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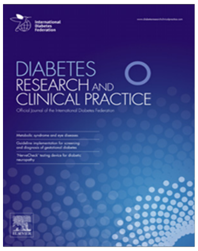

Forecasting the burden of type 2 diabetes mellitus in Qatar to 2050: A novel modeling approach

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ABSTRACT

Aims: We developed and demonstrated a novel mathematical modeling approach to forecast the burden of type 2 diabetes mellitus (T2DM) and to investigate T2DM epidemiology for the purpose of informing public health policy and programming.

Methods: A population-level compartmental mathematical model was constructed and applied to Qatar. The model was stratified according to sex, age group, risk factor status, and T2DM status, and was parameterized by nationally-representative data.

Results: T2DM prevalence increased from 16.7% in 2012 to at least 24.0% by 2050. The rise in T2DM was most prominent among 45–54 years old. T2DM health expenditure was estimated to increase by 200–600% and to account for up to 32% of total health expenditure by 2050. Prevalence of obesity, smoking, and physical inactivity was predicted to increase from 41.4% to 51.0%, from 16.4% to 19.4%, and from 45.9% to 53.0%, respectively. The proportion of T2DM incidence attributed to obesity, smoking and physical inactivity was estimated at 57.5%, 1.8%, and 5.4%, respectively in 2012, and 65.7%, 2.1%, and 6.0%, respectively in 2050. Exploring different scenarios for the trends in risk factors, T2DM prevalence reached up to 37.7% by 2050.

Conclusions: Using our innovative approach, a rising T2DM epidemic is predicted to continue in the next decades, driven by population growth, ageing and adverse trends in risk factors. Obesity was the principal risk factor explaining two-thirds of T2DM incidence. T2DM must be a national priority addressed by preventive and therapeutic interventions targeting T2DM and its modifiable risk factors.

1. Introduction

The burgeoning epidemic of diabetes mellitus (DM) is an eminent global health challenge of the 21st century [1] with a predicted 642 million people living with DM by 2040 [2]. The Middle East and North Africa (MENA) is projected to have one of the largest proportional increases in the number of adults with DM by 2040 (96.2%) [2,3].

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Type 2 diabetes mellitus (T2DM) epidemiology is influenced by several demographic and socio-behavioral health determinants [2]. Socio-demographic factors include globalization, urbanization, and increased life expectancy [4,5], while behavioral risk factors include obesity (BMI > 30 kg/m^2) [6–8] smoking [9,10], and physical inactivity [11,12] among others.

In the first national population-based survey in 2012 [13], Qatar, part of MENA, reported a DM prevalence (for diagnosed and undiagnosed T2DM and Type 1 DM) of 16.7% (95% confidence interval [CI] 13.7–19.8) among adult Qatari nationals aged 18–64 years old; the tenth highest globally [14]. Prevalences of obesity, active smoking, and physical inactivity were reported in this survey as being 41.4% (95% CI 38.8–44.0), 16.4% (95% CI 14.3–18.4), and 45.9% (95% CI 42.2–49.6), respectively [13]. Accordingly, assessing the future T2DM burden in Qatar and its risk factors is critical to inform national public health policy, programming and resource allocation.

Several modeling studies projected DM prevalence in Qatar within the context of global estimations [14–21]. While factoring population aging, all assumed a constant age-specific DM prevalence over time [14–20]—an unrealistic assumption considering predicted increases of key risk factors in MENA [3,22]. While these models are informative, they do not capture dynamically the interactions and trends of risk factors, demography, and T2DM natural history, and are not amenable to assessments of impact of interventions against risk factors.

Against this background, we developed a dynamic forecasting and age-structured mathematical model for T2DM, a novel analytic framework, to *(i)* predict future T2DM prevalence and incidence, *(ii)* estimate health expenditures directly attributed to T2DM, and *(iii)* evaluate the effects of key risk factors and their complex overlap on T2DM. A key strength of our approach is its detailed stratification of the key risk factors of obesity, smoking, and physical inactivity and all of their possible overlaps. We present the methodological approach and results, as applied to Qatar, which can be applied across countries. This analytic framework can be also used to assess impact of interventions against T2DM and risk factors.

2. Subjects, materials and methods

We constructed a deterministic compartmental mathematical model that describes the development of T2DM in a given population—in this case, the Qatari population. The model was based on and informed by existing modeling approaches for non-communicable [23] and communicable diseases [24], and was structured to represent and utilize available epidemiological data. The model was parameterized using nationally-representative epidemiological and demographic data and programmed in MATLAB version 2015a [25].

