Fighting Diabetes: An Analysis of Risk and Solutions to America's Diabetes Crisis

Authors: Qi Zhang[1*], Diana Tang[1]

[1] Adlai E. Stevenson High School, Lincolnshire, IL 60069

[*] First author and corresponding author. Correspondence: qiqi.zhang.2025@gmail.com

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1. Executive Summary

Diabetes is a chronic disease that affects millions of people in the U.S. and the population of diabetics has increased significantly recently. The total percentage of people ages 18 or older in the United States with diabetes has increased from 10.3% in 2001-2004 to 13.2% in 2017-2020. According to a report from the Centers for Disease Control and Prevention (CDC) in 2023, around 38.4 million people in the United States had diabetes and 97.6 million people had prediabetes. Diabetes is also a condition that increases susceptibility to other health conditions and is becoming a leading cause of high mortality.

Moreover, the financial costs of diabetes are extremely high. Based on the report by the CDC, in 2022, it cost $413 billion in the United States alone in medical costs and lost work and wages for those diagnosed with diabetes. Generally, the medical costs for people with diabetes are more than twice the costs for people without diabetes. Both the growing diabetic population and insurance companies are suffering from the diabetes crisis. Therefore, we collect a variety of data, examine the risk of diabetes, and develop solutions to fight the diabetes crisis. The data we collect consists of the following:

- Historical diabetes prevalence data in United States 2017–2020 and 2021 National Diabetes Statistics Report by the CDC
- Incidence rates of diagnosed diabetes in United States 2019-2021
- Diagnosed diabetic population based on race-ethnicity in United States 2000-2022
- Mortality rates of diabetic and non-diabetic population from a national cohort of the U.S. population
- Diabetes risk factor related data including 2019–2021 National Health Interview Survey, 2003-2021 Behavioral Risk Factor Surveillance System, 2015–2018 National Health and Nutrition Examination Survey and US Diabetes Surveillance System.

We started with building the first model to understand how the diabetic population in the U.S. is changing over time. Based on U.S. population trends, we developed a dynamic Markov chain model to project the future diabetic population on both type 1 and type 2 diabetes, with high accuracy and sensitivity. We used a model based on the historical medical costs to estimate the total financial loss of the U.S. diabetic population. A Monte Carlo simulation was run to obtain a clearer picture of the range of diabetic populations we may expect in the future. The simulation showed that one standard deviation below the mean population in 2050 yielded about 63.2 million diabetics, representing 19.8% of the total U.S. population, while the scenario with one standard deviation over the mean population in 2050 yielded about 82.0 million diabetics, representing 24.0% of the total U.S. population. While type 1 is hard to prevent, we applied a multilayer perceptron neural networks model to evaluate high risk factors for type 2 diabetes with the aim to develop prevention and intervention strategies. We observed that high BMI and unhealthy lifestyle are the top risk factors that cause type 2 diabetes.

After extensive analysis of medical costs in 2050 with physical activity interventions, obesity management and stem cell therapy, we conclude that the following type-specific interventions and prevention strategies are valuable in reducing the diabetic population and associated monetary costs to the diabetic population:

Intervention	**Diabetic population in 2050**	**Direct medical costs in 2050**
No intervention	71.3 million	$1.572 trillion
Obese management	55.6 million	$1.227 trillion
Stem cell therapy (10% lower incidence)	67.6 million	$1.491 trillion
Stem cell therapy (50% lower incidence)	52.57 million	$1.159 trillion

Therefore, we recommend that insurance companies offer wellness programs, as well as improve education and communication regarding such programs to increase participation rates. In addition, we recommend obesity management, physical activity interventions and implementation of stem cell therapy to combat America's diabetes crisis.

2. Introduction and Background

Diabetes is defined as a chronic disease which occurs due to the pancreas's dysfunctionality to produce enough insulin or the body's dysfunctionality to effectively use the insulin produced by the pancreas. Insulin is a hormone regulating the level of blood glucose in the human body. The insufficient production or ineffective usage of insulin can raise blood glucose, which consequently leads to many health issues. Diabetes is categorized into three types: type 1 diabetes, type 2 diabetes, and gestational diabetes (1).

