71.2)	67.7(53.9, 79.0)
50-54	56.4(48.5, 64.0)	55.9(49.9, 61.7)	33.8(16.9, 56.2)	21.3(13.1, 32.6)	59.0(39.3, 76.2)	49.5(36.1, 63.1)	58.4(38.7, 75.7)	68.8(55.8, 79.5)
55-59	71.1(60.8, 79.6)	58.4(51.6, 64.9)	49.8(28.6, 71.1)	40.1(26.1, 55.9)	60.2(39.3, 77.9)	45.0(31.6, 59.1)	74.2(54.8, 87.2)	70.0(54.6, 81.9)
60-64	54.1(43.5, 64.3)	66.6(59.5, 73.0)	47.1(25.3, 69.9)	29.7(17.6, 45.6)	56.4(33.6, 76.8)	41.6(27.5, 57.2)	50.5(28.8, 72.0)	67.1(52.2, 79.2)
65-69	69.5(56.6, 79.9)	67.7(58.4, 75.8)	28.6 (9.3, 60.9)	29.0(16.9, 45.2)	40.9(13.8, 75.0)	39.1(23.8, 57.0)	75.4(47.5, 91.2)	54.8(36.2, 72.1)
70-74	75.9(61.9, 85.9)	77.4(69.0, 84.1)	22.1 (7.1, 51.4)	40.2(22.7, 60.5)	39.0(11.3, 76.2)	33.7(17.4, 55.0)	55.4(23.7, 83.2)	57.9(36.9, 76.4)
75-79	59.8(39.6, 77.2)	58.1(43.4, 71.5)	12.8 (1.8, 53.9)	9.9 (3.1, 27.3)	17.8 (2.9, 60.9)	62.6(34.5, 84.2)	16.0 (2.6, 57.7)	75.5(48.5, 90.9)
80+	65.2(43.5, 82.1)	72.6(57.4, 83.9)	10.2 (2.4, 35.0)	19.5 (3.7, 60.4)	20.4 (3.2, 66.6)	47.9(19.9, 77.3)	35.8(10.0, 73.7)	53.3(23.3, 81.0)

Definitions used to estimate this numbers:

Hypertension A) SBP \geq 150 or DBP \geq 90mmHg in \geq 60y B) SBP \geq 140 or DBP \geq 90mmHg in $<$ 60y + A or B or previously diagnosed by a physician

Type 2 diabetes mellitus \geq 126mg/dl (\geq 7.0mmol/L) or previously diagnosed by a physician

Hypertriglyceridaemia \geq 150mg/dl (\geq 1.7mmol/L) or previously diagnosed by a physician

Hypercholesterolaemia \geq 200mg/dl (\geq 5.2mmol/L) or previously diagnosed by a physician

Prevalence of obese individuals without a cardiometabolic risk factor

For the MexOb-Model, the size of the population representing obese individuals without the risk factor of interest was obtained by subtracting the number of the obese population with a cardiometabolic risk factor from the total obese population estimated from 2015.

4.3.2 Mortality and survival rates

Mortality rates and the probability of survival for each of the four obesity-related cardiometabolic risk factors were required as input data to estimate the transition probabilities from the obese (A) and obese-disease (B) states to the death state (C) (obese to obese-death, and obese-disease to obese-disease-death) (Figure 4-2). This section outlines the methods used to estimate the mortality rates and survival probabilities I used to calculate the MexOb-Model transition probabilities.

Life Tables

Sex- and age group-specific mortality rates and probabilities of survival between the exact age groups x and $x+5$ were obtained by a life-table analysis. These were estimated using the most up-to-date data available: all-cause population mortality for 2012 from the Mexican Ministry of Health (222), and the total population for that same year from the Mexican population projections (CONAPO) (63). The Ministry of Health mortality data is based on mortality information from the national registry and death certificates. All-cause mortality data was calculated for adults aged 20 to 79y, stratified by sex and five-year age group. This analysis was performed using R software version 0.98.953.

The required outputs (mortality rate and survival probabilities) from the life table analysis were obtained using the following standard formulas from Chiang II Methodology for Life Expectancy (223):

a) **Mortality rate (m_x):**

m_x =Total deaths by age group and sex/ total population in the same age group and sex

b) **Probability of dying between age group x and age group x+5, given survival at age X (q_x):**

$$q_x = (5 * m_x) / (1 + (1 - a_x) * m_x)$$

a_x = fraction distribution: 0.5 was used for all age groups except for the last age group 80+y where a_x was set to 1.

c) **Probability of surviving between age group x and age group x+5 given survival at age x (p_x):**

$$p_x = 1 - q_x$$

Mortality decomposition

National mortality rates disaggregated by BMI status are not available. To estimate age-group and sex-specific mortality transition probabilities for the obese and the obese-disease populations, it was necessary to transform the general population mortality rates, described above, into separate mortality rates for the obese and obese-disease populations. I applied the mortality decomposition formulas used by Majer et al. (224) and Barendregt et al. (225). The calculations were based on: the population mortality rates from 2012, the total obese and obese-disease prevalence from ENSANUT 2012 and ENSANUT 2006 respectively, and hazard ratios and risk ratios for excess mortality from the literature. These formulae assume that: age-group and sex-specific mortality rates in the general population are the weighted average of the mortality rates for the obese and the non-obese groups with the proportions of the

obese and the non-obese groups as the weights. Likewise, the mortality rates for the total obese population are a weighted average of the mortality rates for the obese with disease and the obese without disease groups.

$$m_x^{(nd)} = m_x / ((HR_x \times p_x^{(d)} + (1 - p_x^{(d)}))$$
$$m_x^{(d)} = m_x^{(nd)} \times HR_x$$

$m_x^{(nd)}$: mortality rate for non-obese

$m_x^{(d)}$: mortality rate for obese/obese-disease

HR_x : estimated hazard ratio or risk ratio

$p_x^{(d)}$: prevalence of obese/obese-disease for each age group(x)

Through the following sections of this Chapter, I will be giving worked examples of the process to calculate the transition probabilities, that build up over the next few pages (Examples 1A to 1E)

Example 1A: Calculating the transition probabilities for obese men aged 30 to 34y with and without hypertension:

m_x (mortality rate for obese population): 0.002911

HR_x : 1.6

$p_x^{(d)}$: 0.43

First I applied the above mortality decomposition formula to the overall mortality rate to estimate obese specific mortality rates. Second, I decomposed the mortality rate for the obese group to estimate the obese-without-disease and the obese-disease specific mortality rates.

In survival analysis, the **hazard ratio** (HR) is the ratio of the hazard rates corresponding to the conditions described by two levels of an explanatory variable. For example, in an obese-mortality study, the obese population may die at twice the rate per unit time as the non-obese population. In statistics and epidemiology, **the relative risk** or **risk ratio** (RR) is the ratio of the probability of an event occurring among the exposed to the risk among the unexposed. For example, a risk ratio for the obese-mortality association could be expressed as the ratio of the probability of dying in an obese group (exposed) to the probability of dying in a non-obese group (non-exposed).

Table 4.8 Risk ratios and hazard ratios used to estimate mortality rates for the obese and obese-with-disease populations

Variable	Hazard Ratio (HR) / Risk Ratio (RR)*	Population	Reference
Obesity (Obese ($\geq 30\text{kg/m}^2$) vs. normal weight)	Age: <65y: HR: 1.13 (1.06-1.19) Age: $\geq 65\text{y}$ HR: 0.98 (0.86, 1.12)	Systematic review Worldwide	Flegal et al. 2013 (226)
Hypertension (Hypertension vs. no hypertension)	RR: 1.6 (1.1, 2.5)	Mexican-Americans. General population	Wei et al. 1996 (227)
T2DM [†] (Obese diabetics vs. normal weight diabetics)	HR: 0.52 (0.31, 0.86)	USA population. obese diabetics	Jackson et al. 2014 (228)
Hypertriglyceridaemia High triglycerides (≥ 150 mg/dl) vs. No high triglycerides	HR: 1.07 (0.82, 1.39)	Mexican-Americans. General population	Hunt et al. 2004 (229)
Hypercholesterolaemia High cholesterol (≥ 240 mg/dl) vs. Cholesterol (160 to 240mg/dl)	RR: 1.6 (1.0, 2.6)	Mexican-Americans. General population	Wei et al. 1996 (227)

*HR/RR assumed to be the same for males and females

†: Type 2 diabetes mellitus

Example IB: Mortality decomposition formula to estimate the mortality rate for obese men 30 to 34y with and without hypertension.

Non-diseased (obese without hypertension) ($m_x^{(nd)}$):

$$m_x^{(nd)}: m_x / ((HR_x \times p_{x2}(d) + (1 - p_{x2}(d))))$$

$$m_x^{(nd)}: 0.002911 / ((1.6 * 0.43) + (1 - 0.43))$$

$$m_x^{(nd)}: 0.002314$$

Diseased (obese with hypertension) ($m_x^{(d)}$)

$$m_x^{(d)}: m_x^{(nd)} \times HR_x$$

$$m_x^{(d)}: 0.002314 * 1.6$$

$$m_x^{(d)}: 0.003702$$

Hazard ratios for modelling studies such as this are typically taken from studies with large nationally-representative datasets (with a large number of events), that have data that is generalizable to the particular country the model is built for (Mexico in this case), that have estimates adjusted for potential confounders, that have findings that are consistent with randomised controlled trials, and have estimates with accompanying 95% confidence intervals. In addition, the studies should show direct comparisons between persons in the general population with and without the disease of interest.

In order to build the MexOb- Model with as much data as relevant to the Mexican population as possible, I performed a comprehensive literature search for disease-specific hazard ratios (HR) and risk ratios (RR) to substitute in the formula above. However, the results from the literature review revealed no examples for the Mexican population of disease-specific HRs and RRs across the BMI categories. The exception was the study by Jackson et al. which provided estimates of the relationship between diabetes status and all-cause mortality by BMI groups such as the obese: giving me the disease-specific HR for the obese population that was needed to feed into the model.

The diabetes-BMI associations with mortality found in this study were independent of smoking, CVD, cáncer, and a range of other potential confounders.

For the other three diseases, I decided to use the published HRs and RRs from the studies based on populations / cohorts that were closest to my target population: i.e. general population Mexican-Americans. Results from the San Antonio Cohort study were used for HT, HTG, and HCl results from San Antonio Cohort Study (227, 229) a cohort study that followed the population for 14 years, with a high percentage of Mexican-American population and one of the few cohorts with Hispanic population data that has been used also as a reference for other studies (230).

The HRs comparing obese persons versus those of normal weight was taken from the worldwide systematic review by Flegal et al. This study was chosen as the published HRs were stratified by BMI and were further stratified by age, and were suitably adjusted for confounders such as sex and smoking status. In addition, the HRs in the Flegal et al study were presented for the general population with and without a health condition, making this a suitable choice for the MexOb-Model. Specific strengths of the Flegal et al study included its large sample size (more than 2.88 million participants; more than 270,000 deaths), made up of a large number of studies that were chosen using a comprehensive search strategy and prespecified standard (WHO) BMI categories .(226).

The common theme of the studies chosen was that they compared the mortality experience of persons in the general population with and without the disease of interest.

4.4 Transition probabilities between health-states

The MexOb-Model second sub-model is formed by a discrete-state Markov chain. A Markov chain is a model that is useful to describe the progression of a chronic disease. A Markov model is formed by a set of states (health states). The process starts in one of these states and moves successively from one state to another during a pre-determined time period called a “*cycle*”. The probability of the individual or of the population as a whole progressing from one state to another is called a “*transition probability*”, and the group of probabilities associated with various state changes is called a “*transition matrix*”. A key characteristic of Markov models is that they are considered memoryless. This characteristic is known as the “Markov property” which states that the conditional probability distribution to any future state is given by the present state, and it is unaffected by any knowledge of the past history (11).

This section describes the methods used to estimate the set of five, age-group and sex-specific transition probabilities between the three health states (obese, obese-with-disease, and death) in the MexOb-Model (Figure 4-2).

MexOb-Model transitions between health states

- Obese to obese (A-A)
- Obese to obese-disease (A-B)
- Obese to death (A-C)
- Obese-disease to obese-disease (B-B)
- Obese-disease to death (B-C)

I estimated the transition probabilities using data stratified by five-year age-groups. The results obtained represent five-year interval transition probabilities. Sonnenberg and Beck mention that the length of the cycle in a Markov model is chosen to represent a clinically meaningful time interval. A one-year cycle length is common for simulation models that can span the entire life history of Individual patients and where events are relatively rare. They state that the choice of a cycle time is also determined by the available data (including the available transition probability data). For example,

if only five-yearly transition probabilities are available (as in this project), then Sonnenberg and Beck mention that there is little advantage to be gained by choosing a life cycle that is shorter than that(231).

The five-year cycle length was chosen based on the method used to estimate the transition probabilities. It was necessary to group the disease prevalence in five-year age groups due to the variability in the prevalence estimates observed when using individual-level data. A five-year cycle has also the cycle length of choice in other recent modelling exercises (i.e. Lymer, A. et al.) (232)).

The five-year interval transition probabilities between health states were estimated via a non-parametric equation. The transition matrices obtained were discrete in time; this means that the transition probabilities are constant over the 15 year projection period. Transition probabilities were calculated assuming that each of the transition states was mutually exclusive and had a zero remission rate; this means that obese individuals flowing into the obese-disease state could not make a transition back to the obese-without-disease state, nor could obese individuals go back to pre-obesity or normal weight. Additionally, the health state “dead” was used as the absorption state: in a Markov model, an absorption state is a state that once entered cannot be left. Table 4.9 describes the non-parametric formulae used to estimate the transition probabilities between the MexOb-Model health states from one age group to another. The formulae use age-group and sex-specific cross-sectional data for the Mexican population. Probability of survival data for the obese and the obese-disease groups was obtained from the life-table method and from applying the mortality decomposition formula described above. Prevalence of obesity with and without the cardiometabolic risk factor of interest (disease) was obtained from the Mexican Health and Nutrition Survey (ENSANUT 2006). The four key inputs for the calculation of the set of transition probabilities are the following:

Prop1: Prevalence of obese without the disease

Prop2: Prevalence of obese with the disease

pnO: Probability of survival of obese without disease between age group intervals

pnD: Probability of survival of obese with disease between age group intervals

Example IC: Calculation of survival rate for obese men 30 to 34y with and without hypertension using the life table formula

Calculation of mortality and survival rate for obese without hypertension population (pnO)

$$M_x = m_x^{(nd)}$$

$$M_x = 0.002314$$

$$q_x = (5 * m_x^{(nd)}) / (1 + (1 - a_x) * m_x^{(nd)})$$

$$q_x = (5 * 0.002314) / (1 + (1 - 0.5) * 0.002314) = 0.01156$$

$$p_x \text{ (pnO)} = 1 - 0.01156 = 0.98844$$

Calculation of mortality and survival rate for obese with hypertension population (pnD)

$$M_x = m_x^{(d)}$$

$$M_x = 0.003702$$

$$q_x = (5 * m_x^{(d)}) / (1 + (1 - a_x) * m_x^{(d)})$$

$$q_x = (5 * 0.003702) / (1 + (1 - 0.5) * 0.003702) = 0.01848$$

$$p_x \text{ (pnD)} = 1 - 0.01848 = 0.98152$$

Prop1: OB without hypertension: $1 - 0.43 = 0.57$

Prop2: OB with hypertension = 0.43

pnO: 0.98844

pnD: 0.98152

Once the calculations were made, smoothing was done to the probabilities obtained to reduce the variability from the original data. Smoothing in statistics refers to a method to minimize irregularities in a data series using an approximation function that

attempts to capture the important pattern in the data series, by reducing the background noise. For the MexOb-Model, this action was necessary due to the variability of the trends in the prevalence of the cardiometabolic risk factors between the adjacent five-year age groups, which was due to the difference in the population size between consecutive age-groups. These differences can be observed in Table 4.7 and in the transition probabilities before smoothing shown in the Appendix C. Calculations of the transition probabilities and smoothing of the estimated data to eliminate irregularities caused by the variability of the obese-disease prevalence from ENSANUT 2006 were made using R software version 0.98.953.

Table 4.9 Non-parametric formulae to estimate transition probabilities between the health states*

	Destination state: Age (x to x+5)+5			
	Health-States	State A (Obese)	State B (Obese-disease)	State C (Dead)
Initial State: Age group (x to x+5)	State A (Obese)	<i>Obese to Obese (A-A)</i> $(prop1[i] * pnO[i]) / prop1[i-1]$	<i>Obese to Obese disease (A-B)</i> $1 - P[i,1,1] - P[i,1,3]$	<i>Obese to Dead (A-C)</i> $1 - pnO[i]$
	State B (Obese-disease)	n/a	<i>Obese-disease to Obese disease (B-B)</i> $pnD[i]$	<i>Obese-disease to Dead (B-C)</i> $1 - pnD[i]$
	State C (Dead)	n/a	n/a	<i>Dead to Dead (C-C)</i> 1

*For a graphic example of the movement between the five health states, see Figure 4-2

Example ID: Calculation of transition probabilities for hypertension in obese men 30 to 34y

	Destination state: Age (x to x+5)+5			
	Health-States	State A (Obese)	State B (Obese-disease)	State C (Dead)
Initial State: Age group (x to x+5)	State A (Obese)	$(prop1[i] * pnO[i]) / prop1[i-1]$ $(0.57 * 0.9844) / 0.67 = 0.8374$	$1 - P[i,1,1] - P[i,1,3]$ $1 - 0.8374 - 0.0156 = 0.147$	$1 - pnO[i]$ $1 - 0.9844 = 0.0156$
	State B (Obese-disease)	n/a	$pnD[i]$ 0.9815	$1 - pnD[i]$ $1 - 0.9815 = 0.0185$
	State C (Dead)	n/a	n/a	1

*For a graphic example of the movement between the five health states, see Figure 4-2

4.4.1 Transition matrices for each of the MexOb-disease models

Transition probabilities for the MexOb-Model were age-group, sex-, and disease-specific. Table 4.10 to Table 4.17 show the estimated transition probabilities for males and for females for moving between the transient health states with the exception of the transition from Dead to Dead (C-C). As described above, death is considered as the absorbing state, therefore the transition probability (C-C) was set as 1.

The set of transition probabilities were calculated with the non-parametric formulae described above. A non-parametric formula has the characteristic of not making any assumption about the probability distributions of the variables. Therefore, some of the transition probability values obtained were <0 or >1. To overcome this limitation, I

rescaled them so that the row transition probabilities summed to 1 using the following formula:

$$\text{New transition probability (TP)} = \text{Absolute number of TP} * ((\text{sum of absolute of TP})/1)$$

The original calculated transition probabilities are outlined in Appendix C.

The following section outlines the transition probabilities for each of the four different modules of the MexOb-Model: hypertension, type 2 diabetes mellitus, hypertriglyceridaemia and hypercholesterolaemia.

Example 1 E. Exercise of calculation of new transition probabilities for hypertension in obese men 30 to 34y

Age group	Obese-Obese (A-A)	Obese-Obese HT (A-B)	Obese-Dead (A-C)
30-34	0.8374	0.147	0.0156

$$\text{New transition probability (TP)} = \text{Absolute number of TP} * ((\text{sum of absolute of TP})/1)$$

Total Sum of absolute values= 0.8374+0.147+0.0156 = 1

New transition probabilities

Obese –Obese = Absolute value (0.8374)*(1/1) =0.8374

Obese –Obese HT = Absolute value (0.147)*(1/1) =0.147

Obese –Dead = Absolute value (0.0156)*(1/1) =0.0156

Transition probabilities for the MexOb hypertension model

Transition probabilities from obese to obese-with-hypertension states (i.e. obese to obese-disease, A-B) were higher for males than for females in the age groups 45 to 64 years. Males from all age groups showed higher transition probabilities to move to the dead state both from the obese and from the obese-disease state than females.

Male transition probabilities from obese to obese with hypertension (A-B) showed an increase with age for most of the age groups, with the exception of the 65 to 69y and 75 to 79 year age groups. A similar association was observed for the transition from obese with hypertension to dead (B-C), but in this case it applied to all age-groups. The estimations also showed that the transition from obese-disease to dead (B-C) for the younger age groups were higher than the transition from obese to dead (A-C)(Table 4.10).

Female transition probabilities from obese to obese with hypertension (A-B) showed an increase with age in all age groups. A similar association was observed for the transition from obese with hypertension to dead (B-C). Female transitions from obese-disease to dead (B-C) were higher in all age groups than the transition from obese without hypertension to dead (A-C) (Table 4.11).

Table 4.10 Transition probabilities between health states in Mexican male obese population for hypertension (MexOb-HT)

Age group	Obese-Obese (A-A)	Obese-Obese-HT (A-B)	Obese-Dead (A-C)	Obese HT-Obese HT (B-B)	Obese HT-Dead (B-C)
20-24	0.9818	0.0152	0.0030	0.9952	0.0048
25-29	0.9668	0.0260	0.0073	0.9890	0.0110
30-34	0.9496	0.0390	0.0115	0.9827	0.0173
35-39	0.9292	0.0552	0.0157	0.9764	0.0236
40-44	0.9006	0.0794	0.0200	0.9695	0.0305
45-49	0.8501	0.1250	0.0249	0.9594	0.0406
50-54	0.7750	0.1921	0.0329	0.9444	0.0556
55-59	0.7243	0.2284	0.0473	0.9240	0.0760
60-64	0.7191	0.2132	0.0677	0.8976	0.1024
65-69	0.8054	0.0991	0.0955	0.8662	0.1338
70-74	*0.8722	*0.0071	*0.1207	0.8339	0.1661
75-79	*0.7804	*0.0993	*0.1203	0.8004	0.1996

* This value was originally <0 or >1. The original transition probability estimates are shown in Appendix table C-1

Table 4.11 Transition probabilities between health states in Mexican female obese population for hypertension (MexOb-HT)

Age group	Obese-Obese (A-A)	Obese-Obese HT (A-B)	Obese-Dead (A-C)	Obese HT-Obese HT (B-B)	Obese HT-Dead (B-C)
20-24	0.9809	0.0190	0.0001	0.9997	0.0003
25-29	0.9614	0.0366	0.0020	0.9967	0.0033
30-34	0.9411	0.0549	0.0040	0.9937	0.0063
35-39	0.9213	0.0725	0.0062	0.9905	0.0095
40-44	0.8991	0.0913	0.0096	0.9856	0.0144
45-49	0.8779	0.1074	0.0148	0.9780	0.0220
50-54	0.8604	0.1176	0.0220	0.9666	0.0334
55-59	0.8469	0.1216	0.0315	0.9508	0.0492
60-64	0.8249	0.1320	0.0431	0.9303	0.0697
65-69	0.7940	0.1491	0.0569	0.9055	0.0945
70-74	0.7621	0.1668	0.0711	0.8800	0.1200
75-79	0.7233	0.1908	0.0859	0.8534	0.1466

The original transition probability estimates are shown in Appendix table C-2

Transition probabilities for the MexOb type 2 diabetes mellitus model

The set of transition probabilities from obese to obese with diabetes (disease) (A-B) were higher for males than for females in all age groups. Males from all age groups showed higher transition probabilities to move to the dead state either from the obese or from the obese with diabetes state than females.

Male transition probabilities from obese to obese with diabetes (A-B) showed an increase with age in the younger age groups up to 49 years old, and then they decreased with age. The transition from obese with diabetes to dead (B-C) showed a constant increase with age. The estimations also showed that the transition from obese-disease to dead (B-C) were lower than the transition from obese without disease to dead for all age groups (A-C) (Table 4.12).

Female transition probabilities from obese to obese with diabetes (A-B) showed an increase with age in the age group 30 to 49 years, and the highest transition probabilities were found in the oldest age groups (70-79y). A clear association with age was observed for the transition from obese with diabetes to dead (B-C). Female transitions from obese with diabetes to dead (B-C) were constantly lower in all the age groups than the transition from obese without diabetes to dead (A-C) (Table 4.13)

Table 4.12 Transition probabilities between health states in Mexican male obese population for type 2 diabetes mellitus (MexOb-T2DM)

Age group	Obese-Obese (A-A)	Obese-Obese T2DM (A-B)	Obese-Dead (A-C)	Obese T2DM – Obese T2DM (B-B)	Obese disease-Dead (B-C)
20-24	0.9540	0.0426	0.0034	0.9983	0.0017
25-29	0.9468	0.0444	0.0088	0.9954	0.0046
30-34	0.9389	0.0467	0.0144	0.9924	0.0076
35-39	0.9298	0.0500	0.0202	0.9894	0.0106
40-44	0.9092	0.0621	0.0287	0.9852	0.0148
45-49	0.8842	0.0727	0.0431	0.9786	0.0214
50-54	0.8670	0.0681	0.0649	0.9699	0.0301
55-59	0.8587	0.0494	0.0918	0.9581	0.0419
60-64	0.8571	0.0191	0.1238	0.9429	0.0571
65-69	*0.8215	*0.0221	*0.1564	0.9257	0.0743
70-74	*0.7621	*0.0592	*0.1786	0.9083	0.0917
75-79	*0.7117	*0.0898	*0.1985	0.8906	0.1094

* This value was originally <0 or >1. The original transition probability estimates are shown in Appendix table C-3

Table 4.13 Transition probabilities between health states in Mexican female obese population for type 2 diabetes mellitus (MexOb-T2DM)

Age group	Obese-Obese (A-A)	Obese-Obese T2DM (A-B)	Obese-Dead (A-C)	Obese T2DM – Obese T2DM (B-B)	Obese disease-Dead (B-C)
20-24	*0.9790	*0.0208	*0.0002	*0.9999	*0.0001
25-29	*0.9935	*0.0042	*0.0023	0.9988	0.0012
30-34	0.9817	0.0132	0.0051	0.9974	0.0026
35-39	0.9609	0.0311	0.0080	0.9959	0.0041
40-44	0.9425	0.0446	0.0129	0.9934	0.0066
45-49	0.9270	0.0519	0.0211	0.9895	0.0105
50-54	0.9285	0.0379	0.0337	0.9840	0.0160
55-59	0.9311	0.0192	0.0497	0.9726	0.0274
60-64	*0.9211	*0.0103	*0.0686	0.9565	0.0435
65-69	*0.8403	*0.0752	*0.0845	0.9380	0.0620
70-74	*0.7778	*0.1247	*0.0975	0.9196	0.0804
75-79	*0.7273	*0.1646	*0.1081	0.9009	0.0991

* This value was originally <0 or >1. The original transition probability estimates are shown in Appendix table C-4

Transition probabilities for the MexOb hypertriglyceridaemia model

Transition probabilities from obese to obese with hypertriglyceridaemia (A-B) were higher for males than for females in the age groups 60 to 79 years. Overall, males from all age groups showed higher transition probabilities to move to the dead state either from the obese or from the obese-disease states than females.

Male transition probabilities from obese to obese with hypertriglyceridaemia (A-B) showed an increase with age in the age groups ≥ 45 years. A similar association was observed for the transition from obese with hypertriglyceridaemia to dead (B-C), but the increase with age occurred in all age groups. The estimations also showed that the transitions from obese-disease to dead (B-C) were higher in most of the age groups than the transition from obese without disease to dead (A-C) (Table 4.14).

Female transition probabilities from obese to obese with HTG (A-B) showed an increase with age in the age groups 45 to 59 years. A constant increase with age was observed for the transition probabilities from obese with the disease to dead (B-C). Female transitions from obese-disease to dead (B-C) were lower than the transition from obese to dead (A-C) for the age groups 30 to 59 years. However, for the age groups ≥ 60 years this changed, with higher transition probabilities from obese-disease to dead (Table 4.15).

Table 4.14 Transition probabilities between health states in Mexican male obese population for hypertriglyceridaemia (MexOb-HTG)

Age group	Obese-Obese (A-A)	Obese-Obese HTG (A-B)	Obese-Dead (A-C)	Obese HTG –Obese HTG (B-B)	Obese HTG-Dead (B-C)
20-24	0.9560	0.0409	0.0031	0.9965	0.0035
25-29	0.9698	0.0224	0.0078	0.9914	0.0086
30-34	0.9844	0.0029	0.0126	0.9861	0.0139
35-39	*0.9648	*0.0184	*0.0169	0.9808	0.0192
40-44	*0.9698	*0.0071	*0.0231	0.9745	0.0255
45-49	0.9618	0.0061	0.0321	0.9655	0.0345
50-54	*0.9402	*0.0160	*0.0438	0.9520	0.0480
55-59	*0.9059	*0.0346	*0.0595	0.9325	0.0675
60-64	*0.8647	*0.0538	*0.0815	0.9066	0.0934
65-69	*0.7954	*0.0979	*0.1066	0.8755	0.1245
70-74	*0.7368	*0.1357	*0.1275	0.8435	0.1565
75-79	*0.6887	*0.1643	*0.1470	0.8102	0.1898

* This value was originally <0 or >1. The original transition probability estimates are shown in Appendix table C-5

Table 4.15 Transition probabilities between health states in Mexican female obese population for hypertriglyceridaemia (MexOb-HTG)

Age group	Obese-Obese (A-A)	Obese-Obese HTG (A-B)	Obese-Dead (A-C)	Obese HTG –Obese HTG (B-B)	Obese HTG-Dead (B-C)
20-24	*0.9303	*0.0685	*0.0012	1.0000	0.0000
25-29	0.9380	0.0603	0.0017	0.9976	0.0024
30-34	0.9461	0.0487	0.0051	0.9950	0.0050
35-39	0.9581	0.0322	0.0098	0.9924	0.0076
40-44	*0.9766	*0.0005	*0.0229	0.9882	0.0118
45-49	*0.9451	*0.0245	*0.0304	0.9814	0.0186
50-54	*0.9185	*0.0438	*0.0377	0.9711	0.0289
55-59	*0.8952	*0.0550	*0.0499	0.9553	0.0447
60-64	*0.8880	*0.0503	*0.0616	0.9344	0.0656
65-69	*0.9109	*0.0152	*0.0739	0.9091	0.0909
70-74	*0.8802	*0.0348	*0.0850	0.8831	0.1169
75-79	*0.8156	*0.0887	*0.0957	0.8560	0.1440

* This value was originally <0 or >1. The original transition probability estimates are shown in Appendix table C-6

Transition probabilities for the MexOb hypercholesterolaemia model

Transition probabilities from obese to obese with hypercholesterolaemia (disease) (A-B) were higher for males than for females in the age groups 35 to 79 years. Overall, males from all age groups showed higher transition probabilities to move to the dead state either from the obese or from the obese-disease states than females.

Male transition probabilities from obese to obese with HCl (A-B) showed an increase with age for most of the age groups. The transition probabilities from obese with hypercholesterolaemia to dead (B-C) showed a constant increase with age in all the age groups. The estimations also showed that the transitions from obese-disease to dead (B-C) were higher than the transition from obese without disease to dead in all age- groups (A-C) (Table 4.16).

Female transition probabilities from obese to obese with hypercholesterolaemia (A-B) showed an increase only in the age groups ≥ 60 years. On the contrary, the transition probabilities from obese with the disease to dead (B-C) increased with age in all age groups. Female transitions from obese-disease to dead (B-C) were higher in all the age groups than the transition from obese without disease to dead (A-C) (Table 4.17).

Table 4.16 Transition probabilities between health states in Mexican male obese population for hypercholesterolaemia (MexOb-HCI)

Age group	Obese-Obese (A-A)	Obese-Obese HCl (A-B)	Obese-Dead (A-C)	Obese HCl – Obese HCl (B-B)	Obese HCl-Dead (B-C)
20-24	*0.9973	*0.0004	*0.0023	0.9955	0.0045
25-29	0.9798	0.0135	0.0067	0.9895	0.0105
30-34	0.9612	0.0278	0.0110	0.9834	0.0166
35-39	0.9453	0.0393	0.0154	0.9773	0.0227
40-44	0.9328	0.0477	0.0195	0.9704	0.0296
45-49	0.9163	0.0598	0.0238	0.9603	0.0397
50-54	0.9260	0.0454	0.0286	0.9450	0.0550
55-59	*0.8279	*0.1287	*0.0434	0.9260	0.0740
60-64	*0.7492	*0.1965	*0.0543	0.9037	0.0963
65-69	*0.6926	*0.2404	*0.0670	0.8790	0.1210
70-74	*0.6508	*0.2750	*0.0742	0.8541	0.1459
75-79	*0.6186	*0.3013	*0.0800	0.8291	0.1709

* This value was originally <0 or >1. The original transition probability estimates are shown in Appendix table C-7

Table 4.17 Transition probabilities between health states in Mexican female obese population for hypercholesterolaemia (MexOb-HCI)

Age group	Obese-Obese (A-A)	Obese-Obese HCl (A-B)	Obese-Dead (A-C)	Obese HCl – Obese HCl (B-B)	Obese HCl-Dead (B-C)
20-24	0.9509	0.0490	0.0001	0.9997	0.0003
25-29	0.9493	0.0489	0.0018	0.9970	0.0030
30-34	0.9490	0.0474	0.0036	0.9941	0.0059
35-39	0.9509	0.0436	0.0055	0.9912	0.0088
40-44	0.9538	0.0371	0.0090	0.9867	0.0133
45-49	0.9598	0.0263	0.0139	0.9795	0.0205
50-54	0.9676	0.0122	0.0202	0.9680	0.0320
55-59	0.9620	0.0071	0.0309	0.9499	0.0501
60-64	0.9371	0.0144	0.0485	0.9261	0.0739
65-69	0.9064	0.0254	0.0682	0.8971	0.1029
70-74	0.8738	0.0381	0.0881	0.8672	0.1328
75-79	0.8362	0.0554	0.1084	0.8360	0.1640

The original transition probability estimates are shown in Appendix table C-8

4.5 Open cohort component and growth ratio

4.5.1 Open cohort definition

Populations for cohort studies can be classified in two groups: static or closed, or dynamic or open. A closed cohort in modelling studies is one with a fixed membership: that is, once a cohort is defined (e.g. an obese population in 2015) and a forecasting period begins, no new members can be added. The number of obese persons in a closed cohort (without remission into normal weight) can only decline because persons progress to other states, including entering the absorbing state of death. In contrast, an open cohort is dynamic, meaning that members can be added over time (e.g. through immigration) (21). Figure 4-3 shows an example diagram of the distribution of the population across the different health states in a Markov model, including the open cohort component (represented by NP, the new population). In an open cohort simulation, the total initial population differs from the final population. In each cycle, the initial population is distributed across the different health states. Additionally, the open cohort component of the Markov model allows new members of the population to enter the health states over time.

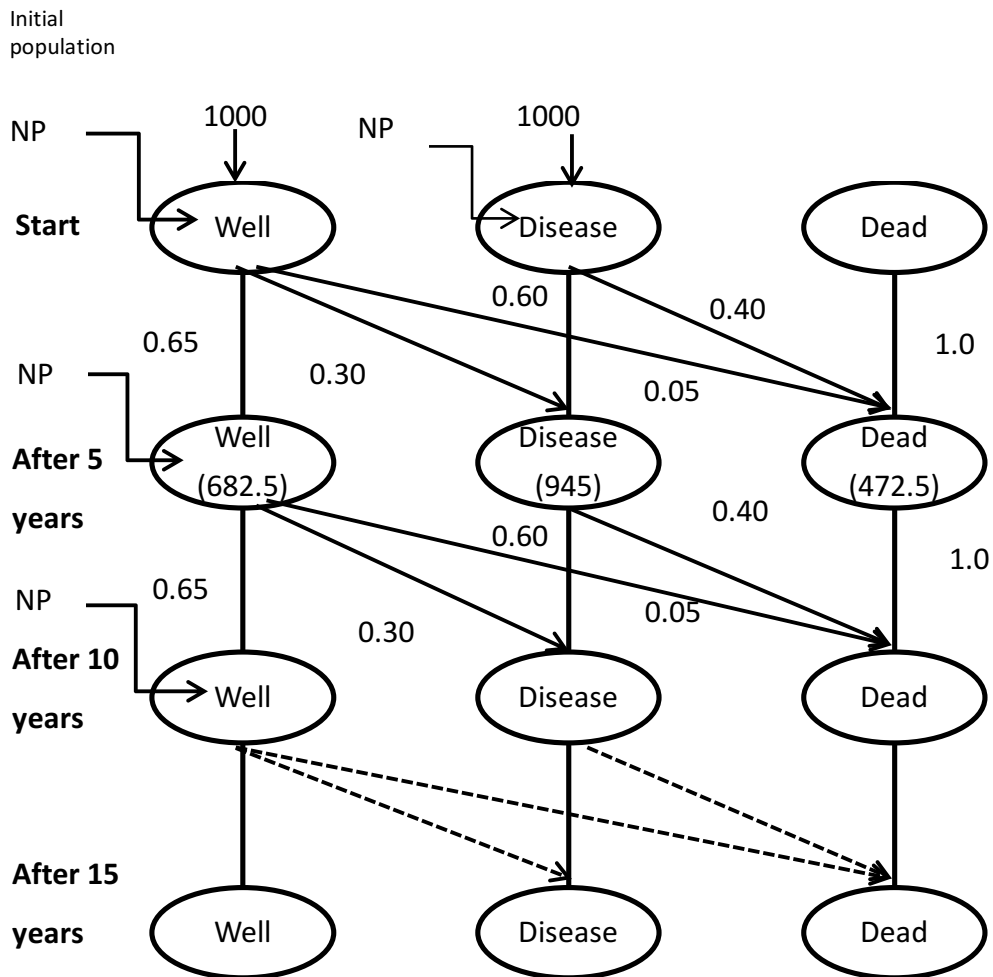
Figure 4-3 Example of an open cohort simulation of distribution across health states after each cycle in a Markov process

Let us imagine that 1000 people began in the well state, and that 1000 people began in the disease state. Let us assume that the beta coefficient (denoting the annual change in obese prevalence) was 0.010, and so amounted to 0.050 over a five-year period. At the beginning of the cycle, applying the beta-coefficient to accommodate new cases increases the size of the well and the disease groups each by 50. After applying the transition probabilities, 682.5 persons remained in the well state ($1050 * 0.65$). 945 persons finished in the disease state, made up of 630 persons who remained in the disease state ($1050 * 0.6$) and 315 people who flowed into the disease state through the obese to disease transition ($1050 * 0.3$). At the end of the cycle, 472.5 persons had reached the absorbing state of death: 52.5 persons from the well state ($1050 * 0.05$)

and 420 persons from the disease state ($1050 * 0.4$). Similar calculations proceed for the remaining five-year cycles.

Transition probabilities:

- well to well (0.65)
- well to disease (0.30)
- well to death (0.05)
- disease to disease (0.60)
- disease to death (0.40)



NP: New population
Diagram adapted from Siebert et al. (188)

The MexOb-Model was developed to follow the progression of an open cohort. The open cohort component of the MexOb-Model was included into the model by adding new cases in every cycle to both the obese-with- and the obese-without- disease populations, and by using a growth ratio for the obese-with-disease population. These two factors were implemented into the MexOb-Model Markov chain model using the following method.

4.5.2 MexOb-Model open cohort component

The open cohort component was included into the MexOb-Model to take into account the addition of new members of the obese population (i.e. new cases of obesity from a population that was not obese at the beginning of the cycle). The number of new cases was obtained by multiplying the total population in each of the health states at the beginning of the cycle by the age-group and sex-specific β -coefficient for the corresponding year simulated (where the baseline year for the linear trend 1999 was defined as year 0; up to 31 for the final year 2030).

Using the β -coefficients obtained from the linear trend equation as described in Chapter 3, the formula for the open cohort component is as follows:

Formula:

$$y = \text{population in health state} * (\beta * \text{year})$$

y =the number of obese persons at the beginning of the cycle

This open cohort component was applied to the population before applying the relevant set of transition probabilities to estimate the number of cases that transition to the next health state.

4.5.3 MexOb-Model growth ratio

A growth ratio (GR) was included as part of the MexOb-Model to adjust the numbers of the population with disease that will correspond to the next obese-disease age group. This age group and sex-specific obese with disease population growth ratio was obtained using the prevalence of the cardiometabolic risk factor within the obese population that was obtained from ENSANUT 2006 (ENSANUT 2012 data was not available at the time of analysis). The growth ratio was calculated using the following formula where x represents the index of the age group:

$$GR = \frac{Ob + D_{x+5}}{Ob + D_x}$$

This growth ratio was kept constant for each of the three five-year cycles but was specific for each of the four obesity-related diseases. It was incorporated into the Markov chain for the MexOb-Model after the population flowed through the relevant transition probabilities to the next health state, just before the end of the five-year cycle. Table 4.18 and

Table 4.19 show the growth ratios for males and for females respectively that were used as components to the Markov chain of the MexOb-Model.

Table 4.18 Growth ratios for the male obese with disease population.

Age group	OB+HT	OB+T2DM	OB+HTG	OB+HCl
20-24	1.074	1.000	1.166	1.060
25-29	1.107	1.357	0.982	0.967
30-34	1.091	1.498	0.992	1.021
35-39	1.079	0.930	0.985	1.232
40-44	1.117	1.120	1.022	0.982
45-49	1.163	1.529	1.209	1.064
50-54	1.261	1.472	1.020	1.270
55-59	0.912	0.945	0.937	0.899
60-64	1.070	0.607	0.726	1.130
65-69	1.093	0.775	0.953	0.735
70-74	0.882	0.577	0.660	0.645
75-79	0.974	0.801	0.793	1.002

OB: obese. HT: hypertension. T2DM: type 2 diabetes mellitus. HTG: hypertriglyceridaemia. HCl: hypercholesterolaemia.

Table 4.19 Growth ratios for the female obese with disease population

Age group	OB+HT	OB+T2DM	OB+HTG	OB+HCl
20-24	1.416	0.819	1.504	1.194
25-29	1.099	1.195	1.107	1.108
30-34	1.172	1.208	1.155	1.056
35-39	1.326	1.294	1.027	1.007
40-44	1.161	2.121	1.008	1.431
45-49	1.231	1.130	1.207	1.016
50-54	1.045	1.136	0.908	1.017
55-59	1.140	0.902	0.925	0.959
60-64	1.017	0.978	0.940	0.893
65-69	1.075	0.908	1.030	0.966
70-74	1.005	0.880	1.193	1.074
75-79	0.993	0.841	0.996	0.856

OB: obese. HT: hypertension. T2DM: type 2 diabetes mellitus. HTG: hypertriglyceridaemia. HCl: hypercholesterolaemia.

4.6 MexOb-Model Markov model structure

4.6.1 MexOb-Model steering parameters

This section describes the steering parameters used in the Markov model to estimate the impact of the increase in the prevalence of obesity on its four related cardiometabolic risk factors (HT, T2DM, HTG, and HCl) over the 15 year period from 2015 to 2030.

The main steering parameters of the Markov model were: the prevalence of obesity with and without the obesity-related cardiometabolic risk factor, the secular increase in obesity prevalence (open cohort and growth ratio), and the mortality and the survival transition probabilities between the transition health states (Figure 4-1).

The initial population in the MexOb-Model uses the projected obesity prevalence in the adult population for 2015, stratified into two groups: obese with, and obese without the risk factor of interest. The prevalence of risk factors within the obese population were held constant at the observed 2006 values. As described above, the

MexOb-Model uses an open cohort component to take into account the number of new individuals that could enter the obese- with and the obese without disease groups during the projected time frame. The open cohort component was incorporated into the MexOb-Model by including into the model: the β -coefficients from the linear trend equation, and the disease-specific growth ratio component. The open cohort component (β -coefficients from the linear trend equation) was included in the Markov chain model before the population progressed to their next health state via the relevant set of transition probabilities. After transitioning to its next health state, and before reaching the end of the cycle terminal node, the disease-specific growth ratio (GR) was included by multiplying the number of surviving obese with disease cases by this growth ratio.

The probabilities of multiple step transitions were calculated by multiplying the transition matrix by itself the number of times (n steps) required to obtain the desired estimations. For example, if the system begins in state P1, then the probability of moving to P3 after n steps will be: $P_{13}(n)$. The individuals could transition from each of the health states during each modelling cycle. For the MexOb-Model, a cycle corresponded to a five-year period. In total for this model, the population completed three five-year cycles covering the time period 2015 to 2030.