2.1. *Mathematical model*

The model describes the four dimensions of sex, age, risk factor status, and T2DM status for a given population leading to a set of 640 differential equations that stratify the population based on these four dimensions (Appendix Fig. S1). The model disaggregates the population into 20 five-year age bands (0–4, 5–9. . . 95–99 years old) and incorporates four main susceptible classes: healthy (i.e. non-obese, non-smoker, physically active, and non-diabetic), obese, smoker, and physically inactive. It accounts for overlaps between risk factors by further stratifying the susceptible population into compartments with overlapping risk factors. Further details on model structure and assumptions can be found in Appendix Text S1.

2.2. *Data sources and model fitting*

The model was parameterized using epidemiological and natural history data, listed in Appendix Table S1. Further discussion of parameter values is provided in Appendix Text S1.

The model was fitted to sex- and age-specific T2DM, obesity, smoking and physical inactivity prevalence data using a non-linear least-square fitting method [25]. Seven sex- and age-specific measures were derived by generating the best fit: T2DM baseline incidence rate (i.e. incidence rate from "healthy" to T2DM), transition rates from healthy to obese, obese to healthy, healthy to smoker, smoker to healthy, healthy to physically inactive, and physically inactive to healthy.

2.3. *Plan of analysis and estimating T2DM and risk factors' future trends*

We used the best-fit parameters to predict trends in T2DM prevalence and incidence among Qataris aged 15–64 years between 2012 and 2050. The year 2012 was the baseline year, representing Qatar's only measured prevalence data.

Predicted risk factor trends and their effects on T2DM were also estimated between 2012 and 2050. The latter were estimated by calculating the total T2DM incident cases attributed to each risk factor, through population attributable fraction (PAF) approach. We adjusted for the overlap between risk factors using an adaptation of established PAF methodologies [26–28].

2.3.1. *The effect of future trends in risk factors on T2DM*

We investigated effects of risk factors on T2DM prevalence through five forecast scenarios. The trends in prevalence of smoking, obesity and physical inactivity in Qatar between 2012 and 2050 were based on WHO's country specific estimates [29,30].

Scenario 1: Forecast scenario assuming constant age-specific risk factor prevalences (demographic change only)

We assumed the age-specific risk factor prevalences remained the same between 2012 and 2050. Accordingly, trends in risk factors depend only on the demographic structure of the population. This was the baseline scenario for comparison.

Scenario 2: Forecast scenario based on increase in obesity

We assumed an annual increase of 1.05% in obesity prevalence [30] and no change in smoking and physical inactivity.