Type 1 diabetes is caused by an autoimmune reaction in which the body is unable to produce sufficient insulin and daily administration of insulin is needed. Type 2 diabetes occurs when the body is unable to effectively and properly use insulin and thus causes high levels of blood glucose. Often, type 2 diabetes is caused by an unhealthy diet and lifestyle. A precursor to type 2 diabetes is prediabetes, when blood glucose levels grow higher than normal but are still under diabetic. Gestational diabetes occurs when blood glucose level is between normal and diabetic for pregnant women and usually reverses after pregnancy (2).

Diabetes is a condition that is becoming increasingly common with the modernization of society. As access to food increases and modern life is made more convenient in various ways, many people in countries, such as the United States, are at higher risk of developing diabetes or prediabetes.

The diabetic population has grown significantly in the U.S. The total percentage of people ages 18 or older in the United States with diabetes has increased from 10.3% in 2001-2004 to 13.2% in 2017-2020 (3) (Figure 1). According to a report from the CDC in 2023, around 38.4 million people in the United States had diabetes and 97.6 million people had prediabetes (3).

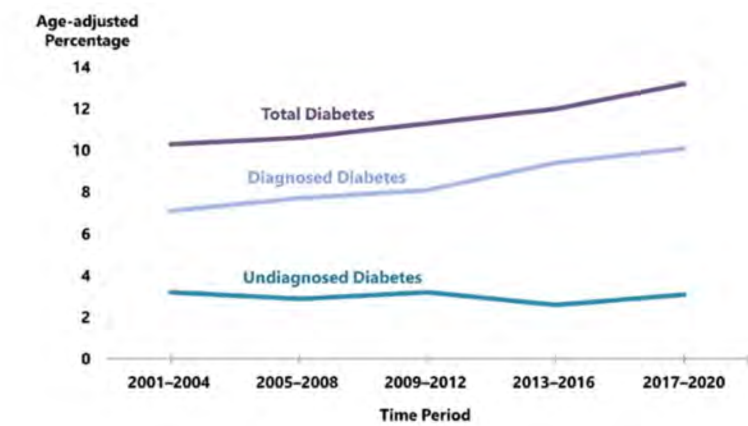

Figure 1: Trends in age-adjusted prevalence of diagnosed diabetes, undiagnosed diabetes, and total diabetes among adults aged 18 years or older, United States, 2001–2020 (3).

Not only is diabetes prevalence rising, but many also remain in the dark regarding the true severity of the diabetes epidemic. Approximately one in five people who have diabetes are unaware of their condition, and more than eight in ten people that have prediabetes don't know that they do. Diabetes is also a condition that increases susceptibility to other health conditions, including blindness, stroke, kidney failure, heart disease, and loss of toes, feet, or legs (4). As a result, those with diabetes or prediabetes not only require treatment for diabetes itself, but potentially other conditions as well.

The financial costs of diabetes are extremely high, and consist of direct costs on health care and indirect costs due to reduced or lost productivity and wages for those diagnosed with diabetes. The medical costs for diabetic care and associated diabetes complications are primarily paid by insurance companies and diabetics, while reduced productivity due to diabetes-related conditions costs employers. The heavy financial burden has raised concerns for insurance companies, patients, employers and the government. Generally, the direct medical costs for people with diabetes are more than twice the costs for people without diabetes (5). According to a report from the CDC, in 2022, it cost $413 billion in the United States alone in direct costs from diabetic care and indirect costs associated with lost work and wages for those diagnosed with diabetes. Due to the high costs, it is in the best interest of both those suffering from diabetes and insurance companies who, for diabetics with insurance, must take on most of the medical costs associated with diabetes.

Fortunately, type 2 diabetes, which makes up around 90-95% of those with diabetes, is largely preventable by keeping a normal body weight, exercising routinely, and maintaining a healthy diet and lifestyle. As opposed to type 2 diabetes, type 1 diabetes is less common, and it is hard to prevent as it is usually caused by genetic and environmental factors (6). However, for those who are already diabetic with type 1 or type 2, diabetes can be managed, and its effect can be delayed or lowered through a healthy diet, routine exercise, regular screening, and medication.