Figure 4-4 shows a graphic description of the structure of the MexOb-Model Markov process that was used to estimate the outcomes as it was implemented in TreeAge Pro version 2015 software.

4.6.2 MexOb-Model outputs

The MexOb-disease Markov models were built independently for each of the four obesity-related cardiometabolic risk factors (MexOb-HT, MexOb-T2DM, MexOb-HTG, and MexOb-HCl).

For every cycle, the following outputs were estimated:

- Prevalence and number of new cases of the obese-without-disease population
- Prevalence and number of new cases of the obese-with-disease population
- Number of deaths in the obese-without-disease and the obese-with-disease populations

Using TreeAge software, the models were run separately for each of the four risk factors. Therefore, it is not possible to estimate the total size of the obese population with or without disease at the end of each five-year cycle (2020, 2025, and 2030) by simply adding the number of obese-disease cases across the four MexOb-disease models, as this would overestimate the true number of obese individuals.

4.7 Key assumptions of the MexOb-Model

The results of simulation models are highly dependent on the data used as inputs for the model, and are also highly dependent on the set of assumptions that the modellers made during the process of building it. It is of great significance to specify the assumptions I took during the development of the MexOb-Model to enable a considered interpretation of the results; and to enable a thorough discussion of its strengths and limitations. The key assumptions made during the process of developing the MexOb-Model were the following:

- I did not take into account the co-morbidity that normally exists within the health state of obesity and in its associated cardiometabolic risk factors (233-235). This, as a consequence, could alter the transition probability estimates. For example, it is highly probable that an obese person with diabetes also has hypertension, and that this obese individual with both diabetes and hypertension will have a higher probability of dying within a five-year cycle than an obese person with diabetes or hypertension but not both.
- I assumed that the prevalence of the four obesity-related cardiometabolic risk factors in the obese population remained steady from 2006 to 2015. The initial population for the model was the total obese population estimated for 2015, divided according to the prevalence of obese adults with, and without, the risk factor of interest. These percentages were based on the number of obese with, and without, the disease as observed in the ENSANUT 2006 data, as the ENSANUT 2012 data were not available at the time of model-development. It is probable that by doing this, I am underestimating to some extent the future levels of obesity and underestimating its future consequences such as the number of deaths.
- To feed the open cohort component of the model, I used the estimates of linear trend (β -coefficient) based on historic data, to increase the size of the obese population with and without the disease to accommodate new members.

Therefore the MexOb-Model assumes that the trends will continue, and that the growth of the overall obese population would be the same for both subgroups (i.e. with and without the cardiometabolic risk factor). The same assumption applies for the disease specific growth ratio.

- The MexOb-Model assumes that persons entering the state of obesity (with or without the cardiometabolic risk factor) do not leave the state of obesity until their death (i.e. zero remission rate). Therefore the MexOb-Model will slightly overestimate the prevalence of obesity as it does not allow for the transition of individuals out of the obese state into non-obese states such as overweight or normal weight possibly as a result of major medical conditions or interventions (236).
- The estimated transition probabilities for the MexOb-Model were assumed to remain static during the 15 year projection period. This reflects our uncertainty about the change over time (if any) in the magnitude of the hazard- and risk-ratios used for the calculations obtained from the literature review that were deemed most relevant for the Mexican adult population. In reality, there could be environmental, biological, and technological factors that could modify the size of the hazard-and risk-ratios during this time period, either increasing or decreasing the probabilities (e.g. obese with disease to death) across the various states.
- Mortality rates for the general population are transformed into mortality rates for the obese and non-obese groups assuming that: (1) the age- and sex-specific mortality rates in the general population are the weighted average of the mortality rates for the obese and non-obese populations, with the proportions of each group serving as the weight; and (2) that the ratio between the mortality rates of the obese and non-obese groups is equal to the HR chosen from the available estimates. A third assumption for this study is that the HRs are assumed constant over the time period.

4.8 Discussion

The MexOb-Model was built with the aim of representing the future of obesity and obesity-associated cardiometabolic risk factors for the Mexican adult population from 2015 to 2030. To build this model the best and most recent available evidence from Mexican data sources was integrated. Epidemiological data for the Mexican population is extensive; still, there was some data needed for the model that was obtained from international sources because it was not available for the Mexican population. Furthermore, some of the estimates used were not specific for my target population (obese) requiring some adjustments to be made to ensure estimates for the general population would also be suitable for application to the obese population.

Transition probabilities between health states

Transition probabilities between health states for epidemiological Markov models have traditionally been estimated using longitudinal data where the transitions across health states (e.g. obese to death) for members of the study population were directly observable over the follow-up period. Several statistical software packages exist that could estimate the transition probabilities based on longitudinal data, such as TPmsm and ets (237, 238). However at the time of this analysis, databases from Mexican longitudinal studies such as The Mexico City cohort were not available to the public, and the studies published to date from this cohort do not contain the data needed to feed the MexOb-Model (239).

Due to the lack of data from Mexican longitudinal studies to feed my model, after a systematic review of available methods and data sources and consultation with colleagues, I decided to estimate the transitions between the three health states of obese, obese-with-disease, and death with a set of non-parametric equations using data on disease prevalence and mortality from cross-sectional data, and data on disease-specific mortality hazard and risk ratios, with the assumption that the transition probabilities remain stable over the 15 year projection period. The statistical

methods necessary to estimate transition probabilities using cross-sectional rather than longitudinal data are complex with few examples reported in the literature (240). These complex methods are also not part of commonly used statistical software packages.

There are a range of other methods that have been used to obtain country-specific epidemiological data, such as: risk factor prevalence, incidence, disease-specific estimates of relative risk, and case-fatality rates to estimate cause-specific mortality, when no data is available. For example, Webber et al. (118) and Al-Quwaidhi et al. (122) used country specific incidence, risk ratios, and case fatality rates to estimate the transition probabilities between health states for their simulation models. They obtained this information using the WHO Software DisMod2 (241). DisMod2 is a model that was originally developed for the Global Burden of Disease (GBD) Study (1990). DisMod software is regularly used to assess disease-specific epidemiological information when country specific data are scarce. This model is formed by a set of differential equations: the objective is to estimate age-sex specific incidence, remission, case fatality and all other cause mortality rates. Recently, an updated version of this software, DisMod-MR, was created for the most recent GBD-2010 study (242). DisMod2 is freely available software that requires data of at least three disease burden parameters as inputs in order to estimate the outputs. It uses input data that is commonly available for the majority of countries and is available for most diseases, such as prevalence, mortality, and disease remission rates. However, as with any model, it has some limitations. The quality of the data used as the input for DisMod software has to be taken into account when interpreting the results obtained. For example, when country specific data is scarce, input data would usually be extracted from different data sources and there could be wide time intervals between data points. To overcome this, the model estimates these missing values by interpolating the values of the given data and smoothing. Additionally, the researchers have to consider using the correct weights for the input data, and the possibility of measurement error (241). Users often require previous knowledge of the inputs used,

and must carefully assess the evidence available to be able to judge if the estimations obtained are fit-for-purpose.

When published, the majority of the simulation models include an extensive and detailed description of the methods used to obtain data and any data manipulation. Unfortunately for the inexperienced user, these detailed descriptions could still be a black box, and this reduces the understanding of the model, its key assumptions, and how to interpret the results. For my modelling exercise, I decided to use a non-parametric equation method in an attempt to use a more transparent method for estimating the transition probabilities using cross-sectional data as input data in the absence of longitudinal data. This method could be easier to understand and replicate by the modelling and public health community even without previous expert knowledge. Additionally, it uses cross-sectional prevalence data that is commonly available in most countries.

Despite the fact that a non-parametric equation could be better understood by non-expert eyes, I am aware that this method also has some limitations. A non-parametric equation by definition is not constrained by the limits of the probability lying between 0 and 1, but instead it follows the data, and as a result it could estimate transition probabilities <0 and >1 . In this particular case, when estimating the sex and age-group specific disease transition probabilities, the data did not show a smooth age-related increase or decrease principally for two of the four cardiometabolic risk factors (diabetes and hypercholesterolaemia (see: Appendix C). This result could have been influenced by the input data used for estimation of the transition probabilities, which for the MexOb-Model came from cross sectional surveys. However, the patterns of the transition probabilities for diabetes and for hypercholesterolaemia could also be a reflection of the obesity paradox, which states that mortality in relation to obesity can have a U-shape or J-shape curve, particular in the older population (243-246). The obesity paradox refers to the hypothesis that obesity may be protective and could be associated with greater survival for certain conditions and for certain groups of people

(247). A J shape curve for the association between BMI and all-cause mortality suggests that the risk of death was generally lowest among persons with BMI of 20 to 24.9kg/m² and higher for persons with a BMI <20kg/m² or a BMI ≥25kg/m². J-shape curves have also been reported for hypertension (SBP and DBP) and all-cause mortality (248). U shape curves for the association between BMI and mortality suggest a higher risk of mortality for persons at the extreme ends of the BMI distribution (i.e. persons underweight and morbidly obese).

There is increasing epidemiological evidence which suggests that there has been a reduction of the effect of obesity on mortality over time. Flegat et al. for example observed that the association between overweight and obesity on mortality have weakened over the last decades. A number of reasons have been put forward for the reduction of the effect of obesity over time. These include: 1) medical advances in the treatment of obesity-related comorbidities such as hypertension; and (2) better access to treatment amongst high-risk groups such as the obese (249).

Other possible cause from Yan et al. also suggest other possible causes. These include the changing distribution of fat free mass (shifting BMI distribution within static BMI categories), and that the observed weakening effect of BMI on mortality over time could be an artefact due to using BMI as a categorical rather than continuous variable(250).

Some researchers have used the population attributable fraction (PAF) as a model steering parameter to estimate only the number of new cases that are attributed to the specific risk factor (122). The PAF refers to the proportion of disease or mortality in the population that is attributable to the risk factor/exposure and thus the proportion of mortality or disease that can be avoided if the risk factor/exposure was eliminated (251). In other words, the PAF could be used to estimate the number of new disease cases that were developed only because the individual was obese. For the purposes of

the MexOb-Model, I decided to include as new cases all members of the population classed as being obese with the cardiometabolic risk factor (obese-disease) regardless of whether the presence of the risk factor (e.g. hypertension or diabetes) was directly due to obesity or not. This model assumption was consistent with the idea that the disease burden to the health services, and any potential reduction in the quality of life for individuals in the obese-with-disease group, are equally affected independently of whether individuals were diagnosed with the cardiometabolic risk factor before or after becoming obese. It is the combination of risk factors that increase the probability of further complications and premature mortality.

Mortality data decomposition

Specific mortality rates for the obese and the obese with a cardiometabolic risk factor groups were not available for the Mexican population. Publically available mortality data bases from the Mexican Ministry of Health routinely report only the principal cause of death from the death certificate. Usually the obesity-associated risk factors, despite being a diagnosis at the time of death, are usually not reported as the first cause of death, making therefore the estimation of disease-specific mortality rates difficult. To overcome this obstacle, I adapted the mortality rates for the general population using a well-established decomposition formula (224, 225). This carries as a consequence a possible over- or under-estimation of my results, depending on the mortality risk I used as an input in the decomposition formula.

The hazard ratio (HR) comparing obese individuals with normal weight individuals was taken from the Felga et al. meta-analysis. The researchers collected data from Mexico, US and European populations. This provides to the HR estimates an heterogeneity that made possible that the value could be generalized to the Mexican population(226). For diabetes, I used a HR for the American obese population: the HR for obese-diabetics was below 1 which indicated a lower risk of death for obese-diabetics compared with normal weight diabetics (228). Previous studies have found that normal weight type 2

diabetic individuals have higher risk of mortality than obese type 2 diabetic individuals (252, 253) Therefore I wanted to take this in consideration for my model as I targeted only obese individuals. This study showed that overall diabetics have a higher mortality rate than non-diabetics. However when stratified by BMI, mortality rates were observed to decrease as BMI increases. However this study has some limitations, it is based on cross-sectional self reported data in the US population.

For hypertension, hypertrygliceridaemia, and hypercholesterolaemia I used HR and RR estimates applicable to the Mexican-American population (227). It is important to consider that these estimates that came from the same cohort. San Antonio Heart Study in which Mexican-Americans constitute 63% of the analytical sample. Unfortunately, this study has some limitations that have to be taken into consideration, It is a cohort with only two waves of information (1979-1982 and 1984-1988). It includes only individuals aged 25 to 64y and that the estimates are not sex or age specific. There is a well-known controversy about the extent of the mortality differences between the Hispanic and non-Hispanic populations. Some studies have shown a lower mortality risk for hypertension or for diabetes for the Hispanic population compared with African American populations (254). Other studies found a higher risk for the Mexican-American population than for non-Hispanic whites after adjustment for confounders (255, 256). Furthermore, when comparing the Mexican and USA populations, it has been observed that the Mexican obese population has a higher all-cause mortality risk than the American population (257). Additionally, a slightly higher mortality diabetes risk between Mexican inhabitants and Mexican-American inhabitants has also been reported (258).

As discussed above, the HR for the American obese population indicated a lower risk of death for obese diabetics compared to non-obese diabetics (228). This article by Jackson et al. observed that death rates in individuals with diabetes fell with increasing BMI, but also observed that death rates among non-diabetic individuals increased with increasing BMI (228). In a similar fashion, the estimated transition probabilities for the MexOb-T2DM were different from the other three diseases in that the transition

probabilities to death were lower for obese persons with diabetes than for obese persons without diabetes. However, the scientific evidence for the association between BMI and mortality in individuals with diabetes has shown different patterns of association: positive, inverse or U-shaped associations (259-261).

4.9 Conclusions

The best available Mexican epidemiological data was used to feed the MexOb-Model. However, due to the scarce data for some parameters, it was necessary to apply widely used formulae to decompose the overall mortality rates for the general population, and use input parameters from external international data sources to achieve a proper functional model. Knowledge about the data sources used for input data, and the set of key assumptions used for the development of the MexOb-Model, should be taken into consideration when interpreting the results presented in the following chapters. The input data, steering parameters, and methods integrated into the MexOb-Model ensure that it has great flexibility, conferring on it the characteristic to be easily modifiable as new and/or better data becomes available.

Chapter 5. Mexican Obesity Forecast Model (MexOb-Model).

Validation

5.1 Introduction

One of the principal characteristics of a population simulation model is that it tries to represent the future trends of a disease based on the historic data as closely as possible to reality. The International Society for Pharmacoeconomics and Outcomes Research (ISPOR)-Society for Medical Decision Making (SMDM) guidelines recommend that a validation process should be included as part of the process of developing a model (32), to observe if the outcomes produced by the population simulation model represent the outcomes from a target population.

Model validation is used to assess the accuracy and reliability of the model within the domain of its applications (262). The ISPOR-SMDM task force states that the validation of a model can be done using: face validity, internal validity, cross-validity, external validity and predictive validity. Validation exercises were used as part of the development of the MexOb-Model, with the aim of strengthening the validity of my results.

To perform the validation of the MexOb-Model, I used three different methods: internal validation, external validation, and cross-validation. Internal validation is used to examine if the calculations of the model are performed correctly; this validation is considered to be internal when the model outcomes are compared with the observed data from a source that was also used in the development of the model. External validation is used to compare the model results with data from an actual event not used as input for the model. Cross-validation involves comparing outputs from the model with results from different models that largely address the same research problem (32).

The validation exercises performed during the development of the MexOb-Model were as follows:

1) Internal validation: Compared the total projected obesity prevalence from each of the four disease models: MexOb-hypertension (MexOb-HT); MexOb-type 2 diabetes mellitus (MexOb-T2DM); MexOb-hypertriglyceridaemia (MexOb-HTG); and MexOb-hypercholesterolaemia (MexOb-HCl) with the obesity prevalence directly observed in the Mexican Health and Nutrition Survey (ENSANUT) 2012.

2) External validation: Compared the results of the MexOb-hypertension model with the prevalence of hypertension among the obese population directly observed in the ENSANUT 2012.

3) Cross-validation: Compared the projected obesity prevalence from the MexOb-Model against the future obesity prevalence produced from my linear trend estimates and from the Foresight model, another population simulation model that estimated future levels of obesity in the Mexican population (115).

This chapter presents the methods and the results of the validation process of the MexOb-Model, as well as a discussion of possible explanations for differences between the sets of estimates.

5.2 Internal validation: Comparison of obesity prevalence model outcomes with ENSANUT 2012 observed data.

The four MexOb-disease models were internally validated by comparing the total obesity prevalence obtained from each disease model with the obesity prevalence estimates directly observed from ENSANUT 2012. The obesity data from ENSANUT 2012 was used to build the linear trend projection estimates for the first component of

the MexOb-Model, and was also used in the mortality decomposition formula (see: Chapter 4). The ENSANUT estimates of obesity prevalence were not disease-specific; therefore each of the four MexOb-disease models was compared against the same set of estimates. Details about the methods used to analyse the obesity data in ENSANUT 2012 was previously described in Chapter 3.

5.2.1 Methods

For the internal validation simulation exercise, I used as the MexOb-Model initial population, the 2007 population obtained from CONAPO stratified by five-year age groups and sex (263). This population was distributed according to the prevalence of obese individuals with, and without, the cardiometabolic risk factor of interest for each of the age groups from ENSANUT 2006, as described in Chapter 4. The MexOb-disease Markov model uses as its steering parameters: the open cohort component, the growth ratio, and the transition probabilities between the health states (obese, obese-disease, and death). These parameters were given the same values derived from the equations described in Chapter 4. These three sets of parameters influence the estimated outcomes of the total projected obesity prevalence from the MexOb-Model. However, the MexOb-Model was developed to estimate the prevalence of obesity as closely as possible to the obesity prevalence estimated from observed survey data and from the linear trend estimated from the repeated cross-sectional surveys.

Each of the four MexOb-disease models was run for one five-year cycle to simulate the time-period between 2007 and 2012. Outcomes were estimated for each of the five-year age groups in the population aged 20 to 79years. The total obesity prevalence for each age group for 2012 was calculated by adding the number of obese individuals with, and without, the cardiometabolic risk factor after the completion of the single five-year cycle for each sex and age group, and dividing the estimated number of obese persons by the estimated total population for 2012 for that same sex and age-

group, from the CONAPO population projections (63). The estimates were then compared with the observed prevalence of obesity from ENSANUT 2012.

5.2.2 Results

Figure 5-1 to Figure 5-8 below show the difference in obesity prevalence between each of the four MexOb-disease models and those estimated directly from ENSANUT 2012.

Overall, the results showed an underestimation of the projected level of obesity for all the models in both sexes when compared with the prevalence estimated from the observed data. However, most of the MexOb-Models' estimates fall within the 95% CI of the ENSANUT 2012 observed obesity prevalence. Of the four models, the MexOb-HT disease model for males and for females showed the lowest difference between the two sets of prevalence estimates. The MexOb-disease models' underestimation of the observed ENSANUT obesity prevalence was $\leq 11\%$ for males and for females (in absolute terms). The results of the internal validation exercise are discussed separately below for each of the four modules.

MexOb-hypertension model (MexOb-HT)

The MexOb-hypertension model for males showed the lowest underestimation of the total obese population in the 20 to 24y, with an absolute difference between the observed prevalence and the model estimates of approximately $<0.1\%$. I observed the highest underestimations in obesity prevalence in the 70 to 74 year age group, with an absolute difference of 9.2% between the modelled estimate for males and the observed data from ENSANUT2012 (Figure 5-1).

The MexOb-hypertension model for females showed the lowest underestimation in the 25 to 29 year age group, with an absolute difference of 0.3% between the model outcomes and observed ENSANUT estimates. I observed that for the population ≥ 40 years old, the MexOb-HT model outcomes showed underestimations in obesity

prevalence between 2.8% and 8.6%, with the highest level of underestimation observed in the 70 to 74 year olds (Figure 5-2).

MexOb-type 2 diabetes mellitus model (MexOb-T2DM)

The MexOb-diabetes model for males estimated obesity prevalence outputs showed the lowest underestimation of the total obese population in the 30 to 34 year olds, with an absolute difference between the model and the observed survey estimates of approximately <1%. The highest underestimations produced by my outcomes were 9.6% in the 60 to 64 year old males and 9.8% in the 70 to 74 year olds (

Figure 5-3).

The diabetes model for females showed the lowest underestimation in the 20 to 29 year age groups, with an absolute difference of <0.5% between the MexOb-T2DM model outcomes and the ENSANUT estimates for both age groups. The highest underestimation was observed in the 55 to 59 year age group (11.4%) (Figure 5-4).

MexOb-hypertriglyceridaemia model (MexOb-HTG)

The MexOb-hypertriglyceridaemia model for males showed the lowest underestimation of 3.2% in the 25 to 34 year age groups and the 75 to 79 year age group. The highest underestimation produced by the MexOb-HTG model showed an absolute difference between the MexOb-Model and ENSANUT prevalence estimates of 10.1% in the 70 to 74 year age group (

Figure 5-5).

The MexOb-HTG model for females showed the lowest underestimation in the 30 to 34 year olds (0.8%). The highest underestimation was observed in the 55 to 59 year

age group with an absolute difference between the model outcomes and the observed ENSANUT estimates of 11.6% (Figure 5-6).

MexOb-hypercholesterolaemia model (MexOb-HCI)

The outcomes from the hypercholesterolaemia model for males showed the lowest underestimation in the 20 to 24 year age group, with an obesity prevalence modelled estimate that was 0.03% lower than the observed prevalence from ENSANUT 2012 for that age group. The highest underestimation (11.0%) was observed in the 70 to 74 year age group (

Figure 5-7).

The hypercholesterolaemia model for females showed the lowest underestimation in the 30 to 34 year age group (1.8%). The MexOb HCI model showed the highest underestimation (11.2%) compared with the ENSANUT prevalence in the 55 to 59 year age group (Figure 5-8).

Figure 5-1 Internal validation of MexOb-hypertension (MexOb-HT) male model. Results for 2012.

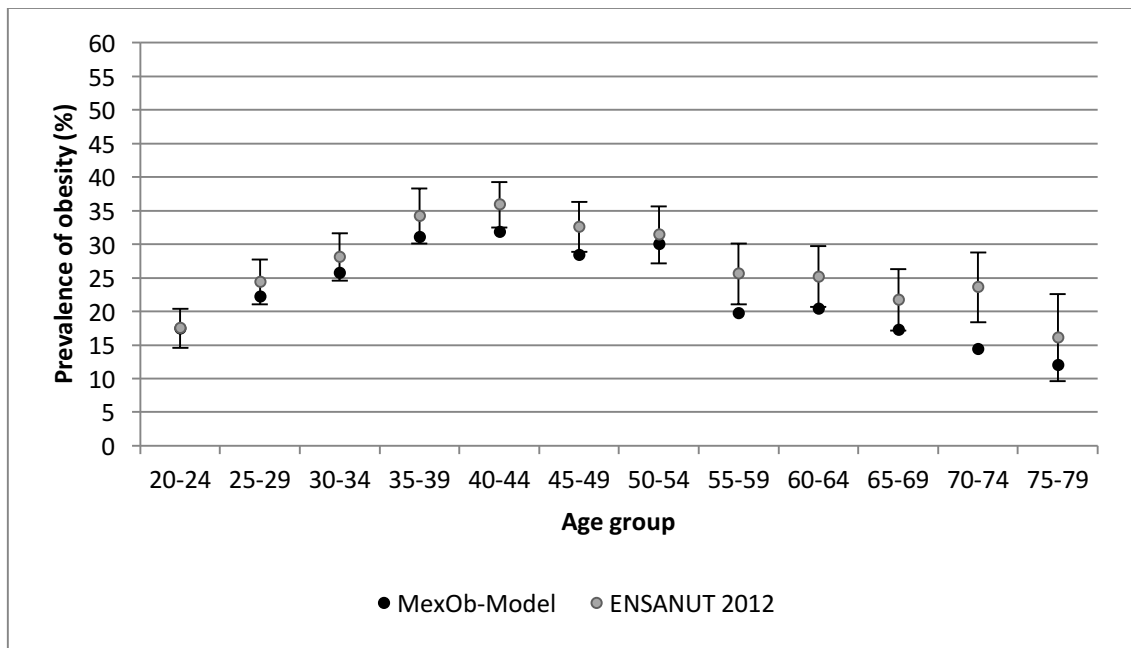


Figure 5-2 Internal validation of MexOb-hypertension (MexOb-HT) female model. Results for 2012.

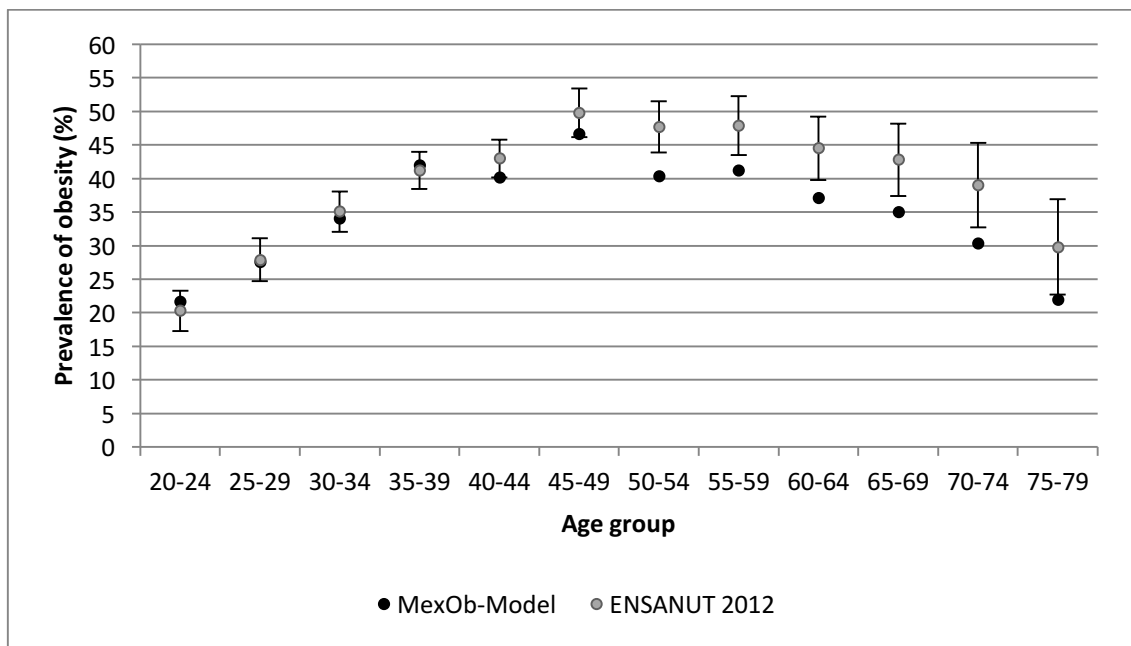


Figure 5-3 Internal validation of the MexOb-type 2 diabetes mellitus (MexOb-T2DM) male model. Results for 2012.

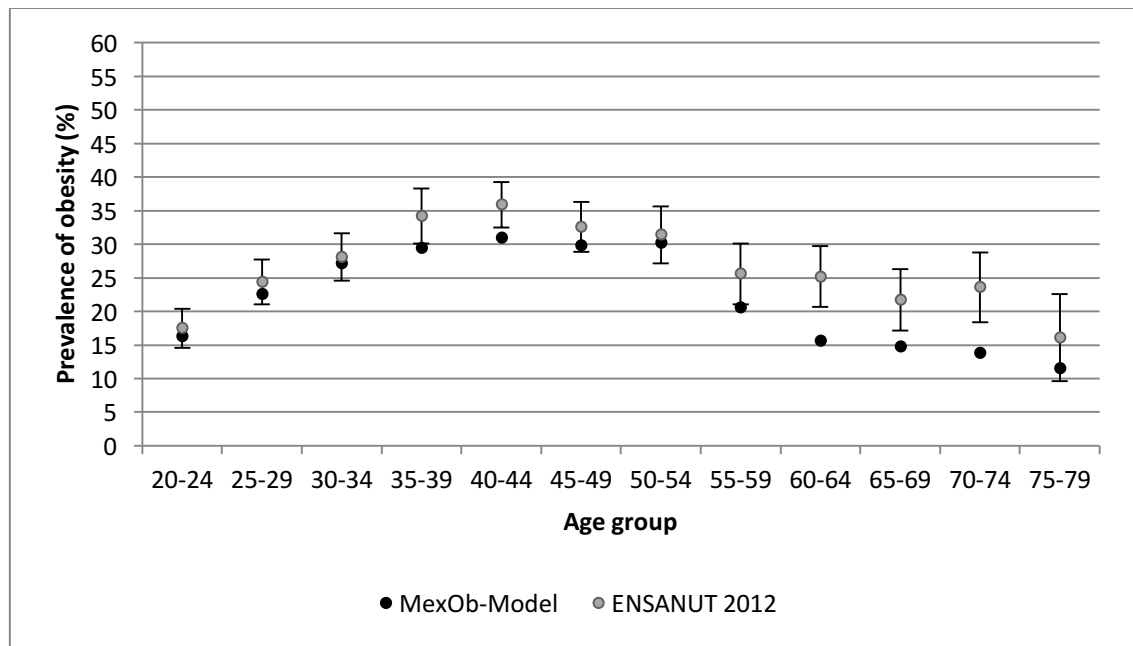


Figure 5-4 Internal validation of the MexOb-type 2 diabetes mellitus (MexOb-T2DM) female model. Results for 2012.

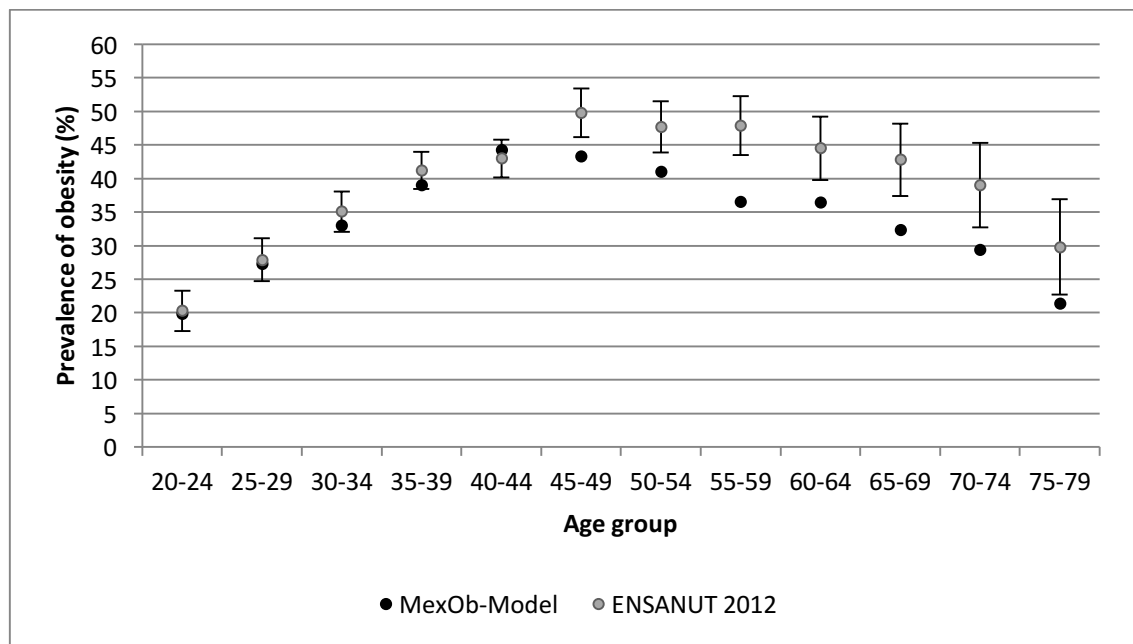


Figure 5-5 Internal validation of the MexOb-hypertriglyceridaemia (MexOb-HTG) male model. Results for 2012.

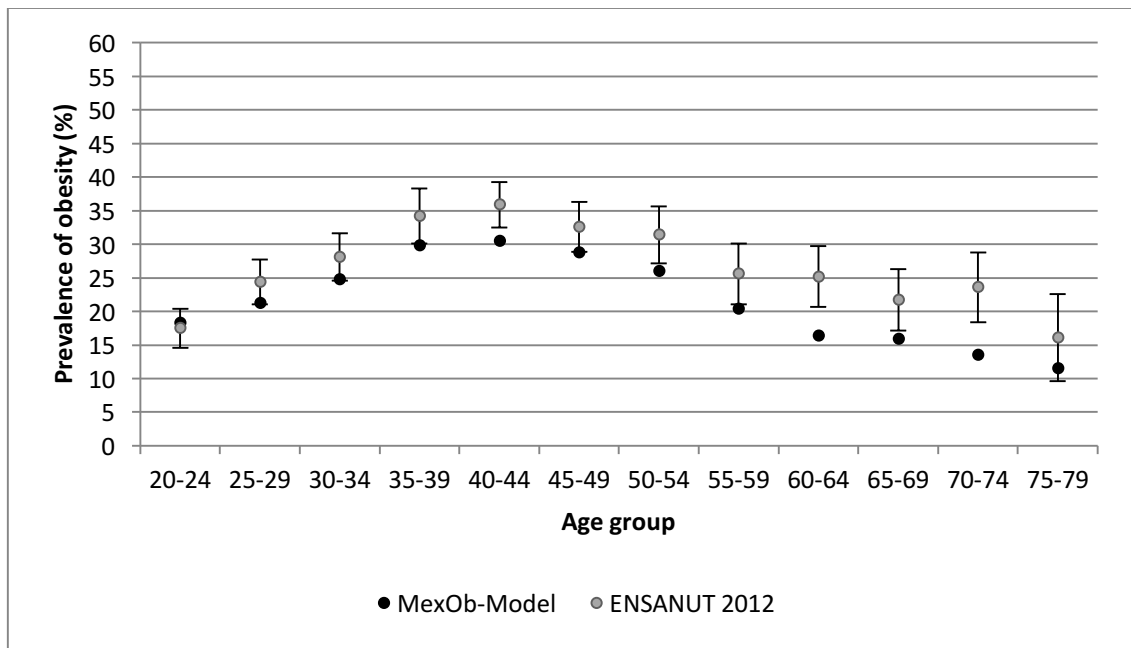


Figure 5-6 Internal validation of the MexOb-hypertriglyceridaemia (MexOb-HTG) female model. Results for 2012.

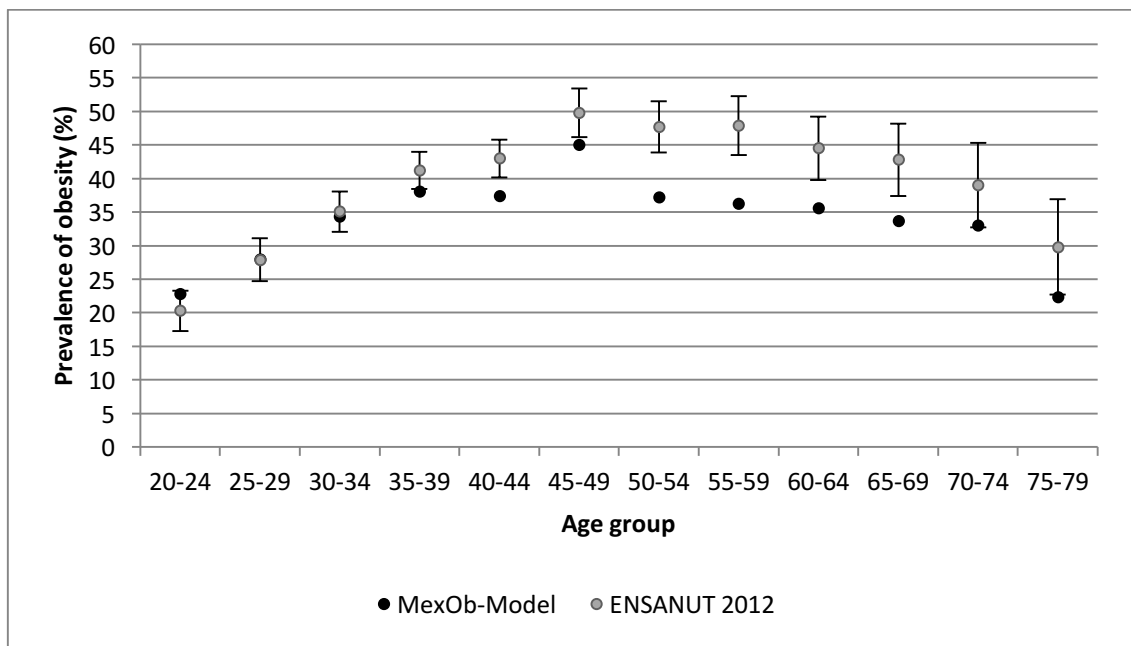


Figure 5-7 Internal validation of the MexOb-hypercholesterolaemia (MexOb-HCI) male model. Results for 2012.

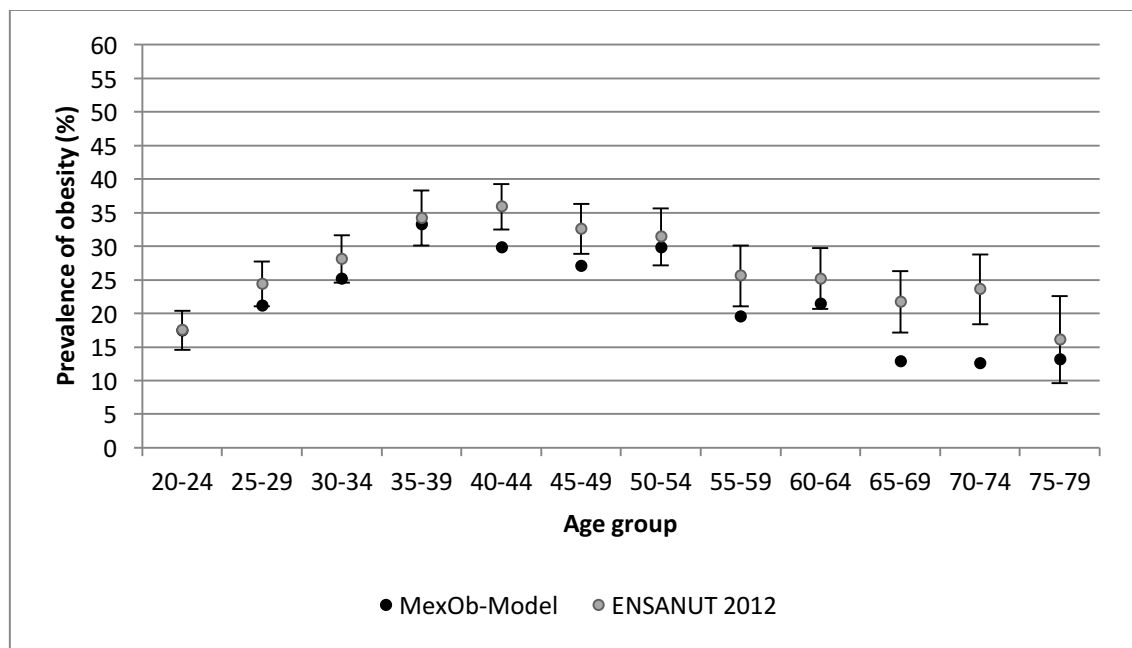
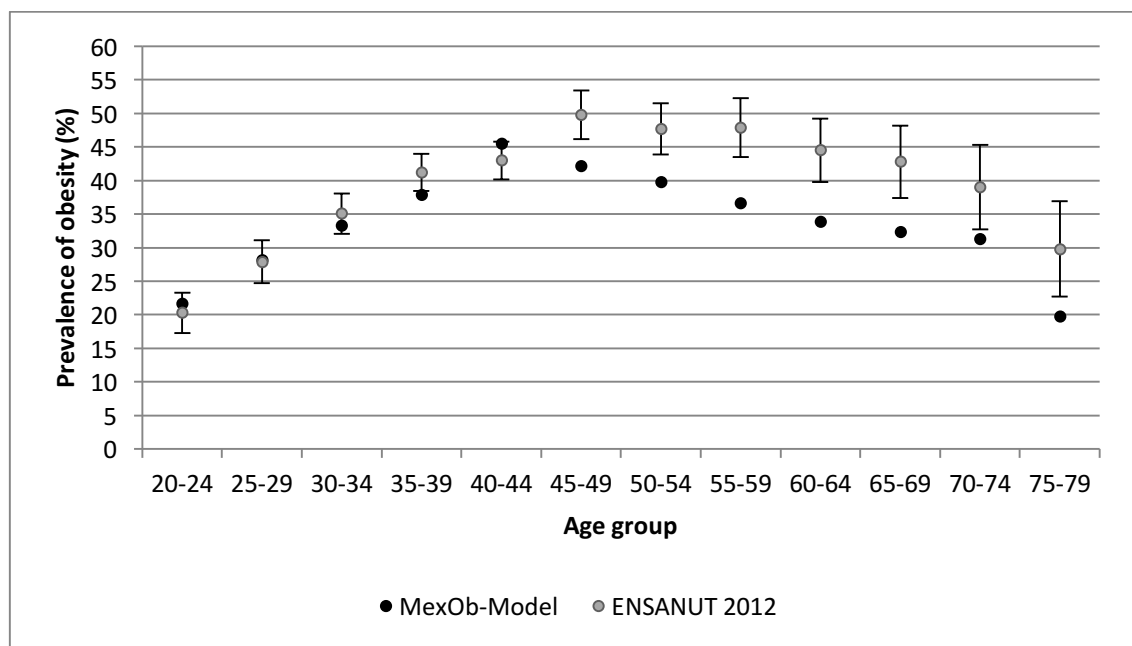


Figure 5-8 Internal validation of the MexOb-hypercholesterolaemia (MexOb-HCI) female model. Results for 2012.



5.3 External validation: Comparison of the MexOb-hypertension model with ENSANUT 2012 observed results.

An external validation exercise was used in order to compare the model estimates against a data source that was not included in the development of the MexOb-Model. In this section I compare the MexOb-Model estimates of the prevalence of hypertension among the obese population (MexOb-HT) for males and for females estimated for the year 2012 with the results for that same population directly observed from ENSANUT 2012. Total obesity prevalence data from ENSANUT 2012 was used in the linear trend analysis and as part of the mortality decomposition equation. However, the particular parameter of interest in this validation exercise, the prevalence of hypertension among the obese population, was not used as an input for the development of the MexOb-HT model. It was only possible to perform this external validation exercise for the MexOb-Model for hypertension, because at the time of the analysis, the results of the biochemical measures from ENSANUT 2012 were not published, and there was no other Mexican population data recently published for these combinations of risk factors (i.e. obese-disease).

5.3.1 Methods

I calculated the prevalence of hypertension among the overall Mexican adult population from the publicly available ENSANUT 2012 database to compare with the prevalence of hypertension reported by Campos-Nonato et al. (84) (Table 5.1). This analysis was performed to confirm that I was using the same survey population as the one used to calculate the published results because it was necessary later on to stratify the sample in different age groups and by BMI status (non-obese / obese), from the ones published, in order to make an adequate comparison between estimates from the ENSANUT 2012 data and the MexOb-Model estimates for each five year age group.

For this validation analysis, I used the same definition and exclusion criteria as Campos-Nonato et al. (84). Hypertension was defined as systolic blood pressure ≥ 140

mmHg or diastolic blood pressure ≥ 90 mmHg or being previously diagnosed by a physician. Outlying observations with blood pressure values of SBP < 80 mmHg and DBP < 50 mmHg were excluded from the analytical sample.

Table 5.1 Prevalence of hypertension in the overall adult Mexican population. ENSANUT 2012

Analysis	Men (%)	Female (%)	Total (%)
This study	32.3	30.7	31.4
Published*	32.3	30.7	31.5

*Published estimates were obtained from Campos-Nonato et al. Hypertension: prevalence, early diagnosis, control and trends in Mexican adults.

