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A mathematical model for determining age-specific diabetes incidence and prevalence using body mass index

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ABSTRACT

Purpose: Few models have been developed specifically for the epidemiology of diabetes. Diabetes incidence is critical in predicting diabetes prevalence. However, reliable estimates of disease incidence rates are difficult to obtain. The aim of this study was to propose a mathematical framework for predicting diabetes prevalence using incidence rates estimated within the model using body mass index (BMI) data. Methods: A generic mechanistic model was proposed considering birth, death, migration, aging, and diabetes incidence dynamics. Diabetes incidence rates were determined within the model using their relationships with BMI represented by the Hill equation. The Hill equation parameters were estimated by fitting the model to National Health and Nutrition Examination Survey (NHANES) 1999-2010 data and used to predict diabetes prevalence pertaining to each NHANES survey year. The prevalences were also predicted using diabetes incidence rates calculated from the NHANES data themselves. The model was used to estimate death rate parameters and to quantify sensitivities of prevalence to each population dynamic. Results: The model using incidence rate estimates from the Hill equations successfully predicted diabetes prevalence of younger, middle-aged, and older adults (prediction error, 20.0%, 9.64%, and 7.58% respectively). Diabetes prevalence was positively associated with diabetes incidence in every age group, but the associations among younger adults were stronger. In contrast, diabetes prevalence was more sensitive to death rates in older adults than younger adults. Both diabetes incidence and prevalence were strongly sensitive to BMI at younger ages, but sensitivity gradually declined as age progressed. Younger and middle aged adults diagnosed with diabetes had at least a two-fold greater risk of death than their nondiabetic counterparts. Nondiabetic older adults were found to be under slightly higher death risk (0.079) than those diagnosed with diabetes (0.073).

Conclusions: The proposed model predicts diagnosed diabetes incidence and prevalence reasonably well using the link between BMI and diabetes development risk. Ethnic group and gender-specific model parameter estimates could further improve predictions. Model prediction accuracy and applicability need to be comprehensively evaluated with independent data sets.

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Introduction

Diabetes prevalence is rising dramatically worldwide and is expected to rise from 366 million in 2011 to 552 million by 2030 [\[1\].](#page--1-0) More than 10% of world health care expenditure and about 14% of U.S. healthcare costs are attributable to diabetes [\[2\]](#page--1-0). Quantifying diabetes prevalence is important to allow rational planning of prevention programs and allocating resources for people affected by diabetes [\[2\]](#page--1-0). Mathematical models can be used effectively to estimate disease prevalence and help understand factors affecting disease development risk. The majority of diabetes-

related mathematical models explain clinical aspects of glucoseinsulin dynamics, whereas few models have been specific to the epidemiology of diabetes [\[3\]](#page--1-0). Diabetes prevalence varies significantly with age implying the mechanisms underlying risk of developing diabetes could be age specific. Boutayeb and Derouich [\[4\]](#page--1-0) proposed a mathematical model for predicting the age-specific prevalence of diabetes and its complications. Accurate prevalence predictions from such a model require reliable estimates of diabetes population dynamics, such as incidence rates and death rates.

Prevalence is the proportion of a population affected by a disease at a particular time point, whereas the incidence rate is the rate of occurrence of new cases of the disease. Incidence rates, indicative of risk of contracting or developing the disease, can be also used to measure the efficacy of disease prevention strategies. Nonetheless, obtaining reliable diabetes incidence rate estimates is often

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Fig. 1. Schematic representation of the model. Boxes, solid arrows and dashed arrows represent pools (Q), flows (F), and effects of body mass index (BMI) on diabetes incidence, respectively. Letter 'D' and 'H' denote diagnosed diabetic and nondiabetic individuals respectively. Time unit for the model is a year (y).

challenging and requires larger survey samples than those required for prevalence estimates. Therefore, a mathematical representation calculating diabetes incidence rates within the model itself can provide a better option for an efficient and more accurate prediction of diabetes prevalence. Mathematical models also allow for estimating parameters and determining sensitivities [\[3\].](#page--1-0) A model representing all major population mechanisms such as births, deaths, aging, migration, and diabetes incidence will help to assess relative sensitivities or strength of associations of each of these mechanisms to diabetes prevalence. Moreover, such a mathematical model also allows for estimating parameters of some critical mechanisms, for example, death rates [\[5\]](#page--1-0). The death rates associated with diseases are often estimated based on the information reported on death certificates. However, the reliability of death certificate-oriented death rate estimates appears to be doubtful [\[6\]](#page--1-0).

Obesity has been a major factor in the recent increase in diagnosed diabetes incidence in the United States [\[7\].](#page--1-0) Therefore, body mass index (BMI) can potentially be a leading diabetes risk predictor. Huang et al. [\[8\]](#page--1-0) constructed a comprehensive Markov chain model for predicting diabetes incidence and prevalence across different BMI categories in the total U.S. population. However, Narayan et al. [\[9\]](#page--1-0) demonstrated that the link between BMI and diabetes development risk can vary significantly with age, suggesting a need for separate mathematical representations of age-specific associations between BMI and diabetes incidence rates. An appropriate mathematical representation quantifying the age-specific associations between BMI and diabetes incidence can be postulated to predict diabetes prevalence accurately. The main objective of this study was to propose a mathematical model to predict diabetes prevalence in different adult age groups. The specific objectives were to (1) develop a mathematical representation for quantifying the effect of BMI on diabetes development risk in adult age groups commonly defined in epidemiology, (2) assess sensitivities of diabetes

prevalence to incidence, death and migration rates, and (3) estimate death rate constants and other parameters for diabetic and nondiabetic adults by fitting the model to National Health and Nutrition Examination Survey (NHANES) 1999-2010 data.

Materials and methods

Model development

The time unit for the model is a year (y) . Total population size was arbitrarily set at 10,000, held constant, and divided into four age groups (x): (1) younger than 20, (2) 20 to 39, (3) 40 to 59, and (4) 60 years or older (Fig. 1). Individuals in each age group were allocated to two pools: Diabetic $(Q_{D(x)})$ and nondiabetic $(Q_{H(x)})$, which also includes undiagnosed cases. The diabetes incidence rate of each age group ($F_{H(x)_D(x)}$) was taken to be a linear function of $Q_{H(x)}$ with corresponding diabetes fractional incidence rate $k_{H(x),D(x)}$:

$$
F_{H(x) = D(x)} = k_{H(x) = D(x)} Q_{H(x)}.
$$

Death rates of nondiabetic ($F_{H(x)$ death) and the diabetic ($F_{D(x)$ death) individuals in each age group were also taken as linear functions of $Q_{H(x)}$ and $Q_{D(x)}$, respectively, with corresponding fractional death rates $k_{H(x)$ death and $k_{D(x)$ death:

$$
F_{H(x)\text{death}} = k_{H(x)\text{death}}Q_{H(x)};
$$

 $F_{D(x)$ death = $k_{D(x)$ death $Q_{D(x)}$.

A fractional rate expresses an absolute rate or a flux (i.e., $F_{H(x)$ death) as a proportion of the pool of interest (i.e., $Q_{H(x)}$). Because units of the rates and pools are individuals per year and individuals respectively, the unit of the fractional rates is y $^{-1}$. For example, a fractional death rate of 0.01 y^{-1} means that 1% of the population dies annually.

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