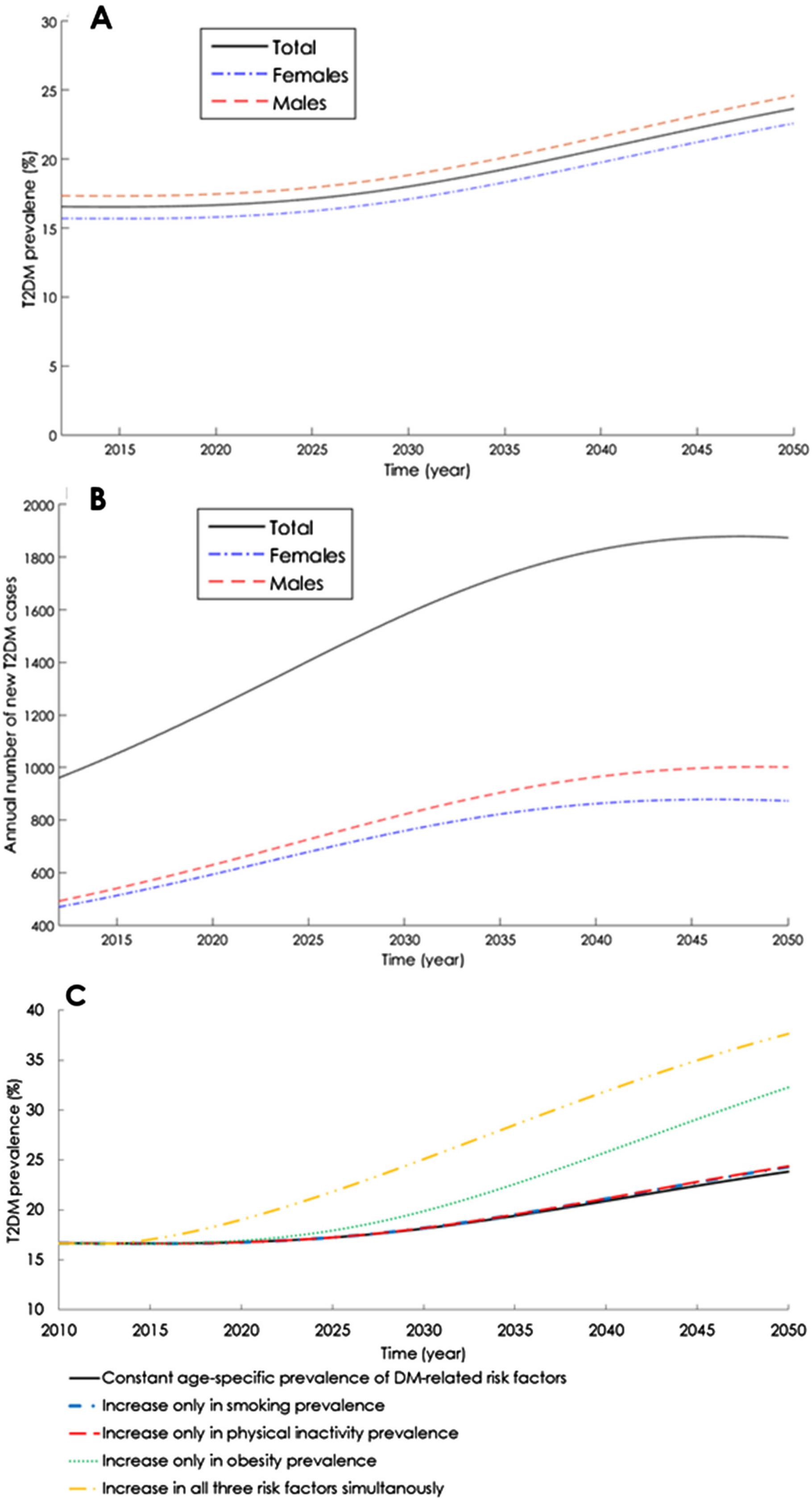

Fig. 1 – Projected type 2 diabetes mellitus (T2DM) among Qataris between 2012 and 2025. (A) Prevalence of T2DM. (B) Annual number of new T2DM cases. (C) Projected T2DM prevalence among Qataris in five forecast scenarios. In panels A and B, the solid black lines are the projections for the total population, the red dashed lines are the projections for males, and the blue dashed lines are the projections for females. In panel C, the lines show the five different projection scenarios of effects of trends in T2DM-related risk factors. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