After my analytical sample was verified, I stratified the analytical sample with valid blood pressure values and with valid BMI values into the obese ($BMI \geq 30 \text{kg/m}^2$) and not obese ($BMI < 30 \text{kg/m}^2$) groups. Afterwards, I calculated the prevalence of hypertension among the analytical sample classified as obese. The analytical sample was stratified by sex and by five-year age-groups (aged 20-79y) (Table 5.2).

For the external validation exercise (MexOb-Model vs. directly observed ENSANUT data) I used the definition of hypertension consistent with that used in the MexOb-HT model. Hypertension was defined as follows:

- a) Aged ≥ 60 y: SBP ≥ 150 or DBP ≥ 90 mmHg or being previously diagnosed by a physician
- b) Aged < 60 y: SBP ≥ 140 or DBP ≥ 90 mmHg or being previously diagnosed by a physician

As above, the outlying observations with blood pressure values of SBP < 80 mmHg and DBP < 50 mmHg were excluded from the sample.

The total analytical sample (obese population ($BMI \geq 30 \text{kg/m}^2$) with valid blood pressure values) from ENSANUT 2012 was 11,250 observations (64% female). 41.5% of the persons classed as obese in ENSANUT 2012 were classified as hypertensive. The prevalence in each sex was very similar, with an estimated prevalence of hypertension

of 41.4% for obese males and 41.6% for obese females. The prevalence estimates shown in Table 5.2 were smoothed by using a moving average fit. Moving averages are commonly used to smooth short-term fluctuations in a data-series in order to reveal the underlying pattern (264); I used a moving average of three data points to smooth the mean prevalence and the 95% confidence intervals (CI) estimates for the adjacent age groups that, due to small sample sizes, showed relatively large fluctuations between estimates.

$$\text{Moving average} = \frac{Y1 + Y2 + Y3}{3}$$

Y1= age group x-5, Y2= age group x; Y3= age group x+5

Table 5.2 Prevalence of hypertension in the obese population, stratified by age group and sex. Results from ENSANUT 2012.

Age group	Obese males			Obese females		
	n(N)	Prevalence (%)	95% CI	n(N)	Prevalence (%)	95% CI
20-24	67 (556,204)	29.1	14.4 , 50.1	115 (691,824)	29.7	18.5 , 44.2
25-29	108 (640,278)	40.9	27.2 , 56.1	170 (860,323)	39.2	23.5 , 57.4
30-34	105 (461,728)	33.0*	21.6 , 45.4	282 (1,378,601)	29.5*	19.7 , 41.4
35-39	135 (944,126)	32.4*	12.9 , 33.2	393 (1,517,237)	30.8	24.2 , 38.3
40-44	152 (888,077)	45.1	32.1 , 58.7	291 (1,251,034)	32.7	25.3 , 41.0
45-49	108 (682,262)	49.5	35.7 , 63.4	293 (1,692,364)	43.0	32.2 , 54.5
50-54	127 (856,911)	50.7*	34.3 , 66.3	236 (1,045,313)	46.8	36.4 , 57.6
55-59	75 (393,288)	62.9	41.4 , 80.2	196 (1,173,887)	57.1	42.1 , 70.9
60-64	81 (297,435)	62.0*	43.6 , 77.5	156 (623,927)	61.2	46.2 , 74.4
65-69	72 (310,935)	67.7	50.9 , 80.9	123 (432,754)	71.8	57.3 , 82.9
70-74	40 (122,403)	64.3*	35.7 , 74.8	84 (281,859)	71.9*	56.6 , 83.3
75-79	24 (121,410)	68.5	38.9 , 88.1	57 (210,556)	79.9	64.9 , 89.5

n: total analytical sample . N: represents the weighted sample size (each sample person is weighted to represent the number of people in the population). 95%CI: confidence interval

* Smoothed data was averaged by using a moving average of three prevalence estimates: i.e. for that five-year age-group and the preceding and subsequent age groups

MexOb-hypertension model (MexOb-HT) simulation

For this external validation exercise, I used the same population for running the MexOb-HT model as in the internal validation exercise. 2007 was used as the start year to estimate results for the year 2012 as the MexOb-Model was developed to run in five-year cycles.

My initial population was the estimated population for 2007 from the CONAPO population estimates database (263). The total adult population was distributed into the obese without hypertension and obese with hypertension groups based on the prevalence of the obese-hypertensive population from ENSANUT 2006 (detailed description in Chapter 4). The open cohort component (β -coefficient), growth ratios and the relevant set of transition probabilities of the MexOb-Model remained unchanged. The prevalence of hypertension among the obese population was calculated as the number of obese persons with hypertension divided by the total number of obese persons estimated for that year.

5.3.2 Results

The figures below show the prevalence of hypertension among the obese adult population that was directly observed from ENSANUT 2012 stratified by age group, and with the 95% confidence intervals (CI). The graphs also show, as dots, the estimated prevalence of hypertension among the obese population for that same year obtained from the five-year cycle (2007 to 2012) of the MexOb-Model for hypertension (Figure 5-9 to Figure 5-10).

MexOb-hypertension model for males

Overall, the outcomes for the MexOb-HT model for males showed an overestimation of the hypertension prevalence among the obese population. However, my results showed that nearly all of the age group specific estimates fell within the 95% CI range of the estimates directly observed from ENSANUT 2012, with the exception of the estimates of hypertension for obese 50 to 54 year olds. The largest difference between the two sets of estimates was the overestimation for the 50 to 54 year age group and the underestimation for the 25 to 29 year age group. The obese population hypertension prevalence among these two age groups showed an absolute difference between the MexOb-Model estimates and the observed ENSANUT estimates of 19.0 pp and 3.6 pp, respectively (Figure 5-9).

MexOb-hypertension model for females

In a similar way to the results for males, the MexOb-Model for hypertension for females showed in general an overestimation of the hypertension prevalence compared with those obtained from the ENSANUT 2012 data. The results from the MexOb-HT Model for females showed that the estimated prevalence for four of the 12 obesity-HT age groups fell outside the 95% CI range of the observed ENSANUT prevalence estimates. Outlier values in all cases showed an overestimation for the model-based estimates compared with the ENSANUT data. The outliers were observed in the 35 to 54 year age groups with an absolute difference between the MexOb-Model estimates and the directly observed ENSANUT hypertension prevalence estimates in the range from 3.0 pp to 7.3 pp. The highest outlier overestimation was observed in the 40 to 44 year age group. The estimated MexOb-Model prevalence closest to the directly observed ENSANUT 2012 estimate was observed in the 65 to 69 year age group with an absolute difference between the two model and survey estimates of 1.7 pp (Figure 5-10).

Figure 5-9. Validation of the MexOb-hypertension male model with the observed hypertension prevalence in the obese population from ENSANUT 2012.

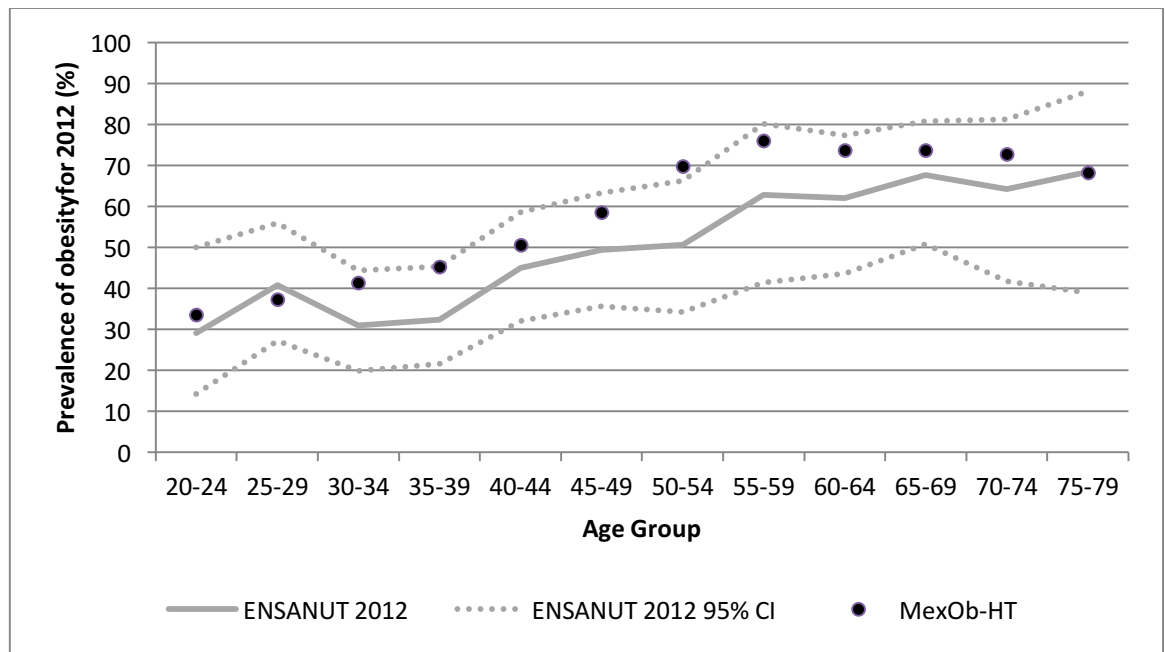
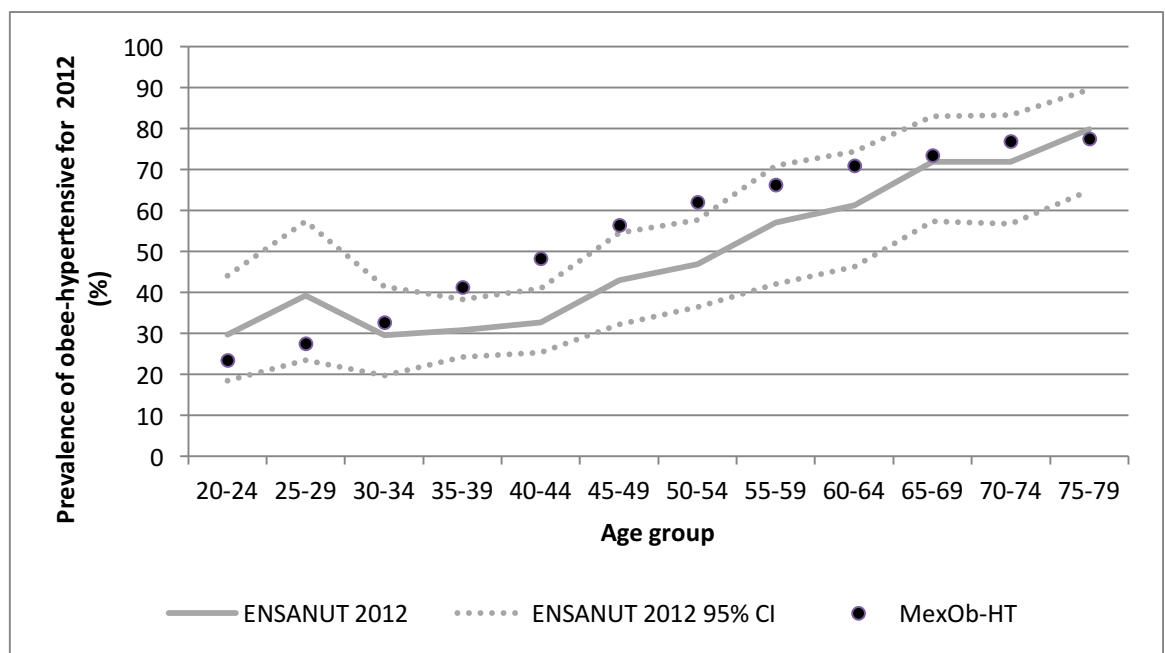


Figure 5-10 Validation of the MexOb-hypertension female model with the observed hypertension prevalence in the obese population from ENSANUT 2012.



5.4 Cross-validation: Comparison of the MexOb-Model with the estimated linear trends and with The Foresight model

The cross-validation exercise consisted of assessing different population-based health forecasting mathematical simulation models that evaluated similar outcomes to the MexOb-Model (32). This validation exercise was used to compare my projected obesity prevalence with the future obesity prevalence estimates obtained from the linear trend estimations, and from another simulation model applied to the Mexican population.

From a literature search I found only a small number of population simulation modelling exercises for chronic diseases that reported projections of obesity or cardiometabolic risk factors in the Mexican adult population. The Foresight model by Rtveldze et al. (115) was used to project future trends in BMI and future trends in the BMI-related diseases and its associated healthcare costs. Reynoso-Noverón et al. (265) used the United Kingdom Prospective Diabetes Study (UKPDS) outcome model to estimate, among the Mexican diabetic population, the future incidence of complications, life expectancy, and diabetes-related mortality. Meza et al. estimated the future levels of the incidence of diagnosed type 2 diabetes (266); Guariguata et al. generated estimates for future levels of diabetes worldwide for the year 2035, including estimates for Mexico (267). Of these four epidemiological models, the Foresight Model was the only model that estimated future levels of BMI and future levels of obesity-related diseases. The other three population simulation models (Reynoso-Noverón (265) , Meza (266) and Guariguata (267)) focused only on the health burden of diabetes among the general population.

The validation exercise between different models was only possible therefore with the Foresight model due to its similarities in the inputs and the outcomes with the MexOb-Model. The comparison of outcomes between the Foresight model and the MexOb-disease models was done only for projected obesity prevalence. Even though the

Foresight model also reported the numbers of new cases of diabetes and of hypertension, two of the four obesity-related cardiometabolic outcomes of the MexOb-Model, a direct comparison with the Foresight model estimates for diabetes and for hypertension was not possible as the numbers shown in the Foresight analyses were not stratified by BMI group (e.g. non-obese / obese) nor by age group. Additionally, I also decided to compare the MexOb-Model estimates with the levels of obesity prevalence projected from the linear trends. I used the linear trend estimates as a benchmark of how close the MexOb-Model estimates were to those based on the historic trends after a simulation of three five-year cycles. This cross-validation exercise was particularly useful as the β -coefficients representing the estimates of the linear trend were also applied in the MexOb-Model to allow for new cases of obesity.

5.4.1 Methods

The projected obesity prevalence estimates from the MexOb-Model were obtained by running the MexOb-hypercholesterolaemia model (MexOb-HCI) during the 15 year period from 2005 to 2020. The results from the MexOb-Model were compared with: (A) the linear trend analysis and the 95%CI for each sex and age group (which was previously described in Chapter 3), and with (B) the projected levels of obesity prevalence from the Foresight model applied to Mexican data published by Rtveldze et al.(115). The comparison between the model outcomes was made for 2010 and 2020. For the purpose of this validation exercise, I only compared obesity prevalence estimates for the population aged 20 to 59y as the Foresight model for the population aged ≥ 60 y used a different set of age bands than the five-year age bands used for the MexOb-Model.

The MexOb-hypercholesterolaemia model (MexOb-HCI) was chosen as the MexOb-disease model to be used for the cross-validation exercise. In the internal validation exercise, estimates from the MexOb-HCI model generally showed the highest underestimation compared with the ENSANUT estimates. Therefore, performing this

validation exercise using the MexOb-HCI model would be expected to show the largest difference between the estimates for the MexOb-Model and the two other sets of estimates.

Model characteristics

Linear trend for Mexico: The first component of the MexOb-Model estimates the future trends of obesity prevalence by using the linear trend modelling technique. I used the average annual rate of change between the past obesity trends of four different National Health Surveys, and used that rate of change to project the future levels of obesity to 2020. Data sources for the MexOb-Model first component were: National Health Survey (ENSA) 2000; Mexican Family Life Survey (MxFLS-1) 2002; and the National Health and Nutrition Survey (ENSANUT) 2006 and 2012 (for full details of the linear trend estimations see: Chapter 3).

MexOb-Model: The MexOb-Model is a Markov chain model that distributes the obese population among different health states (obese-with-disease, obese-without-the-disease, and death). The initial population in the model for this cross-validation exercise used the projected obesity prevalence in the adult population for 2005, stratified into two groups (obese with or without hypercholesterolaemia) held constant at the observed 2006 values extracted from the ENSANUT 2006 database. During each five year cycle, the obese population transitions to the next health state according to their disease, age and sex-specific transition probabilities. Before arriving at the next health state, an open cohort component is added to the total obese population (obese with, and obese without the cardiometabolic risk factor) to accommodate new obese cases. The obese population is progressed through to their next health state through applying the relevant set of transition probabilities. The total number of surviving members of the obese-disease group is then increased or decreased by multiplying by the relevant disease growth ratio.

The MexOb-Model runs over three five-year period cycles to represent a 15 year period (2005 to 2020 for the purposes of this cross-validation exercise) (for full details of the MexOb-Model structure see Chapter 4).

Foresight model (FM) for Mexico: To project the future levels of obesity in the Mexican adult population, the Foresight Model applied to Mexican data by Rtveladze et al. fitted a multivariate categorical regression model to a series of cross-sectional BMI data to build trajectories to 2050. Rtveladze et al. stratified BMI into three categories (normal weight: BMI ≤ 24.9 kg/m²; overweight: BMI 25.0 to 29.9 kg/m² and obese: BMI: ≥ 30 kg/m²), in five-year age groups (20-59y, and 60+y). The Mexican data sources included: National Health Survey (ENSA) 2000; National Health and Nutrition Survey (ENSANUT) 2006; and the Nutrition Health Survey (ENN) 1999 for females 20 to 49 year olds only (115).

5.4.2 Results

Figure 5-11 to

Figure 5-14 show the estimated future obesity prevalence calculated from the three models for each age group and for two years (2010, 2020). All of the obesity projection models showed a substantial increase in obesity prevalence if the past trends of obesity prevalence in the Mexican population continue. However, the MexOb-HCI Model estimates showed an overall lower obesity prevalence for both sexes. The linear trend model prevalence estimates are presented with their 95% CI shown in the Figures as dotted lines. The MexOb-Model did not calculate 95% uncertainty intervals (UI). 95% UI for the Foresight estimates were not documented in the published report (115).

Male projected obesity prevalence: MexOb-Model vs. linear trends and Foresight model estimates.

The MexOb-HCI model projected estimates for 2010 for males showed a lower prevalence of obesity than the linear trend and the Foresight model (FM) for most age groups. The largest difference in prevalence estimates between the MexOb-HCI model and the linear trend estimates was observed in the 55 to 59 year age group (absolute difference of 8.3 pp), and in that same age-group (absolute difference 16.9 pp) when comparing the MexOb-HCI model with the FM. The MexOb-HCI model estimated obesity prevalence for two of the eight age-groups fell outside the 95% CI of the linear trend. Estimates from the FM for four of the eight age-groups fell outside the 95% CI of the linear trend. However, the FM values which were outside the 95% CI of the linear trend estimates were overestimations of the obesity prevalence, whilst the estimates from the MexOb-HCI model were below the lower range of the 95%CI of the linear trend estimates.

The largest absolute difference between the projected obesity estimates from the MexOb-HCI model and the other estimates for 2020 was observed in the 30 to 34 year age group, with the MexOb-HCI estimates being 12.6 pp and 17.4 pp lower than the linear trend model and the Foresight Model respectively. The results for the MexOb-HCI model for males showed four values of the projected obesity prevalence that fell below the lower 95% CI for the linear trend for 2020; one value more than the Foresight model estimates (Figure 5-11 and Figure 5.12).

Female projected obesity prevalence: MexOb-Model vs. linear trends and Foresight model estimates

Projected obesity prevalence estimates from 2010 for females from the MexOb-HCI model were lower than the estimates from both the linear trend and the Foresight model (FM) for nearly all age groups. The largest difference between the MexOb-HCI

model estimates and the linear trend was observed in the 55 to 59 year age group (absolute difference of 11.4 pp). The largest difference was also observed for the same age group (9.4 pp) when comparing the MexOb-HCI model with the FM. Four of the eight age group MexOb-HCI estimates for females fell outside the 95% CI range for the linear trend for 2010; compared with three age-group values from the Foresight model.

The largest absolute difference in estimates between the MexOb-HCI model and the other estimates for 2020 was observed in the 30 to 34y age group, with the MexOb-HCI model estimate being 13.3 pp and 17.0 pp lower than the linear trend model and the Foresight Model, respectively. The estimates of projected obesity prevalence from the MexOb-HCI model for 2020 closest in value to the estimated obesity prevalence from the linear trend were found for the 20 to 24y and the 40 to 44 year age groups (Figure 5-13 and Figure 5.14).

Figure 5-11 Comparison between 2010 projected male obesity prevalence from the MexOb-HCI model, linear trends and the Foresight model.

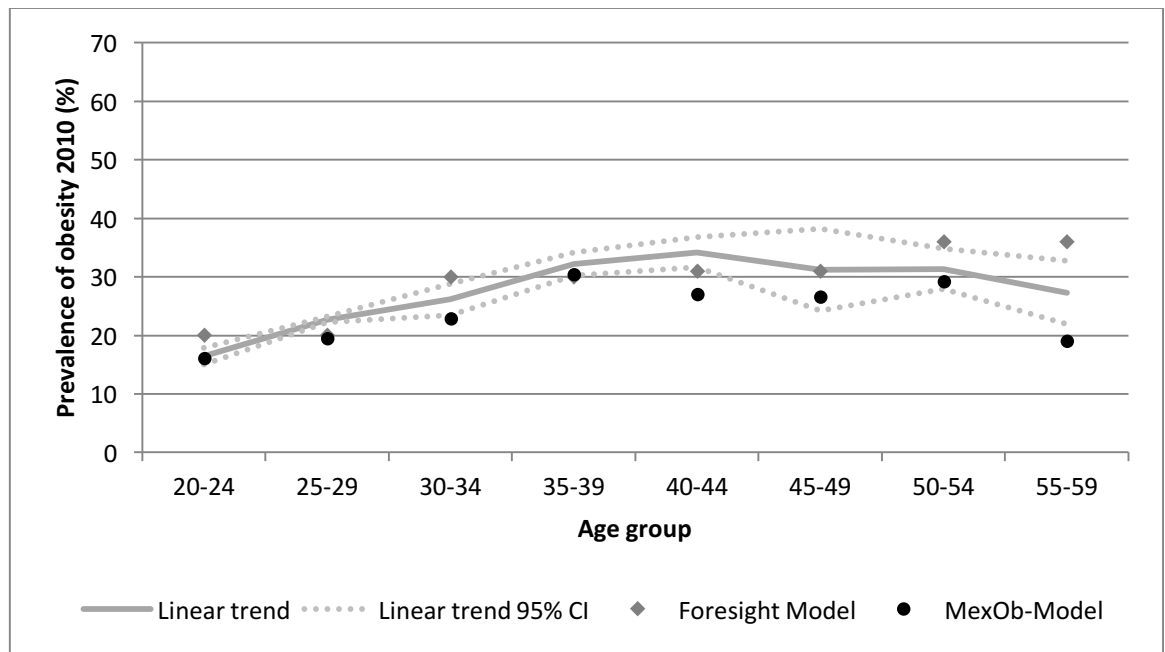


Figure 5-12 Comparison between 2020 projected male obesity prevalence from the MexOb-HCI model, linear trend and the Foresight model.

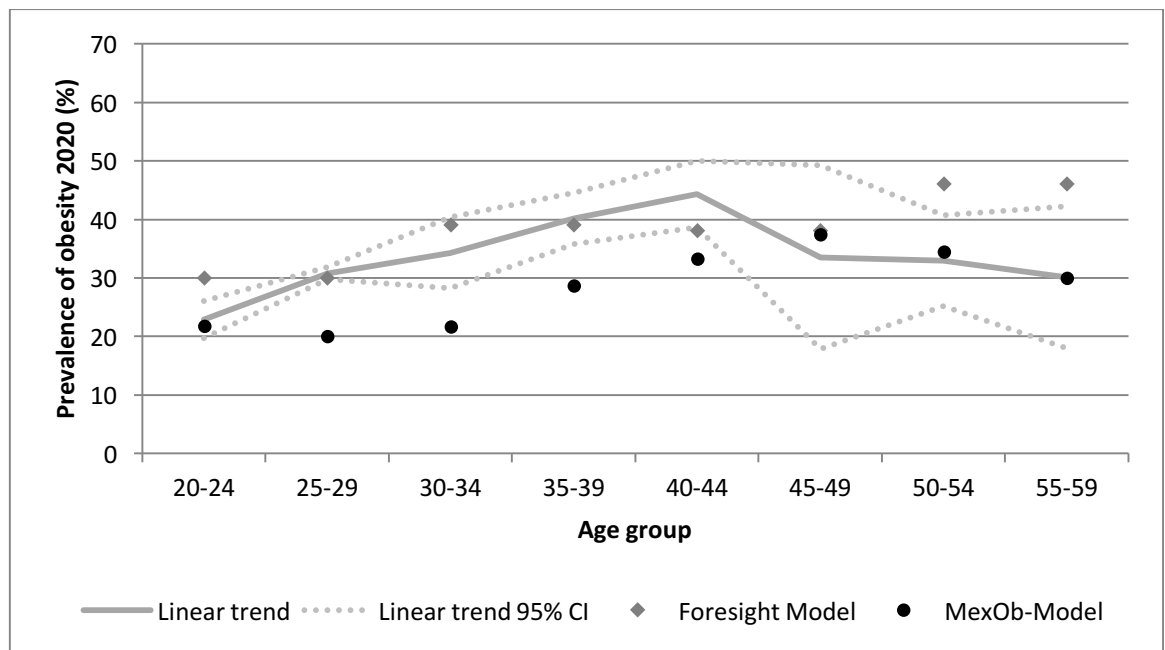


Figure 5-13 Comparison between 2010 projected female obesity prevalence from the MexOb-HCI model, linear trend and the Foresight model.

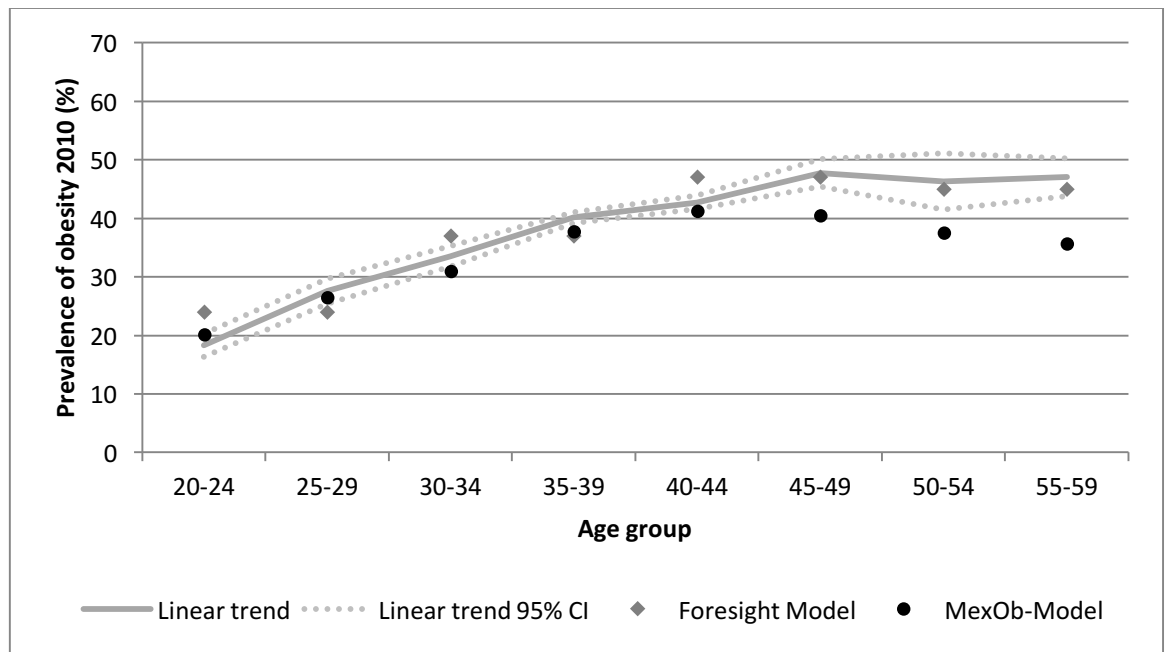
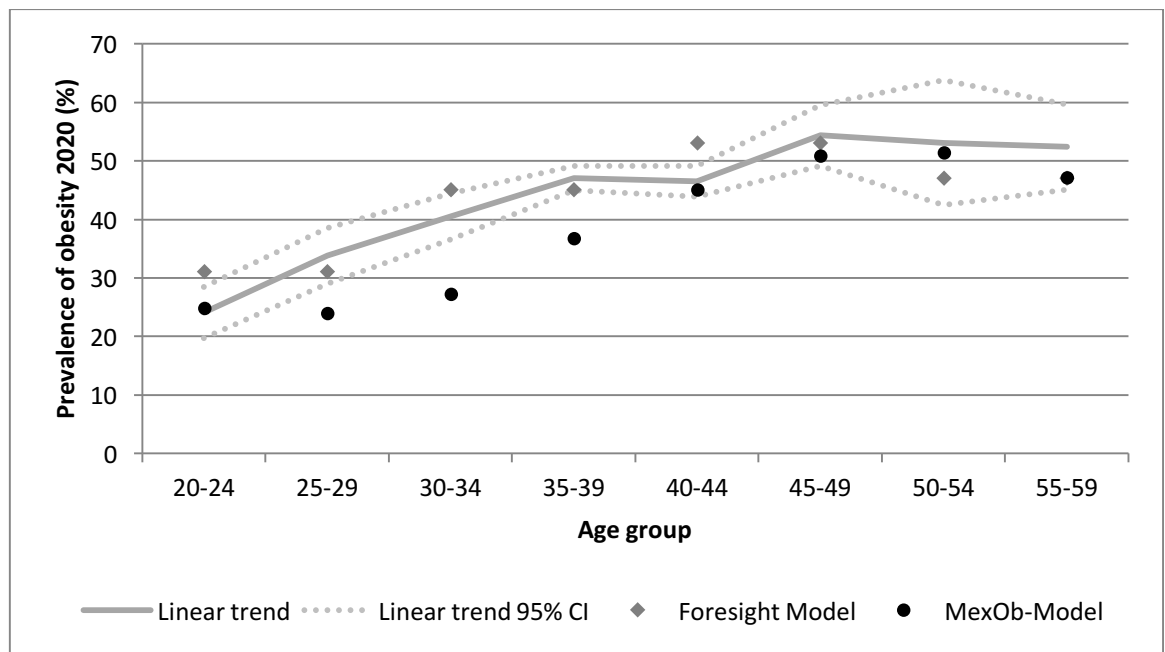


Figure 5-14 Comparison between 2020 projected female obesity prevalence from the MexOb-HCI model, linear trend and the Foresight model.



5.5 Discussion

5.5.1 Internal validation: Comparison of MexOb-disease models with ENSANUT 2012 observed data total obesity prevalence.

This internal validation exercise was performed in order to observe if the parameters chosen for the MexOb-Models produced outcomes (i.e. prevalence of obesity) that were similar to the estimates directly obtained from the ENSANUT 2012 database. The results of my analysis showed that there were minimal differences between the MexOb-Model and those obtained directly from ENSANUT. Overall, the MexOb-disease models estimates of obesity prevalence for females showed a higher underestimation when compared with ENSANUT 2012 than for males. The highest underestimation across all the MexOb-disease models for females was observed in the MexOb-HTG model. Estimates from the MexOb-HCI model for males showed the highest underestimation from the four disease models for males. The observed difference between the two sets of estimates mainly reflect the effect of the chosen model structure for the MexOb Model, including the assumptions of the Markov process and the accuracy of the steering parameters used for estimating the outcomes from the MexOb-Model.

Overall, the estimated obesity prevalence from the MexOb-disease models showed an underestimation compared with the observed ENSANUT data. The over- and underestimation of outcomes for models using a Markov chain has been previously documented, and this has been a particularly common finding for models which have used discrete time parameters, similar to the ones used for the MexOb-Model.

In absolute terms we would expect a larger difference between the observed and modelled estimates for those age-groups where the burden of disease is highest: and the burden of disease is typically highest at higher ages. In addition, the underestimation of obesity prevalence at higher ages may also reflect the limitations of modelling individual diseases separately rather than using a condition of combined

comorbidity such as the Metabolic Syndrome (although that has numerous limitations as well). It is well known that the co-occurrence of diseases increases with age. Finally, the internal validation exercise compares modelled estimates with the directly observed ENSANUT obesity data for 2012. Although nationally representative, estimates obtained from national health examination surveys have accompanying margins of error.

Discrete-time parameters such as the transition probabilities influence the distribution of the population among the health states (268). Discrete-time parameters assume that the transitions between states only occur at fixed times periods: in a Markov process, the transitions are applied at the beginning or at the end of the modelling cycle, instead of influencing the distribution of the population among the health states at the middle of the modelling cycle or at any time. Transitions at any time reflects how transitions occur in most biological systems (18). In order to overcome this limitation, modellers have been recommended to perform a half-cycle correction to the discrete time parameters in order to produce estimates as close as possible to the true health state population (188, 268, 269).

The MexOb-Model structure does not currently include a half-cycle correction when counting the number of persons belonging to each health state. Even though I attempted to correct the absence of a half-cycle correction by adjusting the size of the relevant obese populations before and after application of the transition probabilities, the results for a number of the age groups continued to show an underestimation in the levels of obesity prevalence when compared with the ENSANUT survey data. Future changes to the MexOb-Model structure may include a half-cycle correction to improve model fit and accuracy.

The MexOb-Model structure includes as steering parameters an open cohort component that is derived from the β -coefficients of the linear regression

equations, and also a disease growth ratio. The disease growth ratio (GR) was included as part of the MexOb-Model to adjust the numbers of the population with disease that will correspond to the next obese-disease age group. The disease growth ratio is based on the prevalence of cardiometabolic risk factors within the obese population (taken from ENSANUT 2006) to calculate the input of incoming new obese-disease cases. The main assumption is that the age-, sex- and disease-specific growth ratios estimated using 2006 data will remain constant over the modelling cycles. These estimates are based on comparisons in disease prevalence between age-groups at a single point in time and so do not include any adjustment for birth cohort effects. There is evidence that for obesity simulation exercises, there is only a minimal effect of cohorts and that periods are the ones who drive the growth of obesity prevalence (270, 271)

All the three aforementioned steering parameters were built using historic data, and the outcomes obtained from the MexOb-Model are conditional on holding their values constant for each of the four cardiometabolic diseases over the chosen life-cycles of the model.

There is also some uncertainty that could come from the input data used for the steering parameters that could affect the future levels of obesity generated by the MexOb-Model. The β -coefficients were obtained from the linear trend equation. The linear trends for my analysis only take into account the past prevalence of obesity in the population observed from the repeated cross-sectional national health surveys: it is important to remember that projecting future levels of obesity using repeated cross-sectional survey data inevitably involves levels of uncertainty around the estimates. There is also uncertainty when using national population projections for 2012 compared with the observed data from the subset of the Mexican population who participated in the national health surveys. Although the surveys are carefully designed to be nationally representative, this could cause some variation and error in the sampling method that affect the population estimates. Furthermore, applying a disease specific growth ratio based on estimates from the 2006 ENSANUT data to the

Markov process as part of the MexOb-Model structure also had an impact on the distribution of the total obesity population obtained from the MexOb-Model compared with the total obese population observed data that was collected six years later in the 2012 ENSANUT data.

Additionally, it is also important to remember that once the steering parameters were calculated, I manipulated the data one more time to eliminate the random noise created principally by the variations between the obesity-disease prevalence estimates for consecutive age groups; in the presence of small sample sizes, the prevalence of disease in the participants with obesity does not always smoothly increase with age. To eliminate random noise some of the age group disease prevalence estimates were smoothed. An adjustment was also made for the characteristic of the non-parametric formula to estimate values <0 and >1 for the transition probability calculations, and this could potentially had an effect on the projections for the older age groups for which some estimates of disease prevalence decrease as age increases.

5.5.2 External validation: Comparison between projected estimates and observed survey data

In the external validation exercise of comparing the estimates of hypertension prevalence among the obese population from the MexOb-HT model with the equivalent estimates observed directly from the survey data (ENSANUT 2012), my results showed that in general, the MexOb-HT model estimates showed higher mean prevalence of hypertension than the survey data. However, the majority of the MexOb-HT model estimates fell within the 95% CI range of the observed data. From this exercise, I also observed that the MexOb-HT model estimates for females showed more outlying values of hypertension prevalence among the obese population than for males.

The ENSANUT 2012 estimates of the prevalence of hypertension among the obese population showed stronger evidence of a linear relationship with age than the MexOb-HT model estimates. This effect could be the result of the imprecision in the survey data due to small sample sizes for the ENSANUT 2006 analytical sample within my selected age ranges (five-year age group). The difference between sample sizes for consecutive age groups had an impact on the estimates of the prevalence of hypertension among the obese population from ENSANUT 2006. The directly observed ENSANUT 2006 prevalence estimates of cardiometabolic risk factors among the obese population has a large effect on the outcomes as it is one of the main inputs for the steering parameters of the MexOb-Model. It was used for the initial population distributions (obese without disease / obese with disease), the disease growth ratio, and for the calculation of the disease-, age-group, and sex-specific transition probabilities (see: Chapter 4). Furthermore, the obese population in each age group ages with each Markov cycle (e.g. the cohort aged 20-24y in the first five-year cycle enter the second five-year cycle as the 25-29y cohort), therefore, also having an effect for subsequent age groups. Hence the magnitude of the absolute differences between the MexOb-HT model and the observed ENSANUT estimates were largest for those age groups whose survey-based estimate of hypertension among the obese population clearly departed from the general increasing pattern with age.

5.5.3 Cross-validation: Comparison between population simulation models.

MexOb-Model vs. Linear trends and the Foresight Model

In general, the obesity projections from the MexOb-HCI model showed lower projected obesity prevalence than the estimates obtained from the linear trend and from the Foresight model. The difference between the sets of estimates was closer for females than for males. The differences in data sources and the differences in methods of simulation calculations between the three models clearly resulted in different levels of obesity five years after baseline (2010) and at the end of the forecasting period (2020).

The MexOb-HCI model, the linear trends, and the Foresight model use a number of similar data sources as input to feed the model: namely ENSA 2000 and ENSANUT 2006. Other data sources not shared across the three models were of the same high quality (nationally representative health surveys with objectively measured anthropometry). However, the projections produced by the Foresight model were based on only three data points for women and two data points for men, compared with the four data points for both sexes used for the linear trend estimations and the MexOb-HCI model. From previous modelling exercises, it has been observed that the number of data points used for projecting future levels of non-communicable diseases such as obesity can have a large influence on the estimates of disease levels.

Using more data points is useful as it increases the precision of the estimates, and is better placed to capture any changes in the pattern over time. For example, both the linear trend estimates and the MexOb-HCI model used the obesity prevalence obtained from ENSANUT 2012 as the most recent data point for estimating the trends in obesity prevalence. The final data point used by the Foresight model was 2006. This could have had a large effect on the comparisons. Obesity prevalence among women aged 20 years and older showed a larger and steady increase over each six year period: from 28% in 2000 to 34.7% in 2006, and finally reaching a level of 38% in 2012. In contrast, obesity prevalence for adult males showed a higher increase between 2000 and 2006 than from 2006 to 2012: from 19% in 2000 to 24% in 2006, and reaching 27% in 2012. Therefore, the seemingly slower rate of increase in obesity prevalence for males from 2006 to 2012 was not accounted for in the projections of the Foresight model. In addition to the historic trends in obesity levels, the MexOb-HCI model uses as input data other growth and distribution parameters that also have an important influence on the overall projected levels of obesity prevalence, as has been mentioned throughout this thesis.

Furthermore, it is not only the data input that matters, but also the methods chosen to calculate the projections that influence the results. The forecasting methods for the

MexOb-HCI model and for the linear trend took into account the past changes in the prevalence of obesity to estimate the future levels. However, the multivariate categorical regression method used by the Foresight model for forecasting takes into account the changes between BMI categories (normal weight, overweight, and obese), thereby considering the movement of populations between the three BMI categories, something that the linear trend analysis does not do.

It is important to remember that linear projections are extrapolations from available past data, and that this could alone create uncertainties in the predictions, as it is possible that the direction or pace of change that is observed from past trends may not continue into the future. Using linear equation estimations to continue the historic trend fails to take into account any possible curvature in the trend which could better represent the distribution of populations across the BMI categories (155). Additionally, the distribution of the adult population between the health states implemented by the structure of the MexOb-Model during the simulation period is based on the assumption that the steering parameters (e.g. growth ratio and transition probabilities) are constant throughout the modelling cycle (a 15 year period from 2005 to 2020 in this case). As in every simulation model, the levels and the shapes of future trends in disease rely heavily on the precise details and assumptions made about the disease progression based on the data used as input, and the equations used to fit the trend.

The discrepancies between the sets of obesity prevalence estimates in this cross-validation exercise, particularly for the projections for the final year of 2020, highlight one of the main limitations of the use of population simulation projections. The longer the forecasting period used, the larger the magnitude of differences between the observed data and the forecasted outcomes from other modelling studies. Compared with a five-year projection period (2005 to 2010), the differences between the three sets of estimates were much larger for the 15-year projection period (2005 to 2020). Users of my model have to be aware of this limitation when interpreting population

simulation results, and consider that a shorter term projection period of five to ten years could produce more accurate results than a longer projection period of more than ten years.

5.6 Conclusion

The MexOb-Model validation exercises showed that the model estimates are a close representation of the observed obesity panorama in Mexico (obese prevalence and disease prevalence in the obese population). The results from these analyses conferred the MexOb-Model's outcomes the credibility to be used for future decision making. As with all epidemiological models, outcomes from the MexOb-Model rely heavily on the parameters used to estimate the outcomes. The characteristics of the data and the details of the methods used for estimation of the steering parameters used to run the model can provide the main explanation for the variation in the different sets of estimates that have been shown in this chapter. Detailed validation of population simulation models is always a continual exercise, as more data is published in future years.

One of the advantages of the methods I have used to develop the MexOb-Model is that due to its transparency, it would be relatively easy for users to modify the model as new data is released. This will make it adaptable to the new circumstances of the population and so confers on the model the ability to estimate future levels of obesity and its associated diseases more precisely.

Chapter 6. Mexican Obesity Forecast Model (MexOb-Model). Baseline simulation results 2015 to 2030

6.1 Introduction

Growth in the number of individuals with a BMI $\geq 30\text{kg/m}^2$ in Mexico's population during the past years has brought as a consequence an increase in morbidity and mortality from its associated diseases, particularly hypertension and diabetes. This has increased the health and economic burden on Mexico and its inhabitants. One of the principal objectives of my PhD research project was to forecast the health impacts of future changes in obesity prevalence on four of its associated cardiometabolic risk factors: hypertension, type 2 diabetes mellitus, hypertriglyceridaemia and hypercholesterolaemia in the Mexican obese adult population from 2015 to 2030 using the MexOb-Model.

This chapter describes the baseline or base-case model results from the MexOb-Model. This baseline scenario represents the future health burden of obesity-related cardiometabolic risk factors if the past trends of obesity prevalence continue. The results include: the projected prevalence of cardiometabolic risk factors in the obese population, the number of new cases of obese-disease, and the number of accumulated deaths from all-causes from each of the four MexOb-disease models: MexOb-hypertension (MexOb-HT); MexOb-type 2 diabetes mellitus (MexOb-T2DM); MexOb-hypertriglyceridaemia (MexOb-HTG); and MexOb-hypercholesterolaemia (MexOb-HCI).

6.2 Methods

6.2.1 MexOb-Model

The MexOb-Model is composed of two sub-models, as described in chapters 3 and 4. The first sub-model corresponds to the projections of obesity prevalence, estimated from past trends (see: Chapter 3). The second sub-model is an open cohort Markov

model of Mexican adults aged 20 to 79y classed as obese (BMI $\geq 30\text{kg/m}^2$), that aims to estimate the impact of the future obesity trends on the future levels of four of its associated cardiometabolic risk factors: hypertension, type 2 diabetes mellitus, hypertriglyceridaemia and hypercholesterolaemia from 2015 to 2030, stratified by sex and five-year age group (see: Chapter 4).