The purpose of this report is to understand the growth of diabetes in the U.S. population through 2050, quantify the direct medical costs on diabetic care, and explore effective ways to mitigate the cost for both type 1 and type 2 diabetes. Ultimately, we aim to lower or avoid risk for both types of diabetics who are suffering from the "quiet epidemic" and are combatting America's diabetes crisis.

Firstly, we recommend insurance companies offer wellness programs, improve education and communication to increase participation rates. Next, we recommend communities, governments, and healthcare providers offer education and resources to manage obesity and increase physical activity. Finally, we explore the promise of stem cell therapies in treatment and cure for diabetic patients and review the barriers preventing them from coming to the market. We recommend the federal government support the development and implementation of stem cell therapies to treat both type 1 and type 2 diabetes in the near future.

3. Data Methodology

The data methodology for the mathematics models depends on identifying and collecting data sources to achieve the following goals: develop a model to project diabetic population in the future, project the associated medical costs per capita, quantify the financial loss of the diabetic population and evaluate the high-risk factors. These will be described in detail in the next section for mathematics methodology.

3.1 Data Collection

The collected data were classified into the five categories defined in the Actuarial Process Guide (Table 1).

To define historical trends and project the population changes of each gender, race and ethnicity group, we collected data from the United States Census Bureau 2023 national population projection tables (7).

To analyze historical trends and forecast the diabetic population changes, we collected and analyzed the historical diabetes prevalence data in the United States 2017–2020 and 2021 National Diabetes Statistics Report by the CDC (3), incidence rates of diagnosed diabetes in the United States 2019-2021 (3), diagnosed diabetic population based on race-ethnicity from 2000 to 2022 (8) and mortality rates of the diabetic and non-diabetic populations from a national cohort of the U.S. population (9). By using these data sources, we can build a model to study the historical data, find the trend and project the diabetic population in the future.

To study the severity and quantify the financial loss associated with the risk of diabetes, we collected data regarding the economic costs of diabetes in the United States in 2002, 2007, 2012 and 2017 (10-13). To meet the goal of developing recommendations and mitigation strategies, we need to study the relationship between diabetes and its risk factors to separate the outcomes. Therefore, we collected diabetes risk data from the 2019–2021 National Health Interview Survey (NHIS) (14), 2003–2021 Behavioral Risk Factor

Surveillance System (BRFSS) (15), 2015–2018 National Health and Nutrition Examination Survey (NHANES) (16) and U.S. Diabetes Surveillance System (17).

Table 1: data collected in the five categories defined in the Actuarial Process Guide		
Data	**Data categories**	**Model**
United States Census Bureau 2023 national population projection tables	● Defining historical trends ● Projecting future trends ● Defining the frequency of potential outcomes	Project diabetic population
Diabetes prevalence data in United States 2017–2020 and 2021	● Defining historical trends ● Projecting future trends ● Defining the frequency of potential outcomes	
Incidence rates of diagnosed diabetes in United States 2019-2021	● Defining historical trends ● Projecting future trends ● Defining the frequency of potential outcomes	
Mortality rates of diabetic and non-diabetic population	● Defining historical trends ● Projecting future trends ● Defining the frequency of potential outcomes	
Economic costs of diabetes in the United States	● Defining historical trends ● Projecting future trends ● Defining the severity of potential losses	Project direct medical costs per capita Quantify financial loss
Diabetes risk data	● Separating potential outcomes	Evaluate high risk factors

United States Census Bureau 2023 national population projection tables

- **Type of Data**: The projected population of the United States (7)
- **Source**: United States Census Bureau
- **Variables**: gender, race and ethnicity, year
- **Purpose**: This dataset will be used to estimate population changes of each gender, race and ethnicity group every year

Incidence rates of diagnosed diabetes in United States 2019-2021 (people with onset in the past year are considered incident cases**)**

- **Type of Data**: The diabetes incidence rate of the United States (3)
- **Source**: CDC
- **Variables**: gender, race and ethnicity
- **Purpose**: This dataset will be used to project the diabetic population of each gender, race and ethnicity group every year

Diabetes prevalence data in United States 2017–2020 and 2021 (prevalence rate is the number of diagnosed diabetes per 100 people during the year**)**