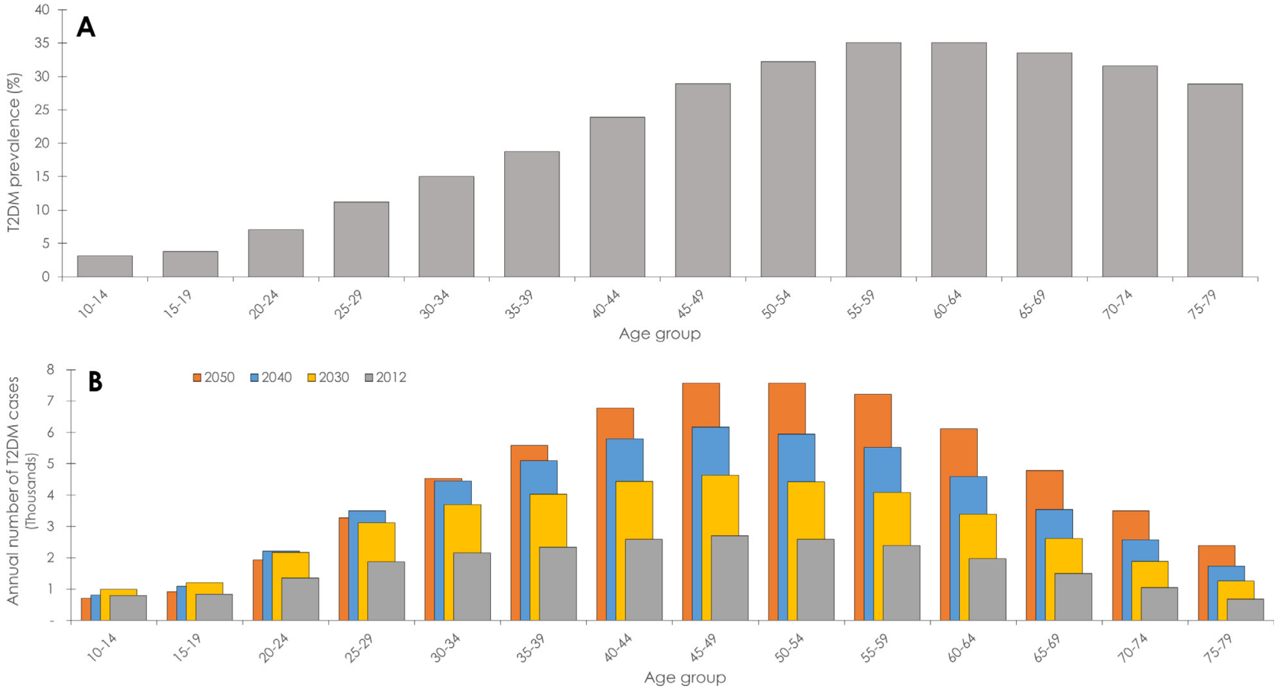

Fig. 2 – Age-specific characteristics of type 2 diabetes mellitus (T2DM) among Qataris. The figure shows (A) the age-specific T2DM prevalence (constant between 2012 and 2050), and (B) the age-specific T2DM incidence (annual number of new T2DM cases) in four different timeframes; 2012, 2030, 2040, and 2050.

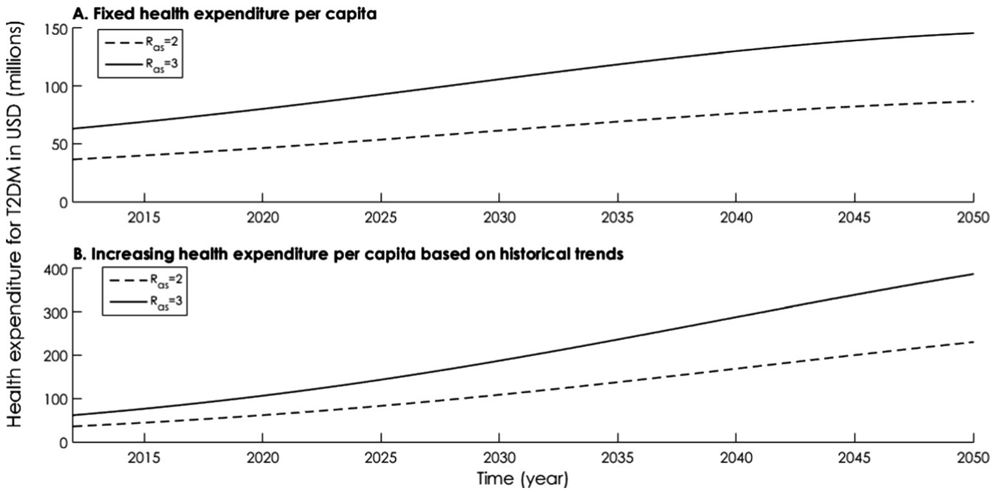

Fig. 3 – Projected total health expenditure for type 2 diabetes mellitus (T2DM) among Qataris between 2012 and 2050. The figure shows the expenditure assuming (A) fixed *per capita* health expenditure between 2012 and 2050, and (B) differential *per capita* health expenditure per year between 2012 and 2050 based on the historical increasing trend of *per capita* health expenditure in Qatar as provided by World Bank data [35]. The health expenditure directly attributed to T2DM out of Qatar's total healthcare expenditure on Qataris is calculated per the Jönsson's approach [31] of assuming a ratio of medical care expenditures for individuals with T2DM to individuals without T2DM in the range between 2 (dashed line) and 3 (solid line).

Scenario 3: Forecast scenario based on increase in smoking

We assumed an annual increase of 0.42% in smoking prevalence [29] and no change in obesity and physical inactivity.

Scenario 4: Forecast scenario based on increase in physical inactivity

In absence of reliable trend data on physical inactivity in Qatar, we assumed that trends in physical inactivity were similar to trends in obesity. Accordingly, we assumed an annual increase of 1.05% in physical inactivity prevalence and no change in obesity and smoking.