6.2.2 Simulations

For the baseline scenario analyses, I ran the four MexOb-disease models for three five-year cycles to simulate a 15 year period (2015 to 2030). The initial population was taken from the 2015 CONAPO population projection estimates (63). The initial population was distributed into obese persons without and obese persons with a cardiometabolic risk factor. Risk factor prevalence among obese individuals was held at 2006 levels, based on estimates from ENSANUT 2006. Transition probabilities between the health states (obese without cardiometabolic risk factor, obese with cardiometabolic risk factor, and death) used for the Markov chain process were assumed to be constant during the 15-year modelling period. The main outcomes predicted were prevalence, number of new cases, and number of total deaths in the obese without- and the obese with disease populations. Outcomes were produced for the four disease-specific MexOb-Models separately, and separately by sex.

The analyses for the baseline simulation were run in TreeAgePro version 2015. Details about the development of the two-part modelling process can be found in the previous chapters. In summary, the MexOb-Model estimates the number of persons in the population aged 20 to 79 years that will be obese with or without a cardiometabolic risk factor during the next 15 years in Mexico.

The MexOb-Model was developed to produce age-specific estimates. In addition, to provide estimates for the total population, the age-specific estimates of the total projected prevalence of the cardiometabolic risk factors in the obese population were

directly age-standardised to the age group, gender and to the 2022 population distribution from the National Population Council of Mexico (CONAPO) estimates to be able to compare the changes through time (63) (Figure 6-1 to Figure 6-6).

6.3 Baseline simulation results

The Mexican total population (aged $\geq 2y$) is expected to grow from 128 million in 2015 to 148 million by 2030 (63). The results from the linear trend analysis projected that the proportion of the population (aged $\geq 2y$) classified as obese is expected to increase from 35% to almost 44%, which means that by 2030 there could be around 48 million obese individuals ($\geq 2y$). Past survey data consistently shows that obesity prevalence is higher among women than men. From the linear trends, it is estimated that one in every two women aged 20 to 79y (around 24 million), and around 40% of men aged 20 to 79y will be classified as obese (around 16 million) by 2030 (see: Chapter 3). In the following section I present the results of the baseline simulation separately for men and for women, and show the main projected results: total prevalence of disease; number of new disease cases; and number of deaths.

6.3.1 Male MexOb-disease models baseline simulation results

Total prevalence of disease within the obese population

In the baseline simulation with the initial population distributed according to the obesity-related cardiometabolic risk factors prevalence at 2006 levels, projections estimated from the MexOb-disease models for males showed that by 2030, the prevalence of hypertension and the prevalence of dyslipidaemias (HTG and HCl) in the obese population will be between 52% and 57%. The highest projected prevalence for 2030 from the four male MexOb-disease models was observed for hypercholesterolaemia (57%).

The increase in the size of the male obese population during the next 15 years is projected to have the biggest effect on the prevalence of hypertension and the prevalence of diabetes. Estimates from these models showed an annual increase in prevalence of 0.7 percentage points (pp) between 2015 and 2030. Hypertension prevalence is estimated to increase from 46.8% to 54.6%, and diabetes prevalence is estimated to increase from 20.9% to 30.9% (Figure 6-1)**Error! Reference source not found.** The increase in the projected risk factors prevalence was mainly due to the increase in the number of obese people aged 50 to 54y and 60 to 69y with hypertension. Large increases in obese-disease cases were also due to increases in prevalence among males aged 40 to 54y and 65 to 79y with diabetes, and to the high increase in obese individuals with HCl and HTG among those aged 65 to 79y (Figure 6-2 to Figure 6.5)

Total number of cumulative new obese-disease cases

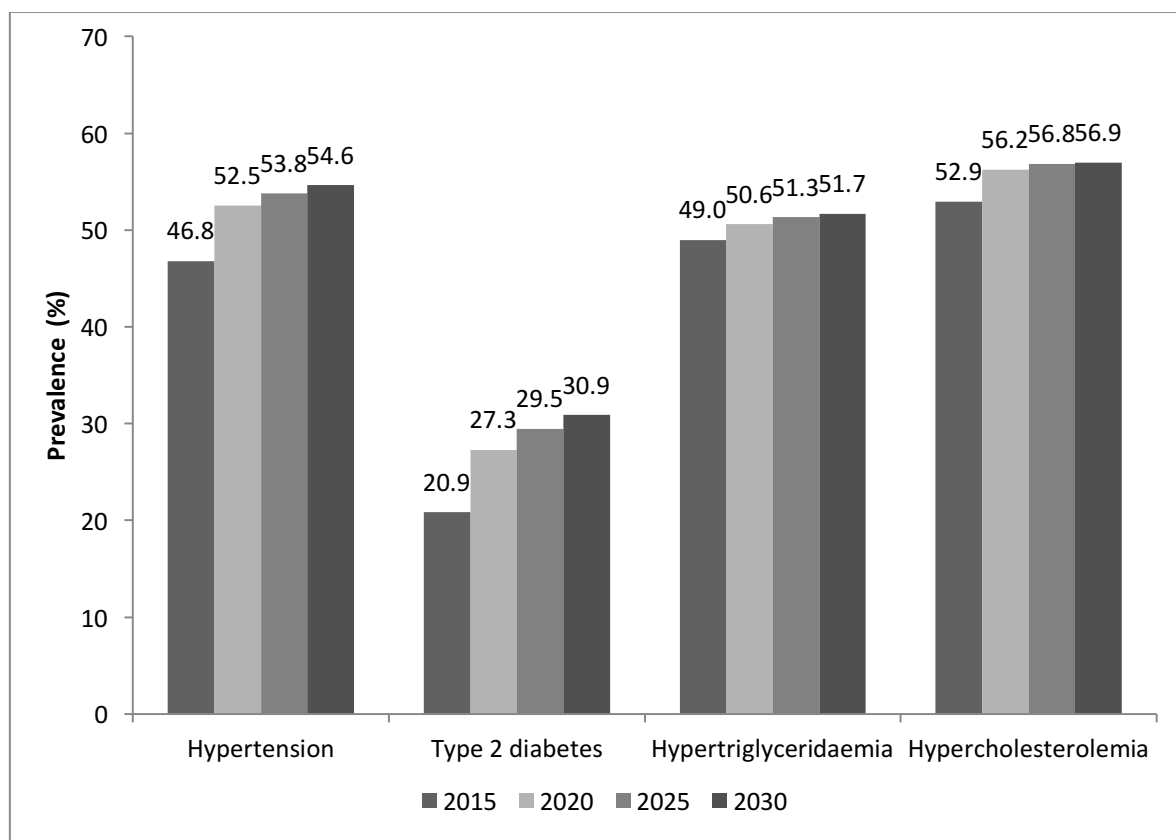
Table 6.1 shows the cumulative number of new cases of obesity-related cardiometabolic risk factors in the future male obese population in this 15 year period. The numbers of new obese-disease cases are projected to double in this time period. In 2020, the projected number of new cases in the four models was estimated to be between 0.6 and 1.3 million. However, by 2030, these numbers were projected to increase to approximately six million for hypertension, four million for diabetes and for hypertriglyceridaemia, and five million for hypercholesterolaemia.

Total number of projected deaths in the obese and obese with disease population

The projected increases in the prevalence of obesity from 2015 to 2030 among males could lead to between 1.4 million and 1.6 million deaths from each of the four cardiometabolic risk factors by 2030. The MexOb-HT model predicted the highest number of total deaths in the obese population (1.6 million) by 2030, of which 70% were deaths in obese individuals with hypertension. The second highest total estimate of all-cause deaths was observed in the MexOb-T2DM model (1.6 million), with 21% of

the deaths from the obese diabetic individuals. However, it was the MexOb-HCI model which projected the highest percentage of deaths in the obese population with presence of the cardiometabolic risk factor (72%) (Table 6.2).

Figure 6-1 Total age-standardised projected prevalence of obesity-related cardiometabolic risk factors in the male obese population 2015-2030



The age-specific estimates of prevalence were directly age-standardised to the projected population for 2022

Definitions used to estimate this numbers:

Hypertension A) SBP \geq 150 or DBP \geq 90mmHg in \geq 60y or B) SBP \geq 140 or DBP \geq 90mmHg in <60y+; A or B or previously diagnosed by a physician

Type 2 diabetes mellitus \geq 126mg/dl (\geq 7.0mmol/L) or previously diagnosed by a physician

Hypertriglyceridaemia \geq 150mg/dl (\geq 1.7mmol/L) or previously diagnosed by a physician

Hypercholesterolaemia \geq 200mg/dl (\geq 5.2mmol/L) or previously diagnosed by a physician.

Figure 6-2 Projected hypertension prevalence in obese male population 2015 to 2030 by age group.

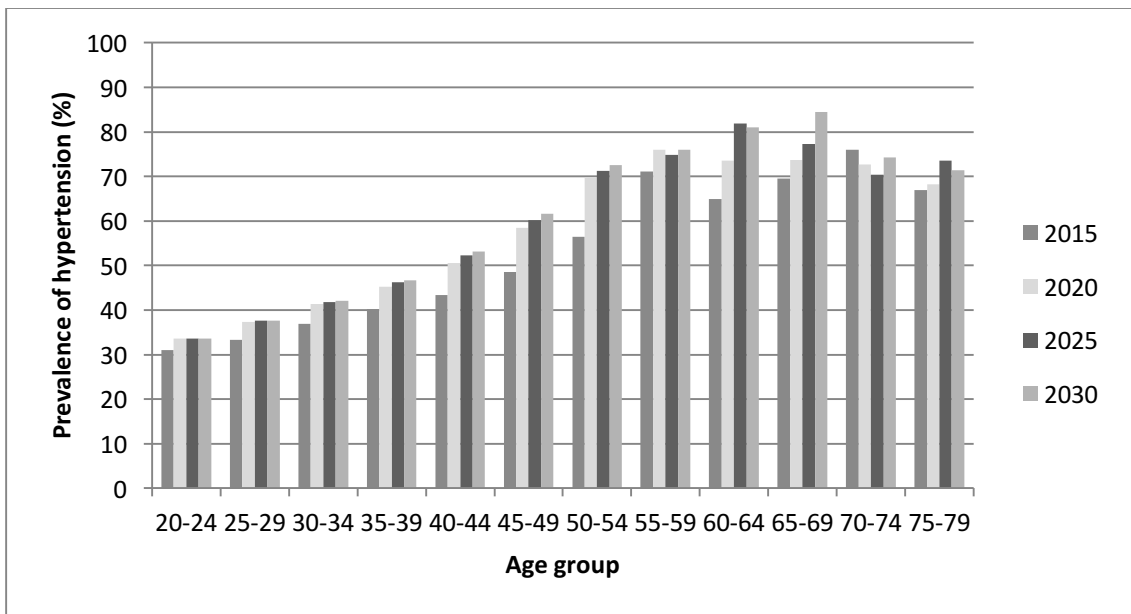


Figure 6-3 Projected type 2 diabetes mellitus prevalence in obese male population 2015 to 2030 by age group.

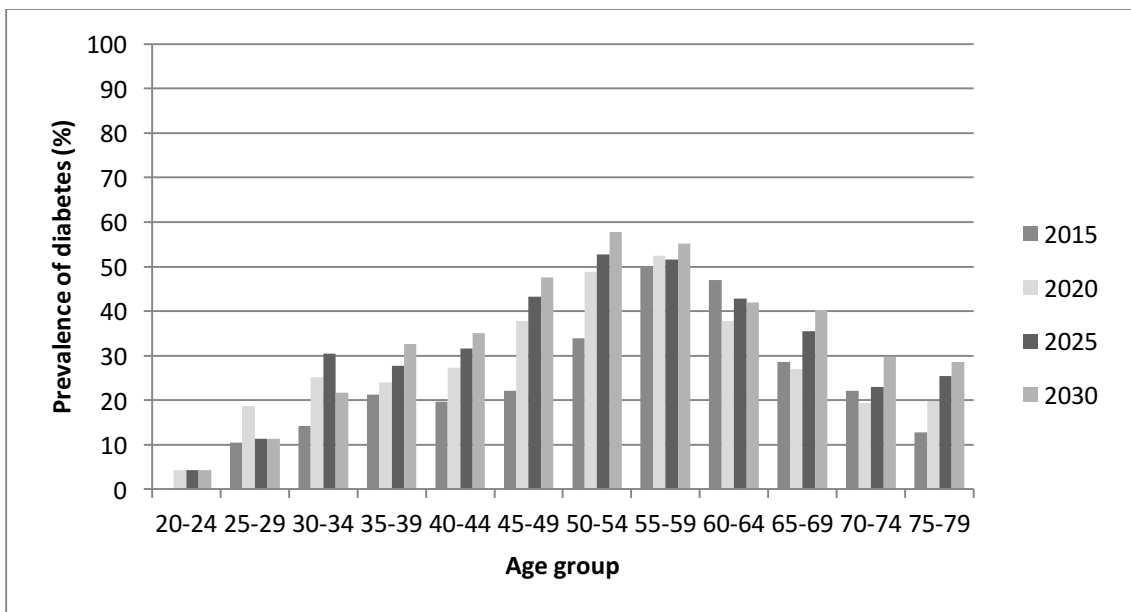


Figure 6-4 Projected hypertriglyceridaemia prevalence in obese male population 2015 to 2030 by age group.

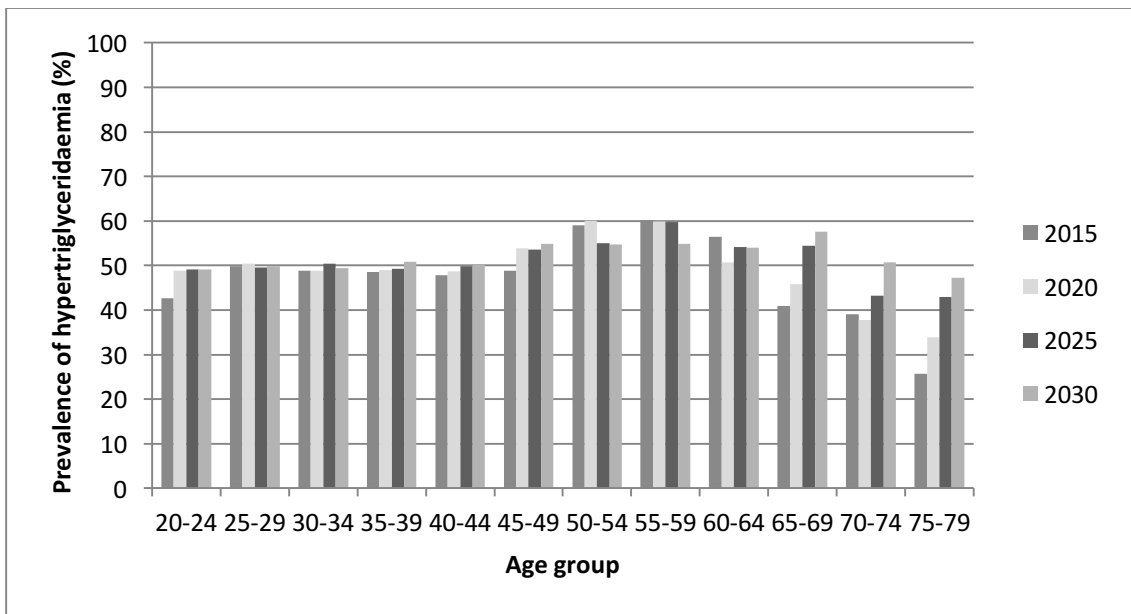


Figure 6-5 Projected hypercholesterolaemia prevalence in obese male population 2015 to 2030 by age group.

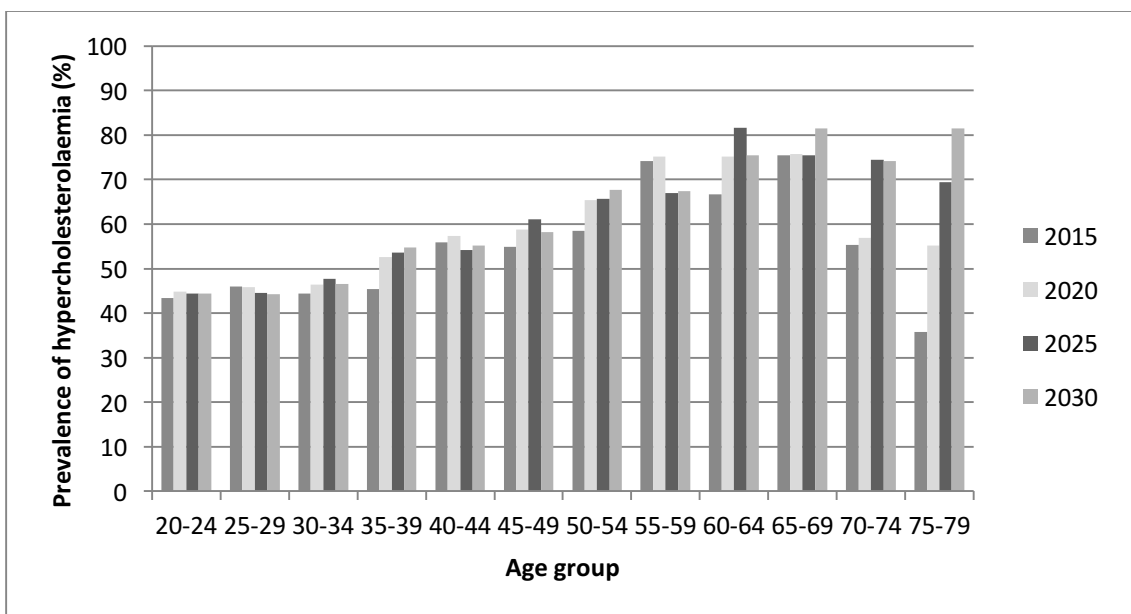


Table 6.1 Cumulative number of new cases of obesity-related cardiometabolic risk factors from 2015 to 2030 among Mexican males 20 to 79 years old in thousands.

Cardiometabolic risk factor	2020	2025	2030
Hypertension	1,250	3,263	5,885
Type 2 diabetes mellitus	1,050	2,516	4,394
Hypertriglyceridaemia	640	2,034	3,738
Hypercholesterolaemia	941	2,629	4,778

Table 6.2 Cumulative number of deaths from each MexOb-disease model in obese males 20 to 79 years to 2030 in thousands.

Cardiometabolic risk factor	2020		2025		2030	
	Obese	Obese + disease	Obese	Obese + disease	Obese	Obese + disease
Hypertension	127	250	288	612	485	1,128
Type 2 diabetes mellitus	326	66	741	170	1,266	331
Hypertriglyceridaemia	171	190	386	448	659	790
Hypercholesterolaemia	102	244	236	584	403	1,042

Obese: Category that refers to all the obese population without the cardiometabolic risk factor of interest for each of the MexOb-disease models

6.3.2 Female MexOb-disease models baseline simulation results

Total prevalence of disease within the obese population

Projections estimated from the MexOb-disease models for females showed that by 2030 the prevalence of hypertension and the prevalence of hypercholesterolaemia in the obese population will be above 50%. Similarly to males, the highest projected prevalence of the four obese-related cardiometabolic risk factors was observed for hypercholesterolaemia (56%).

The rise in the number of obese persons among females is projected to have the biggest effect on the prevalence of hypertension, which showed an approximately 0.7pp annual increase between 2015 and 2030 (from 40.1% to 50.4%). Diabetes prevalence in the obese population showed the second highest increase, with an annual growth in prevalence of approximately 0.6 pp/year (17.0% in 2015 to 26.2% in 2030). In contrast, I observed that the projected prevalence of the obese population with hypercholesterolaemia (around 55%) remained steady during a 15 year period, (Figure 6-6). The observed increase in the projected obese-related cardiometabolic risk factor prevalence was mainly due to the increases among the following groups: obese women aged 35 to 49y with hypertension; obese women aged 40 to 54y and 70 to 79y with diabetes; and obese women aged 40 to 44y and 70to 74y with hypercholesterolaemia and 20 to 34y and 60 to 74y with hypertriglyceridaemia (Figure 6-7 to Figure 6.10).

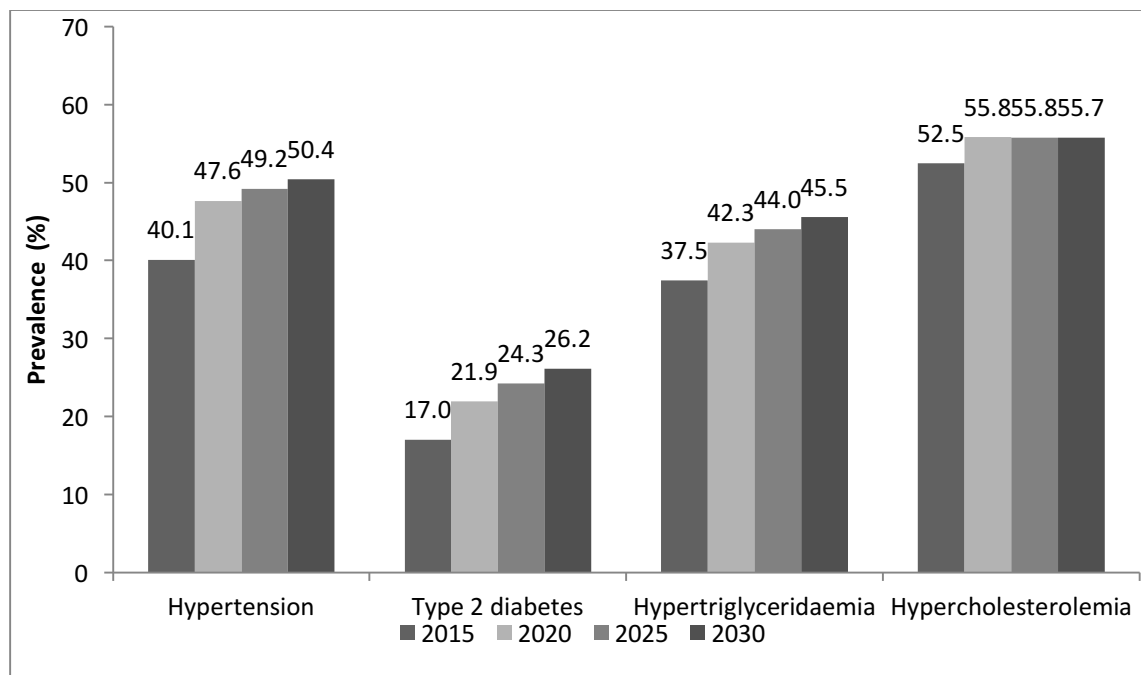
Total number of cumulative new obese-disease cases

Table 6.3 shows the cumulative number of new cases of obese individuals with the presence of a cardiometabolic risk factor in the future female population over the 15 year period. As with males, the number of new cases are projected to nearly double in 15 years' time. In 2020, the projected number of new disease cases from three of the four MexOb-disease models was around 1.5 million in each, with the exception of hypertension (2.5 million). By 2030, my model results showed that the highest number of new disease cases in obese females was observed for hypertension, with 10.3 million new cases expected from 2015 to 2030. The lowest number was found for diabetes (almost six million obese persons with diabetes). Even though the results from the MexOb-Model for diabetes showed a smallest number of new cases (reflecting its lowest prevalence among the four risk factors), the proportional growth in the projected number of obese persons with diabetes in this 15 year period was similar to that estimated by the other three MexOb-disease models for females.

Total number of projected deaths in the obese and obese with disease population

The projected future increase in the prevalence of obesity among women aged 20 to 79y in a 15 year period could lead to between 1.8 million and 2 million deaths by 2030. The MexOb-HTG model predicted the highest number of all-cause deaths (2.07 million) by 2030, of which 44% were estimated to be deaths in obese women with hypertriglyceridaemia. Also the MexOb-HT model estimated a similar number of total deaths (2.06 million) by 2030. This MexOb-disease model also showed the highest projected percentage of deaths in the obese with a cardiometabolic risk factor group from the four MexOb-disease models (72.7%). The next highest estimates of the number of projected deaths was observed in the MexOb-HCl model (2 million), with 72.5%% of the deaths in the obese population projected to come from obese persons with hypercholesterolaemia.(Table 6.4).

Figure 6-6 Total age-standardised projected prevalence of obesity-related cardiometabolic risk factors in the female obese population 2015-2030.



The age-specific estimates of prevalence were directly age-standardised to the projected population for 2022

Definitions used to estimate this numbers:

Hypertension A) SBP ≥ 150 or DBP ≥ 90 mmHg in ≥ 60 y; B) SBP ≥ 140 or DBP ≥ 90 mmHg in < 60 y+. A or B or previously diagnosed by a physician

Type 2 diabetes mellitus ≥ 126 mg/dl (≥ 7.0 mmol/L) or previously diagnosed by a physician

Hypertriglyceridaemia ≥ 150 mg/dl (≥ 1.7 mmol/L) or previously diagnosed by a physician

Hypercholesterolaemia ≥ 200 mg/dl (≥ 5.2 mmol/L) or previously diagnosed by a physician.

Figure 6-7 Projected hypertension prevalence in obese female population 2015 to 2030 by age group.

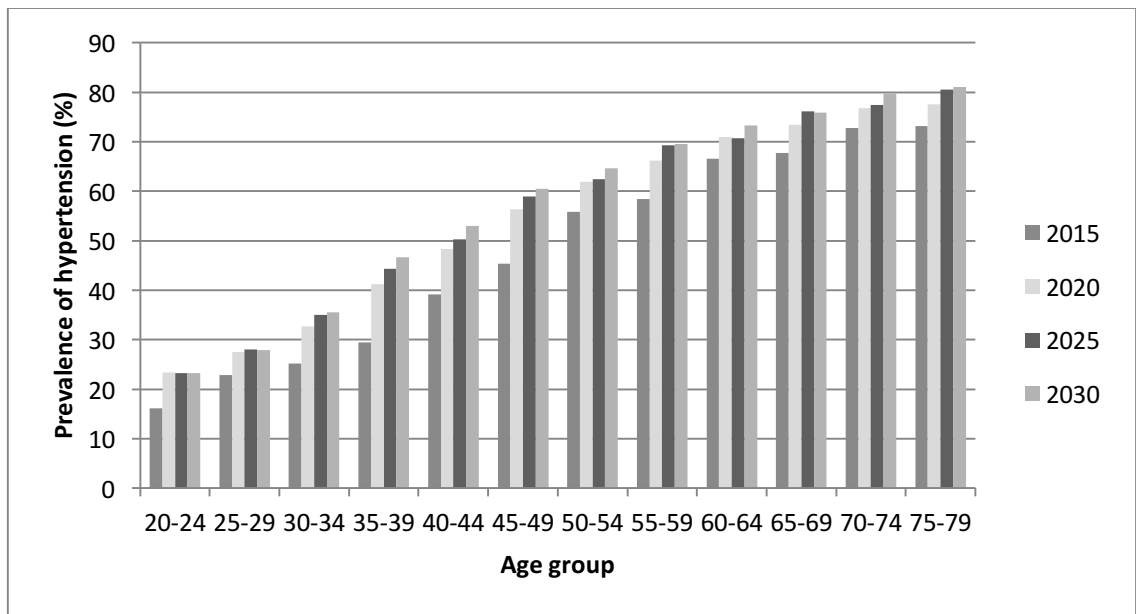


Figure 6-8 Projected type 2 diabetes mellitus prevalence in obese female population 2015 to 2030 by age group.

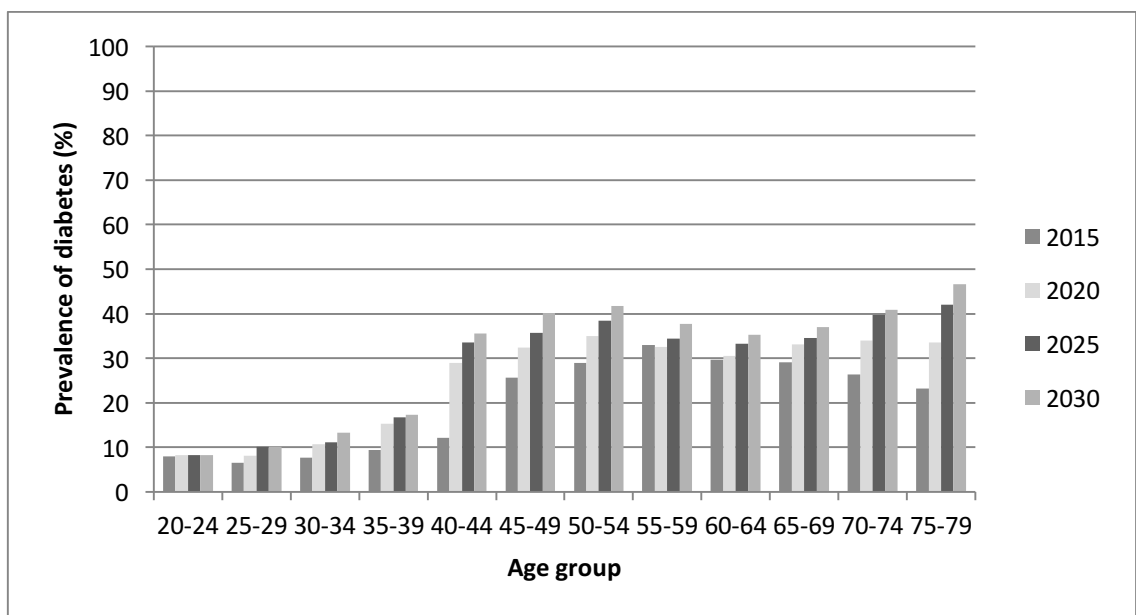


Figure 6-9 Projected hypertriglyceridaemia prevalence in obese female population 2015 to 2030-by age group.

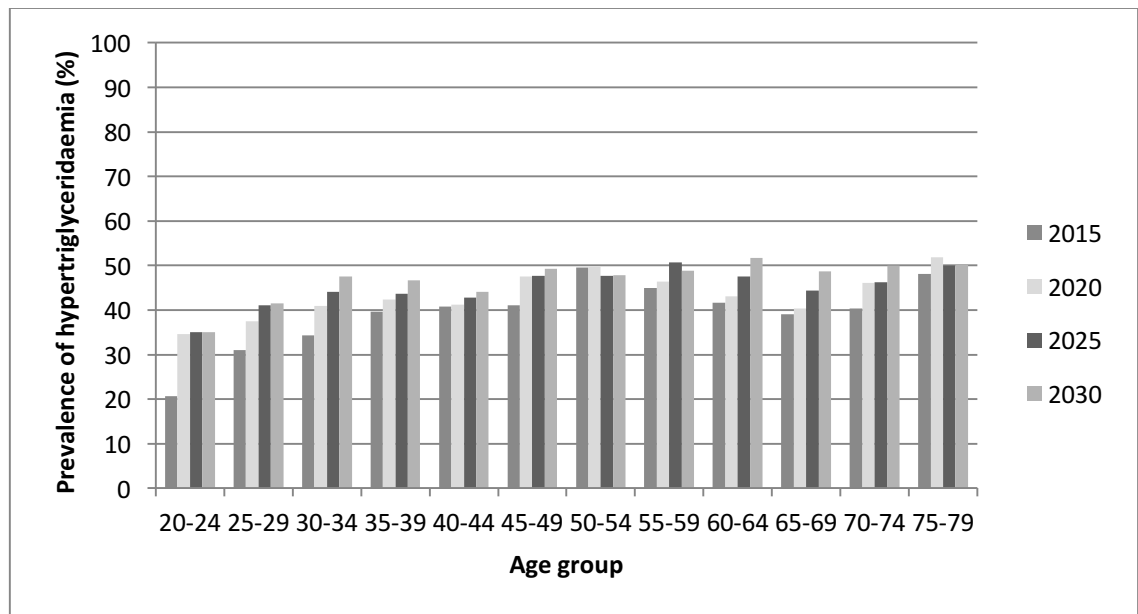


Figure 6-10 Projected hypercholesterolaemia prevalence in obese female population 2015 to 2030 by age group.

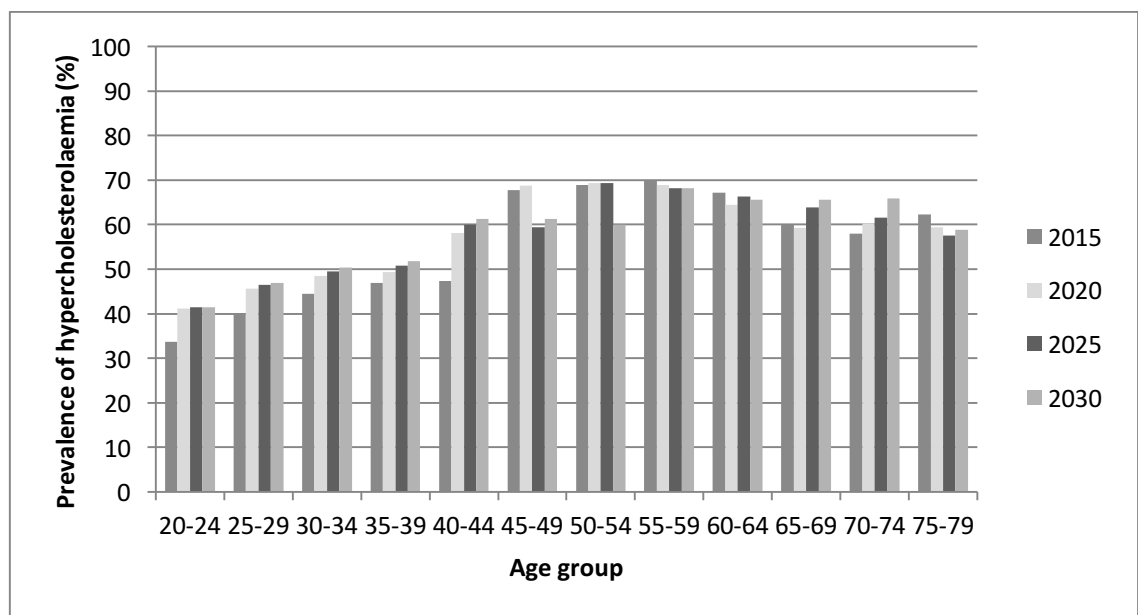


Table 6.3 Cumulative number of new cases of obesity-related cardiometabolic risk factors from 2015 to 2030 among Mexican female adults 20 to 79 years old in thousands.

Cardiometabolic risk factor	2020	2025	2030
Hypertension	2,446	5,824	10,280
Type 2 diabetes mellitus	1,300	3,201	5,643
Hypertriglyceridaemia	1,468	3,524	6,130
Hypercholesterolaemia	1,639	4,134	7,183

Table 6.4 Cumulative number of deaths from each MexOb-disease model in obese female adults 20 to 79 years from 2015 to 2030.

Cardiometabolic risk factor	2020		2025		2030	
	Obese	Obese + disease	Obese	Obese + disease	Obese	Obese + disease
Hypertension	135	296	316	769	564	1,499
Type 2 diabetes mellitus	345	76	819	206	1,447	414
Hypertriglyceridaemia	285	194	665	489	1,152	919
Hypercholesterolaemia	127	321	304	789	548	1,449

Obese: Category that refers to all the obese population without the cardiometabolic risk factor of interest for each of the MexOb-disease models

6.4 Sensitivity analysis

I performed a sensitivity analysis to estimate the possible best-case and worst-case scenarios of the base-case model projected prevalence of the four obesity-related cardiometabolic risk factors in the simulated population. The MexOb-Model parameters were originally programmed to remain static during the 15 year simulation period (divided into three five-year cycles). Therefore it is relevant to undertake sensitivity analyses to estimate possible variations of the baseline model to show a range of data that could possibly happen into the future, in order to represent what could happen in real life, should the parameters of the MexOb-Model change over time.

6.4.1 Methods

These sensitivity analyses were performed via a deterministic sensitivity analysis in which the values of a parameter were modified manually to estimate the uncertainty of the model outcomes around specific parameters (7). The analyses performed while developing the MexOb-Model showed that the most important steering parameter affecting the variability in the model outputs was the estimated size of the annual increase in the obese population during the 15 year period, and the prevalence of the four cardiometabolic risk factors in the obese population used for the distribution of the initial population into the obese without disease and obese with disease groups. Therefore, for this analysis, I modified the main steering parameters of the MexOb-Model: the initial population distribution, transition probabilities, the open cohort component, and the growth ratio parameters of each of the four MexOb-disease models for males and for females.

These deterministic sensitivity analyses were performed by using the lower and the upper limits of the 95% confidence interval for the best and worst-case scenario respectively, instead of the mean values of the data used for the base-case model. For the initial population distribution and the growth ratio, I used this approach to modify the values of the ENSANUT 2006 prevalence of the cardiometabolic risk factors in the obese population. For the open cohort component (used to accommodate new cases), I used this approach to modify the values of the β -coefficients estimated from the linear trends. For the transition probabilities, I used the values as 95% CI for the Hazard Ratios Please refer to Chapter 3 and Chapter 4 for more details on the data and the equations used to estimate these parameters.

Additional adjustment for the MexOb-T2DM for males

As shown in Table 4.7, the prevalence of diabetes in the male obese population in the youngest age group (20-24y) from the National Health and Nutrition Survey (ENSANUT) 2006 was 0% (i.e. no cases of diabetes among obese men aged 20-24y).

This zero estimate reflects both the small number of obese males aged 20 to 24y in the survey data, and the lower prevalence of diabetes at younger ages.

This figure of zero prevalence was used for the mean baseline estimation and also for the best-case scenario simulation, as this could be a plausible value for a best-case scenario of the prevalence of diabetes in that age group (i.e. zero number of obese diabetics). However, this prevalence does not represent a potential value for a possible worst-case scenario. To overcome this, I decided to substitute, for the worst-case scenario simulations, the prevalence of 0% by a prevalence of 39%. This value was estimated from two calculations. Firstly, the prevalence of diabetes in the total population was 15% higher among the 25 to 29y group compared with the 20 to 24y group in ENSANUT 2006 (3% and 4% respectively). Secondly, the upper limit of the confidence interval for the prevalence of diabetes among obese men aged 25 to 29y was 46% (representing the worst-case scenario). Applying a 15% reduction to the value of 46% gave a value for the worst-case scenario for obese males aged 20 to 24y of 39%. The rationale for using this strategy was to ensure that the prevalence of diabetes in the obese population had a value that was plausible for the worst-case scenario for the male MexOb-T2DM model.

Directly age-standardised prevalence estimates for the total obese population with the presence of a cardiometabolic risk factor for each of the four MexOb-disease models were estimated for the three five-year cycles (amounting to a 15 year period). Weights for the age-standardisation to apply to the age-group specific estimates were calculated using the age group, gender and calendar year specific projected population distribution from the National Population Council of Mexico (CONAPO) estimates (63).

6.4.2 Results

Figure 6-11 to Figure 6.18 show the projected age-standardised to 2022 prevalence estimates for the four cardiometabolic risk factors in the estimated total obese population aged 20 to 79y, separately by sex. The analyses based on the worst-case scenario estimated that the prevalence of three of the four cardiometabolic risk factors in the obese population by 2030 could reach $\geq 53\%$ for both sexes, with higher prevalence projected for males than for females, with the exception of diabetes. A more optimistic panorama, the best-case scenario, showed that the prevalence of T2DM, HTG and HCl among obese men and T2DM and HTG among obese women could be between 15% and 40%.

The MexOb-disease models for males showed a bigger variability in the estimated prevalence of the cardiometabolic risk factors among the obese population between the best and the worst-case scenarios than the female disease models simulations. The range of difference observed between the projected outcomes for 2030 from the two different scenarios for the four MexOb-disease models for males varied between 14 pp to 40 pp. For women, the difference between the best and worst-case scenarios estimates was between 9 pp and 24 pp.

From all the four MexOb-disease models, for both sexes, the MexOb-HT model showed the smallest difference between the best and the worst-case scenario projected prevalence. By 2030 there could be between 11 million (45%) and 22 million (54%) obese women and between 6 million (47%) and 15 million (61%) obese men with hypertension, for the best and worst-case scenario respectively. The biggest change observed from the sensitivity analyses for the four MexOb-disease models for the male and female obese population was from the MexOb-HTG model. By 2030, the projected prevalence could vary between the best and worst-case scenario by 40 percentage points (pp) for obese males and by 17 pp for obese females. This represents that by 2030 there could possibly be between 4 million (31%) and 15 million (71%) men and between eight million (36%) and 17 million (53.4%) women

classified as obese with hypertriglyceridaemia for the best and worst-case scenario respectively. Appendix C shows the total cumulative number of new disease cases projected to be observed every five years under the best-case and worst-case scenarios stratified by sex.

Figure 6-11 Total projected hypertension prevalence in the obese male population 2015 to 2030.

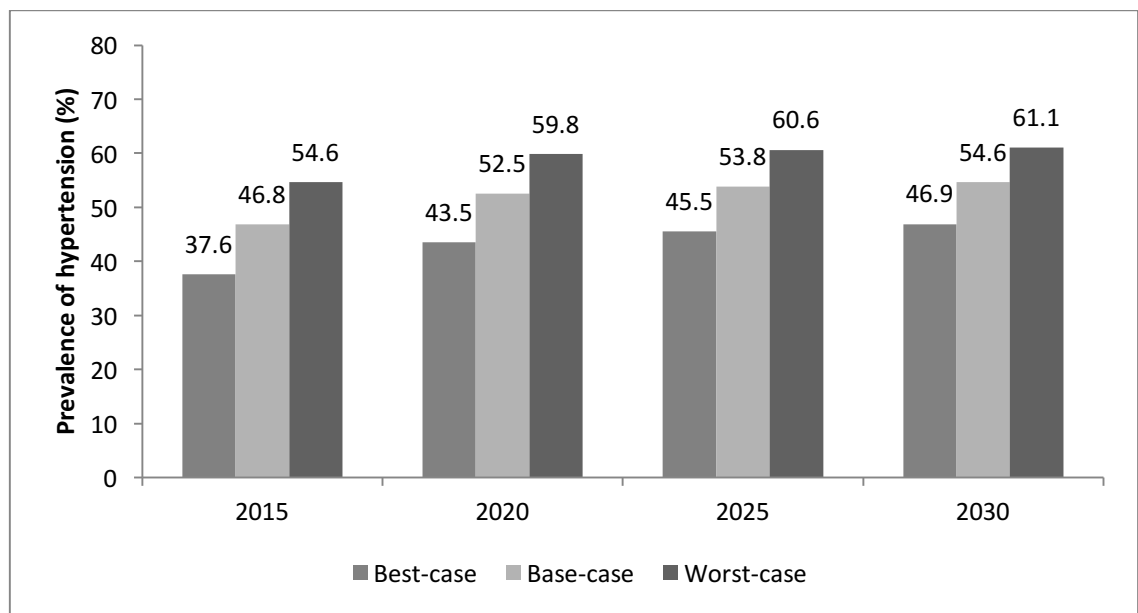


Figure 6-12 Total projected type 2 diabetes prevalence in the obese male population 2015 to 2030.