- **Type of Data**: The diabetes prevalence of the United States (3)
- **Source**: CDC
- **Variables**: gender, race and ethnicity
- **Purpose**: This dataset will be used to project the diabetic population of each gender, race and ethnicity group every year

Mortality rates of diabetic and non-diabetic population

- **Type of Data**: The mortality rate data from a national cohort of the United States population (9)
- **Source**: CDC
- **Variables**: gender, race and ethnicity
- **Purpose**: This dataset will be used to project the diabetic population of each gender, race and ethnicity group every year

Economic costs of diabetes in the United States

- **Type of Data**: the economic costs of diabetes in the United States in 2002, 2007, 2012 and 2017 (10-13)
- **Source**: American Diabetes Association (ADA)
- **Variables**: year
- **Purpose**: This dataset will be used to forecast the medical costs of diabetes per capita every year and furthermore calculate the total medical costs of the diabetic population

Diabetes risk data

- **Type of Data**: 2019–2021 NHIS (14), 2003–2021 BRFSS (15), 2015–2018 NHANES (16), U.S. Diabetes Surveillance System (17)
- **Source**: National Center for Health Statistics, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion
- **Variables**: Diabetes binary, high blood pressure, high cholesterol, BMI, smoker, stroke, heart disease attack, physical activity, fruits, vegetables, heavy alcohol consumption, any healthcare, general health, mental health, physical health, difficulty in walking, gender, age, education, and income.
- **Purpose**: This data will be used to examine the relationship between diabetes and risk factors.

The diabetes related data were collected for each race- and ethnicity-, gender- group, for which the incidence and prevalence vary. We have made every effort to search for age-specific or diabetes type-specific incidence and prevalence for these subgroups, as that could differentiate diabetic population by separating the diabetics into age subgroups, or type 1 and type 2 subgroups for each race- and ethnicity-, gender-specific group. However, age- and type- specific data were not available for these race- and ethnicity-, gender-specific groups. Thus, we estimated the number of type 1 and type 2 diabetes from the total population of diabetes as it was known that approximately 5.8% of diabetics had type 1 diabetes and 90.9% of diabetics had type 2 diabetes (18).

3.2 Data Reliability

We have made our best efforts to search for the most reliable sources of data for what our models need. The data we utilize largely originates from nationally renowned organizations such as the U.S. Census Bureau and the CDC, which have numerous fail safes in place to ensure the accuracy of their data. Participating in the census is mandated by law, and although people can choose to skip questions, the Bureau is able to use a combination of statistical techniques and alternative data sources to provide more accurate data. National organizations also employ professionally trained statisticians and, in the case of the CDC, epidemiologists to collect, compile, and confirm their data, indicating the reliability of such data sources. The information we use from the ADA comes from state and federal agencies as well.

Due to their reliability, we have no need to clean the data we collect. Additionally, we preprocessed data from various sources to prepare for the following section on Mathematics Methodology. The United States Census Bureau 2023 data provided national populations project in every 5-year interval based on race and gender (7). The population for each race and gender subgroup was extracted from the population table and estimated for each year from 2018 to 2050. The incidence rate of diagnosed diabetes and the mortality rate were provided as a number per 1,000 people in the data sources (3, 9) and were converted to a fraction for the following calculation in the math modeling. For the economic costs of diabetes, direct medical costs each year were collected from the data sources (10-13) and classified into three main cost components to project future trends. For the diabetes risk factors data, it contains 20 variables, with 2 classes for target variable "Diabetes binary": 0 for no diabetes and 1 for diabetes.

4. Mathematics Methodology

Our methodology is to create models to forecast the diabetic population in the future, predict the associated medical costs and develop recommendations for intervention strategies. The progression of our models is shown in the flow chart below (Figure 2).