Scenario 5: Forecast scenario based on simultaneous trends in all risk factors

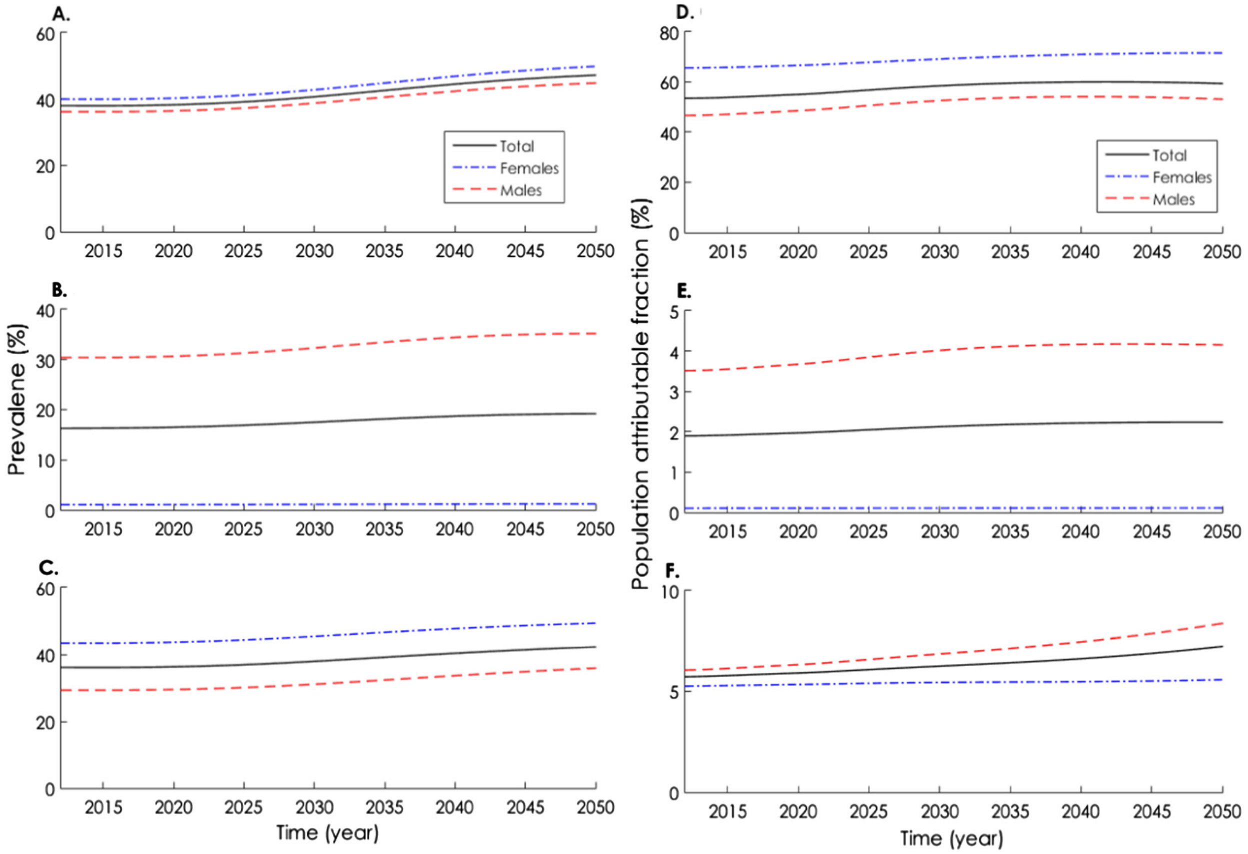

Fig. 4 – Projections for type 2 diabetes mellitus (T2DM) related risk factors among Qataris between 2012 and 2050. The figure shows projected prevalence of (A) obesity, (B) smoking, and (C) physical inactivity, and proportions of T2DM cases that are attributable to (D) obesity, (E) smoking, and (F) physical inactivity. The solid black lines are the projections for the total population, the red dashed lines are the projections for males, and the blue dashed lines are the projections for females. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

We assumed that prevalence of each risk factor would increase simultaneously—i.e. 1.05% increase in obesity and physical inactivity, and 0.42% increase in smoking.

2.3.2. *Projection of health expenditure for T2DM*

We used an approach developed by Jönsson to estimate health expenditures directly attributed to T2DM from a country's total health care expenditure (Appendix Text S1) [31]. Briefly, the relative ratio (R_{as}) of all health care expenditures between T2DM and non-T2DM individuals is the key parameter in the conversion of *per capita* health expenditure to estimates of T2DM attributable spending. Based on evidence, R_{as} was assumed to be between 2 and 3 [32]. We included the possibility of discounting on future expenditures. The main outcomes were reported with no discounting, but for comparison purposes, we applied an annual discount rate of 3% [33] for some of the results.

For projections of T2DM attributable national health expenditure, we applied two assumptions for Qatar's *per capita* health expenditure over time. First, we assumed that *per capita* health expenditure remained constant between 2012 and 2050 as estimated in 2012 (i.e. $2270 United States dollars) [34]. Second, we assumed that *per capita* health expenditure changed with time, based on the historical trend of *per capita* health expenditure in Qatar as provided by World Bank data (Appendix Fig. S4) [35].

2.3.3. *Sensitivity and uncertainty analyses*

Several univariate sensitivity analyses were conducted to assess robustness of model predictions to variations in relative risk (RR) of risk factors, RR of mortality in T2DM compared to the general population, and prevalence of physical inactivity at baseline year. The latter was conducted because of evidence suggesting that self-reported physical activity is inflated relative to objective biomarkers [36].