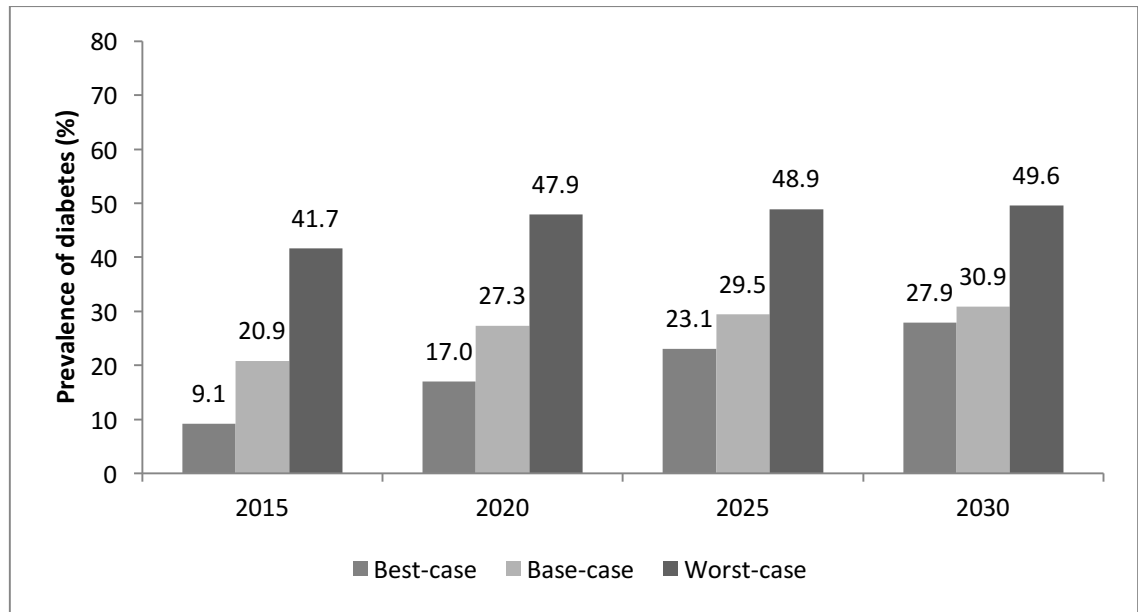


Figure 6-13 Total projected hypertriglyceridaemia prevalence in the obese male population 2015 to 2030.

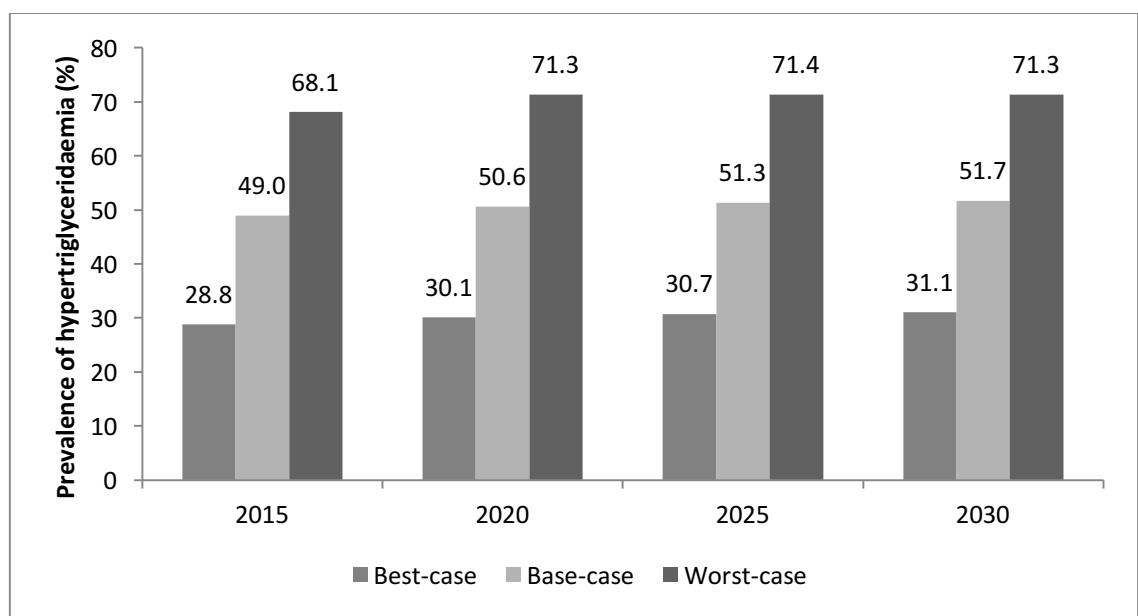


Figure 6-14 Total projected hypercholesterolaemia prevalence in the obese male population 2015 to 2030.

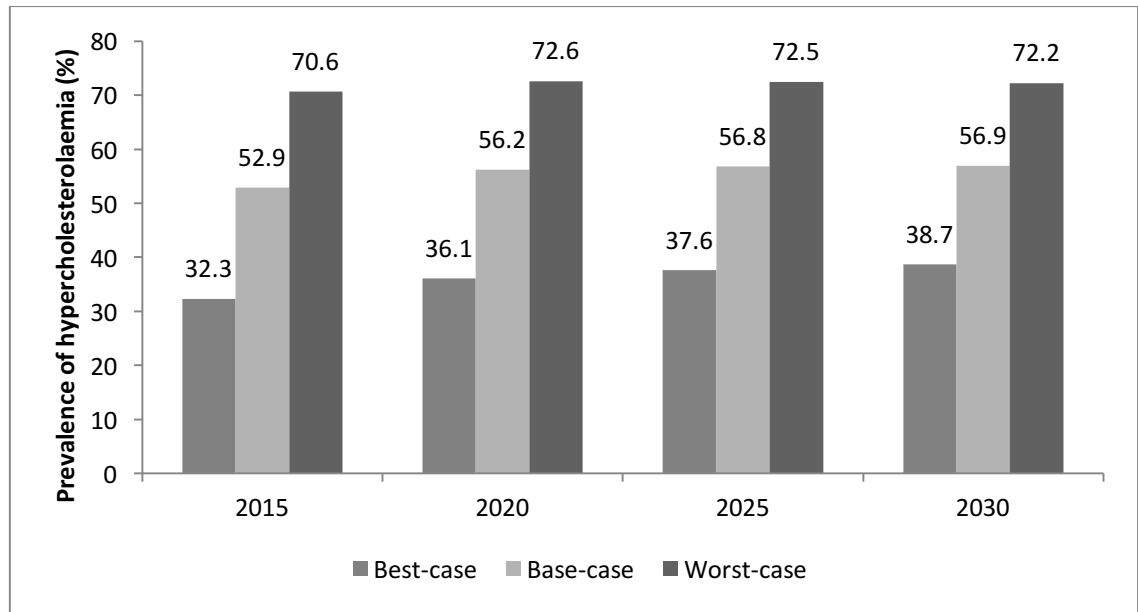


Figure 6-15 Total projected hypertension prevalence in the obese female population 2015 to 2030.

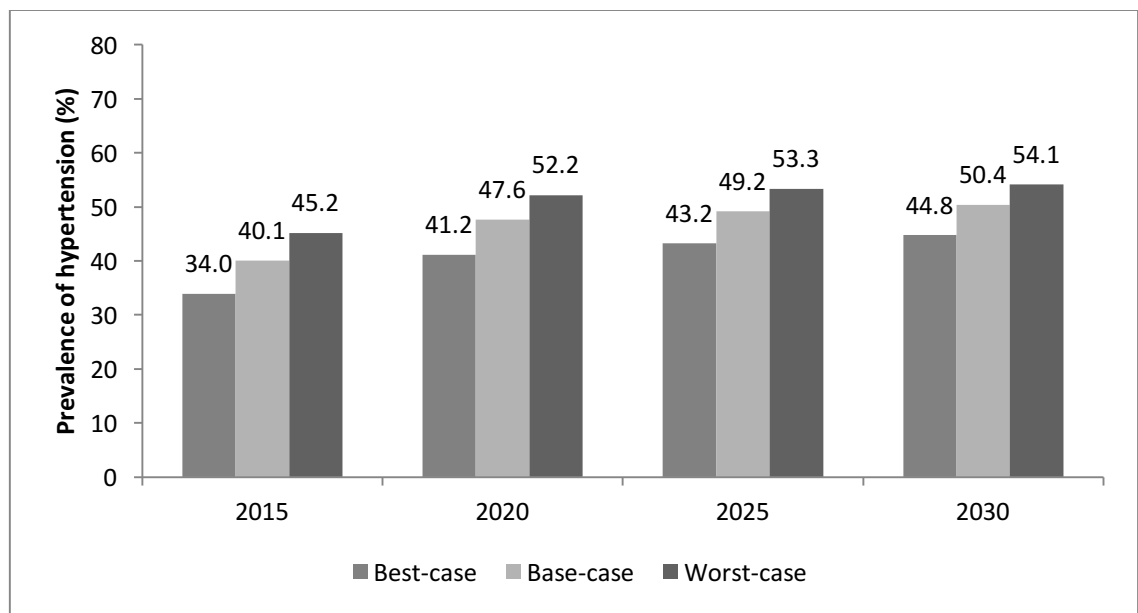


Figure 6-16 Total projected diabetes prevalence in the obese female population 2015 to 2030.

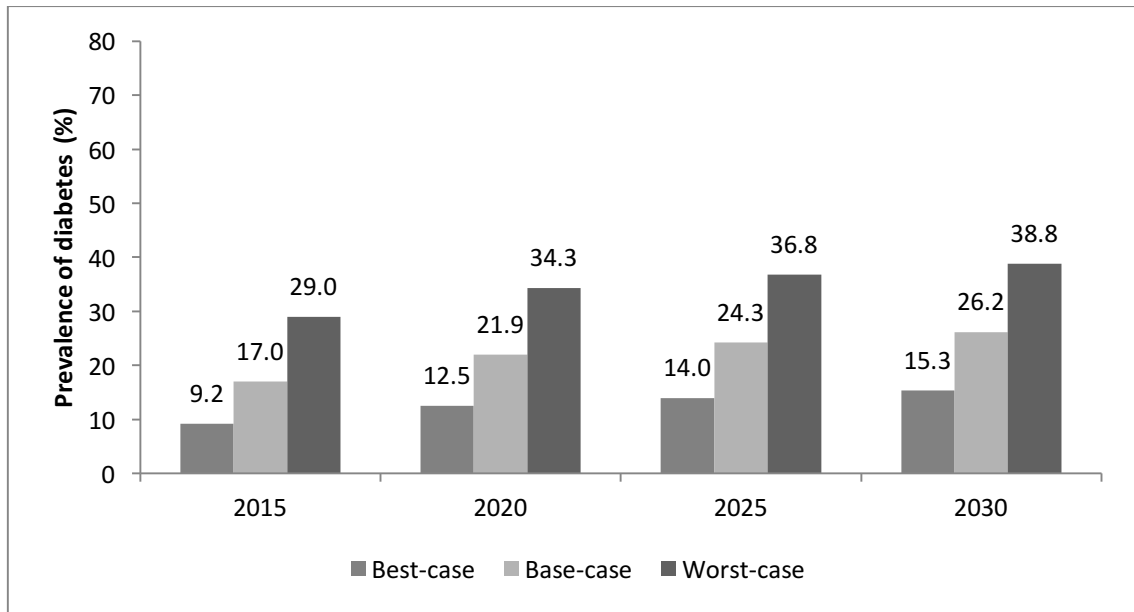


Figure 6-17 Total projected hypertriglyceridaemia prevalence in the obese female population 2015 to 2030.

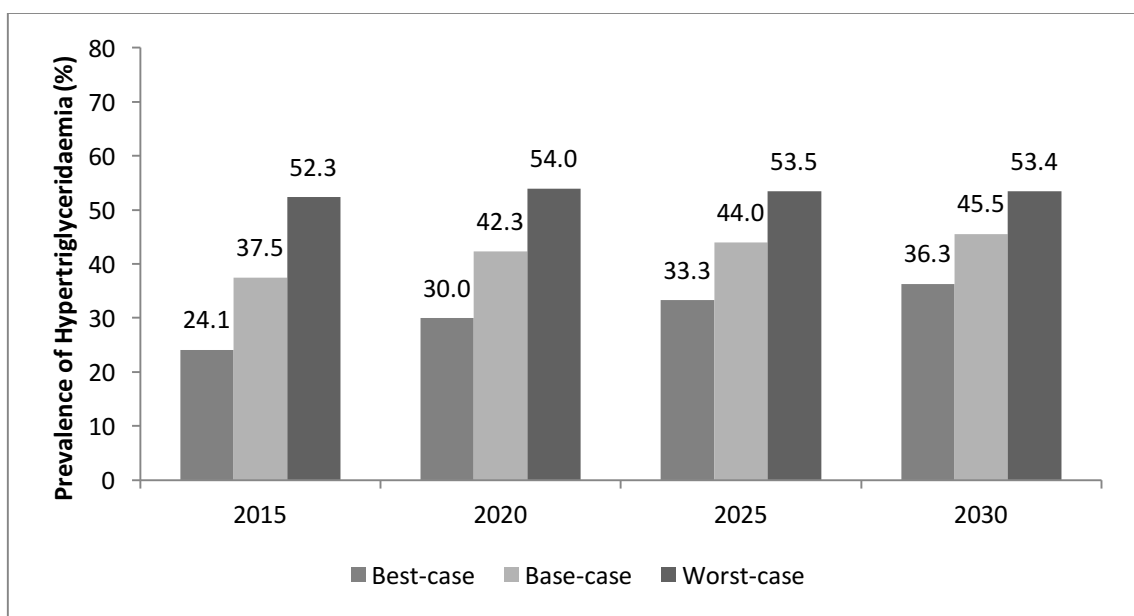
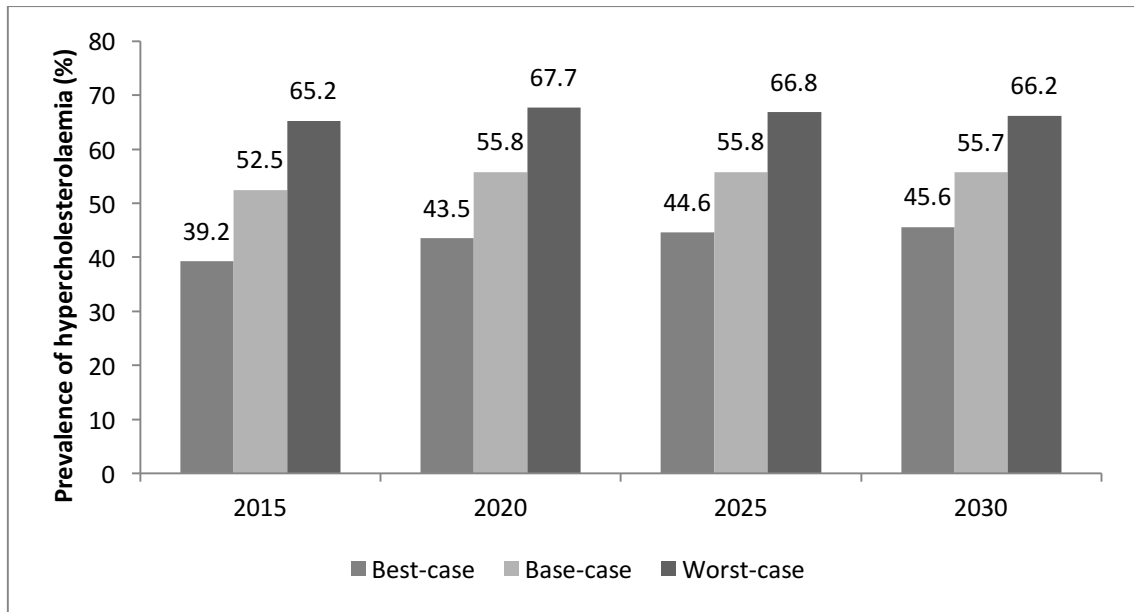


Figure 6-18 Total projected hypercholesterolaemia prevalence in the obese female population 2015 to 2030.



6.5 Discussion

6.5.1 Summary of results

Based on the best available Mexican data, and with the prevalence of the obesity-related cardiometabolic risk factors among the initial obese population at 2015 held constant at 2006 levels, my study showed that if the obesity trends continue, the prevalence of the obese population with a cardiometabolic risk factor, for both sexes, will be approximately 55 % for HT, and between 47% and 60% for HTG and HCl and around 30% for diabetes by 2030 (reflecting the influence of the open cohort component, growth ratio and transition probabilities). The MexOb-disease models forecasted that the highest increase in the prevalence of a cardiometabolic risk factor among the obese population in the 15 year projection period for males and for females would be for hypertension and diabetes.

My results showed that by 2030, the increase in obesity trends will have a greater impact in the number of obese individuals with the presence of a cardiometabolic risk factor in the oldest age groups (60y and older). Additionally, the expected increase in the number of obese persons with diabetes and the number of obese persons with hypertension will come from the growth of this disease in the younger population. Projected results from the sensitivity analyses from the four MexOb-disease models showed the lowest difference in the prevalence of obese with disease between the best and the worst-case scenarios by 2030 for the MexOb-HT model (47% to 61% respectively for males, and 45% to 54% respectively for females). This means that even in the best-case scenario, there could be a high health burden among the obese population coming from the number of hypertensive cases.

Overall, the MexOb-disease models for females showed a higher projected cumulative number of deaths than the MexOb-disease models for males. The number of cumulative deaths from 2015 to 2030 was projected to be around 1.5 million and 2 million for males and for females, respectively. I observed that the highest number of

deaths among the obese population with a cardiometabolic risk factor was estimated from the MexOb-HCI model and from the MexOb-HT model, with >70% of the cumulative estimated number of deaths coming from obese males and obese females with hypercholesterolaemia or with hypertension.

Overall my outcomes reported a higher number of new cases of obesity-related cardiometabolic risk factors in obese females than in obese males. These differences in the projected estimates could be the effect of the higher prevalence of obesity in Mexican women than in men, a pattern that has been observed in the national health surveys from past years (see: Chapter 3). This increase in obesity prevalence is projected to bring as a consequence an increase in the prevalence of obesity-related risk factors.

This gender difference in obesity prevalence is not exclusive to the Mexican population; it has also been observed worldwide. In 2013, the worldwide prevalence of overweight, including obesity ($\text{BMI} \geq 25 \text{ kg/m}^2$) was 36.9% in men and 38% in women. Obesity prevalence was observed to be higher for women (13%) than for men (9%), and this pattern was more frequently seen in developing countries, like Mexico, than in developed countries (272). Gender differences in overweight/obesity prevalence have been attributed to various factors such as biological factors (273, 274) or sociocultural dynamics (275). In Mexico, results from the 2006 national health examination survey reported that Mexican men were more active than women (69). Mexican women in both rural and urban areas had a significantly higher BMI than their male counterparts; the same pattern was observed when men and women were compared by education or socioeconomic status (276). Additionally, results from a meta-analysis showed that there is a stronger association between obesity and hypertension, and between obesity and diabetes, in women than in men (46).

The MexOb-HCI and MexOb-HT models for males and females estimated the highest number of projected cumulative deaths by 2030. The calculation of these outcomes

were highly influenced by the risk ratio (RR) of mortality, and by the prevalence of HT and HCl in the obese population that were used for the mortality decomposition formula to estimate the transition probabilities. The RR used for this formula for HT and HCl was 1.6 for both sexes, which was the highest RR used in the MexOb-disease models (see: Chapter 4).

6.5.2 Comparisons with other studies

Other modelling studies have reported projections of the prevalence of these cardiometabolic risk factors in the Mexican population. For example, Meza et al.(266) reported that by 2030 the number of people with diagnosed diabetes in the total population 20+ years of age is expected to be approximately ten million women (prevalence of 20%), and seven and a half million men (prevalence of 17%), with a growth of diabetes prevalence increasing with age and having its peak in the 65 to 70 year olds in both sexes.

The MexOb-T2DM model projected for 2030 a total number of obese diabetic individuals of 6.5 million men (4.8 to 13 million for the best and worst-case scenario respectively) and eight million women (four to 15 million). My model projections showed a peak in the prevalence of diabetes among the obese population in the 50 to 59y male population, and an increase associated with age in women aged 40 years and older, with the highest prevalence observed in the 75-79 year age groups. The number of projected diabetes cases among the obese population from the MexOb-T2DM model was calculated considering both diagnosed and undiagnosed diabetes in the obese population. In contrast, estimates from the study by Meza and colleagues (266) reported only the diagnosed cases in the total population. According to the results by Villalpando et al., 50% of the total prevalence of diabetes in the Mexican population in 2006 came from cases that were undiagnosed (217), so it could be expected that the estimates from Meza would at least double if they had taken into account the cases of undiagnosed diabetes. Another study, by Guarioguata et al. (267), reported that by 2035, the number of Mexican people with diagnosed diabetes will be around 16

million. They also reported that across the world regions evaluated, the highest prevalence of diagnosed diabetes was found in people between 60y and 79y of age, but the largest number of diabetic people was in the 40 to 59 year age groups. Similar to the results by Meza and colleagues, they predicted a higher increase in the number of diabetes cases than my model; this is expected due to their models estimating values for the total adult population (whilst the MexOb Model focuses on the obese population), but the age groups reported that could present the highest prevalence of diabetes were similar between the models. Additionally, recent projections from the International Diabetes Federation (IDF) reported that by 2040 the prevalence of diabetic adults in Mexico will be around 20.6 million. This is in the same ballpark as the results produced by the MexOb-T2DM (by 2030 14.4 million obese-T2DM), taking into consideration that the model focusses only models obese population compared to IDF who reported future estimates for the general population(277).

Overall, the MexOb-disease models projected a higher prevalence of cardiometabolic risk factors in the obese population aged 60 years and older than in the obese population in the younger age groups. This is of extreme relevance to the Mexican population as it is expected that the older population will increase significantly in the next few years, and with this, the associated health burden (278, 279). This is consistent with other projection studies (Meza and Guarioguata) which estimated that the highest projected disease prevalence in the Mexican population would be observed in the elderly ($\geq 60y$) (266, 267). Other studies have also reported that the elderly population normally present a higher prevalence of cardiometabolic risk factor clusters than the younger population and with that, a lower quality of life (280).

The increase in the health burden from the increase in the size of the elderly population is a problem that affects not only Mexico, but all countries. It has been estimated that 23% of the global burden of disease is attributable to diseases that occur to the population aged ≥ 60 years of age, and its highest contributor is cardiovascular disease. The higher contributors of disability adjusted life years (DALYs)

per person come from the older population in the low-income and the middle income regions (281). In Mexico, the healthcare costs for the elderly population create a big burden, particularly for household incomes. It was reported that in 2006, the average household expenditure for hospitalization of the elderly was \$309 USD per year (2010 exchange rate from Mexican Peso to USD) (282).

My projected prevalence estimates from the four MexOb-disease models showed that by 2030, hypercholesterolaemia and hypertension are projected to have the highest prevalence among the obese population for both men and women (58% for HCl and 56% for HT in men; 56% for HCl and 52% HT in women). These results are in line with the previous results from the ENSANUT survey data for 2006 for the total population that showed that after low HDL, hypercholesterolaemia and hypertension were the risk factors with the highest levels of prevalence in the total adult population (81, 86). Additionally, according to results from ENSANUT 2012, hypertension levels in the total population when stratified by age group showed a similar pattern of prevalence distribution as those estimated from the MexOb-HT model. Male hypertension prevalence results from ENSANUT 2012 showed the highest prevalence in the 60 to 69 years old groups and hypertension levels in women were observed to increase with age, and showed the highest prevalence in the population aged 70 to 79y (35). A similar pattern was observed in my estimated prevalence of hypertension in the obese population (MexOb-HT model) which showed the highest prevalence in the same age groups as ENSANUT 2012 for both sexes by 2030 (Figure 6-2 and Figure 6-7).

The annual increase in cardiometabolic risk factor prevalence from my estimates from 2015 to 2030 are in agreement with the increase in prevalence reported by Villalpando et al. for diabetes and hypercholesterolaemia from 1993 to 2006, considering that the trends observed in the obese population are similar to the trends observed for the total population (81). Villalpando et al. reported that in the 13 year period from 1993 to 2006 the prevalence of diabetes increased by 0.6 pp/year. My diabetes projected prevalence for obese men and for obese women showed a slightly higher increase of

0.7 pp/year. Villalpando et al reported an increase in the prevalence of hypercholesterolaemia of 1.3 pp/year between 1993 and 2006. However, the reported increase between 2000 and 2006 was lower, at 0.2 pp/year. The latter annual increase was similar to the one reported from my MexOb-HCl model (0.35 pp/year for both sexes).

In contrast, the annual increase in the observed prevalence from past trends for hypertension and for hypertriglyceridaemia was higher than those obtained from my MexOb-Model estimates. The reported annual increase in hypertension prevalence from past trends (from 1993 to 2006) was 1.5 pp/year, and it was observed to be higher for women than for men (1.2 pp/year for males, and 1.9 pp/year for females) (81). My projected prevalence of hypertension among the obese population also showed a bigger annual increase in prevalence for females than for males, but it was lower than the increase reported from past trends, 0.7 pp/year and 0.9 pp/year for obese males and obese females respectively. However, it was recently reported that the prevalence of hypertension in the total adult population from 2006 to 2012 remained steady for males and for females (84).

Contrary to the other cardiometabolic risk factors, the past trends of the prevalence of hypertriglyceridaemia showed a decrease from 42.3% to 31.5% from 1993 to 2006 (81). According to the researchers, this was due to changes in definition and to changes in the methods of biochemical evaluation. The prevalence estimates produced from the MexOb-HTG model using the definition of total triglycerides ≥ 150 mg/dl or previously diagnosed by a physician showed instead an increase in prevalence over the 15 year time period (2015 to 2030).

6.5.3 Strengths and Limitations

Strengths

The MexOb-Model is the first population simulation model that focuses exclusively on the Mexican adult obese population, and that produces future estimates of the prevalence of hypertension, type 2 diabetes, hypertriglyceridaemia and hypercholesterolaemia among the obese population. It is also the first model for the adult Mexican population that produces future estimate of HTG and HCl. This model was developed exclusively for the Mexican population, taking into consideration the best epidemiological data available for the Mexican population. The validation exercise and the base-case scenario results show a future epidemiological panorama that is consistent with the observed data. Furthermore, the results from the MexOb-T2DM model were also similar to what has been produced by other Mexican population simulation models (266, 267).

The projected outcomes presented by the four MexOb-disease models have been shown to be a good estimation of a possible future panorama of the prevalence of hypertension, type 2 diabetes, hypertriglyceridaemia and hypercholesterolaemia in the Mexican obese population. However as with any simulation model it has some limitations that the user has to account for when interpreting the results.

Limitations

The MexOb-disease models were developed to run as independent models, therefore caution is required when interpreting the model outcomes as they cannot be combined together to estimate the total number of obese persons or more specifically the total number of obese persons with disease. Based on previous evidence, it is highly probable that individuals with one of the four cardiometabolic risk factors have at least one other (81). The prevalence of metabolic syndrome (using ATP III definition) in the Mexican adult population is around 37% (283), and it was also observed in the Mexican population that individuals with hypertension are more likely to also have

type 2 diabetes or a dyslipidaemia (83). Saydah et al. also reported that obese individuals in the United States had a higher prevalence of having at least three of four cardiovascular risk factors (total diabetes, total hypertension, total dyslipidaemia, and self-reported smoking) than overweight or normal weight individuals (284).

The MexOb-Model used as its initial population the expected obese population for 2015, but the prevalence of each of the four cardiometabolic risk factors among the obese population in 2015 was set at the same level as observed in ENSANUT 2006, as the cardiometabolic risk factor data collected in ENSANUT 2012 has not been released at the time of the analyses. The structure of the MexOb-Model assumes that these prevalence levels remained unchanged during the nine year period from 2006 to 2015. Additionally, I assumed that the transition probabilities which progress the flow of persons through the three health states (obese, obese-with-disease, and death), and which are based on cross sectional data, will remain steady during the 15 year simulation period (2015 to 2030). These assumptions about the steering parameters, together with the use of the extrapolation of historical trends to account for the secular increase in the size of the obese population, could lead to uncertainties around the forecasted estimates. The sensitivity analyses were performed to illustrate plausible values for the uncertainty around the model outcomes. They were performed by using the lower (best-case) and the upper (worst-case) limits of the 95% confidence interval from the 2006 ENSANUT estimates of cardiometabolic risk factors prevalence among the obese population, and the lower and upper limits of the 95% confidence interval for the β -coefficients from the linear trends.

These deterministic sensitivity analyses were relatively easy to implement (by modifying the values of the key parameters for the baseline model) but the reader has to be aware that this type of analysis fails in considering a broader uncertainty in the outcomes of interest by focusing only on values chosen arbitrarily compared with a stochastic sensitivity method like Monte Carlo simulation where the uncertainty around model outcomes is calculated using random selected values. Monte Carlo

simulation is a probabilistic sensitivity analysis (PSA) in which probability distributions are defined around a factor/parameter that has uncertainty (e.g. β -coefficients). Random values are selected within the chosen parameter distribution (e.g. a normal distribution for a parameter has a specified mean and variance). Each model iteration (e.g. out of a total of 1000) estimates a value from that distribution and uses it as a model input. The different results obtained after each run using the different values of the selected parameter are ranked in order and are then used to estimate the uncertainty values around the simulation model's main outcomes (20).

Another limitation of the MexOb-Model comes from the definitions used for the cardiometabolic risk factors. Even though I tried to use definitions that were closest to the ones used in the ENSANUT 2006 outcome reports, some of the differences in definitions could have had an effect on the outcomes produced from the models. A clear example of this was shown in the study by Rojas et al.(283) where the authors compared three definitions of metabolic syndrome (NCEP 2001, AHA/NHLBI 2005, and IDF 2005) and showed that for women, the diagnosis of metabolic syndrome varied from 42% with NCEP 2001 to 52.7% with IDF 2005. For hypertension, the Mexican cut-off points were adults with SBP >140mmHg or DBP >90mmHg. However, for the population aged 65y and older, I used the different cut-off point of SBP \geq 150mmHg, and as a result I observed a small decrease in the prevalence of hypertension for older age groups. It is probable that the different definition I used for dyslipidaemias (HTG and HCl) could have had a similar effect in my estimations. In addition to the recommended cut off points of total triglycerides \geq 150mg/dl (\geq 1.7mmol/L) for HTG, and total cholesterol \geq 200mg/dl (\geq 5.2mmol/L) for HCl, I included the condition of "being previously diagnosed by a physician", which would have had the effect of producing higher outcomes compared with modelling studies which would only use the \geq 150mg/dl and \geq 200mg/dl cut offs. For the MexOb-Model I considered that the obese population with normal values of TG or TC levels, but being previously diagnosed by a physician, could have normal values of TG or TC because of pharmacological treatment or lifestyle changes, and so those members of the obese population could present higher values again later in life. Therefore, they should be

included within the future burden of disease. These differences in definition should be considered when computing the MexOb-Model estimates with other modelling studies.

Moreover, the MexOb-Model does not take into account the transition of the population from the obese (BMI $\geq 30\text{kg/m}^2$) state to the states of overweight or normal weight. I also did not consider the possible effect that changes in the obesity trends among children and adolescents could have on future adult obesity prevalence and on the outcomes produced from the models. The future levels of obesity estimated from the linear trends showed that obesity prevalence for younger age groups, particularly for boys, is not increasing significantly, but even a small increase could have an effect on the number of cases and the number of deaths from the obesity-related cardiometabolic risk factors in early adulthood. Results from a recent meta-analysis showed that obese children and obese adolescents are approximately five times more likely to become obese adults than children and adolescents who are not obese (285). Additionally having a high BMI during childhood could moderately increase the risk of non-communicable diseases such as diabetes and heart disease in adulthood (286).

6.6 Conclusion

If the obesity trends for adults aged 20 to 79y keep increasing as I have projected, by 2030 one of every two obese adults would have at least one obesity-related cardiometabolic risk factor. Even under the assumption of the best-case scenario, my outcomes showed that it is unlikely that the base-case projected estimates for morbidity and mortality change substantially. By 2030, the projected health impact will not only be affected by the increase in the size of the Mexican population, or by the ageing of the population. The projected health impact will also be affected by the increase in the prevalence of cardiometabolic risk factors among the younger age groups. It will be the obesity health burden from the younger population that could bring greater long-term implications for the healthcare services and individual's quality of life.

Chapter 7. Health impact of three possible future obesity prevalence reduction scenarios

7.1 Introduction

If the past trends in obesity continue, obesity and its associated cardiometabolic risk factors are expected to increase the health burden in Mexico. As observed from the base–case results, by 2030 the prevalence of cardiometabolic risk factors in the obese population could reach $\geq 50\%$ for HT, HTG and HCl and around 30% for diabetes for men and women. Nowadays, there is extensive literature about the estimated health benefits that a reduction of obesity prevalence could bring at an individual and at a population level. Additionally, many studies have been published about a range of cost-effective interventions or policies that could achieve a reduction in obesity prevalence. The enormous size of this public health problem has driven international agencies such as the WHO to set a list of voluntary targets in order to encourage countries to reduce the health and economic burden from non-communicable diseases (NCDs) (287).

A number of population-based simulation modelling studies have assessed the future impact of reducing the burden of obesity at the population level, and have observed that even with a small reduction in population mean BMI and/or obesity levels there could be important improvements in the overall population health, including a reduction in the number of deaths from chronic diseases, as well as healthcare costs savings (92, 116, 117).

This chapter describes the possible future effects on the number of cases (obese, obese with disease, and deaths) of three possible scenarios of obesity prevalence reduction by 2030 in Mexican adults 20 to 79 year olds, predicted using the MexOb-Model.

7.2 Three obesity prevalence reduction scenarios

The results of my literature review showed that the most frequent strategy used for simulating obesity prevalence reduction scenarios was that of applying a direct reduction to mean levels of BMI in the population (i.e. shifting the centre of the BMI distribution) (117, 118) (see: Chapter 2). However, the MexOb-Model does not use mean BMI population values as a model component; it uses the commonly used obesity threshold ($\text{BMI} \geq 30 \text{ kg/m}^2$) to obtain prevalence values. Based on this, I decided to apply a similar approach to the one used in the population simulation analyses of Finkelstein et al.(147); Lo et al. (160); and Saidi et al. (165), which apply direct reductions to obesity prevalence.

Mexico has not set any national obesity reduction target(s). Therefore, for the obesity prevalence reduction scenarios analyses, I decided to use goals that had been set by other countries and international agencies. Additionally, I also considered as a scenario the future health effect of a sugar-sweetened beverage (SSB) tax; an initiative that has been implemented in Mexico since 2014.

The measures of assessment that were applied to these analyses to observe the differences between the *base-case model* and the three obesity reduction scenarios were: avoided number of total obesity cases, avoided number of expected new obese-disease cases, and number of deaths avoided.

Base-case model: Refers to the outcomes obtained if the projected obesity prevalence from 2015 to 2030 continues (see: Chapter 6).

The three hypothetical scenarios simulated to estimate the effect of a reduction of obesity prevalence in the Mexican population as estimated by the MexOb-Model were as follows:

- **Scenario A:** A slowing down in the rate of increase of obesity prevalence to achieve a 3% relative reduction of 2030 projected base-case model levels.
- **Scenario B:** A zero increase from 2015 obesity prevalence.
- **Scenario C:** A relative reduction of 10% of the 2015 projected obesity prevalence by 2030.

7.3 Methods

7.3.1 Overview

All the scenarios were targeted directly at reducing the obesity prevalence of the Mexican adult population (aged 20 to 79y). The estimated effects of these reductions were directly applied to the age-group and sex specific open cohort component, as this one of the parameters which affects the growth in the size of the obese population (i.e. the open cohort component allows for the inclusion of new obese cases in a modelling cycle) (see Chapter 4). Each of the four MexOb-disease models (MexOb-HT, MexOb-T2DM, MexOb-HTG and MexOb-HCI) for males and females was run for three five-year cycles to estimate the impact of the specified reduction in adult obesity prevalence during the fifteen year period (2015 to 2030) using the model outcomes described above.

7.3.2 Hypothetical scenarios description

The three scenarios for reducing the prevalence of obesity are discussed below.

Scenario A: I simulated a deceleration in the rate of increase of obesity prevalence in each age group and sex to alter the trend so that by 2030, the total obesity prevalence for adults aged 20 to 79y for each sex (males and females) was approximately 3% less than the prevalence estimated by the base-case model.

To achieve this goal, changes could be made to one or more of the parameters that modified the growth of the obese population in the MexOb-Model (i.e. open cohort component, disease growth ratio or transition probabilities). For my analysis, I decided

to apply the change only to the open cohort components (age group and sex specific beta-coefficients). The beta-coefficient is the slope of the linear trend equation (for a 1-unit increase in year): the parameter in the model that affects the number of new obese cases entering into the modelling cycle.

To reach this target of reduction in obesity prevalence (3% from the 2030 projected prevalence) using only modifications to the beta-coefficients, I applied a relative reduction of 3% every five years to the age–group and sex specific beta-coefficient obtained from the linear trend calculations (see: Chapter 3) starting from 2015 onwards (2020, 2025 and 2030). With this gradual deceleration in rate of increase the target of relative reduction of approximately 3% from 2030 projected obesity prevalence will be achieved.

Table 7.1 shows the adjusted age group and sex specific open cohort component (new beta-coefficient * year) values used for this analysis for each of the three five-year cycles (scenario A).

Under scenario A, the formula to estimate the new beta-coefficient was follows:

$$\beta_{eta_x} = \beta_{eta_{x-5}} * 0.97(3\%)$$

x: represents the cycle year

For example: the beta-coefficient (annual rate of change) for 20-24y in the base case model was 0.575 for 2015. The adjusted beta-coefficient under scenario A for 2020 was the original base-case value of 0.575 multiplied by 0.97 =0.557 (i.e. 1-0.97= 0.03 or 3%). For 2025, the adjusted beta-coefficient was 0.541 (0.557 *0.97); and for 2030, the value was 0.524 (0.541* 0.97).

Once the new beta-coefficients for each five year cycle were calculated, they were used as the input to estimate the open cohort parameter which estimates the number

of obese cases (existing plus new) in the initial population of each model cycle as follows (see: Chapter 4):

$$y = \text{population in health state} * (\beta * \text{year})$$

year= baseline year for the linear trend: 1999 was defined as year 0; up to 31 for the final year 2030.

Table 7.1 Open cohort component values used for the simulation of a slowing down in the rate of obesity prevalence increase to achieve a 3% relative reduction to 2030 projected values (Scenario A).

Age group	Males			Females		
	2015-2020	2020-2025	2025-2030	2015-2020	2020-2025	2025-2030
20-24	1.132	1.158	1.182	1.117	1.140	1.162
25-29	1.164	1.197	1.227	1.127	1.152	1.175
30-34	1.166	1.199	1.229	1.144	1.172	1.199
35-39	1.161	1.193	1.223	1.140	1.168	1.194
40-44	1.205	1.246	1.284	1.077	1.092	1.107
45-49	1.048	1.058	1.067	1.134	1.160	1.185
50-54	1.032	1.038	1.044	1.139	1.166	1.192
55-59	1.057	1.068	1.078	1.109	1.130	1.150
60-64	1.030	1.036	1.041	1.111	1.133	1.154
65-69	0.956	0.948	0.940	1.135	1.162	1.187
70-74	1.061	1.074	1.085	1.175	1.210	1.243
75-79	1.039	1.047	1.054	1.070	1.084	1.096

Applying the reduction in the β -coefficient slowed down the rate of increase of the estimated total obesity prevalence to ensure that the total prevalence by 2030 was 3% less than the base case model estimate. As mentioned above, the total obesity prevalence under the MexOb-Model is not only influenced by the open cohort component (β -coefficient), but it is also influenced by the other steering parameters, i.e. the disease growth ratio and the transition probabilities, and these were not modified in this scenario. The gradual reduction in obesity prevalence under scenario A in 2020 and 2025 and the final target of 3% by 2030 is shown in Table 7.2 and Table 7.3 for males and females respectively.

Table 7.2 Reduction and percentage (%) relative change from base-case model in total male obesity prevalence (20-79y) in each five-year cycle to achieve scenario A target in 2030.

MexOb-disease model	2020		2025		2030	
	Base-case model	Scenario A (% change)	Base-case model	Scenario A (% change)	Base-case model	Scenario A (% change)
MexOb-HT	30.6	30.5 (0.4%)	36.3	35.8 (1.5%)	43.6	42.2 (3.4%)
MexOb-T2DM	30.3	30.2 (0.4%)	35.9	35.3 (1.5%)	43.1	41.6 (3.4%)
MexOb-HTG	29.4	29.3 (0.4%)	33.8	33.2 (1.6%)	39.3	37.9 (3.6%)
MexOb-HCI	30.0	29.9 (0.4%)	34.9	34.4 (1.5%)	41.2	39.8 (3.5%)

Scenario A: a gradual reduction to achieve a 3% relative reduction from 2030 projected prevalence.

Table 7.3 Reduction and percentage (%) relative change from base-case model in total female obesity prevalence (20-79y) in each five-year cycle to achieve scenario A target in 2030.

MexOb-disease model	2020		2025		2030	
	Base-case model	Scenario A (% change)	Base-case model	Scenario A (% change)	Base-case model	Scenario A (% change)
MexOb-HT	42.9	42.7 (0.4%)	50.8	50.1 (1.4%)	61.3	59.3 (3.2%)
MexOb-T2DM	41.6	41.4 (0.4%)	48.0	47.3 (1.4%)	56.4	54.6 (3.2%)
MexOb-HTG	41.3	41.1 (0.4%)	47.0	46.3 (1.4%)	54.3	52.5 (3.2%)
MexOb-HCI	41.6	41.5 (0.4%)	47.8	47.2 (1.4%)	55.8	53.9(3.2%)

Scenario A: a gradual reduction to achieve a 3% relative reduction from 2030 projected prevalence.

This scenario was based on the approach used by Lo et al. (160) and Zainal et al. (136), and it was planned to be a close representation of reality in which the effect of national obesity policies or interventions are unlikely to produce a sudden step response. There has to be a gradual change over the years.

The target of scenario A was set to simulate the effect that the implementation of a sugar sweetened beverages (SSB) tax could have on the future levels of obesity prevalence and its impact on the obesity-related cardiometabolic risk conditions in the Mexican population. An exercise for the possible effect of the implementation of a 20% tax in SSBs on the Mexican population showed that it could reduce the prevalence of overweight and obesity in adults by 2% in relative terms in ten years (288). Basu et al. (120) also estimated that the implementation of a 20% tax in SSBs among the Indian population, could reduce its adult obesity prevalence by 3% in relative terms (95%CI: 1.6% to 5.9%) in a nine year period (2014-2023).

Using these two modelling studies as reference, I decided to assess the potential future impact of a 20% SSB tax on the future health of the Mexican obese population by using a 3% relative reduction from the projected 2030 obesity prevalence as estimated by the base-case model. Mexico's current SSB tax implemented is of 10%. However I decided to use the potential effect of a 20% SSB tax to estimate results that could be comparable with other modelling studies which have simulated the effect of a 20% SSB tax (120, 289). But more importantly, I chose this approach to generate evidence that supports the increase of the percentage of SSB taxation in Mexico to 20%, as was originally planned.

Scenario B: Represents the direct effect of a halt in the increase of total obesity prevalence at 2015 levels as estimated by the base-case model. The effect of this hypothetical scenario was estimated by keeping constant the open cohort

component of the MexOb-Model at 1.0 (i.e. no allowance for new cases of obesity into the model).

The WHO has set nine voluntary global non-communicable diseases (NCDs) targets for 2025 in their quest for reducing the global mortality burden from NCDs by 25% by 2025 (287). These targets are actions against the principal NCDs risk factors. One of the nine targets is a zero increase in obesity prevalence by that year. I decided to apply this approach as one of the three simulated hypothetical scenarios presented in this analysis by holding the obesity prevalence at 2015 levels to estimate the beneficial health effect that achieving the WHO target for NCDs could bring to the Mexican population. Simulating a halt in the increase of obesity prevalence has been a popular scenario assessed in population-based simulation models. Recently, Roth et al. used this approach to estimate the impact of obesity reduction on worldwide levels of cardiovascular disease mortality by 2025 (290).

Scenario C: Using the 2015 projected prevalence as a starting point, scenario C assumes a 10% relative reduction in obesity prevalence by 2030. To achieve this target, the size of the age-group and sex specific obese population with and without disease was reduced by approximately 3.33% in relative terms in each of the three five-year cycles; this resulted in a 10% relative reduction over the 15 year period by 2030. Scenario C represents the most optimistic scenario of obesity reduction from the three scenarios evaluated.