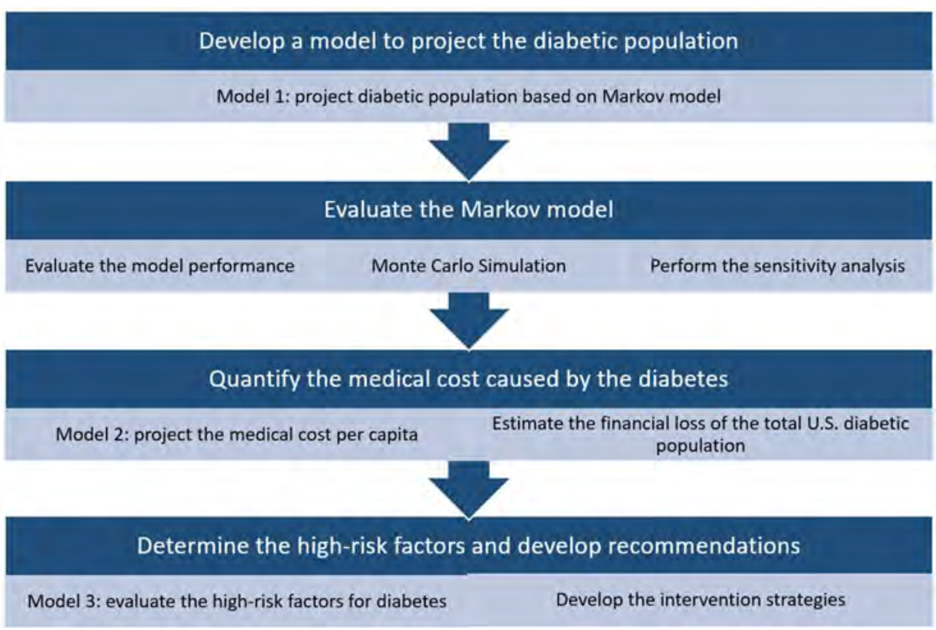

Figure 2: Flowchart of the models and risk mitigation strategies development.

We start with building a dynamic Markov chain model in model 1 to project the diabetic population. In model 2, the medical costs per capita is projected based on historical data and then used to estimate the total financial loss of the U.S. diabetic population.

Our final goal is to develop mitigating strategies and recommendations to reduce diabetes prevalence and financial loss. Therefore, we build model 3, a multilayer perceptron neural networks model, to evaluate the high-risk factors of diabetes and develop intervention strategies to lower the risk of diabetes and reduce the associated financial loss.

4.1 Model the Diabetic Population

4.1.1 Markov Chain Model

4.1.1.1 Assumption and Justification

Assumption: The U.S. population is mainly composed of Hispanic, non-Hispanic White, Black, Asian and other races including American Indian, Alaska Native, Native Hawaiian and other Pacific Islanders.

Justification: The U.S. has a racially and ethnically diverse population which has been categorized at the federal level. The most recent U.S. Census classifies the population into five groups: Hispanic, White, Black, Asian, and Native Hawaiian and other Pacific Islanders (7).

Assumption: The disease transition probability is gender, race and ethnicity-specific.

Justification: According to diabetes data during 2019-2021, the estimated crude incidence rates of diagnosed diabetes are different between men and women and vary for each race and ethnicity group (1).

Assumption: The mortality rate of the diabetic population is gender-specific.

Justification: Based on the NHANES during the follow up from 1971 to 1993, the mortality rate of individuals with diabetes was gender-specific (9).

Assumption: The mortality rate of the non-diabetic population is gender-specific.

Justification: The mortality rate of the non-diabetic population is lower than that of the diabetic population (9). The data of NHANES during the follow up from 1971 to 1993 showed that mortality rate of individuals without diabetes was gender-specific.

Assumption: The transition probability from non-diabetes to diabetes for obese women is higher than overweight women and normal weight women. The same trend is applied to men.

Justification: The previous case study from 2015 reported that the transition probability from non-diabetes to diabetes for obese women was about 3.9 times higher than normal weight women and about 2.3 times higher than overweight women, and the transition probability from non-diabetes to diabetes for obese men was about 4.0 times higher than normal weight men and about 2.3 times higher than overweight men (18).

Assumption: Age-standardized total diabetic prevalence is higher in males than in females.

Justification: It is known that global age-standardized total diabetic prevalence was higher in males than in females and the ratio of the male to female diabetic population is 1.12:1 (20).

Assumption: The general rate of inflation is stable in the future until 2050.