A multivariate uncertainty analysis was also performed to specify uncertainty ranges in projected prevalence estimates relative to variations in structural parameters of the model. We used Monte Carlo sampling from log-normal distributions for confidence intervals or ranges of plausibility of the epidemiological parameters of the model (Appendix Table S1). Random values from specified ranges were selected for the parameters at each run. This set of new parameters was employed to refit T2DM prevalence. We implemented 1000 runs of the model and determined the likelihood distributions and the 95% uncertainty intervals (UI) for the measures.

3. Results

3.1. Projections of T2DM prevalence and incidence

Fig. 1 illustrates the predicted T2DM prevalence and incidence between 2012 and 2050 among Qataris aged 15–64 years. Based only on the demographic structure change of Qataris (Appendix Fig. S3), the prevalence was predicted to increase from 16.7% in 2012 to 24.0% by 2050 (Fig. 1A). T2DM prevalence was higher among males than females; 17.5% in males compared to 15.9% in females in 2012, and predicted to be 24.9% compared to 22.9%, respectively, by 2050 (Fig. 1A).

Given the population size and its future projection (Appendix Fig. S2), a total of 20,953 Qataris had T2DM in 2012, with 978 new cases (Fig. 1B). The number of T2DM cases was predicted to increase to 51,921 cases by 2050, with 1907 new cases in that year.

T2DM prevalence was insignificant in the younger age groups and increased with age (Fig. 2A). T2DM prevalence peaked at 35.0% among 55–64 years old and decreased among those over 65 years old. The rise in T2DM cases in 2012–2050 was most prominent among 45–54 years old (Fig. 2B). The largest relative increase was found among 75–79 years old: T2DM cases in 2050 were 3.3 times higher than in 2012.

3.2. Health expenditure for T2DM

In 2012, the total T2DM health expenditure among Qataris ranged between $38.3 million (for a ratio of health care expenditure of $R_{as} = 2$) and $66.0 million ($R_{as} = 3$; Fig. 3). An average between $1800 ($R_{as} = 2$) and $3103 ($R_{as} = 3$) was expected to have been spent on each T2DM case in 2012.

Assuming a fixed health expenditure *per capita* per 2012, total T2DM health expenditure by 2050 was projected to be more than twice as large as that in 2012 (Fig. 3A); between $90.0 million ($R_{as} = 2$) and $150.3 million ($R_{as} = 3$). An average between $1734 ($R_{as} = 2$) and $2895 ($R_{as} = 3$) was expected to be spent on each T2DM case by 2050. Applying an annual discount rate of 3% on future expenditures, total T2DM health expenditure by 2050 was projected to range between $33.9 million ($R_{as} = 2$) and $56.7 million ($R_{as} = 3$).

Assuming continuation of the historical trend for *per capita* health expenditure in Qatar (Appendix Fig. S4), total T2DM health expenditure by 2050 was estimated to be about five times larger than that in 2012 (Fig. 3B); between $241.8 million ($R_{as} = 2$) and $400.8 million ($R_{as} = 3$). An average between $4658 ($R_{as} = 2$) and $7777 ($R_{as} = 3$) was expected to be spent on each T2DM case by 2050. Applying an annual discount rate of 3% on future expenditures, total T2DM health expenditure by 2050 was projected to range between $91.2 million ($R_{as} = 2$) and $152.2 million ($R_{as} = 3$).

3.3. Projections of T2DM-related risk factors

Fig. 4A–C illustrates the predicted prevalence of T2DM-related risk factors based only on the demographic structure change of Qataris. Prevalence of obesity, smoking, and physical inactivity was 41.4%, 16.4%, and 45.9%, respectively in 2012, and increased to 51.0%, 19.4%, and 53.0%, respectively by 2050.

Prevalence of obesity, smoking, and physical inactivity differed by sex. Males had much higher smoking prevalence compared to females: 30.5% versus 1.0% in 2012 and 35.3% versus 1.2% by 2050 (Fig. 4B). However, females had higher obesity prevalence compared to males: 43.2% versus 39.3% in 2012, and 53.4% versus 48.3% by 2050 (Fig. 4A). Similarly, females had higher physical inactivity rates compared to males: 54.2% versus 37.4% in 2012, and 60.7% versus 45.2% by 2050 (Fig. 4C).