The structure of the MexOb-Model, and the chosen input values of the steering parameters used for the calculation of the final outcomes, meant that at the end of the 15 year period the total projected prevalence of obesity was slightly different in each of the four MexOb-disease models. Therefore, it was necessary to vary slightly the target value of the percentage reduction (3.33%) in each five –year cycle to ensure that the 10% relative reduction by 2030 from the initial 2015 estimated prevalence could be achieved in each model. The range of reduction used as the input for this

scenario varied across the models by between 3.5% and -1.0%. The percentage reduction values used were sex and disease model specific. Table 7.4 shows the sex-specific percentage reduction (in relative terms) used as the modified open cohort component in each MexOb-disease models. For example, a cohort component of 0.965 represents a $(1-0.965) = 0.035$ or 3.5% relative reduction in the number of new cases added to the model at the beginning of a modelling cycle.

Table 7.4 Open cohort component values to achieve a 10% relative reduction from 2015 projected obesity prevalence (Scenario C).

MexOb-disease model	Males	Females
MexOb-HT	0.970	0.965
MexOb-T2DM	0.978	0.995
MexOb-HTG	0.994	0.999
MexOb-HCI	1.030	1.010

HT: hypertension; T2DM: type 2 diabetes mellitus; HTG: hypertriglyceridaemia; HCI; hypercholesterolaemia

Achieving a 10% relative reduction in the prevalence levels of obesity is a target that has been set for the US population under the Healthy People (HP) 2020 programme (291). HP 2020 is a set of 10-year goals created by the US Department of Health to reduce the level of preventable diseases in the population (292). Until now, levels of obesity among adults in Mexico have continued to increase; therefore I decided to incorporate this target assuming that it will be achieved by 2030, 15 years after the chosen baseline year (2015) for the MexOb-Model. This scenario, scenario C, is an updated version of the approach used by Finkelstein et al. in their obesity projections exercise (147).

7.3.3 Methods to verify that that the targets of reduction in obesity levels were achieved

I verified that the target for obesity prevalence reduction was achieved in each of the four MexOb-disease models for males and females by calculating the relative decrease

in obesity prevalence for 2030 relative to the prevalence of obesity used as the comparison baseline for each of the scenarios (obesity prevalence in 2030 for scenario A; and obesity prevalence in 2015 for scenarios B and C). As in the base-case model, obesity prevalence was calculated by the ratio of the number of obese cases and the total projected population from CONAPO (63).

7.3.4 MexOb-disease Model outcomes to compare the scenarios

For each of the three scenarios, the number of avoided cases relative to the base-case model was estimated by calculating the difference between the original projected number of cases (total obese, obese-disease and deaths) in the base-case model (should the projected obesity trends from 2015 to 2030 continue at the same pace as the historic trends) and the number of cases projected at the new obesity level under each scenario. The numbers for the outcomes presented in this section were rounded to the nearest thousand.

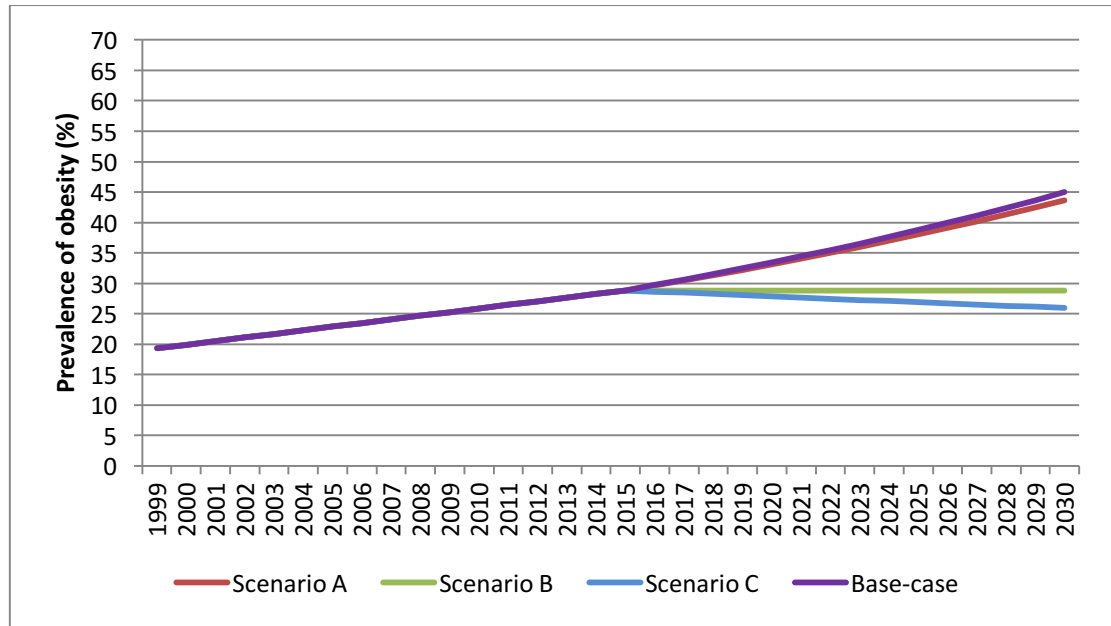
7.4 Results

7.4.1 Changes in total population obesity prevalence by 2030 for each of the MexOb-disease models under three different obesity prevalence reduction scenarios.

Table 7.5 and 7.6 show the total obese population among Mexican adults aged 20 to 79y that could be expected if the targets for obesity reduction for the three hypothetical scenarios were achieved by 2030. Results from the base-case model showed that if the historic trends in obesity prevalence continue, around 44% of males and 60% of females would be obese. Over the 15 year period from 2015 to 2030, this represents approximately a 50% relative increase in male obesity prevalence and a 48% relative increase in female obesity prevalence. Under the base-case model, this means that by 2030 there will be approximately 46 million obese adults (20-79y) in Mexico, 20 million more than was estimated for 2015. However, under the most optimistic obesity prevalence reduction scenario, a 10% relative reduction from the

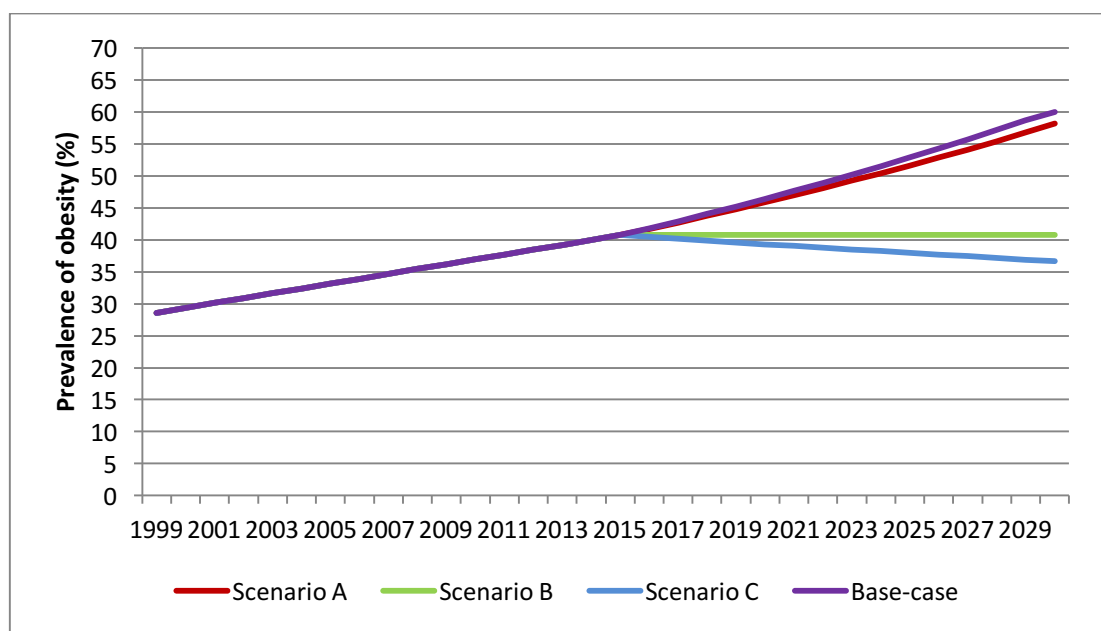
estimated obesity prevalence in 2015 (scenario C), the total expected obese population in 2030 would only reach 28 million (Figure 7-1 and Figure 7-2)

Figure 7-1 Projected obesity prevalence for males by 2030 from base-case and three different obesity reduction scenarios*



*Prevalence of obesity for base-case model was estimated from the average of the projected total obese male adult population prevalence from the base-case of the four MexOb-disease models. A similar approach was used to estimate scenario A expected obesity prevalence **Scenario A**: a gradual reduction to achieve a 3% relative reduction from 2030 projected prevalence. **Scenario B**: obesity prevalence held constant at 2015 levels. **Scenario C**: 10% relative reduction of 2015 obesity prevalence.

Figure 7-2 Projected obesity prevalence for females by 2030 from base-case and three different obesity reduction scenarios*



*Prevalence of obesity for base-case model was estimated from the average of the projected total obese female adult population prevalence from the base-case of the four MexOb-disease models. A similar approach was used to estimate scenario A expected obesity prevalence. **Scenario A:** a gradual reduction to achieve a 3% relative reduction from 2030 projected prevalence. **Scenario B:** obesity prevalence held constant at 2015 levels. **Scenario C:** 10% relative reduction of 2015 obesity prevalence.

Averted cases of obesity for males

A slowing down in the rates of increase in obesity prevalence to achieve a 3% reduction in the 2030 projected obesity prevalence (scenario A), relative to the base-case, could reduce the number of obese men in the Mexican population by an estimated 623,000-644,000. In order to achieve this goal, Mexico would need to reduce the average annual increase in total obesity prevalence from the base-case scenario by 0.1% during the 15 year period (Table 7.5).

A scenario that maintained obesity prevalence at 2015 levels (scenario B), estimated that by 2030 the number of obese cases avoided compared with the base-case scenario would be between 4.8 million and 5.7 million. The most optimistic scenario, a 10% relative reduction (scenario C) from estimated 2015 obesity prevalence, would

lead to between 5.7 million to 7.6 million fewer obese men by 2030 than the base-case model. Achieving this target would mean a relative reduction of 40% from the projected total obesity prevalence in the base-case model (43% in 2030 from the base-case model to 26% in 2030 from scenario C). This panorama represents the most ambitious target to be achieved (Table 7.5).

Averted cases of obesity for females

Compared with the base-case model, a deceleration in the rate of increase in obesity prevalence to achieve a 3% reduction from 2030 projected prevalence (scenario A) would lead to around 9 thousand fewer obese women by 2030. Holding the total obesity prevalence at 2015 levels would result in an average of 8.5 million fewer obese women (aged 20 to 79y) for 2030 than originally projected with the base-case model. A 10% relative reduction in the 2015 projected prevalence (scenario C) would lead to the highest reduction in the number of obese women from the three hypothetical scenarios. Compared with the base-case model, the number of avoided cases of obese women could reach nearly 12 million if the obesity reduction target for scenario C was achieved. Achieving this target for obesity reduction would mean on average an approximately 40% relative reduction in obesity prevalence by 2030 compared with the base-case model (average of approximately 57% in the base-case model, 36% in scenario C) (Table 7.6)

Table 7.5 Total reduction in projected male obese population by 2030 under three different obesity prevalence reduction scenarios*.

MexOb-disease model	Base-case model		Scenario A		Scenario B		Scenario C	
	Total estimated obese population	Projected obesity prevalence (%)	Projected obesity prevalence (%)	Averted cases of obesity	Projected obesity prevalence (%)	Averted cases of obesity	Projected obesity prevalence (%)	Averted cases of obesity
Total projected obese population for 2015[†]	10,338,000	29.1						
Total projected obese population for 2030:								
MexOb-HT	18,934,000	43.6	42.2	644,000	30.4	5,743,000	26.1	7,609,000
MexOb-T2DM	18,684,000	43.1	41.6	641,000	29.8	5,777,000	26.1	7,349,000
MexOb-HTG	17,050,000	39.3	37.9	614,000	28.1	4,851,000	26.1	5,723,000
MexOb-HCI	17,889,000	41.2	39.8	623,000	28.1	5,690,000	26.2	6,539,000

Scenario A: a gradual reduction to achieve a 3% relative reduction from 2030 projected prevalence. **Scenario B:** obesity prevalence held constant at 2015 levels. **Scenario C:** 10% relative reduction of 2015 obesity prevalence.

HT: hypertension; T2DM: type 2 diabetes mellitus; HTG: hypertriglyceridaemia; HCI; hypercholesterolaemia

*Number of obese cases rounded to their nearest thousand.

† 2015 obesity prevalence was estimated using the linear trend analysis (see: Chapter 3)

Table 7.6 Total reduction in projected female obese population by 2030 under three different obesity prevalence reduction scenarios*

MexOb-disease model	Base-case model		Scenario A		Scenario B		Scenario C	
	Total estimated obese population	Projected obesity prevalence (%)	Projected obesity prevalence (%)	Averted cases of obesity	Projected obesity prevalence (%)	Averted cases of obesity	Projected obesity prevalence (%)	Averted cases of obesity
Total projected obese population for 2015[†]	15,512,000	39.7						
Total projected obese population for 2030:								
MexOb-HT	29,382,000	61.3	59.3	938,000	39.6	10,405,000	35.5	12,338,000
MexOb-T2DM	27,058,000	56.4	54.6	861,000	38.6	8,562,000	35.7	9,933,000
MexOb-HTG	26,050,000	54.3	52.5	861,000	38.5	7,564,000	35.7	8,924,000
MexOb-HCI	26,740,000	55.8	53.9	868,000	38.1	8,479,000	35.7	9,599,000

Scenario A: a gradual reduction to achieve a 3% relative reduction from 2030 projected prevalence. **Scenario B:** obesity prevalence held constant at 2015 levels. **Scenario C:** 10% relative reduction of 2015 obesity prevalence.

HT: hypertension; T2DM: type 2 diabetes mellitus; HTG: hypertriglyceridaemia; HCI: hypercholesterolaemia

*Number of obese cases rounded to their nearest thousand.

† 2015 obesity prevalence was estimated using the linear trend analysis (see: Chapter 3)

7.4.2 Total number of obese-disease cases avoided by 2030 from base-case model based on three difference obesity prevalence reduction scenarios.

Under the base-case model, if the historic trends in obesity continue, the number of obese with disease cases could double for HT, HTG and HCL or even more than triple for T2DM by 2030.

Under the base-case model, the biggest increase (in absolute terms) in the number of obese persons with disease by 2030 is projected for the number of obese males and obese females aged 20 to 79y with hypertension, followed by the increase in number of obese persons with hypercholesterolaemia (Table 7.7).

Table 7.7 Total number of projected obese with disease population in 2015 and 2030. Results from the base-case model. (Thousands)*

Cardio-metabolic risk factors	Obese males		Obese females	
	2015	2030	2015	2030
Hypertension	4,727	10,611	6,449	16,729
Type 2 diabetes mellitus	2,171	6,565	2,782	8,424
Hypertriglyceridaemia	5,108	8,845	6,013	12,143
Hypercholesterolaemia	5,430	10,207	8,398	15,581

*Numbers of obese individuals presented in thousands.

Figure 7-3 and Figure 7-4 present the decrease in the expected number of obese persons with disease for 2030 under the three hypothetical scenarios compared to the base-case model. The results showed that even a modest relative reduction of 3% in the projected obesity prevalence for 2030 (scenario A), compared to the base-case model, is estimated to reduce the expected number of obese individuals with a cardiometabolic risk factor considerably.

Avoided cases of obese-disease for males

Compared with the base-case model, a deceleration in the rates of increase in obesity prevalence to achieve a 3% reduction from the projected obesity prevalence of 2030 (scenario A) could lower the number of new cases of cardiometabolic risk factors in the

obese male population by between 34 and 8% in relative terms. In absolute terms this means that between 160,000 and 317,000 cases of cardiometabolic risk factors in the obese population could be avoided. Achieving the obesity prevalence reduction target for scenario A (3% relative reduction of the expected obesity prevalence in 2030) would be expected to have the largest impact in reducing the number of obese persons with hypercholesterolaemia (reflecting its highest prevalence among the obese population) (Figure 7-3).

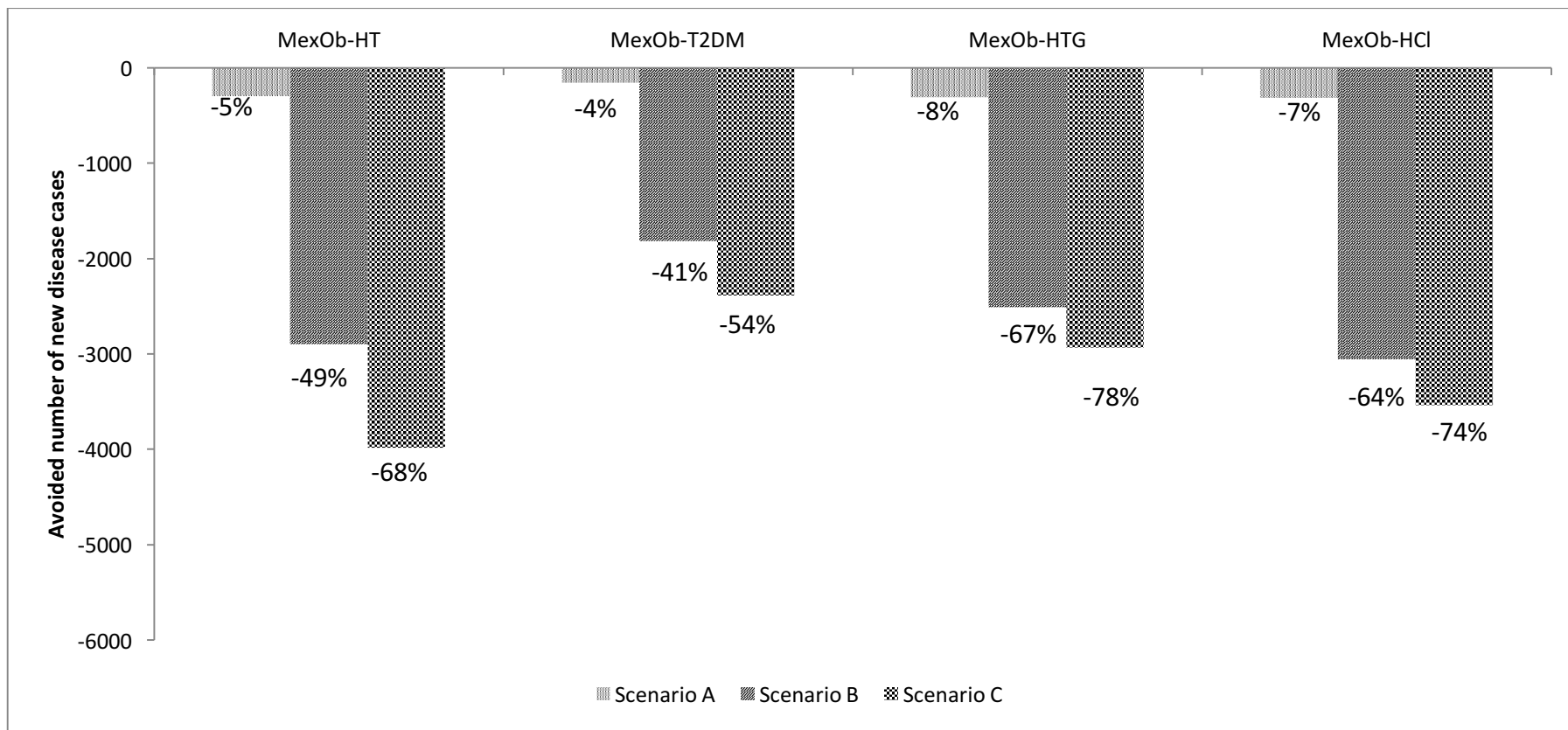
A halt in the prevalence of obesity at 2015 levels (scenario B) could potentially reduce the expected number of cases of cardiometabolic risk factors among the obese population for 2030 between 40% and 67% in relative terms, compared with the base-case model estimates. The largest impact of this reduction scenario was observed for hypertension, with a decrease in the number of expected cases of around 29 million by 2030. However, if a 10% relative reduction from 2015 projected obesity prevalence was achieved (scenario C), the number of obese persons with disease by 2030 could be reduced by almost 80% in relative terms for some diseases compared with the levels estimated under the base-case model.

Avoided cases of obese-disease for females

Compared with the base-case model, assuming a deceleration in the rates of obesity prevalence increase to achieve a 3% relative reduction (scenario A) in female projected obesity prevalence by 2030 would reduce the number of expected new cases of cardiometabolic risk factors among the obese population between 230,000 and 480,000. This represents a relative decrease from the projected base-case model of between 4% and 7%. The biggest impact in the reduction of expected cases was observed in the number of obese individuals with hypertension (Figure 7-4).

Holding the prevalence of obesity at 2015 levels (scenario B) could potentially reduce the number of expected cases of cardiometabolic risk factors among the obese population by 2030 between three and six million from the number expected under the base-case model. The largest impact of this reduction on the expected number of obese persons with disease was observed for hypertension as was shown above for scenario A. However if the target level for obesity reduction for the most optimistic scenario was achieved (scenario C), there would be on average a 70% relative reduction in the number of obese-disease cases compared with the base-case model estimates for three of the four cardiometabolic risk factors, with the exception of type 2 diabetes which would have a relative reduction of nearly 55% in the number of obese-disease cases by 2030 (Figure 7-4).

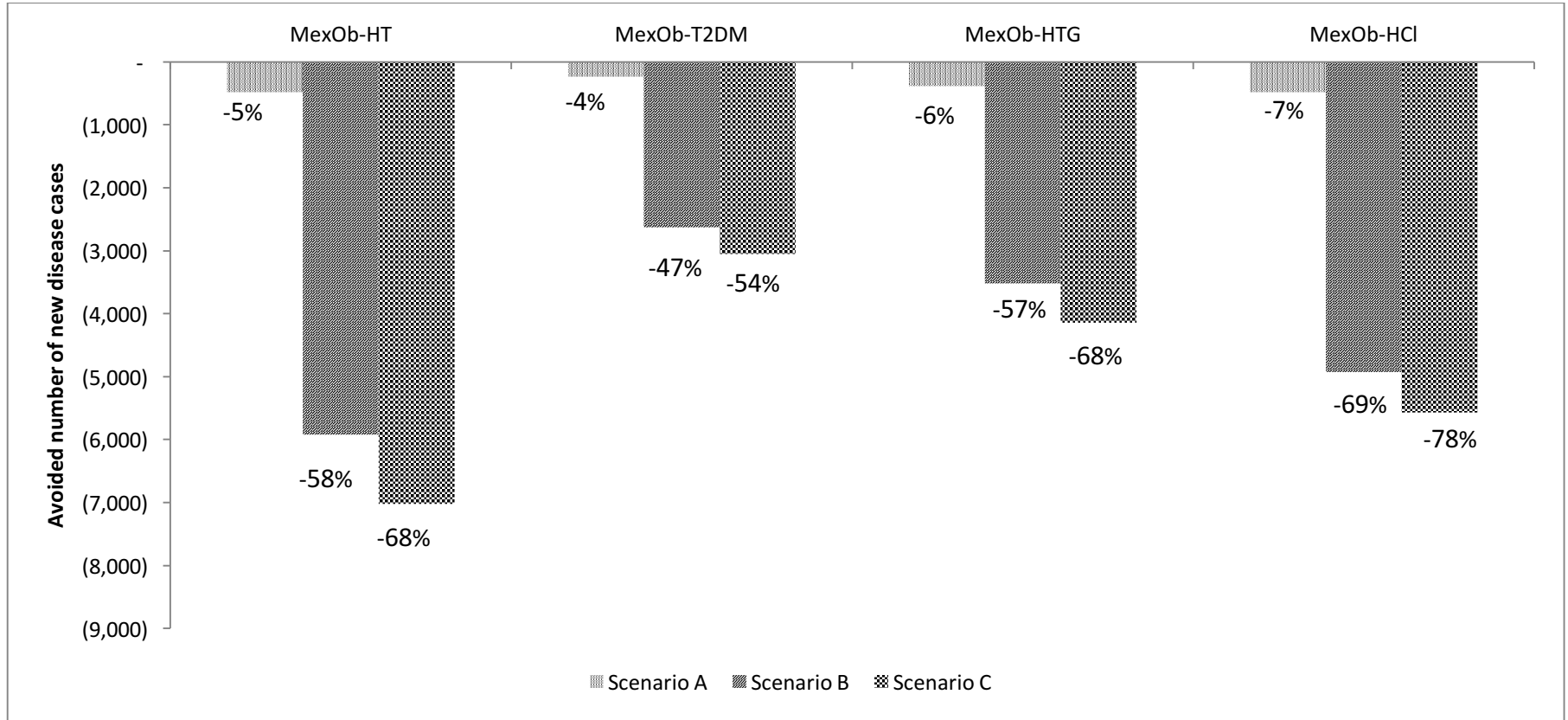
Figure 7-3 Estimated percentage reduction from base-case model in the cumulative number of new disease cases for obese males from 2015 to 2030 by MexOb-disease model, under three different obesity prevalence reduction scenarios. (Thousands).



Scenario A: a gradual reduction to achieve a 3% relative reduction from 2030 projected prevalence. **Scenario B:** obesity prevalence held constant at 2015 levels. **Scenario C:** 10% relative reduction of 2015 obesity prevalence

HT: hypertension; T2DM: type 2 diabetes mellitus; HTG: hypertriglyceridaemia; HCl; hypercholesterolaemia

Figure 7-4 Estimated percentage reduction from base-case model in the cumulative number of new disease cases for obese females from 2015 to 2030 by MexOb-disease model, under three different obesity prevalence reduction scenarios (Thousands).



Scenario A: a gradual reduction to achieve a 3% relative reduction from 2030 projected prevalence. **Scenario B:** obesity prevalence held constant at 2015 levels. **Scenario C:** 10% relative reduction of 2015 obesity prevalence

HT: hypertension; T2DM: type 2 diabetes mellitus; HTG: hypertriglyceridaemia; HCl; hypercholesterolaemia

7.4.3 Total number of deaths avoided by 2030 from base-case model based on three difference obesity prevalence reduction scenarios.

Table 7.8 shows the decrease in the expected cumulative number of deaths among obese males and females by 2030 based on the three different obesity prevalence reduction scenarios compared to the base-case model. Achieving the most conservative scenario (scenario A), a slowing down in the rates of increase to achieve a 3% relative reduction in obesity prevalence from the 2030 levels under the base-case model, would avoid around 16,000 deaths from the total obese male population and around 34,000 deaths from the total obese female population from 2015 to 2030 (obese persons with and obese persons without disease). The total number of deaths avoided would augment to around 150,000 and 200,000 in obese men, and between 400,000 and 550,000 in obese women if the obesity levels by 2030 remain at 2015 levels (scenario B). If Mexico achieved a 10% relative reduction of 2015 projected levels by 2030 (scenario C), it would be possible to reduce the number of deaths by up to 110,000 in obese males and up to 115,000 in obese females.

Obese-disease cumulative deaths avoided in males

Compared to the base-case model, a deceleration in the rate of obesity prevalence increase to achieve a 3% relative reduction in 2030 projected obesity prevalence (scenario A), could reduce the cumulative number of deaths among the obese population with disease by between 3,000 and 10,000 deaths; with a similar reduction in the number of deaths shown in the results from three of the four MexOb-disease models, except for diabetes. Achieving the obesity prevalence reduction target for scenario B (a zero increase in 2015 prevalence) would reduce up to 136,000 deaths in the obese with disease population from the base-case model. If the most aggressive reduction of obesity prevalence is achieved by 2030 (a 10% relative reduction of the 2015 prevalence levels: scenario C), around 64,000 to 228,000 fewer deaths among obese persons with disease could be achieved compared to the base-case model by 2030. Under this scenario (scenario C), the biggest reduction in the number of deaths would be for obese persons with hypertension.

Obese-disease cumulative deaths avoided in females

Compared with the base-case model, between 30,000 and 36,000 deaths in the obese with disease population could be avoided if a 3% relative reduction in the projected obesity prevalence for 2030 is achieved by gradual reduction in the rate of increase (scenario A). A more aggressive obesity prevalence reduction target, a zero increase from 2015 obesity levels (scenario B), would lead to between 420,000 and 550,000 fewer deaths compared with the base-case model. A larger reduction in obesity prevalence, a 10% relative reduction in the 2015 prevalence levels(scenario C), could achieve up to 111,000 fewer obese-with-disease deaths than the number of deaths estimated from the base-case model. The biggest impact on the number of deaths avoided from this scenario (scenario C) was estimated for obese females with hypertension, followed by the reduction in the number of deaths for obese females with hypertension.

Table 7.8 Reduction in projected cumulative number of deaths in obese population 20 to 79y from 2015 to 2030 under three different obesity reduction prevalence scenarios for each MexOb-disease models.

MexOb-disease models	Obese males		Obese females	
	Obese-with-disease deaths	Total deaths	Obese-with-disease deaths	Total deaths
MexOb-HT model				
Base-case total number of cumulative deaths 2015-2030	1,128,000	1,613,000	1,499,000	2,063,000
Scenarios absolute number of deaths avoided (% relative change from base-case)*				
Scenario A	-10,000 (1%)	-16,000 (1%)	-27,000 (2%)	-36,000 (2%)
Scenario B	-123,000(11%)	-203,000(13%)	-408,000(27%)	-551,000(27%)
Scenario C	-228,000(20%)	-348,000(22%)	-489,000(33%)	-662,000(32%)
MexOb-T2DM model				
Base-case total number of cumulative deaths 2015-2030	3,331,000	1,597,000	414,000	1,861,000
Scenario A	-3,000 (1%)	-17,000 (1%)	-7,000 (2%)	-30,000 (2%)
Scenario B	-38,000(11%)	-205,000(13%)	-100,000(24%)	-421,000(24%)
Scenario C	-64,000(19%)	-324,000(20%)	-117,000(28%)	-495,000(27%)
MexOb-HTG model				
Base-case total number of cumulative deaths 2015-2030	790,000	1,449,000	919,000	2,071,000
Scenario A	-9,000 (1%)	-16,000 (1%)	-16,000 (2%)	-34,000 (2%)
Scenario B	-83,000(11%)	-153,000(11%)	-194,000(21%)	-419,000(20%)
Scenario C	-113,000(14%)	-207,000(14%)	-231,000(25%)	-502,000(24%)
MexOb-HCI				
Base-case total number of cumulative deaths 2015-2030	1,042,000	1,445,000	1,449,000	1,997,000
Scenario A	-10,000 (1%)	-15,000 (1%)	-25,000 (2%)	-34,000 (2%)
Scenario B	-136,000(13%)	-208,000(14%)	-337,000(23%)	-459,000(23%)
Scenario C	-177,000(17%)	-263,000(18%)	-383,000(26%)	-523,000 (26%)

Scenario A: a gradual reduction to achieve a 3% relative reduction from 2030 projected prevalence. **Scenario B:** obesity prevalence held constant at 2015 levels. **Scenario C:** 10% relative reduction of 2015 obesity prevalence
HT: hypertension; T2DM: type 2 diabetes mellitus; HTG: hypertriglyceridaemia; HCl; hypercholesterolaemia
*Number of deaths from the different scenarios rounded to their nearest thousand.

7.5 Discussion

7.5.1 Main findings

In this analysis, I examined the impact of three possible obesity reduction prevalence scenarios: a slowing down in the rates of increase of obesity prevalence to achieve a 3% relative reduction of 2030 obesity projected levels, maintaining obesity prevalence at 2015 levels, and a 10% relative reduction of 2015 levels over a 15 year period. Achieving the obesity prevalence reduction targets in any of these hypothetical scenarios would have important health benefits for the obese population. The MexOb-Model results showed that reducing the number of obesity cases could have larger gains in health benefits for obese females than for obese males by reducing in absolute terms a larger number of disease cases and reducing a larger number of deaths compared with the base-case estimates.

From all the four MexOb-disease models, it was the MexOb-HT model for males and for females that showed the greatest potential gains through reductions in obesity prevalence. A reduction in obesity levels could avoid between 300,000 and four million cases of hypertension for obese men and between 500,000 and seven million cases of hypertension for obese women; and reduce up to 350,000 deaths depending on the target achieved compared to the base-case model.

Of the three scenarios of obesity prevalence reduction evaluated, achieving a 10% relative reduction from 2015 projected obesity levels would be expected to lead to the highest reduction in the number of cases (obese, obese-disease and deaths) with reduction between 55% and 80% in the number of potential expected disease cases by 2030. However, holding obesity prevalence constant at 2015 levels would have a similar impact. The MexOb-Model results suggest that a reduction in obesity prevalence could bring important health benefits in the four obesity-associated cardiometabolic risk factors: HT, T2DM, HTG and HCl. Achieving reductions in obesity prevalence would also help to decrease the burden of disease in Mexico by decreasing

one of the principal risk factors that contribute to the number of years of life lost and the number of years lost due to disability (80). Additionally, the benefit of a reduction in these four obesity-related risk factors would also contribute to reductions in the potential number of new cases of other chronic diseases like cardiovascular disease and chronic kidney disease, two of the principal causes of morbidity and mortality in the Mexican population (35, 46, 80).

To my knowledge there are very few studies that have reported the future health impact on the levels of obesity-related cardiometabolic risk factors of a reduction of obesity prevalence in Mexico (115, 265, 266). None of these studies have focused specifically on the effects on the obese population, nor assessed similar hypothetical scenarios of obesity prevalence reduction, as shown here by the MexOb-Model. However, the three scenarios assessed in this exercise have been used to estimate the size of potential future health gains in other populations. The most common of the three assessed scenarios found in the literature was the potential effect of a SSB tax. The SSB taxation is an intervention that has gained momentum during recent years, and has been already implemented in cities like Berkeley, California and Philadelphia, Pennsylvania in the US and countries like Chile and Belgium (293). In the MexOb-Model, the potential long-term health benefits of this intervention was assessed by estimating the effect of a deceleration in the rate of increase of obesity prevalence to achieve a 3% relative reduction in the 2030 projected prevalence (from the MexOb base-case model) over the 15 year period from 2015 to 2030 (scenario A); the choice of a 3% relative reduction in 2030 levels was based on the projected reduction in obesity prevalence from a decrease in SSB consumption by a SSB taxation initiative estimated by other simulation exercises (120, 288). Using this assumption, adjusting the MexOb-Model to lower obesity prevalence in 2030 by 3% in relative terms produced results that showed that a 20% SSB tax in Mexico if maintained, could result in around 630,000 fewer cases of obesity for males and around 900,000 fewer cases of obesity for females in 15 years' time compared to those projected in the base-case model.

Other population projection simulation studies have also shown similar benefits in the number of avoided cases. Implementation of a US\$ 0.03/ounce tax in the city of Philadelphia, Pennsylvania could lead to the prevention of around 36,000 cases of obesity over a ten year period (294). The implementation of a \$0.01/ounce tax in New York State, USA could potentially save 145,000 obesity cases over a nine year period (295). Moreover, it has been estimated that this intervention could start to be effective almost immediately. Briggs et al. projected that the implementation of a 10% SSB tax in Ireland could reduce the number of obese cases by 9,900 in a one year period (296). A 20% SSB tax implementation in the UK could reduce the number of obesity cases in adults by 180,000 from current levels (297), and the same percentage tax could avert 220,000 cases of obesity in South Africa from current levels (298).

The positive health effects of the SSB intervention is not confined to reductions in the number of obese cases: it would also help to reduce the incidence of obesity-related cardiometabolic risk factors. Under scenario A (a 3% relative reduction in the 2030 projected prevalence of obesity from the base-case model), the relative reduction in the number of new obese-disease cases could range from 4% to 8% for males and females. Similar scenario projections in other population modelling studies showed that the implementation of a 10% or a 20% SSB tax could reduce the number of projected diabetes incident cases by between 1.8% and 3.4% in California's adult population over a 9 year period (289), and a 20% SSB tax could reduce the number of projected diabetes incidence cases by around 1.6% in the Indian adult population during a similar time period (120). My results from the MexOb-T2DM model showed that under scenario A, the number of new diabetes cases in the obese population could be reduced in relative terms by around 3% for males and 4% for females over the 15 year period.

The cardiometabolic risk factor from the four MexOb-disease models that would have the biggest reduction in the number of cases, regardless of the scenario of obesity prevalence reduction, was hypertension (reductions of 300,000 to four million for

obese males, and reductions of 500,000 to 7 million for obese females). Given the strong associations between high blood pressure and the global burden of disease (49), this reduction would be expected to translate into important reductions in cardiovascular mortality. Similarly, Roth et al reported that a reduction in hypertension prevalence showed the largest impact on premature mortality from cardiovascular diseases for almost all the regions across the world (290).

As in other countries, the increase in obesity levels over recent decades has had an important effect for the population of Mexico. Soto-Molina et al. projected that the total direct cumulative healthcare costs for Mexican obese patients with hypertension could increase by 13 times (up to €4,925 per person) and could increase by 14 times for obese patients with diabetes (up to €1,830, per person) from the cost of the first year of treatment during a 20 year period; with the biggest increase in health care costs seen during the first five years after diagnosis of the disease (299). There are also other wider economic costs. In 2006, it was estimated that around 26% of the total health expenditure associated with obesity-related disease in Mexico for that year came from out of pocket expenses (95). The economic impact of obesity also comes from the loss of productivity that has been observed in obese-disease individuals. In Mexico, it was estimated that an overweight or obese individual with diabetes lost on average 3% of productivity during one year, and this was estimated to increase up to 5% if the person presented disease-related complications (41). Obesity by itself may not seem that expensive, but it is the cost that comes from its associated diseases that increases the overall economic burden that is associated with obesity. In 2012, health care expenditures from chronic kidney disease, chronic ischaemic heart disease and type 2 diabetes accounted for around 85% of the total financial burden (between US\$1.4 and US\$4 billion) from chronic disease treatment in the Mexican Healthcare Institutions (96). Reducing the number of obese cases could therefore have important economic benefits. Rtveldadze et al. estimated that reductions of 1% or 5% in the 2010 BMI levels among the Mexican population could save approximately US\$43 million or US\$117 million, depending on the BMI percentage reduction, in obesity healthcare costs over a twenty year period (115).

From the three scenarios examined in this chapter, the potential future health effects observed under scenario A (the most modest scenario: slowing down in the rates of increase of obesity prevalence to achieve a 3% relative reduction of the 2030 obesity levels observed under the base-case model), are the ones that have the highest probability to become a reality. First, because this scenario is assumed in this study to represent or approximate the future effect of an intervention that has already been implemented in Mexico (a SSB tax), and that has proven to be effective in reducing taxed SSBs purchase (300). Second, this scenario tried to recreate the real effect of the implementation of an intervention. In real life, it is expected that this intervention could gradually reduce the prevalence of obesity until it reached the set goal of a 3% relative reduction in the 2030 projected obesity levels. Additionally, considering this approach, using base-case model estimates to set reduction targets has been recommend as it gives an overview of what percentage of reduction is needed to achieve the set target, and if that is reduction is feasible (160). Finally, achieving a 3% relative reduction in the projected prevalence in 15 years' time is a goal that refers to the potential effect of a 20% SSB tax. In Mexico the current intervention is a 10% SSB tax and it has been reported that a 10% tax in SSBs could potentially halve (relative change) the estimated projected reduction in obesity prevalence achievable by a 20% SSB tax (120). Fortunately, a 3% reduction target can potentially be achieved by a combination of the current 10% SSB tax and the other obesity preventive interventions or health programmes already implemented in Mexico.

Even though the health benefits estimated from a 3% relative reduction of 2030 projected obesity levels are small in comparison with those achievable from meeting more ambitious or aggressive targets, this could still bring significant benefits, but maybe not enough to reduce or even reverse the size of the health burden associated with obesity, particularly in the context of population ageing. To have an important impact on the health of the population, a more aggressive approach has to be implemented, like scenario B (a halt in the increase of obesity levels from 2015) or

scenario C (a 10% relative reduction in 2015 levels). Either of these could be achieved by a combination of strategies that emphasize the influence of environmental and individuals responsibility (156, 301, 302).

Obesity reduction targets have been set worldwide in order to help to reduce the burden of obesity on morbidity and mortality of non-communicable disease (287). Unfortunately, an evaluation of the worldwide obesity trends showed that there has not been an important decline in the rates of obesity (272). As a consequence, it seems highly improbable that the target set by WHO of halting the increase in obesity prevalence by 2025 could be achieved in most countries. Furthermore, Roth et al. reported that in many countries, including Mexico, the current increasing trends of the cardiometabolic risk factors means that there will not be the expected decrease in the rates of premature CVD by 2025 (290).

In Mexico, achieving the target of a zero increase of 2015 obesity prevalence during a 15 year period would mean that there had to be approximately a 40% relative reduction from the 2030 estimated obesity prevalence for males and females under the base–case model (see: Chapter 6). But even though the obesity prevalence in adults keeps increasing, results from the past trends have shown that the increase in obesity prevalence for younger age groups (children and adolescents) has started to slow down recently (see: Chapter 3) and it could be possible that the future levels of obesity among the adult population may not reach the projected values estimated under the base-case model (42% for males and 60% for females aged 20 to 79y). However it seems that Mexico still has a long way to go before a meaningful reduction in obesity prevalence can be achieved.

The aforementioned cast doubt on the potential of Mexico to achieve this particular target of a halt in obesity prevalence or achieve the higher more ambitious goal of a 10% reduction of 2015 obesity prevalence levels by 2030. The WHO recommended in

the “Global Status Report on non-communicable disease 2014” that each country has to set its own national target of reduction, and to measure their progress towards the set goal of a 25% reduction in CVD mortality rates by 2025 (287). Results from the MexOb-Model showed that these targets may be very hard to reach without important changes in the current trends in obesity prevalence. In Mexico, policy makers, the public health community and the wider population are aware of the importance of this problem and the relevance of reducing the prevalence of obesity. A number of national strategies have already been implemented to prevent or reduce obesity and to reduce the levels of obesity-related diseases. These include the following:

Mexican beverage guidelines for healthy hydration. This is a graphic recommendation, like the food pyramid, of the different type of beverages and the amount recommended for consumption; it was published in 2008 (303).

National Agreement for Healthy Nutrition (ANSA): This consists of a list of ten objectives which aim to help reduce Mexico’s obesity problem. This agreement was published in 2010. Besides the list of objectives, it also includes recommendations on the strategies to be implemented and the responsibilities of each of the different sectors: government, industry, civil societies and individual in order to achieve the planned objectives (304).

Under the umbrella of the ANSA, the Mexican government has developed and implemented four strategies for obesity prevention:

- *School guidelines for food and beverages.* Guidelines that help to promote the consumption of healthy foods inside schools and reduce the intake of high calorie, low-nutrient dense foods. It was implemented in 2011.
- *Front-of package labelling system.* In 2014 the government released new mandatory guidelines for front of pack labelling based on the Guideline Daily Amount (GDA) system. The products should contain information on sugar, sodium, fats and caloric content per portion (305). This information may be complemented by a voluntary “seal of recommendation” that will be awarded to the top 20% foods with the best nutritional profile in each food group.

- *Regulations of marketing of foods and beverages to children:* In 2014, the Ministry of Health issued an order of mandatory regulation of advertising of foods and sweetened beverages, defined according to a nutrient profiling model. The restrictions apply to TV programmes with over 35% of the audience being under age 13 (306).
- *Sugar Sweetened Beverage (SSB) and nonessential foods tax initiative.* In 2014 the Mexican government passed a tax initiative that combined: A) \$1 Mexican peso per litre (10% tax). The SSBs taxed were: sodas, energy drinks, bottled coffees and teas, and fruit drinks (307). B) An 8% tax on nonessential food with energy density of ≥ 275 kcal/g (308).