Justification: The inflation rate in the U.S. has been relatively low and stable since the 1980s. The exception, the 2021 and 2022 spike, could have been caused by factors such as COVID-19 pandemic spending, which added constraints on various aspects of the U.S. economy (21).

Assumption: No new live births have diabetes.

Justification: Young children usually have a low prevalence rate of diabetes, but it would still help to obtain the prevalence rate of new live births for accurate forecast. We performed extensive research but did not find available diabetic data for new live births.

4.1.1.2 Variables

The variables used for the Markov chain model are defined in the below table (Table 2).

Table 2: Variables and description	
Variables	**Description**
ND(t)	non-diabetic population at year t
D(t)	diabetic population at year t
Dead(t)	number of deaths at year t
P(t)	prevalence rate of diabetic population
M(t)	new population due to migration at year t
B(t)	new population due to new births at year t
pNdToDead (t)	probability of non-diabetes to death at year t
pNdToDb (t)	probability of non-diabetes to diabetes at year t
pDbToDead (t)	probability of diabetes to death at year t
U(t)	total U.S. population at year t
C(t)	direct medical costs per capita at year t
F(t)	total medical costs at year t

4.1.1.3 Model Development

The Markov chain has frequently been applied to model disease states and transition probabilities (Figure 3). The states in a Markov chain model either stay in the same state or transition to another state and the state transition is determined by the transition probabilities.

Herein we build a Markov chain model with three states— "No Diabetes", "Diabetes" and "Death"—within a one-year cycle (Figure 3). The No Diabetes can go to Diabetes or Death. The Diabetes either stays the same or goes to Death, but can't go back to No Diabetes, as diabetes is a chronic condition with no medical evidence showing that diabetes can become non-diabetes. To build an accurate model, we consider the new population every year due to the U.S. births and migration and add the new population to the existing cohorts.

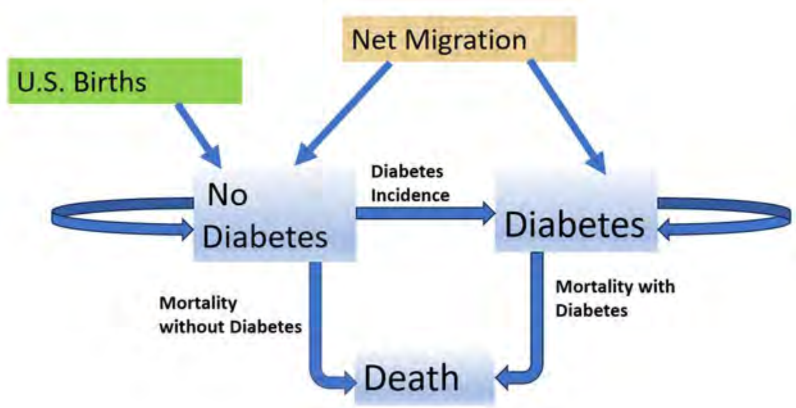

Figure 3: The diabetes disease states and transition probabilities in the Markov chain model. The arrows point to the next disease state in the transition at discrete intervals.

Prevalence rate was calculated as the number of people with diabetes divided by the total population in the sample. People with onset in the past year were considered incident cases. Since the diabetes prevalence and incidence are gender, race and ethnicity-specific, the projections were divided into 10 subgroups based on gender (male, female), race and ethnicity (Hispanic, non-Hispanic White, non-Hispanic Black, Asian, others including American Indian, Alaska Native, Native Hawaiian and other Pacific Islanders). The projected diabetic population of each subgroup was combined for the U.S. diabetic population.

Input parameters and parameter estimations for the Markov model were described as the following:

- The year 2018 was used as the start cycle of the Markov chain model.
- The diabetic population for 2018 was obtained from national surveillance data by the CDC. The non-diabetic population was calculated using the equation base on diabetes prevalence:
  ND (t) = U(t) – D(t)   (equation 1)

- This transition probability from non-diabetes to diabetes was guided using the crude incidence rate (Table 3).