3.4. Proportion of T2DM cases attributable to risk factors

Fig. 4D–F shows the proportions of T2DM cases among Qataris that are attributed to obesity, smoking, and physical inactivity. In 2012, T2DM incident cases attributed to obesity, smoking and physical inactivity were 57.5%, 1.8%, and 5.4%, respectively. By 2050, the proportions were projected to increase to 65.7%, 2.1%, and 6.0%, respectively. The proportions of T2DM cases attributable to risk factors differed by sex and are illustrated in Fig. 4D–F.

3.5. Effects of future trends in risk factors on T2DM

Fig. 1C and Appendix Table S2 quantify the effects of future trends in T2DM–related risk factors on T2DM prevalence by 2050. Four forecast scenarios were compared to the baseline scenario of constant age-specific distribution for the risk factors (*Scenario 1*). In the baseline scenario, T2DM prevalence reached 24.0% by 2050. The predicted T2DM prevalence by 2050 was slightly higher in *Scenario 3* (24.4%), in which only smoking prevalence increased, and in *Scenario 4* (24.5%), in which only physical inactivity increased. However, the predicted T2DM prevalence was considerably higher in *Scenario 2* (32.4%), in which only obesity increased, and was highest in *Scenario 5* (37.8%), in which all risk factors increased simultaneously. Of notice, as risk factors act simultaneously in overlapping compartments, their individual effect changes as the RRs are combined multiplicatively, thereby amplifying their effects on T2DM prevalence.

4. Discussion

We introduced a novel analytical mathematical modeling approach to investigate T2DM epidemiology, assess the role of key risk factors and their overlap in driving T2DM incidence and prevalence, and forecast T2DM-related health expenditures. The new model is an improvement to previous studies as it captures dynamically interactions and trends of risk factors, demography, and T2DM natural history. The model predicts T2DM over decades and provides a framework for generating strategic information to inform T2DM public health policy, programming and resource allocation at the national level. We applied the model to Qatar, a high-burden T2DM country, as an example, but can be applied across countries. The approach also offers a platform for extensions to assess the impact and cost-effectiveness of interventions against T2DM and risk factors.

Armed with nationally-representative population-based data, we projected T2DM burden in the Qatari population through 2050 along with its associated economic cost. T2DM prevalence in Qatar was projected to increase by at least 43%, in the most optimistic scenario, despite being already over twice the global average. Factoring in population growth and aging, the number of people with T2DM was projected to grow by 147% by 2050. Though T2DM health expenditure is already consuming nearly 20% of national health expenditure, it is projected to reach 32% by 2050. These findings highlight the urgency for cost-effective preventive and therapeutic interventions for T2DM and its risk factors as a national priority in Qatar.

A striking finding is that T2DM prevalence is driven by the high prevalence of obesity in this nation (41.4% in 2012). Smoking and physical inactivity contributed to T2DM's high and growing levels. While less than 10% of T2DM cases were attributed to smoking and physical inactivity combined, nearly 60% were attributed to obesity, and more so for females than males. If obesity prevalence among Qataris aged 20–79 years in 2012 was as low as that in Japan (around 4% [37]), T2DM prevalence would have decreased from 16.7% to 9.8% and stood at two percentage points higher than that in Japan (7.6% [38]; Appendix Fig. S5)—highlighting obesity as the leading driver of the T2DM epidemic in Qatar.

Demography influences the growing T2DM epidemic over the coming decades. The Qatari population was projected to grow by 73% between 2012 and 2050 (Appendix Fig. S2). A fairly rapid aging of this population (Appendix Fig. S3) leads to higher T2DM prevalence through its direct effect on T2DM, and its indirect effect on the risk factors that drive T2DM incidence. Obesity, for example, was projected to increase by 23% between 2012 and 2050 due to population aging (Fig. 4). If the prevalence of risk factors will increase due to factors other than population aging, our baseline projections will underestimate future T2DM prevalence. For example, an annual 1.05% increase in obesity, would result in an 8.5 percentage points increase in T2DM prevalence by 2050, from 24.0% to 32.3%.

There has been a debate about the role of genetic factors in Qatar's rising T2DM epidemic [39,40]. Our study indicates that more than two-thirds of T2DM incidence is attributed to modifiable risk factors including obesity, smoking and physical inactivity (Fig. 4). Genetic factors may have a significant role in T2DM epidemiology, but are not the main drivers of T2DM in Qatar. A public health focus on modifiable risk factors may prevent or even reverse the rising T2DM burden. Evidence indicates that lifestyle interventions can prevent the progression of impaired glucose tolerance, and therefore reducing the projected rise in T2DM prevalence [41,42]. The Finnish Diabetes Prevention Study has demonstrated that such preventive measures can lead to a 40% decrease in T2DM incidence [42]. Further to individual-based approaches that rely on behavioral change, population-based strategies such as taxation and marketing restrictions may prove to be more impactful [43]. However, adapting and testing such approaches to the Qatari context require further research on the feasibility and practicality of intervening against modifiable risk factors, such as physical activity, but this research continues to be underdeveloped in Qatar and the region [44].