These interventions have only recently been implemented, and the majority have yet to be evaluated, except SSB and nonessential foods taxation (300, 308). At this moment it is not possible to assess if they have been effective in reducing the number of obese persons in the population. This will only be possible after the monitoring of BMI levels in the population using the next National Health and Nutrition Survey in 2018. Furthermore, Mexico has not set a clear specific target on the reduction of obesity prevalence, or set other recommendations for other health indicators (physical activity, sodium consumption, fruit and vegetables consumption) (287). It is of great importance that the Mexican government, besides using as guidelines the WHO voluntary targets, sets a clear and achievable national target of obesity prevalence reduction according to the country's context, ideally starting with targets that focus on slowing down the increase in projected trends, like the scenario A presented in this chapter. Implementing a well-set goal will play a relevant role in assessing and monitoring the performance of these programmes, it will provide accountability, and as a consequence would be expected to improve these health outcomes. The evidence generated from a detailed evaluation of these initiatives could help to give continuity to the public health programmes aimed at reducing obesity and non-communicable diseases.

7.5.2 Strengths and Limitations

The MexOb-Model is one of the few simulation models that estimate the future effects of future trends in obesity on levels of the four main obesity-related cardiometabolic risk factors in the Mexican population. To my knowledge, this is the first population simulation model for Mexico that also estimates the future prevalence of dyslipidaemias within the obese population. This is of great relevance because it was reported from ENSANUT 2006 that the prevalence of hypertriglyceridaemia and hypercholesterolaemia in the total Mexican adult population is >40%. Additionally it has been observed from ENSANTU 2006 published reports that hypercholesterolaemia had the highest prevalence in the Mexican adult population of all the four obesity-related cardiometabolic risk factors (86).

The evidence provided by these analyses show an overview of the increase of the health burden from obesity and obesity-related diseases that could occur if the historic trends continue, and also show the estimated benefits of achieving different targets for obesity prevalence reduction. Estimates of the potential future increase in levels of hypertension, type 2 diabetes, hypertriglyceridaemia and hypercholesterolaemia in the obese population could help the Mexican government to set clear goals for obesity prevalence reduction, and also help with obesity and obesity-related preventive programme planning and resource allocation. This could also be useful particularly at the primary level of attention where more cases are detected and which could be controlled, leading to reductions in the health burden from obesity and from its associated diseases as well as reductions in the economic costs at both the individual and population level.

Nevertheless, estimating the future health effects of hypothetical scenarios of potential obesity prevalence reduction has some limitations. Each MexOb-disease model was run separately; therefore this analysis does not consider the co-morbidity that exists between the diseases, and how this co-morbidity can affect the risk of morbidity or mortality. The results give an overview of future projections of the

population levels of the different cardiometabolic risk factors on their own, but in reality they are usually presented in the same person. Moreover, the MexOb-Model estimates are calculated specifically only for the obese population. The results presented here therefore represent only a portion of the potential benefits. In reality, the implementation of obesity intervention policies in the population, such as the SSB tax, not only target members of the adult population who are currently obese, they also affect the total adult population (normal weight and overweight) as well as children and adolescents, so that the potential health benefits of obesity reduction policies could be much bigger.

Evidence from the US in the study by Saydha et al.(284) suggests that levels of treatment for hypertension and for dyslipidaemia have been greater amongst the obese population, suggesting that obese individuals are more likely to be screened and tested for the risks associated with cardiovascular disease. It could be reasonable to expect therefore that the proportion of obese persons with adverse levels of cardiometabolic risk factors (with the exception of diabetes) may decrease over time (although the proportion of obese persons on treatment may show an increase over time). However limitations of data availability mean that we cannot quantify this with any certainty at this stage in Mexico.

The high percentage of undiagnosed diseases in the Mexican Population suggest that despite the Ministry of Health increasing the scope of disease prevention programmes, there is still a long way to go before seeing important changes in obesity-related diseases prevention and treatment.

The user has to be aware that the results estimated for scenario A present an overestimation of the effect of the current Mexican SSB tax initiative. Scenario A, a slowing down in the rates of increase in obesity prevalence to achieve a 3% relative reduction of 2030 projected obesity levels, was designed to reflect the sustained effect

of a 20% SSB tax which was estimated to reduce the prevalence of obesity in relative terms by 2% over a ten year period, and I assumed it would increase to 3% after 15 years. However, in reality, it is possible that a 3% relative reduction in the projected obesity levels by 2030 could not only be achieved by a SSB tax. Price elasticity exercises for Mexico estimated that a 10% increase in price of SSB could reduce the consumption by 10% (309). However, the reported evaluation study showed that after one year, implementation of the 10% SSB tax reduced SSB purchases by 6%, which could represent that the expected target of reduction of taxed SSBs consumption has not yet been achieved (300, 309). Additionally, it remains possible that the effect of the SSB tax may not be sustained during the long-term, and that the effect of the SSB tax over a 15 period on obesity prevalence could be less than those projected by the MexOb-Model. This evidence supports the argument that it is necessary to combine different interventions and programmes in order to achieve even a small reduction in obesity prevalence.

The MexOb-Model continues forward the historic trends in obesity growth (calculated from five nationally representative health examination surveys) and the scenarios examined in this chapter assumed that the targeted percentage reduction in obesity prevalence would be maintained over the 15 year period to 2030. In reality, the pace of change represented by the historic trends will be altered by those factors that influence the future levels of obesity among children and adolescents in the Mexican population, and other possible environmental changes like: increase of taxation, effectiveness of other preventive interventions, new drugs, and new technology.

Moreover, comparing my results with other population-based modelling studies is difficult as the studies have been performed on diverse populations. As mentioned above, the MexOb-Model only estimates the health effects on the obese population. In general, many population projection models focus on general populations. Also, estimates from the MexOb-Model are calculated for a 15 year period (2015 to 2030) and some of the studies used here for comparison used a ten year period.

7.6 Conclusions

Obesity is a multifactorial disease that requires the implementation of effective actions from multiple sectors. A small reduction in projected obesity prevalence is estimated to have important benefits for the population's health. However, to achieve the impact needed to reduce its associated health and economic burden requires large reductions in the projected prevalence. The results presented in this chapter using the MexOb-disease population simulation model, along with those of other simulation models specific for the Mexican population, provide important evidence for policymakers to set realistic targets for the reduction of obesity prevalence as well as for monitoring health indicators. The MexOb-Model as a tool in itself is also useful for the planning and the evaluation of preventive and control interventions or programmes that are aimed at obesity reduction.

Chapter 8. Discussion

8.1 Introduction

Obesity is one of the principal public health problems in Mexico. In 2012, the latest Mexican National Health and Nutrition Survey reported that approximately 9.7% of children aged <5y and 34.4% (5.6 million) of children five to 11 years were classified as overweight or obese using the WHO cut-off points. 6.3 million (35%) adolescents (12 to 19 years old) were classified as overweight or obese. This represented in 2012 that one of every five adolescents was overweight and one of every ten adolescents was classed as obese. Of the total adult population (≥ 20 years), 25 million (38.8%) were classified as overweight (BMI 25 to $< 30 \text{ kg/m}^2$), and approximately 22 million (32.4%) adults were classified as obese (BMI $\geq 30 \text{ kg/m}^2$ (35, 276)). However, despite the country's efforts to reduce it, obesity prevalence keeps growing. For example, the prevalence of obesity in women aged 20-49y increased from 26% in 1999 to 34.2% in 2006 and to 35.2% in 2012. For men aged ≥ 20 y, the prevalence of obesity increase from 19.4% in 2000 to 24.2% in 2006 and 26.8% in 2012 (35).

The main aim of this thesis was to project the future prevalence of obesity in the Mexican population and estimate the health impacts of these future levels of obesity on four obesity-related cardiometabolic risk factors. To estimate those outcomes, I developed the Mexican Obesity Forecast Model (MexOb-Model), a population-based computer simulation model created to quantify the future trends of obesity and estimate its health consequences on hypertension, type 2 diabetes mellitus, hypertriglyceridaemia and hypercholesterolaemia in the Mexican adult obese population (20-79y) from 2015 to 2030.

An extensive discussion and interpretation of the methods used in the development of the MexOb-Model, and of the results obtained, was presented in each chapter of the thesis. This section presents an overall discussion of my complete research work. It summarizes the main results obtained and the strengths and limitations of the MexOb-

Model. It also discusses the policy implications of the findings and outlines potential future improvements for the MexOb-Model.

8.2 Summary of the main findings

The MexOb-Model was created in order to have a simulation tool specially developed to address Mexico's obesity problem. Other population simulation models have been adapted to estimate future health outcomes among the overall Mexican population (115, 265). However, these models were originally developed to answer other countries' health questions and, as discussed in Chapter 2, these could produce estimates that over- or under-estimate the burden of disease in the Mexican population.

My PhD thesis had four objectives:

1. To develop a population-based forecasting simulation model for the obese Mexican population (MexOb-Model).
2. To project the Mexican population obesity trends to 2030 stratified by age group and sex.
3. To estimate the impact of projected obesity trends on the incidence, prevalence, and mortality of four obesity-related cardiometabolic risk factors (hypertension, type 2 diabetes, hypertriglyceridaemia and hypercholesterolaemia) in the obese adult population in Mexico
4. To explore the effects of three national level hypothetical scenarios for obesity prevalence reduction on the health of the future obese population in Mexico.

Below I will discuss how each of the objectives was achieved

8.2.1 Objective 1

The first objective was to develop a population-based forecasting simulation model for the obese Mexican population (MexOb-Model). This objective was achieved by the

combination of the information described in four chapters: Chapter 2, literature review of population simulation methods; Chapters 3 and 4, that described the methods used to build the MexOb-Model; and Chapter 5, which presented the validation of the MexOb-Model against observed data and other data from a model that largely addresses the same research problem.

The MexOb-Model was developed based on some of the most frequently used population-based simulation models that forecasted future obesity prevalence found from my literature review described in Chapter 2: the Foresight model (115, 118) and the Impact model (165). Having a similar design to other simulation models made it possible to compare the MexOb-Model outcomes with other similar population simulation models. It also enables the model to be used in the future to perform validation exercises or international comparisons of the estimated outcomes. The methods used in the MexOb-Model for forecasting were also chosen considering: my question of interest, my knowledge about the progression of the disease, the target population, the data quality and availability, my modelling skills and constraints in time for the analysis.

The Mexican Obesity Forecast Model (MexOb-Model) is a population-based computer simulation model composed of two sub-models:

- 1) a linear trend model that projected the future prevalence of obesity among the adult population (Chapter 3).
- 2) a discrete-state Markov model that estimated the health impacts of the increases in the levels of obesity on the prevalence, incidence and mortality of four related cardiometabolic risk factors in the adult population (Chapter 4).

The MexOb-Model was implemented in TreeAge Pro 2015 Software, Inc., software designed to implement decision analysis techniques. The MexOb-Model Markov

process used for this project runs in three five year cycles to account for a 15 year period (2015 to 2030).

The MexOb-Model was built using as inputs the best and most recent available Mexican data. For the first sub-model, the primary sources of data were four nationally representative health examination surveys: Encuesta Nacional de Nutrición (ENN) 1999 “*National Nutrition Survey*”; Encuesta Nacional de Salud (ENSA) 2000 “*National Health Survey*”; Encuesta Nacional sobre Niveles de Vida en los Hogares-1 (MxFLS-1) 2002 “*Mexican Family Life Survey*”; and Encuesta Nacional de Nutrición y Salud (ENSANUT) 2006 and 2012 “*National Health and Nutrition Survey*”. For the second sub-model, the Markov model, I fed the main steering parameters (initial population distribution, open cohort component, growth ratio and transition probabilities) with information from: ENSANUT 2006, national population projections, national mortality databases, and risk of mortality from international published studies. ENSANUT 2006 was one of the principal databases used to develop this model, as it was the latest available survey that provided more complete health examination data on the Mexican population. This database contains: anthropometric measures, blood pressure measures for hypertension, and biochemical measures from blood samples for type 2 diabetes mellitus, hypertriglyceridaemia, and hypercholesterolaemia.

Mexico’s epidemiological data cannot be compared with the amount of health data from the USA or UK, but it is one of the countries in Latin America that has more health data available. Unfortunately, due to the lack of published data from the Mexican population for the key inputs (incidence, risk ratios and hazard ratio for mortality from the four cardiometabolic risk factors, normally obtained from data collected from longitudinal studies) that are needed to estimate one of the most important model parameters - the transition probabilities between the states of obese, obese with disease, and death - I had to use information from the literature and manipulate the available data to estimate specific parameters for the Mexican obese population. I used a decomposition formula (224, 225) to calculate the disease specific

risk of mortality for the Mexican obese population, and a non-parametric formula to estimate the transition probabilities between my model's health states using the available cross-sectional data from the health surveys listed above. It is probable that this data manipulation and use of non-Mexican data as input would also have an impact on my projected estimates.

Validation of population-based simulation models is a highly important step when developing a model (31, 32). Validity refers to the degree to which the model represents the real world. The MexOb-Model as seen in Chapter 5 was validated in three different forms: 1) Internal validation, by comparing the total obesity prevalence estimated from running the MexOb-Model over one five-year cycle (2007-2012) with the obesity prevalence estimates directly observed from ENSANUT 2012; 2) External validation, by comparing the prevalence of hypertension among the obese male and the obese female populations forecasted with the MexOb-HT model estimated over one five-year cycle (2007-2012) with the hypertension prevalence directly observed among the obese population from ENSANUT 2012; and 3) Cross-validation, by comparing the total obesity population levels from the MexOb-hypercholesterolaemia (MexOb-HCI) model outcomes estimated from running the MexOb-Model over three five-year cycles (2005-2020) with the obesity levels estimated from the linear trend regression and from the Foresight model (115). In general, the results from these exercises were consistent with what was reported by observed data and by other forecasting models, with slight underestimations when comparing total obese population prevalence and slight overestimations when comparing obese-disease (hypertension) prevalence. The results observed from the validation exercises conferred credibility on the outcomes produced by the MexOb-Model for potential users.

The small differences between MexOb-Model outcomes and observed and projected data from other simulation models are mainly due to the characteristics of the amount and quality of data used as input in the model (e.g. the number of previous cross-

sectional studies used to estimate historic trends), the distribution of the initial population and growth ratio which were based on 2006 data; the structure of the MexOb-Model (e.g. the use of discrete time parameters, cohort distribution between health states), and the assumptions made during the modelling process (e.g. holding values such as the transition probabilities constant during the simulation period). All these characteristics of the MexOb-Model had an influence on the estimated outcomes that could cause small variation when compared with other estimates of obesity prevalence. Besides the aforementioned concepts, when doing the cross-validation exercise (MexOb-HCI estimates vs. linear trend regression and the Foresight model), I observed that there were other aspects that could be the cause of the differences between the MexOb-Model outcomes and the projections estimated by other simulation models. The population simulation model chosen to do the cross-validation (the Foresight model) used the similar high-quality databases as input data (ENSA 2000 and ENSANUT 2006) to calculate its projections. However, the difference in statistical methods for forecasting (the MexOb-Model used linear regression analysis, and the Foresight model used multivariate categorical regression) and the difference in the number of past trend data points used for forecasting obesity prevalence (the MexOb-Model four points and the Foresight model three points) had an effect on the estimated future prevalence. This exercise also highlighted the importance of the length of the projection period. As the results showed, the longer the forecasting period used, the larger the magnitude of differences between the observed data and the forecasted outcomes from modelling studies.

8.2.2 Objective 2

The second objective was to project the Mexican population obesity trends to 2030 stratified by age group and sex. This objective was addressed in Chapter 3 using a linear regression model based on the historic obesity prevalence trends from five national health examination surveys (MexOb-Model first sub-model). The MexOb-Model projected that in 2015 approximately 30 million people 2 years and older would be classified as obese (using the IOTF cut-off points for children and adolescents). If these trends continue, by 2030 the obese population ($\geq 2y$) in Mexico is estimated to

be about 48 million. This represents approximately 36% of the total Mexican population projected for that year. Analysis of the historical trends showed that the increase in obesity prevalence has started to level off for males and females younger than 20y, but in adults - particularly in women - the growth of obesity levels is still large. As discussed extensively in Chapter 3, there are some important limitations to consider when interpreting these results.

The use of linear trends for calculating long-term projections could potentially overestimate future levels of obesity should there be any levelling-off in the trends. Levelling off of the prevalence has already been observed in younger age groups in the Mexican population and could possibly be observed in the adult population in the near future. Additionally, projections of future trends based on historic trends (linear or non-linear) assume that those trends will continue until 2030, but is highly probable that these trends may depart from reality because of the influence of external factors (e.g. education, other interventions or even medical advances). Furthermore, it is important not to forget that the projection estimates for younger age groups could vary according to the choice of BMI thresholds used to classify children and adolescents as obese. My results showed that using the IOTF-BMI classification projected lower obesity prevalence than the prevalence obtained using the WHO BMI cut-off points.

8.2.3 Objective 3

The third objective was to estimate the impact of projected obesity trends on the incidence, prevalence, and mortality of four obesity-related cardiometabolic risk factors in the obese adult population; it was addressed in Chapter 6. This chapter presented the results from the base-case model which represents the future impact of obesity on hypertension, type 2 diabetes, hypertriglyceridaemia and hypercholesterolaemia assuming the historic trends in obesity prevalence will continue. I also performed sensitivity analyses around these outcomes. Based on the best available epidemiological Mexican data, and with the prevalence of obesity-

related cardiometabolic risk factors held constant at 2006 levels for the initial population distribution, the MexOb-disease models projected that by 2030 the prevalence of HT, HTG and HCl in obese males and obese females aged 20 to 79y would be approximately 50% (ranging from 30% to 70% for the best and worst-case scenarios respectively). The prevalence of T2DM in the obese population could reach nearly 30% for both sexes by 2030 (ranging from 15% to 50% for the best and worst-case scenarios respectively). Of all the four cardiometabolic risk factors, the highest prevalence among the obese population by 2030 would be observed for hypercholesterolaemia and for hypertension for both sexes, but the biggest increase from 2015 levels would be for the number of cases of obese-hypertensives and obese-diabetics in both sexes. The continued increase in obesity prevalence could result in around 1.5 million deaths in obese males and around 2 million deaths in obese females over the 15 year period from 2015 to 2030.

These estimates of future disease prevalence are a clear representation of Mexico's actual cardiometabolic risk factors panorama. The Mexican National Health and Nutrition Survey (ENSANUT) 2006 reported that hypercholesterolaemia was the second most prevalent risk factor in the total adult population (43.6%) after low HDL (60.5%) (86), but hypertension and diabetes prevalence were the ones with the most rapid growth. Hypertension prevalence increased from 23.8% in 1993 to 30.7% in 2006. Diabetes prevalence increased from 6.7% in 1993 to 14.4% in 2006 (81). The results from the MexOb-Model projected a bigger burden of obesity and obese-related cardiometabolic risk factors for Mexican women than for men, which reflects the already observed higher prevalence of obesity in women (38%) than in men (27%) in 2012 (276). The difference in obesity prevalence between sexes has also been observed in other developing countries (272). The higher levels of obesity for women than for men have been attributed to different biological and sociocultural factors. Unsurprisingly, the age groups in which we could expect the biggest burden from all the four cardiometabolic risk factors were individuals aged ≥ 60 years, according to the projected results from the MexOb-Model. Additionally, for hypertension and type 2 diabetes mellitus, the burden could also come from younger age groups (40-59y). The

higher number of cardiometabolic risk factors cases in the older population are influenced by the increase in the number of the elderly population. The percentage of people aged ≥ 60 y in Mexico is expected to increase from 9% in 2012 to 14% by 2030 (63).

Moreover, the projected numbers of obese-diabetic cases under the base-case scenario from the MexOb-Model were in line with the projected number of diabetes cases reported from other population simulation models for the Mexican population. Projections by Meza et al. (266) and Guariguata et al. (267), predicted a higher number of diabetes cases for the Mexican adult population than my model. These differences were expected, as their estimate referred to the total adult population and not only obese individuals as in the MexOb-Model.

8.2.4 Objective 4

The fourth objective was to explore the potential health effects on the number of obese cases with cardiometabolic risk factors and the number of deaths by calculating the difference in the number of cases estimated by the MexOb base-case model and the number of cases estimated by the MexOb-Model under three different obesity prevalence reduction scenarios. The base-case model estimated that approximately 48 million adults aged 20 to 79y would be obese by 2030. Achieving the most optimistic of the three scenarios evaluated, a 10% reduction in obesity 2015 projected prevalence in 15 years, would mean that the new expected obese population would be around 28 million, 20 million fewer obese cases than the number estimated from the base-case model (i.e. if the historic trends in obesity prevalence continue at the same pace).

The MexOb-Model projected that a slowing down in the rate of increase in obesity prevalence to achieve a 3% reduction in the 2030 projected obesity prevalence (scenario A) would produce an important decrease in the number of obese-disease cases, approximately 300,000 fewer disease cases for obese men and nearly 4800,000

fewer disease cases for obese women. In order to achieve a relevant health impact a bigger reduction of obesity prevalence has to be achieved. Compared to the base-case model, maintaining obesity prevalence at 2015 levels (scenario B) would achieve around 3 million fewer disease cases for men and around 4 million fewer disease cases for women with obesity. A relative reduction of 10% in the obesity prevalence levels of 2015 (scenario C) would achieve 4 million fewer disease cases for obese men and just over 5 million fewer disease cases for obese women, projecting an important reduction in the burden of obesity.

Of the four cardiometabolic risk factors, the biggest benefit could be observed from the reduction in the number of obese-hypertensive individuals. The results showed that a reduction in obesity prevalence would be extremely beneficial for the country. However it also acknowledged that achieving those targets of obesity prevalence reduction and observing the estimated benefits in population's health may be difficult in the context of the historic increases in obesity prevalence among the Mexican adult population.

8.3 Strengths and Limitations

8.3.1 Strengths

To my knowledge, The MexOb-Model is the first obesity population-based simulation model that projected future health estimated in the Mexican obese adult population, and the first to estimate future cases of hypertriglyceridaemia and hypercholesterolaemia. The transparency of the MexOb-Model in its methods of data manipulation and projection estimations confers to the model the characteristic of being an easily understandable tool by non-expert modellers, and this will help potential users to have a better understanding of its limitations but also offers opportunities to easily implement possible modifications, in order to address other important obesity-related policy and research questions. The MexOb-Model does not require an extensive amount of data, and it uses for its inputs epidemiological or

health examination survey data that is commonly available in most countries (e.g. cross-sectional data from health examination surveys, general mortality data, and population projections), this gives the possibility to adapt the MexOb-Model forecasting methods to be used by researchers in other countries which have less rich epidemiological data than countries such as the UK and the USA. Its structure and statistical methods used in its two sub-models are easy to understand and do not require highly advanced programming skills, making the MexOb-Model an easily replicable simulation tool.

The process of developing the MexOb-Model to achieve the four objectives discussed above highlighted the gaps in epidemiological data from the Mexican population. This was particularly observed for the lack of incidence data, one of the most important input parameters used for the calculation of the transition probabilities between the health states of obese without disease, obese with disease, and death. Funding resources for science in Mexico are limited, and the high cost of studies that could allow for the direct estimation of the transition probabilities using Mexican data (e.g. incidence and morbidity and disease-specific relative risks of mortality for obese individuals vs non-obese from longitudinal studies) has been an important barrier for the estimation of transition probabilities. I overcome this barrier by using statistical methods that could estimate transition probabilities using the cross-sectional health examination data that is available in Mexico. A number of longitudinal studies have begun in Mexico (239, 310) and hopefully data from these studies could be used to estimate the input parameters required in future modelling exercises.

The MexOb-Model was implemented in TreeAge software (213). This software is commercial (i.e. not freely available), and this could be a potential barrier for its replicability in middle and low income countries. I decided to use TreeAge for the development of the MexOb-Model as it helped me to achieve a better understanding of the transition of the model cohort between the chosen health states. However the

MexOb-Model structure could be implemented in Microsoft Excel, a Microsoft Office application that is widely available.

8.3.2 Limitations

Population-based simulation models, as other simulation models, are highly dependent on the quality of the data used as input, the statistical methods used for forecasting and the assumptions made by the modellers. All these variables need to be fully understood to allow for a proper interpretation and use of the outcomes produced (112). To estimate the MexOb-Model outcomes I made the following assumptions: firstly, the prevalence of the four main cardiometabolic risk factors in the obese population used to distribute the initial population of the model (obese persons with and obese persons without the disease) remained unchanged since 2006. Secondly, the steering parameters used for calculating the distribution of the obese population among the health states also remained static during the period of simulation (open cohort component, growth ratio, and transition probabilities). Thirdly, the model assumed a zero remission rate from each of three states (e.g. that obese persons flowing into the obese-disease state could not make a transition back to the obese-without-disease state, nor could obese individuals go back to normal weight or overweight).

All population simulation models also have limitations that affect their projections and that as with their key modelling assumptions, it is important to clearly identify them. The MexOb-Model does not consider the rates of transition between the BMI groups in the population (normal, overweight and obese) or consider the changes to those transition rates that could occur during this 15 year period. The transition probabilities do not include the effect of co-morbidity between the cardiometabolic risk factors and so the model does not consider that the potential co-morbidity could have had an impact on the number of new disease cases and number of deaths projected. The MexOb disease models were run separately for each of the cardiometabolic risk factors. The outcomes from the MexOb-Model cannot be simply summed to estimate

the overall size of the disease burden. As I mentioned in previous chapters, it is frequently observed that clusters of these risk factors occur among individuals with obesity.

Data from the literature review showed that most of the simulation models covered in the review used a 1 year cycle length. However, due to the methodological constraints explained previously (see: Chapter 4), a five year cycle was chosen for the MexOb-Model. This could, of course, have a number of limitations. For example, it is possible that the choice of a longer cycle length could result in overlooking important changes in disease prevalence that could modify the estimated outcomes.

For a future analysis, it will be important to compare the MexOb-Model outcomes obtained using a five-year cycle with outcomes obtained by the same model run using a 1-year cycle.

Moreover, blood pressure measurements were assessed in the total adult population from ENSANUT 2006, however the MexOb-Model uses data only from the obese population and that reduced my total analytical sample for blood pressure values. Additionally, only a sub-sample of the surveyed population, as describe in Chapter 4, was selected for venous blood sampling reducing even more the size of my analytical sample. These small sample sizes meant that smoothing had to be used for some values due to the variation of estimates between consequent age groups caused by the reduce sample sizes.

The validation exercise undertaken to compare projected levels of disease among the obese population could only be conducted for one of the four cardiometabolic risk factors (hypertension) at the time of writing. Although collected, blood sample data from ENSANUT 2012 to estimate levels of diabetes, hypertriglyceridaemia and

hypercholesterolaemia among the obese population were not available to data users. This created a limitation for the MexOb-Model as I could not use as an input the most recent data on prevalence of cardiometabolic risk factors. Hence the potential users or readers should be aware of this when interpreting the prevalence of the cardiometabolic risk factors among the obese population.

8.4 Policy Implications

Obesity has been estimated to be one of the top three global causes of the social burdens generated by humans in conjunction with smoking and armed violence. Obesity's economic impact was estimated as 2.8% of the global GDP in 2012 (\$2 trillion) (311). In Mexico, the healthcare expenditure from obesity-related disease complications projected for 2017 would be approximately £3.2 billion (around 78 billion , Mexican pesos, £1=24.4 MXN), this represents nearly 70% of the total health budget for Mexico for 2014 (41). The economic and social costs of obesity are expected to increase as obesity prevalence is projected to keep rising, with the number of obese individuals aged 20 to 79y expected to reach a total of 48 million by 2030 should the historic trends in obesity prevalence continue.

As observed from the results presented in Chapter 7 that showed the potential gains through three hypothetical scenarios of obesity prevalence reduction compared with the base-case results for the MexOb-Model, a small relative reduction in obese prevalence is something that could potentially be achieved by the implementation of a small group of obesity prevention interventions. However, a slowing down in the rate of increase in obesity prevalence to achieve a 3% reduction from 2030 projected prevalence would not create sufficient impact to decrease the size of the health burden of obesity in Mexico. My results highlight the enormous benefit that a more significant reduction in obesity levels, such as sustaining the 2015 obesity projected prevalence or achieving 10% reduction of the 2015 projected obesity levels, could bring to the population. But achieving this level of decrease in obesity prevalence will

require big efforts. Mexico has already implemented a series of actions to reduce obesity levels: school guidelines for food and beverages, that promote the consumption of healthy foods inside and outside schools; front of package labelling system; marketing regulation of food and beverages for children; and a 10% tax on sugar sweetened beverages and a 8% tax on nonessential foods, but no decrease in obesity prevalence has been observed yet. The Mexican Health and Nutrition Survey (ENSANUT) is conducted every six years; the next ENSANUT is planned for 2018. Therefore, ENSANUT obesity data available post implementation of the SSB tax and other obesity prevention interventions that allows us to assess whether obesity prevalence has changed since 2012 is not yet available.

The Mexican government needs to start exploring the cost-effectiveness of the implementation of obesity prevention interventions in other areas like portion control, reformulation, subsidies, parental education and weight management programmes, as well as modifications to the environment like active transport that complement the interventions already in place and help accomplish changes in obesity levels sooner (302, 312). Therefore, joint action between government institutions, non-governmental organizations (NGOs) and industries (e.g. food and beverage manufactures, and retailers) is vital (302, 313).

The MexOb-Model outcomes could also be used as evidence to support the implementation of new obesity preventive interventions, and monitor and maintain the ones already in place. This will help to present a stronger argument in favour of obesity preventive actions and will help to overcome potential barriers from stakeholders that could affect the implementation of effective interventions (314). Furthermore, having knowledge of the age groups that would be most affected, and the magnitude of the prevalence of the main cardiometabolic risk factors among the obese population that could happen if obesity levels reach the projected levels, will help to properly allocate resources where it clearly reflects the population's health needs.

Preventing the potential future obesity trends and its consequences from happening will have an important economic benefit for the healthcare institutions and for the population's economy. It has been observed that obese individuals have lower productivity (41), lower quality of life (280, 315) and higher healthcare costs (89) than non-obese individuals. A recent review of the Mexican Healthcare System by the OECD observed that Mexico allocates fewer of its national resources to health than other OECD countries, this is reflected in the low amount of health resources Mexico has and as a consequence low rates of care delivery compared with other OECD countries. Therefore it is one of the countries with higher out-of-pocket health expenditure (316).

8.5 MexOb-Model potential future improvements

The results of the validation analyses showed that the MexOb- model produces estimates that have credibility in Mexico's context. However, like all other population based simulation models, the MexOb-Model will have to be improved constantly in order to estimate more precise and specific outcomes. Modification of the model is an ongoing process as more data becomes available and other obesity relevant policy questions become of interest to the country.

Future modifications could be implemented progressively as more resources become available. The most immediate modification that could be made to the model would be to update the prevalence estimates for the four obesity-related cardiometabolic risks factors with ENSANUT 2012 results, which are expected to be published later this year. At the moment only the hypertension data is available but there is no data reported for T2DM, HTG or HCL. Another short-term modification could be to estimate the future obesity prevalence by a log-regression method instead of using a linear trend method. The first sub-model of the MexOb-Model projected future levels of obesity using a linear-regression method. As discussed extensively in Chapter 3, using a linear trend to estimate long term projections could overestimate future obesity

prevalence. Instead, a log-regression analysis of trends has the ability to consider potential change in the dynamic of the population historic trends (e.g. levelling-off) and as opposed to a linear trend, it will probably produce lower estimates of obesity prevalence (147). Moreover, log-regression was also one of the most popular mathematical methods to estimate future obesity trends that I found from my literature review.

Finally, I calculated 95% uncertainty intervals around the main outcomes from the base-case model using a deterministic sensitivity analysis. As previously described in Chapter 6, I estimated the best and worst case scenario for the base-case model outcomes to assess what could possibly happen in the future if the MexOb-Model changes over time. These sensitivity analyses were performed by using the lower (best-case) and the upper (worst-case) limits of the 95% confidence interval instead of the mean values of two MexOb-Model steering parameters: a) the ENSANUT 2006 prevalence of the cardiometabolic risk factors in the obese population; this had an effect on the initial population distribution and the growth ratio; and b) β -coefficients estimated from the linear trends, which affected the open cohort component. Instead of using these manually allocated values to calculate uncertainty, the MexOb-Model could be modified to use Monte Carlo simulations, to produce uncertainty estimates in different ways by using random values of the distribution of the parameters (7).

In addition, medium term modifications to the MexOb-Model could include changing the static transition probabilities to dynamic transition probabilities that account for the effect of the comorbidities between the four obesity-related cardiometabolic factors, as well as including the effects on the obese adult population of the future obesity trends among children and adolescents. As previously described in Chapter 4, the transition probabilities used in the MexOb-Model remain static during the modelling period (15 years), and the open cohort (the β -coefficients from the linear trends that allow new members of the obese population to enter the health states

over time) only refers to the increase of the trends of obesity levels in the adult population.

Longer-term improvements to the MexOb-Model will imply bigger modifications to the main model structure and will require more intensive work as well as results from specific scientific research. As described in Chapters 3 and 4, the MexOb-Model includes only obesity prevalence as the main outcome. A long-term improvement could be the inclusion of the effect of behavioural obesity risk factors like diet and physical activity. This will enable the model to evaluate preventive obesity interventions that target reducing the consumption of certain macronutrients (fat, sugar and sodium), and assess the future effect on obesity-related cardiometabolic risk factors of an increase or decrease in physical activity levels among the obese population. The model structure could also be expanded to include information to estimate the future health and economic burden associated with obesity and obesity-related disease using measures like disability adjusted life years (DALYS) or quality adjusted life years (QALYS), and provide estimates of the total direct and indirect disease costs. Furthermore, the MexOb-Model could be expanded to estimate specific morbidity and mortality outcomes from other obesity-related disease like cardiovascular disease, chronic kidney disease or cancer by using the estimated future cardiometabolic risk factors outcomes as mediators to estimate the impact of obesity on those diseases. Finally as described in Chapter 5, the validation of simulation models such as the MexOb-Model is a constant effort. Once the results of the new ENSANUT 2018 are published, I could use those observed obesity prevalence values to validate the current MexOb-Model predictions, and also use the data to assess if obesity levels have changed after the implementation of the national obesity preventive interventions.

8.6 Conclusion

The obesity trends in the adult population are still increasing and as a result, the number of individuals with obesity-related cardiometabolic risk factors will also keep increasing. This health panorama will be affected also by the increase in the size of the Mexican population, the ageing of the population, and also by the increase in the prevalence of cardiometabolic risk factors among the younger population. By 2030, the burden of morbidity and mortality from the obese-disease population could exceed the health services budget and capacity and so negatively impact on the population's quality of life. Mexico could therefore be facing a big risk of not being able to attend to the health needs of its inhabitants, and this will have a great impact on the economic development of the country.

Obesity is a public health problem that affects developed and developing countries (272). Knowing the potential future health burden of this disease is of great relevance to all. The purpose of this research was to build a transparent population model that integrated information from the most recently available current evidence to estimate the medium to long term impact of increasing obesity levels on the levels of its four main cardiometabolic risk factors in the Mexican adult population by 2030. Population-based simulation model like the MexOb-Model estimated outcomes which otherwise would require much time to produce. The information will potentially be used for obesity prevalence reduction goal setting, obesity prevention and control programme planning and monitoring, and resource allocation that could help prevent and control Mexico's obesity's health burden.

The results of this research project highlight the importance of each country creating their own population-based simulation model. Usually population predictions are made based on models built in developed countries. However when adapted to developing countries that usually have less health data available to feed the models, the quality of the outcomes produced by these models could be altered as they will

need to fill the gaps in data with data obtained from other countries and that could not reflect the country's own specific health panorama. The MexOb-Model was built taking into consideration the limitations of Mexican epidemiological health data and the validation exercises showed that it produces good quality and credible estimates. It is still important to recognize that more country specific health data will produce more precise projections, so we should not underestimate the importance of collecting epidemiological data. These research findings open the possibility to other lower and middle income countries, where the obesity epidemic is also striking but that have limited health data and economic resources, to create country-specific population simulation models that could help them assess the future impacts of obesity. Developing a country-specific population-based simulation model will empower countries to be able to create this type of evidence for other relevant public health problems.

Chapter 9. References

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Appendix A. Mexico's nationally representative health surveys

A.1 National Nutrition Survey (ENN) 1999

The ENN had the objective to estimate the prevalence of and identify the risk factors for undernutrition, micronutrient deficiencies and malnutrition due to excessive intake in different age groups. This information was also obtained to create epidemiological evidence to support the development of social policies and national food and nutrition programmes. The data was collected between October 1998 and March 1999 (1, 2).

A.1.1 Survey design

The survey had a probabilistic multistage, stratified, clustered sample design. It was designed to be nationally representative, with stratification between four geographical regions and between urban (≥ 2500 inhabitants) and rural areas.

Sample design

Geographical regions

The country was divided into four geographical regions.

- 1) **North:** Baja California, South Baja California, Coahuila, Chihuahua, Durango, Nuevo León, Sonora and Tamaulipas
- 2) **Centre:** Aguascalientes, Colima, Guanajuato, Jalisco, México, Michoacán, Morelos, Nayarit, Querétaro, San Luis Potosí, Sinaloa and Zacatecas.
- 3) **South:** Campeche, Chiapas, Guerrero, Hidalgo, Oaxaca, Puebla, Quintana Roo, Tabasco, Tlaxcala, Veracruz, Yucatán.
- 4) Mexico City

Zones

Each of Mexico's states was first divided to create a total of six different zones. The zones were built based on the sample frame of the Population Census, INEGI, which classified the communities according to the number of inhabitants.

Appendix table A-1 Description of the zones created for the sample selection

Zone	Characteristics	No of households in Primary sampling unit
I	Cities and metropolitan areas (defined in the Mexican National Employment Survey)	480
II	Cities with $\geq 100,000$ inhabitants	280
III	Communities with 20,000 to 99,999 inhabitants	280
IV	Communities with 15,000 to 19,999 inhabitants	280
V	Communities with 2,500 to 14,999 inhabitants	280
VI	Communities with $< 2,500$ inhabitants	100

Additionally, the communities were stratified in sample units, as described below, to identify the households to be surveyed.

Primary sampling units (PSUs): They were formed by one, part or several basic geo-statistical areas (BGSA). The number of households per BGSA varied by zone (**Error! Reference source not found.**). The BGSA in localities with $\geq 2,500$ inhabitants were constructed of a number of household blocks delimited by streets (urban BGSAs). Localities with $< 2,500$ inhabitants (rural BGSAs) were formed by households within an area of 10,000 hectares or of several BGAs to achieve the required number. Furthermore, every PSU selected was stratified by socioeconomic status within each state and zone.

Secondary sampling units (SSUs): For zone I, SSUs were formed by one or more adjoining blocks with a minimum of 40 inhabited houses. For zones II to VI, it was constituted by the households.

Tertiary sampling unit (TSU): TSU was exclusively for zone 1 and it was formed by the households.

Sample selection

1) Cities or metropolitan areas (zone I): First the PSU were selected with a probability proportional to size. Secondly, the SSU were selected from each PSU. Finally, within each SSU five households were chosen to be in the survey sample.

2) Urban and rural areas (zones II-V): At the first stage, the PSU were selected with a probability proportional to size. In the second stage, the households to be interviewed were selected.

3) Rural areas (zone VI): Firstly the PSUs were selected. In the second stage, they selected two or four groups of 10 households to collect data from.

Sample size

The total calculated sample included 21,000 households (6,200 for each region (north, south and centre); and 2,400 for Mexico City). All children (0 to 11 years old) in the household and only one woman 12 to 49 years old per household were selected to be included in the survey.

A.1.2 Survey content

The units of analysis were the household and individuals. The population was divided into three age groups: two children's groups (from 0 to 4 years, and 5 to 11 years); and adult women (12 to 49 years). The survey included: four questionnaires, two dietary evaluations, and anthropometric and biological measurements. A sub-sample of venous blood was collected.

Subsample: A subsample of 4,200 households for each of the three age groups was selected for dietary evaluation. A secondary subsample was created to obtain blood samples measurements from adult women. This secondary subsample was built by selecting one of every three households that comprised the first subsample. This subsample included a total of 1,400 households.

1) Questionnaires

- *Household questionnaire:* collected information about socioeconomic and demographic characteristics.
- *Morbidity questionnaire:* information about acute and chronic morbidity and health services usage.
- *Infant feeding questionnaire:* the survey collected breastfeeding and complementary feeding data for children 2 years and younger.
- *Women's questionnaire:* collected data on obstetric history, physical activity, and alcohol and tobacco consumption. This questionnaire was applied only to a subsample of 4,200 households.

2) Measurements

- *Anthropometric measures:* height and weight was measured in all the population, and waist and hip circumference for adult women only.
- *Capillary blood sample:* obtained to measure haemoglobin.
- *Blood and urinary sample:* obtained for a subsample of 1,400 households that included all age groups.

3) Diet evaluation

- *24 hour dietary recall:* collected information from a subsample about food, energy, and macro and micronutrients.
- *Food frequency questionnaire:* applied only to a subsample of women 12 to 49 years of age.

A.1.3 Response rates

This survey reported a response rate of 82%.

A.2 National Health Survey (ENSA) 2000

The ENSA 2000 provided information about the prevalence of acute and chronic diseases, the quality of health services and their usage. Furthermore, the data collected was used to evaluate national programmes implemented five years prior to the survey. The data was collected between November 1999 and June 2000 (3-5).

A.2.1 Survey design

This nationally representative survey had a probabilistic multistage, stratified, clustered sample design.

Sample selection

The researchers stratified by urban and rural areas. They classified as rural areas those communities with <15,000 inhabitants.

To select the sample, first a proportional number of households was calculated for each urban and rural area. Secondly, a total of 14 boroughs by state were selected and within each borough, five BGSA's were selected to be included. Three blocks were chosen from each BGA previously selected. Then seven houses from each block were chosen. Finally, within each household, the household inhabitants were randomized to select one individual for each age group sub-populations.

Sample size

The total sample calculated was 47,040 households, (1,470 households in each of the 32 states). Within each household the following sub-populations were selected:

Healthcare outpatient or inpatient services user, one child (0-9y), one adolescent (10-19y) and one adult ($\geq 20y$).

A.2.2 Survey content

The survey included a total of five questionnaires and measurements:

1) Questionnaires

- *Household and population*: collected information about socioeconomic status and house physical characteristics.
- *Health services usage*: collected data from people that used the health services in the 12 months before the interview, reasons for health service usage, quality of health services and health services' characteristics.
- *Individual questionnaire*: Collected data in three age groups: children (0 to 9 years of age), adolescents (10 to 19 years) and adults (≥ 20 years).

2) Measurements

The survey obtained: anthropometry, blood pressure, capillary blood samples, and urine sample (urine test strips) from the surveyed population.

- *Anthropometric measures*: height and weight in all the population, and waist circumference in adults were collected in situ.
- *Blood pressure*: two blood pressure evaluations were obtained using a mercury sphygmomanometer with a five-minute interval between each other.
- *Blood samples*: Two finger prick blood samples were obtained to measure blood glucose and haemoglobin in situ. Additionally, non-fasting venous blood samples were collected in children, adolescent and adults. A second non-fasting venous blood sample was obtained in adults to separate the plasma and collect white cells.
- *Urine sample*: A urine sample from the first urine in the morning was collected and analysed by dipstick.

A.2.3 Fieldwork

Data was collected by face to face interview (interview time was two hours). The information on the household was obtained by interviewing an adult (usually the housewife). On average, each household received three visits. All the measurements and samples were obtained by trained personnel using standardised protocols.

A.2.4 Weights

Weights were calculated to allow for non-response, and further weights were calculated to adjust for sampling design. The calculated weights were used to adjust

for the effect of over or under representation for population subgroups and to reflect the population numbers from the Population and Household Census in 2000.

A.2.5 Response rate

A total of 45,726 households were surveyed, approximately 1,429 households per state. A total of 190,214 individual questionnaires were collected. This represented a response rate of 97%. A total of 82,152 biological samples were obtained, which represented 88% of the expected blood samples.