Table 3: Estimated crude incidence rate per 1,000 (95% CI) of diagnosed diabetes (3)

Race/ethnicity	lower	upper	middle
Hispanic	4.8	7.7	6.1
White, non-Hispanic	4.5	5.8	5.1
Black, non-Hispanic	5.3	8.7	6.8
Asian, non-Hispanic	2.4	5.9	3.8
Others	1.3	33	2.3

- The transitions from the non-diabetes state to the death state was based on the previously reported data (9).
- The mortality rates were estimated based on the data from a national cohort of the U.S. population (9).
- The number of live births for each year was obtained from the 2023 National Population Projections Tables (7).
- The number of migrations for each year was obtained from the 2023 National Population Projections Tables (7).

Since both prevalence and incidence are critical parameters which affect the diabetic population, we tuned both parameters to match the historical data and literature, and produce an accurate forecast:

- The estimated annual percentage change (EAPC) of 198% for the incidence rate of diabetes was reported to be the largest globally for North America high income countries such as the U.S. (22). The EAPC of diabetes incidence rate was used for the dynamic model (22).
- The prevalence was estimated based on the data in the past year.

If we did not consider annual population changes, the following transition matrix would be generally used for each subgroup in the Markov chain model:

	ND(t)	D(t)	Dead(t)
ND(t-1)	[1- pNdToDead (t-1)]* [1- pNdToDb (t-1)]	[1- pNdToDead (t-1)]* pNdToDb (t-1)	pNdToDead (t-1)
D(t-1)	0	1- pDdToDead (t-1)	pDdToDead (t)
Dead(t-1)	0	0	1

However, we need to incorporate annual population changes every year to build an accurate model, so we further tuned the model with the addition of new births and migration to match the outcomes of the historical data set and annual population changes in the U.S. The following equations (2) and (3) were used in our Markov chain model:

ND(t)=ND(t-1) * [1- pNdToDead (t)] *[1- pNdToDb (t)]+B(t) + M(t) * [1- P(t)]   (equation 2)

D(t) = D(t-1) * [1- pDdToDead (t)] + M(t) * P(t)   (equation 3)

The Markov chain model was run cycle by cycle from 2018 to 2050. The diabetic population in 2050 was projected to reach 71.3 million, representing 19.8% of the total U.S. population, with 4.1 million type 1 and 64.8 million type 2 diabetics (Figure 4).

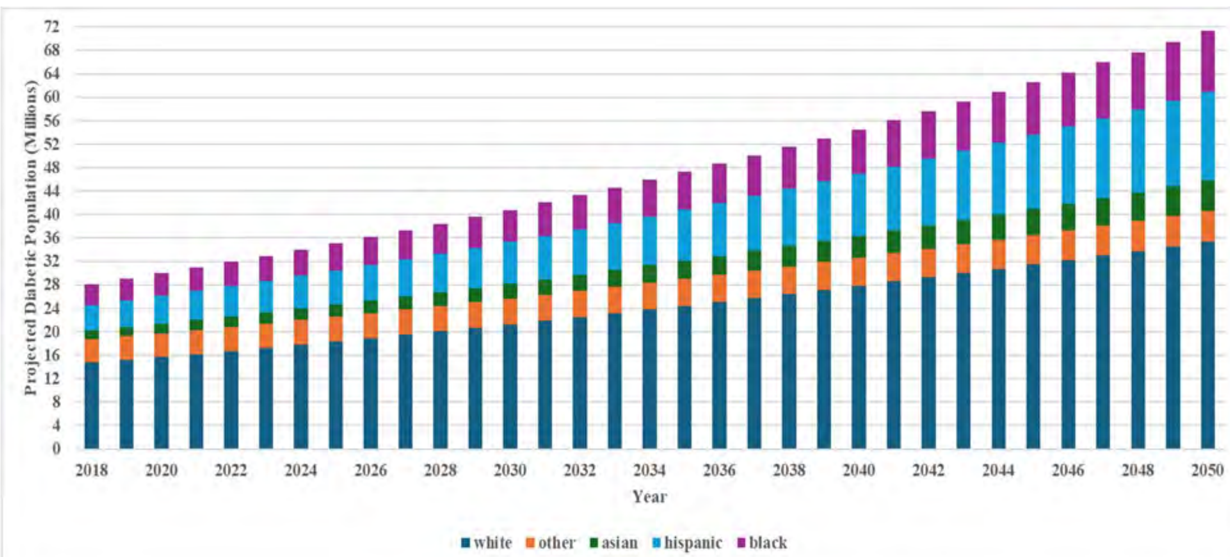

Figure 4: The diabetic population projected using the Markov model.