Our projections for the rise of T2DM among Qataris are lower than those reported by the International Diabetes Federation (IDF) [45]. IDF estimated T2DM prevalence for those aged 20–79 at 13.5% in 2015 and at 21.0% in 2040—an increase of 56% [45]. Our study predicts an increase of 26%, from 16.7% in 2015 to 21.1% in 2040. IDF uses a logistic regression method for estimation rather than a dynamical population-level model, and uses data from Qatar's neighboring countries for its projections [46–51], while we parameterized our model using Qatar's population-based data.

Our predictions are consistent with the increasing T2DM in MENA, and in the Arabian Gulf countries in particular [45]. T2DM prevalence among Qataris is similar to other neighboring countries including Bahrain (15.6%), Saudi Arabia (17.6%), Kuwait (14.3%), and the United Arab Emirates (14.6%) [45].

Limitations may have affected our results. Although we used an elaborate mathematical model to capture the complexity of T2DM dynamics, our predictions may depend on the type of mathematical model used. Our predictions rely on availability of representative epidemiological, demographic and economic data for T2DM, but limitations in input data can lead to limitations in model predictions. There has been one nationally-representative population-based survey in Qatar for T2DM and its risk factors [13], however, the precision of our projections would have been enhanced, if more trend data were available. In the STEPwise survey, fasting capillary blood glucose testing was used as opposed to venous testing, but data suggests reliability of capillary testing for measuring T2DM prevalence [52]. The relative ratio of healthcare expenditure between T2DM and non-T2DM individuals has not been formally assessed in Qatar. However, this ratio has been assessed for other countries in the range of 2–3 [31], and we used this range to bracket our estimate for T2DM economic burden. Estimates of the RRs associated with the three risk factors were obtained from large, recent systematic reviews which were global in scope, but it is possible that their magnitude may be different in Qatar.

Given potential limitations and to assess the reliability of our predictions, we conducted several sensitivity analyses (Appendix Fig. S7). These analyses demonstrated that our results are sensitive to the RR of developing T2DM if obese, as expected given that nearly 60% of T2DM is attributed to obesity. The analyses have also shown sensitivity to large biases in self-reported prevalence of physical inactivity, highlighting the need for use of objective biomarkers in physical activity surveys. Otherwise our results were insensitive to variations in the rest of explored parameters.

Given the sensitivity to the RRs of developing T2DM, we conducted a multivariate uncertainty analysis to assess the uncertainty in model output given the uncertainty in model input for the RRs of risk factors and other parameters (Appendix Fig. S6). The results demonstrated narrow UIs around our point estimates, thanks to the narrow 95% CIs around the input parameters. Therefore, the sensitivity and uncertainty analyses affirmed the validity of our predictions.

5. Conclusions

We developed and demonstrated the utility of an analytical approach to investigate T2DM epidemiology, drivers of T2DM incidence and economic burden, and to provide a strategic framework to inform public health policy, programming and resource allocation. The model was applied to Qatar where we predicted a rising T2DM epidemic driven by population growth and aging, and growing levels of risk factors. Importantly, we found that obesity is the driver of over half of T2DM incidence among Qataris, and that at least one-third of Qatar's health expenditure is destined to be spent on T2DM by 2050. These expenditures should be seen in context of the wider burden of T2DM on individuals, their families, and society in terms of premature departure from the workforce, reduced quality of life, and early mortality. The high cost of T2DM even in a wealthy country like Qatar should receive the attention that it deserves.

These findings highlight the urgency for introduction and expansion of cost-effective preventive and therapeutic interventions targeting T2DM and its modifiable risk factors as a national priority. If effectively implemented, lifestyle interventions can prevent or even reverse the expansion of this epidemic in a nation that is already burdened by this disease.

Disclaimer

The statements made herein are solely the responsibility of the authors. The funders had no role in the design, conduct, or analysis of the study.

Author contributions

SFA, JC, and LJA conceived the study. SFA designed the model and conducted the analyses. LJA contributed to the model design and conduct of the analyses. SFA, JC, MO, and LJA analyzed and interpreted the results. SFA wrote the first draft of the article. All authors contributed to the writing of the manuscript.

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Competing interests

The authors have declared that no competing interests exist.

Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.diabres.2017.11.015.

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