A.3 Mexican Family Life Survey 1 (MxFLS)

The objective of the Mexican Family Life Survey was to create a longitudinal data base that collected information on health, demographics and economic at the individual, household and community level. The MxFLS was planned for a 10 year period. A total of three surveys were collected (baseline and two waves): MxLFS-1 (2002), MxLFS-2 (2005-2006) and MxFLS-3 (2009-2012) (6-8).

A.3.1 Survey design

The survey has a probabilistic, multi-stage, stratified, clustered design. The survey was designed to be nationally representative and to provide urban/rural and regional representation.

Sample design

The national regions were created with accordance to the National Development Plan 2000-2006, Mexico. The sample selection was made in three stages by cluster and stratification.

Geographical regions

- 1) **South-Southeast:** Oaxaca, Veracruz, Yucatan
- 2) **Centre:** Mexico City, México, Morelos, Puebla
- 3) **Centre West:** Michoacán, Jalisco, Guanajuato
- 4) **North West:** Baja California Sur, Sinaloa, Sonora
- 5) **North East:** Coahuila, Durango y Nuevo León

Zones

The PSUs were grouped in three different zones:

- 1) **Cities and metropolitan areas (ENEU zone):** It was formed by 48 cities and metropolitan areas.
- 2) **Urban areas:** Boroughs with $\geq 100,000$ inhabitants that do not belong to the ENEU zone and by communities with 2,500- 99,999 inhabitants.
- 3) **Rural areas:** Communities with populations of $<2,500$ inhabitants.

Additionally, the PSU were classified in three strata: high, medium and low, based on health, education and economic indicators collected during the “The Mexican National Employment Survey-2001” (*Encuesta Nacional de Empleo (ENE)*).

Sample Selection

The sample size was equal for the five regions; within each region the sample was selected proportional to the zones and within each zone the sample was selected proportional to the strata.

- 1) **Cities or metropolitan areas (ENEU):** Within each region, the states were selected with equal probability; within each state and stratum, the PSUs were selected with a probability proportional to size. A total of six SSUs were chosen, with a probability proportional to size, within each PSU. Finally they selected the households within each SSU.
- 2) **Urban areas:** For each region, they selected each state with equal probability. Within each state, the PSUs were selected with equal probability by randomization; within each PSU, they selected 20 households with equal probability by randomization.
- 3) **Rural areas:** The selection of PSUs was similar to that described for urban areas, except that within each PSU they selected two groups of approximately 10 households each for data collection.

Sample size

The total sample size was calculated to be of 10,000 households distributed within the five geographical regions (2,000 households per region). MxFLS-1 has oversampled rural communities with less than 2,500 inhabitants.

A.3.2 Survey content

The MxFLS collected information on demographic and socioeconomic indicators at a community, household and individual level.

1) Questionnaires

- *Individual:* Data on education, social programmes, income, migration and health status perception. Additionally, it also collected health measurements (weight, height, blood pressure and haemoglobin), health service usage, marital status history and victimization. Furthermore, the cognitive ability of the population 6 to 64 years was evaluated by Raven's progressive matrices.
- *Household:* Questionnaire that collected information about food expenditure, land usage, violence, economic shock and participation in economic activities.
- *Community:* The survey also collected qualitative and quantitative information on characteristics of the population, health, commerce, education and transport. The community questionnaire included retrospective information on schools, health centres, private small health providers, stands, stores, supermarkets, farmers' markets and pharmacies.

2) Measurements

The health measurements included:

- *Anthropometric measures:* weight, height, waist and hip circumference. Additionally, each individual was asked about their self-perception of their height and weight
- *Blood pressure:* were assessed using a mercury sphyngmomanometer
- *Blood samples:* haemoglobin levels were measured using a finger prick.

A.3.3 Fieldwork

Household information on socioeconomic characteristics and demographic composition was obtained from one or two adult members. Additionally, individual data from all household members was obtained in the population ≥ 12 years. The aforementioned interviews were made face-to face. Additionally, a parent or a care taker was interviewed to obtain data on children < 12 years old. Measurements were obtained from all household members by trained personnel using standardised protocols.

A.3.4 Weights

The adjusted weights were calculated to consider the non-response of each group of interest (individual and household weights).

A.3.5 Response rate

The MxFLS-1 collected information from 35,677 individuals and 8,440 households from 150 communities in the country. MxFLS-2 and MxFLS-3 achieved a re-contact rate of 90% of the original sample. Additionally, the researchers were able to contact more than 91% of the individuals that migrated to the USA or relocated within the country.

A.4 National Health and Nutrition Survey (ENSANUT) 2006

The objective of this survey was to collect data related to the health and nutritional status of the Mexican population, and the quality and response of the health services. Additionally, it was also designed to collect information related to national health policies and programmes, and household expenditure on health services. They collected information for the population of all ages. The data collection took place between October 2005 and May 2006 (9, 10).

A.4.1 Survey design

Sample design

The survey had a probabilistic multistage, stratified, clustered sample design. The design of the survey allowed differentiation between the rural and urban populations and four different geographic regions (North, Centre, South and Mexico City). These regions were the same as described above in ENN 1999. Furthermore, the stratification was made considering if the area belonged or not to the National Programme

“Oportunidades/Prospera”, a government created cash-transfer programme that targets poor and extreme poor households (11).

Zones

The communities were classified in three different types of stratum according to their size, using a similar classification as ENN 1999:

Stratum I: Cities or metropolitan areas with $\geq 100,000$ inhabitants.

Stratum II Urban areas that had a population between 99,999 and 2,500 inhabitants.

Stratum III: Rural areas with $< 2,500$ inhabitants.

Sample Selection

There was a small variation in the sample selection between cities and urban areas, and rural areas.

1) Cities and metropolitan areas and urban areas (stratum I and II): Firstly, the basic-geo-statistical areas (BGSA), were randomly selected for each of the 32 states by probability proportional to size. Secondly, within each BGSA, six blocks of households were randomly selected. Thirdly six households were randomly selected from each of the blocks. Finally, by randomization, they selected one individual from each group (child, adolescent, adult and health service user).

2) Rural areas (stratum III): The PSUs were BGSAs formed by rural communities. The probability of the BGSA being selected was proportional to the number of households in it. The SSUs were formed by a community or a group of communities to group 120 households. For every community or group of communities, they selected at random three segments, each of them with 12 households.

In all the strata, the survey was applied to each of the selected households. If the characteristics of the household inhabitants allowed it, one individual from each group (child, adolescent, adult, and health user) was selected by randomization to be surveyed.

Sample size

The calculated sample size included 48,600 households; it included 1,620 households from each of the 32 Mexican states

The survey identified as their unit of analysis six different groups:

- *Home*: defined as a group of people that have or not a family liaison but that live in the same household, and that benefit from the same income contributed by one or more members of the household.
- *Health services users*: people that sought or received ambulatory health attention in the six months before being interviewed. They included people looking for disease treatment, accident, rehabilitation, dental health, or appointments as part of hypertension and diabetes disease control (prevention/treatment) programmes.
- *Four different age groups*: children (0 to 4y); school age children (5 to 9y); adolescents (10 to 19y) and adults ($\geq 20y$).

A.4.2 Survey content

The survey included a total of five different questionnaires, dietary information collections and measurements.

1) Questionnaire

- *Household survey*: The household survey collected information on socio-demographic characteristics of the household, health service usage, physical characteristics of the house, "Seguro Popular Programme" utilization and acceptance, and nutrition information.
- *Children's questionnaire*: This collected information on immunization, diarrhoeal disease, acute respiratory tract infections and asthma, breastfeeding practices, complementary feeding in children <2 years old and diet information for children 1-9 years of age.

- *Adolescents' questionnaire*: This questionnaire asked about risk factors, sexually transmitted diseases, reproductive health, physical activity, eating behaviour, violence and accidents and diet.
- *Adults' questionnaire*: collected data on risk factors (tobacco, alcohol, physical activity, overweight and obesity), chronic diseases (diabetes mellitus, hypertension, cardiovascular diseases, renal diseases, dyslipidaemias and cancer), reproductive health, accident and violence, preventive programmes usage and diet.
- *Health services user s' questionnaire*: data on ambulatory, preventive and treatment services usage, accessibility and quality of attention, health services utilization patterns, and usage and accessibility of the ambulatory health services.

2) Measurements

Measurements were obtained for all the four age groups (children and school age children, adolescents and adults).

Measurements included: height, weight, capillary blood samples and venous fasting blood samples. Additionally, blood pressure was assessed in the adult group (greater detail of these has been described in Chapter 4) (10).

3) Dietary evaluation

- *7-day food frequency questionnaire*: Dietary data were collected. Energy and nutrient intake by day were estimated from these data (12).

Furthermore, the survey also collected information about the participation of the population in food aid and health programmes, including "*Oportunidades/Prospera*".

A.4.3 Fieldwork

The information was obtained by face-to face interview by personnel trained in standardized measures. The data was collected by two different groups (health and nutrition groups).

Health team: this team applied the questionnaires for all age groups, health users and households.

Nutrition team: this team obtained anthropometric measurements, data on food frequency consumption inside the household and outside, information on low birth weight children born in the previous five years and the usage of food programmes. During a second visit the next day, they collected fasting blood samples and measured blood pressure.

Blood samples: A sub-sample of 6,613 individuals from the adult survey were randomly selected, with a total of 91% of the selected sample in the fasting state. The blood subsample had a statistical power to detect differences in prevalence of T2DM and dyslipidaemias $\geq 8\%$ by geographical regions.

A.4.4 Weights

Survey weights were estimated at household and individual level, for the main sample. Additional weights for the subsample were calculated to estimate nationally representative values. The population of the subsample included a higher number of younger persons and were more likely to be females. All weights were adjusted for survey non-response.

A.4.5 Response rates

ENSANUT obtained data on 48,304 households, and 24,098 children, 25,166 adolescents, 45,446 adults' individual questionnaires. Additionally, they collected 50,027 blood samples and 90,267 anthropometric measurements. Dietary data was obtained for a total sample of 40,018 individuals $\geq 1y$ (12).

A.5 National Health and Nutrition Survey (ENSANUT) 2012

The objective of the survey was to measure the trends, distribution and frequencies of the health and nutrition status of the Mexican population, as well as to assess the coverage and the quality of health services and some specific preventive health

programmes at a national level, and differences between urban and rural areas, and by socioeconomic status. In addition, ENSANUT 2012 provides evidence about the health coverage of Mexican families (13, 14).

A.5.1 Survey Design

The survey had a probabilistic multistage randomised design that was nationally representative and could distinguish between urban and rural areas and by state.

Sample design

ENSANUT 2012 had a similar sample design as ENSANUT 2006. The survey design allowed differentiation between the rural and urban populations and between four different geographic regions (North, Centre, South and Mexico City).

The sampling unit BGSAs were built based on information of the “*Conteo de Población y Vivienda, 2005*” following the methodology used for ENSANUT 2006. Additionally, for this survey, they included communities of new creation that were identified in the 2010 population census. Compared with ENSANUT 2006, households in the 2012 survey from the most vulnerable sector of the country were over-sampled. This over-representation had the objective of increasing the estimation precision of the information regarding the high vulnerability population.

To account for this over-representation, the researchers built a deprivation index to apply to the BGSA. After the BGSAs were classified according to the deprivation index, 20% of the population was classified as high in the deprivation index. The calculated sample included 1,440 households by state and 288 households with the highest deprivation index within each state. BGSA were classified by: cities and metropolitan areas, urban areas, rural areas; each of the aforementioned stratified by high or low deprivation index, and communities of new creation.

Sample selection

1) Cities, metropolitan areas and urban areas: For the first stage, the BGSA were selected with a probability proportional to size, according to the total number of households. In the second stage, six blocks were selected with the probability proportional to the number of households in the block. Within each block six households were selected using a randomized sampling method.

2) Rural areas and communities of new creation: In the first stage they selected the BGSAs were selected according to the total number of households. During the second stage, three communities with probability proportional to size (number of households) were selected. During stage three, because of the characteristics of rural areas, groups of household, called pseudoblocks, were built that contained approximate 50 households. After a pseudoblock was selected, by randomization, groups of 12 households were classified into groups and by randomization one of these groups of 12 households was chosen to be surveyed.

Sample Size

The total sample calculated was of 55,008 homes, including 1,719 homes by state. This number took into account the expected response rate. If the population of the households allowed it, an individual from each group of interest, children (0- 4y); school age children (5-9y); adolescents (10-19y) and adults ($\geq 20y$), and one or two health services users, was selected by randomization.

The survey identified as their unit of analysis six different groups as also defined in ENSANUT 2006: Home, health services users, and four different age groups.

A.5.2 Survey content

The survey included a total of six questionnaires (household, health services user, child, school age children, adolescent and adult), anthropometric measurements and collection of blood samples (capillary and venous) and dietary information. The researchers collected dietary information using two methods: a food frequency

questionnaire and a 24hr dietary recall. The content of the questionnaires was similar to the one describe for ENSANUT 2006.

The survey also collected information about the participation of the population in food aid and health programmes, including “*Oportunidades/Prospera*”.

A.5.3 Fieldwork

The method for data collection used was face to face interview and the tools (measurements and interviews) were taken by trained personnel.

The survey was applied in three stages by two different groups: a health and a nutrition team as in ENSANUT 2006.

Subsamples

Blood samples: One-third of the surveyed population (37%), which included all age groups ≥ 2 years old, was selected as a subsample to obtain blood samples.

Dietary information: A food frequency questionnaire was administered in 11% of the population and 24hr dietary recall was assessed in a subsample of 13% of the interviewed population.

A.5.4 Weights

Survey weights were estimated at household and individual level, for the main sample and for the subsamples. Weights were adjusted for survey non-response.

A.5.5 Response rate

The ENSANUT 2012 had a response rate of 87% with a total of 50,528 household surveyed, 96,031 individual interviews and 14,104 health services user questionnaires. By age group, information was collected about: 13,614 children 0 to 4y; 14,595 aged 5 to 9y; 21,519 adolescents (10 to 19y); and 46,303 adults (≥ 20 y).

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Appendix B. Future trends of obesity prevalence by 2030 by different statistical methods for projected

Appendix table B-1 Predicted male obesity prevalence by 2030 using different methods of projections

Age group	Linear Trends		Aggregated Data		Squared	
	%	95% CI	%	95% CI	%	95% CI
20-24	29.4	24.3, 34.5	28.9	22.0, 35.9	28.9	-12.4, 68.9
25-29	38.9	37.2, 40.6	38.8	30.9, 46.8	43.9	-4.8, 92.6
30-34	42.5	32.7, 52.2	42.4	33.4, 51.4	67.4	19.7, 115.1
35-39	48.0	41.0, 55.1	48.5	38.2, 58.8	52.9	-12.0, 117.8
40-44	54.4	45.3, 63.5	54.2	44.6, 63.7	32.1	-33.0, 97.3
45-49	35.9	10.8, 61.1	36.6	24.8, 48.4	40.1	-43.2, 123.5
50-55	34.5	22.0, 47.0	34.1	21.7, 46.4	10.6	-70.0, 91.3
55-59	32.9	13.4, 52.4	30.0	18.1, 42.0	-43.8	-122.9, 35.3
60-64	28.3	18.7, 38.0	27.7	15.9, 39.5	1.4	-70.0, 72.7
65-69	17.0	5.0, 29.0	18.1	5.9, 30.3	54.4	-24.4, 133.2
70-74	27.2	10.8, 43.7	28.7	14.9, 42.5	79.8	-0.9, 160.5
75-79	20.8	-7.9, 49.6	17.2	-3.1, 37.4	-50.0	-167.5, 67.6
80+	8.2	3.4, 12.9	8.8	-3.9, 21.5	23.0	-43.6, 89.7

Appendix table B-2 Predicted female obesity prevalence by 2030 using different methods of projection

Age group	Linear Trends		Aggregated Data		Squared	
	%	95% CI	%	95% CI	%	95% CI
20-24	29.8	22.8, 36.8	29.9	23.0, 36.9	59.0	20.0, 98.0
25-29	40.0	32.4, 47.6	39.8	32.3, 47.3	8.3	-33.4, 49.9
30-34	47.6	41.3, 53.9	47.9	40.9, 54.8	63.5	24.3, 102.7
35-39	53.9	50.6, 57.2	53.8	46.6, 61.0	45.5	3.0, 88.1
40-44	50.3	46.2, 54.5	50.0	42.5, 57.5	35.1	-11.2, 81.4
45-49	61.0	52.6, 69.3	61.9	51.9, 71.9	90.5	29.4, 151.6
50-55	59.9	42.8, 77.1	60.6	50.8, 70.5	74.3	16.5, 132.2
55-59	57.7	46.0, 69.5	57.1	45.0, 69.3	41.7	-33.3, 116.7
60-64	56.5	37.5, 75.5	54.2	41.2, 67.3	-23.0	-101.1, 55.1
65-69	54.5	48.3, 60.6	55.1	41.0, 69.3	70.9	-10.5, 152.2
70-74	54.9	40.7, 69.2	55.3	37.9, 72.6	52.6	-44.4, 149.6
75-79	36.0	25.2, 46.7	35.4	17.8, 52.9	31.2	-68.6, 130.9
80+	23.5	3.5, 43.4	24.0	8.1, 40.0	56.2	-27.6, 140.1

Appendix C. Calculations estimated for each disease for the MexOb-Model

The set of tables below shows the transition probabilities that were originally obtained by the non-parametric equation, as described in Chapter 4.

C.1 Hypertension (HT)

Appendix table C-1 Transition probabilities between health states in the Mexican male obese population for hypertension

Age group	Obese-Obese (A-A)	Obese-Obese-HT (A-B)	Obese-Dead (A-C)	Obese HT – Obese HT (B-B)	Obese HT-Dead (B-C)
20-24	0.9842	0.0152	0.0007	0.0152	0.0009
25-29	0.9717	0.0264	0.0019	0.0264	0.0022
30-34	0.9571	0.0399	0.0030	0.0399	0.0035
35-39	0.9394	0.0565	0.0042	0.0565	0.0047
40-44	0.9132	0.0815	0.0054	0.0815	0.0061
45-49	0.8649	0.1283	0.0067	0.1283	0.0081
50-54	0.7924	0.1983	0.0093	0.1983	0.0113
55-59	0.7467	0.2389	0.0145	0.2389	0.0160
60-64	0.7442	0.2334	0.0224	0.2334	0.0221
65-69	0.8328	0.1331	0.0341	0.1331	0.0296
70-74	0.9157	0.0390	0.0453	0.0390	0.0374
75-79	1.0074	-0.0642	0.0568	-0.0642	0.0456

Appendix table C-2 Transition probabilities between health states in the Mexican female obese population for hypertension

Age group	Obese-Obese (A-A)	Obese-Obese-HT (A-B)	Obese-Dead (A-C)	Obese HT – Obese HT (B-B)	Obese HT-Dead (B-C)
20-24	0.9811	0.0189	0.0000	0.0189	0.0001
25-29	0.9628	0.0367	0.0005	0.0367	0.0007
30-34	0.9439	0.0551	0.0010	0.0551	0.0013
35-39	0.9255	0.0730	0.0015	0.0730	0.0019
40-44	0.9054	0.0921	0.0025	0.0921	0.0029
45-49	0.8873	0.1087	0.0040	0.1087	0.0043
50-54	0.8743	0.1195	0.0061	0.1195	0.0068
55-59	0.8669	0.1239	0.0091	0.1239	0.0104
60-64	0.8526	0.1345	0.0129	0.1345	0.0147
65-69	0.8304	0.1520	0.0176	0.1520	0.0197
70-74	0.8075	0.1701	0.0224	0.1701	0.0250
75-79	0.7779	0.1946	0.0275	0.1946	0.0305

C.2 Type 2 diabetes mellitus (T2DM)

Appendix table C-3 Transition probabilities between health states in the Mexican male obese population for type 2 diabetes mellitus

Age group	Obese-Obese (A-A)	Obese-Obese-T2DM (A-B)	Obese-Dead (A-C)	Obese T2DM – Obese T2DM (B-B)	Obese T2DM-Dead (B-C)
20-24	0.9564	0.0429	0.0007	0.0429	0.0003
25-29	0.9534	0.0450	0.0016	0.0450	0.0009
30-34	0.9500	0.0474	0.0026	0.0474	0.0015
35-39	0.9453	0.0510	0.0036	0.0510	0.0021
40-44	0.9313	0.0633	0.0054	0.0633	0.0029
45-49	0.9180	0.0730	0.0089	0.0730	0.0042
50-54	0.9197	0.0661	0.0142	0.0661	0.0061
55-59	0.9347	0.0458	0.0195	0.0458	0.0087
60-64	0.9612	0.0129	0.0260	0.0129	0.0122
65-69	0.9996	-0.0341	0.0345	-0.0341	0.0163
70-74	1.0397	-0.0824	0.0427	-0.0824	0.0205
75-79	1.0780	-0.1291	0.0511	-0.1291	0.0249

Appendix table C-4 Transition probabilities between health states in the Mexican female obese population for type 2 diabetes mellitus

Age group	Obese-Obese (A-A)	Obese-Obese-T2DM (A-B)	Obese-Dead (A-C)	Obese T2DM – Obese T2DM (B-B)	Obese T2DM-Dead (B-C)
20-24	1.0219	-0.0219	0.0000	-0.0219	0.0000
25-29	1.0037	-0.0042	0.0005	-0.0042	0.0002
30-34	0.9856	0.0134	0.0010	0.0134	0.0005
35-39	0.9671	0.0315	0.0015	0.0315	0.0008
40-44	0.9522	0.0455	0.0024	0.0455	0.0013
45-49	0.9426	0.0536	0.0038	0.0536	0.0019
50-54	0.9544	0.0394	0.0062	0.0394	0.0028
55-59	0.9708	0.0198	0.0094	0.0198	0.0067
60-64	1.0003	-0.0143	0.0140	-0.0143	0.0104
65-69	1.0875	-0.1084	0.0209	-0.1084	0.0143
70-74	1.1735	-0.2015	0.0280	-0.2015	0.0182
75-79	1.2613	-0.2967	0.0354	-0.2967	0.0221

C.3 Hypertriglyceridaemia (HTG)

Appendix table C-5 Transition probabilities between health states in the Mexican male obese population for hypertriglyceridaemia

Age group	Obese-Obese (A-A)	Obese-Obese-HTG (A-B)	Obese-Dead (A-C)	Obese HTG – Obese HTG (B-B)	Obese HTG-Dead (B-C)
20-24	0.9581	0.0413	0.0006	0.0413	0.0007
25-29	0.9755	0.0229	0.0017	0.0229	0.0017
30-34	0.9938	0.0035	0.0027	0.0035	0.0028
35-39	1.0147	-0.0185	0.0038	-0.0185	0.0038
40-44	1.0003	-0.0055	0.0052	-0.0055	0.0051
45-49	0.9848	0.0082	0.0070	0.0082	0.0068
50-54	1.0065	-0.0164	0.0099	-0.0164	0.0097
55-59	1.0264	-0.0405	0.0141	-0.0405	0.0145
60-64	1.0487	-0.0693	0.0205	-0.0693	0.0206
65-69	1.1126	-0.1430	0.0304	-0.1430	0.0280
70-74	1.1800	-0.2205	0.0405	-0.2205	0.0356
75-79	1.2410	-0.2921	0.0511	-0.2921	0.0437

Appendix table C-6 Transition probabilities between health states in the Mexican female obese population for hypertriglyceridaemia

Age group	Obese-Obese (A-A)	Obese-Obese-HTG (A-B)	Obese-Dead (A-C)	Obese HTG –Obese HTG (B-B)	Obese HTG-Dead (B-C)
20-24	0.9314	0.0689	-0.0003	0.0689	0.0000
25-29	0.9391	0.0605	0.0003	0.0605	0.0005
30-34	0.9500	0.0489	0.0011	0.0489	0.0010
35-39	0.9658	0.0321	0.0020	0.0321	0.0015
40-44	0.9964	-0.0013	0.0049	-0.0013	0.0023
45-49	1.0205	-0.0272	0.0067	-0.0272	0.0036
50-54	1.0411	-0.0499	0.0088	-0.0499	0.0058
55-59	1.0524	-0.0645	0.0121	-0.0645	0.0099
60-64	1.0485	-0.0634	0.0149	-0.0634	0.0149
65-69	1.0398	-0.0551	0.0153	-0.0551	0.0209
70-74	1.0286	-0.0438	0.0152	-0.0438	0.0270
75-79	1.0173	-0.0327	0.0154	-0.0327	0.0334

C.4 Hypercholesterolaemia (HCl)

Appendix table C-7 Transition probabilities between health states in the Mexican male obese population for hypercholesterolaemia

Age group	Obese-Obese (A-A)	Obese-Obese-HCl (A-B)	Obese-Dead (A-C)	Obese HCl –Obese HCl (B-B)	Obese HCl-Dead (B-C)
20-24	0.9995	0.0001	0.0004	0.0001	0.0009
25-29	0.9848	0.0134	0.0017	0.0134	0.0021
30-34	0.9698	0.0272	0.0030	0.0272	0.0033
35-39	0.9574	0.0383	0.0043	0.0383	0.0045
40-44	0.9478	0.0468	0.0054	0.0468	0.0059
45-49	0.9338	0.0596	0.0066	0.0596	0.0080
50-54	0.9449	0.0476	0.0075	0.0476	0.0112
55-59	1.1775	-0.1938	0.0163	-0.1938	0.0155
60-64	1.3425	-0.3670	0.0245	-0.3670	0.0207
65-69	1.5018	-0.5358	0.0340	-0.5358	0.0267
70-74	1.6679	-0.7110	0.0431	-0.7110	0.0330
75-79	1.8338	-0.8861	0.0524	-0.8861	0.0394

Appendix table C-8 Transition probabilities between health states in the Mexican female obese population for hypercholesterolaemia

Age group	Obese-Obese (A-A)	Obese-Obese-HCI (A-B)	Obese-Dead (A-C)	Obese HCI – Obese HCI (B-B)	Obese HCI-Dead (B-C)
20-24	0.9509	0.0491	0.0000	0.0491	0.0001
25-29	0.9506	0.0490	0.0004	0.0490	0.0006
30-34	0.9515	0.0475	0.0009	0.0475	0.0012
35-39	0.9548	0.0437	0.0014	0.0437	0.0018
40-44	0.9602	0.0374	0.0025	0.0374	0.0026
45-49	0.9695	0.0266	0.0039	0.0266	0.0037
50-54	0.9818	0.0124	0.0058	0.0124	0.0061
55-59	0.9834	0.0075	0.0091	0.0075	0.0124
60-64	0.9696	0.0157	0.0146	0.0157	0.0185
65-69	0.9514	0.0277	0.0209	0.0277	0.0252
70-74	0.9313	0.0414	0.0272	0.0414	0.0319
75-79	0.9064	0.0599	0.0337	0.0599	0.0388

Appendix D. Diabetes prevalence in obese population using a different hazard ratio for mortality

Projection models, as it has been said in previous chapters, are highly dependent of the data used to feed the model. For the MexOb-T2DM model, I decided to use Jackson et al. hazard ratio (HR: 0.52) as it was the reference that gave information specifically for my target group “obese-with or without disease population”. However, to assess if my results were different if I used a HR like the ones used for the other diseases targeting general population.

To do this exercises, I used the HR published by Hunt et al. which used for their calculation Mexican-American population born in Mexico.

Appendix Table D-1 Risk ratios and hazard ratios used to estimate mortality rates for the obese obese-with-diabetes populations

Variable	Hazard Ratio (HR) / Risk Ratio (RR)*	Population	Reference
T2DM [†] (diabetes vs. no diabetes)	HR: 1.65 (0.92, 2.96)	Mexican-Americans General Population	Hunt et al. 2011

*HR/RR assumed to be the same for males and females

†: Type 2 diabetes mellitus

1. Hunt KJ, Gonzalez ME, Lopez R, Haffner SM, Stern MP, Gonzalez-Villalpando C. Diabetes is more lethal in Mexicans and Mexican-Americans compared to Non-Hispanic whites. *Ann Epidemiol.* 2011;21(12):899-906.

D.1 Results

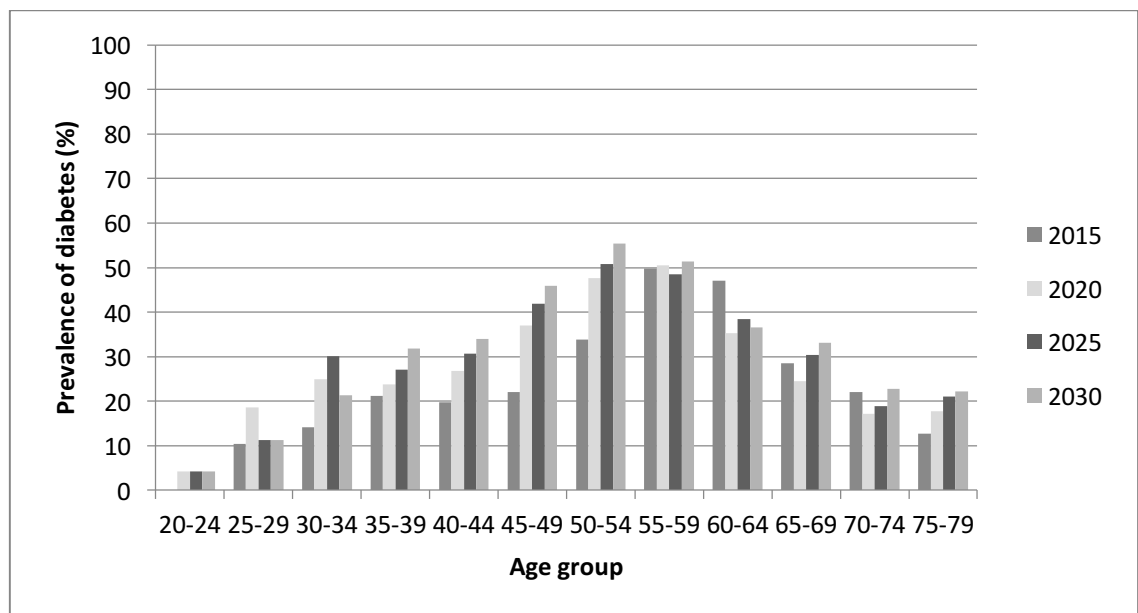
D.1.1 Cumulative number of new cases

Appendix figure D-1 and Appendix figure D-2 show the prevalence of obese-diabetes male and female population. The results predicted that the obese population 45 to 54y will have the highest increase in diabetes prevalence in the 15year period.

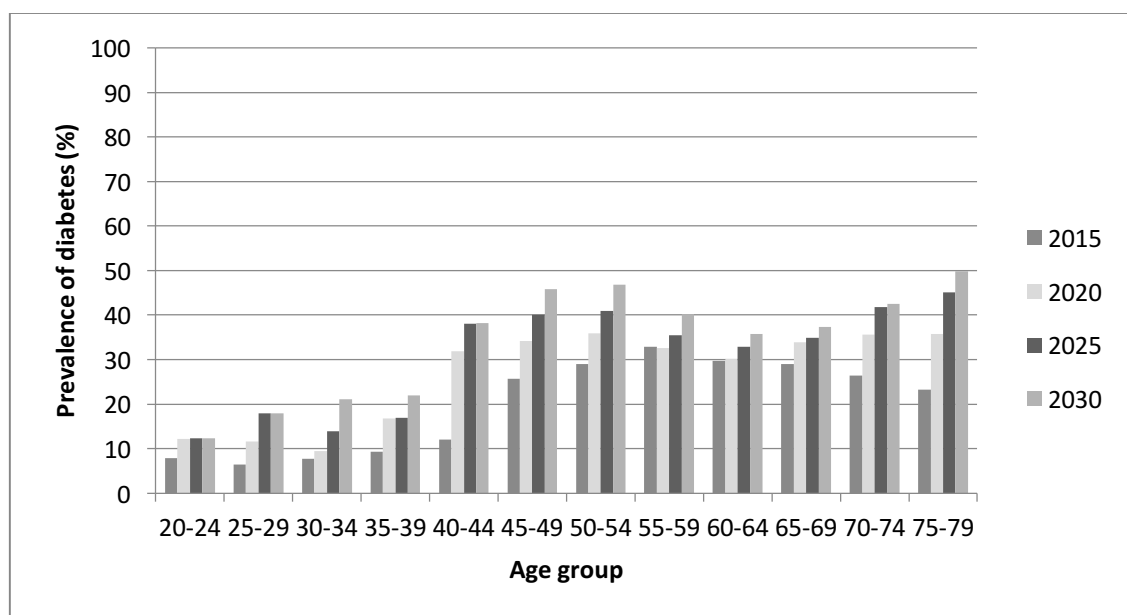
For males, the large increase in obese-diabetes prevalence were due to the increase in the disease prevalence of the males aged 45 to 54y. These age groups showed the biggest annual increase from all the age groups (1.6 pp/year and 1.4 pp/year, respectively).

The diabetes model for females showed the biggest increase an disease prevalence in the aged 40 to 54y female population with approximately 1 pp annual increase on obese-disease prevalence between 2015 and 2030 with the highest annual increase in the obese women aged 40 to 44y (1.7 pp/year).

Appendix figure D-1 Projected type 2 diabetes mellitus prevalence in obese male population 2015 to 2030 by age group



Appendix figure D-2 Projected type 2 diabetes mellitus prevalence in obese female population 2015 to 2030 by age group



D.1.2 Cumulative number of cases and deaths

Appendix table D-2 shows the cumulative number of new cases of type 2 diabetes are projected to growth almost four times in a 15 year period. The model results showed a higher number of new obese-diabetes females than males. From 20150 to 2030 there is expected to be approximately 4 million and 6 million new diabetes cases in the obese Mexican population.

Appendix table D-2 Cumulative number of new cases of obesity-related diabetes from 2015 to 2030 among Mexican males and females 20 to 79 years old in thousands.

	2020	2025	2030
Males	974	2,328	4,042
Females	1,565	3,850	6,806

The projected increase in obesity prevalence in a 15 year period could lead to around 1.6 million and 2 million deaths by 2030 for males and females respectively. The results showed that the number of deaths in obese-DM males will be higher than in females

(Appendix table D-3 Cumulative number of deaths from each the MexOb-DM model in obese males and females 20 to 79 years from 2030 in thousands Appendix table D-3).

Appendix table D-3 Cumulative number of deaths from each the MexOb-DM model in obese males and females 20 to 79 years from 2030 in thousands

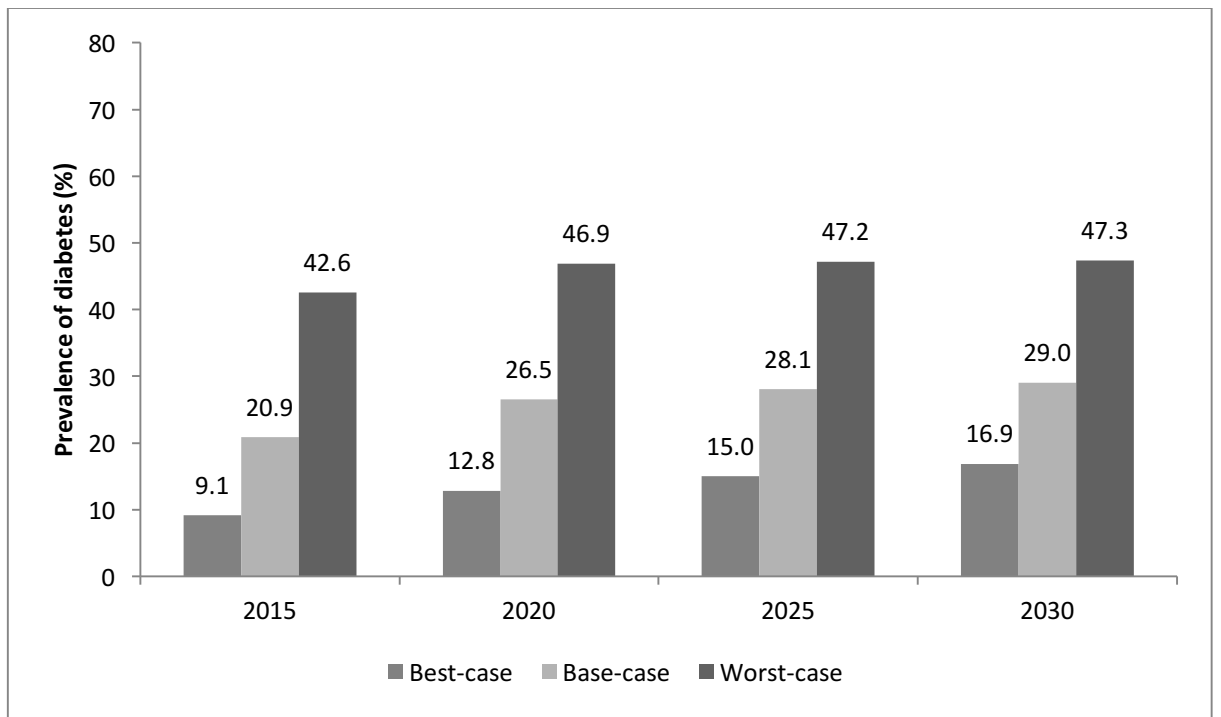
	2020		2025		2030	
	Obese	Obese + disease	Obese	Obese + disease	Obese	Obese + disease
Males	250	145	572	362	984	690
Females	354	112	837	309	1,466	627

Obese: category that refers to all the obese population without the cardiometabolic risks factor of interest

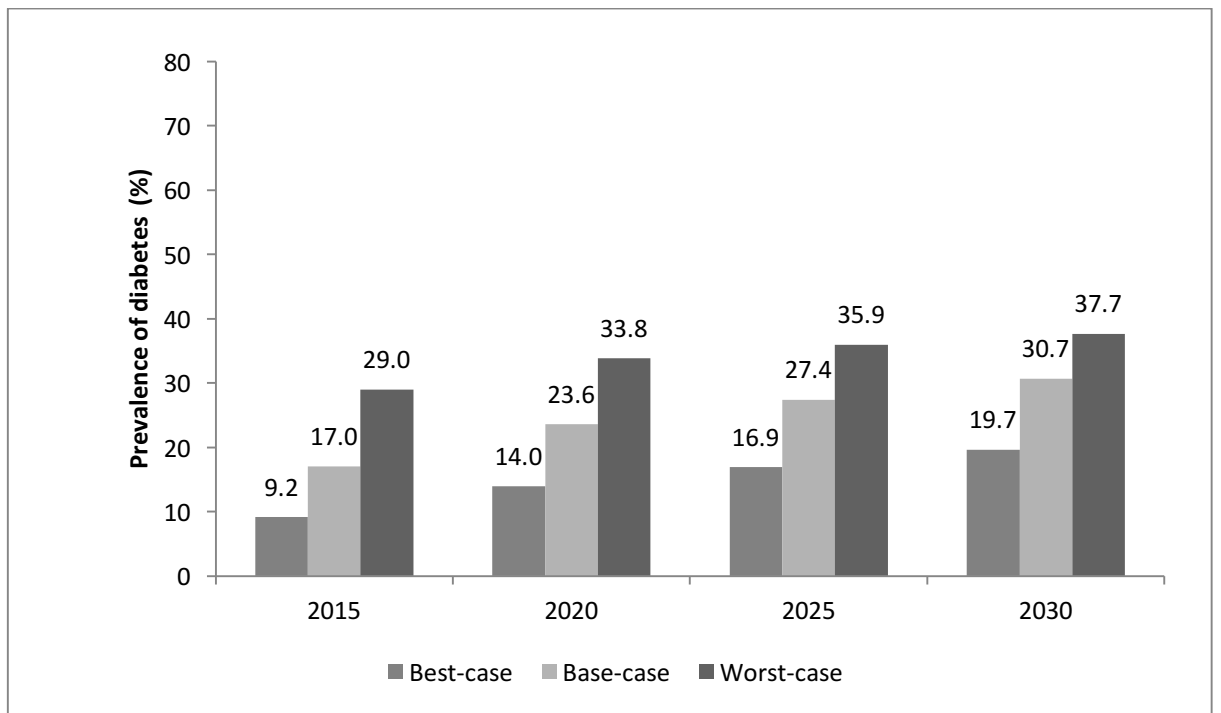
D.2 Sensitivity Analysis

The sensitivity analysis estimated that by 2030 the prevalence of obese female with diabetes could be between 38.9% and 20.4%, for the best and worst scenario respectively. For that same year, there could be between 48% and 17% obese men with diabetes, for the best and worst scenario respectively.

Appendix figure D-3 Total projected age standardized type 2 diabetes prevalence in the obese male population 2015 to 2030.



Appendix figure D-4 Total projected age standardized type 2 diabetes prevalence in the obese female population 2015 to 2030.



D.3 Discussion

The hazard ratios/risk ratios are an important component of the simulations models. There exist in the literature vast information about the risk of dying from a chronic disease in different populations. The results from these analysis using Hunt et al. hazard ratio compared to Jackson et al. used for the main simulation exercise. Overall the future estimated prevalence of diabetes for 2030 was lower for males and higher for females than the ones estimated for the main analysis.

For males, the results showed that the estimated prevalence of diabetes in obese males with the Hunt et al. hazard ratio was lower than the one from the main analysis. For the baseline prevalence, this difference was approximately 1% less, in absolute terms that the one originally estimated (30.9% main analysis vs. 29.0% in comparison analysis). Compared to the number of new disease cases from the main analysis, for 2030 the estimated number was approximately 7 hundred less cases.

A similar difference to the estimated prevalence with the two different HR between estimated percentage was observed for the estimated disease prevalence for the worst case-scenario. Between these estimates the highest absolute difference between percentages was observed for best-case scenario estimates (approximately 10%).

For females, the Hunt et al. hazard ratio estimates a higher prevalence of diabetes in obese women compared to the one obtained for the main analysis, a difference of around 4% in absolute terms (30.7% vs 26.2 %, respectively). However, the estimates obtained for best and worst case scenario do not showed a clear pattern of differences compared to the observed for men. Contrary to the pattern observed for males in the new cumulative number of cases, the use of this new HR estimated that by 2030 there will be seven hundred new cases of obese-diabetes more than with the HR from the main analysis.

Appendix E. Sensitivity analyses number of cumulative cases

Appendix table E-1 Best and worst-case scenario cumulative number of new cases of obesity-related cardiometabolic risk factors among Mexican obese males (20-79y) in thousands.

Cardiometabolic risk factor	2020		2025		2030	
	Best	Worst	Best	Worst	Best	Worst
Hypertension	983	2,083	2,200	5,837	3,542	11,578
Type 2 diabetes mellitus	945	1,954	2,376	5,081	4,115	9,790
Hypertriglyceridaemia	245	1,921	812	5,340	1,421	10,126
Hypercholesterolaemia	680	1,875	1,405	5,577	2,218	10,887

Best-case: using the lower 95%CI obesity projection linear trends β coefficients and obesity cardiometabolic risk factor prevalence from ENSANUT 2006

Worst-case: using the upper 95%CI obesity projection linear trends β coefficients and obesity cardiometabolic risk factor prevalence from ENSANUT 2006

Appendix table E-2 Best and worst-case scenario cumulative number of new cases of obesity-related cardiometabolic risk factors among Mexican obese females (20-79y) in thousands.

Cardiometabolic risk factor	2020		2025		2030	
	Best	Worst	Best	Worst	Best	Worst
Hypertension	2,054	2,846	4,474	6,996	7,332	12,563
Type 2 diabetes mellitus	985	1,834	2,268	4,738	3,808	8,408
Hypertriglyceridaemia	1,191	2,026	2,562	5,200	4,200	9,392
Hypercholesterolaemia	1,114	2,190	2,590	5,636	4,172	9,956

Best-case: using the lower 95%CI obesity projection linear trends β coefficients and obesity cardiometabolic risk factor prevalence from ENSANUT 2006

Worst-case: using the upper 95%CI obesity projection linear trends β coefficients and obesity cardiometabolic risk factor prevalence from ENSANUT 2006