4.1.1.4 Evaluate the Model

We compared our results with historical diabetes prevalence data in the United States from 2019-2022 (17). Combining the diabetic population of the all race and ethnicity subgroups used in the surveillance of the CDC (17): the Hispanic, White, Black, and Asian subgroups, we found our forecast was very close to what was recorded in the CDC dataset during the same period (Figure 5). Our forecast on these subgroups were slighter higher than CDC, with 2.320 million in 2019, 3.245 million in 2020, 3.198 million in 2021 and 3.962 million in 2022. This could not only demonstrate the strength of our Markov model in forecast the diabetic population but also reflect the effect of COVID-19 on the health care system and hospital strains.

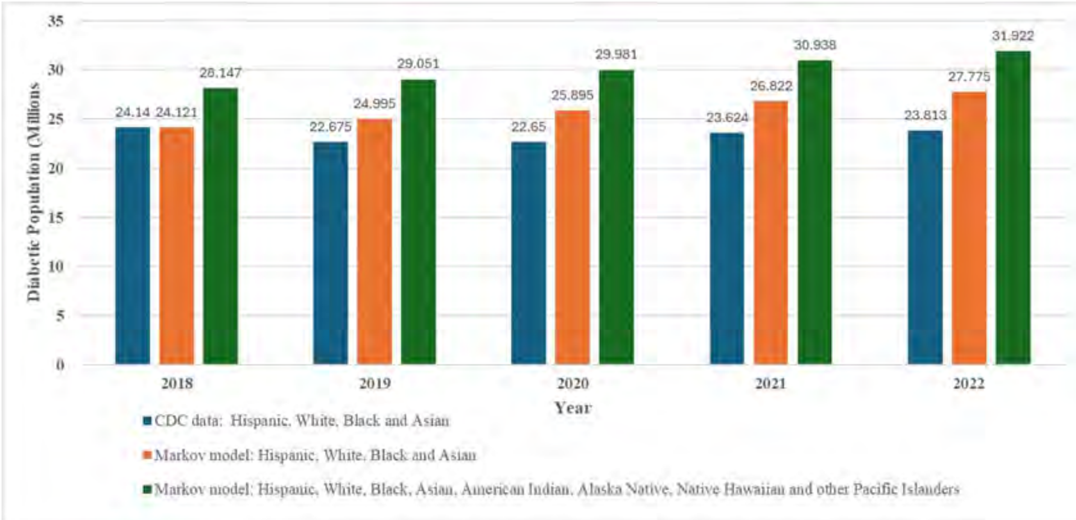

Figure 5: Comparison of the diabetic population in millions between CDC surveillance data (17) and the forecast by the Markov model during 2018-2022. Blue bar represents the historical diabetic population recorded in CDC surveillance, which only included four subgroups: the Hispanic, White, Black and Asian subgroups. Orange bar stands for the sum of these four subgroups forecast by the Markov model. Green bar stands for the total diabetic population including additional minority groups: American Indian, Alaska Native, Native Hawaiian and other Pacific Islanders.

The CDC data showed a diabetic population of 24.140 million in 2018, 22.675 million in 2019, 22.650 million in 2020, 23.624 million in 2021 and 23.813 million in 2022. The slightly lower diabetic population in record from 2018 to 2020 could be caused by COVID-19, as a portion of diabetes cases were likely undiagnosed or not recorded due to the long quarantine period and hospital strains during the pandemic. The total difference between our forecast and the report in the surveillance of the CDC was 6.4 million in 2019, 7.3 million in 2020, 7.3 million in 2021 and 8.1 million in 2022. In addition to what was explained above regarding the CDC dataset during the pandemic period, the difference mainly consisted of the diabetic population for minority groups including American Indian, Alaska Native, Native Hawaiian and other Pacific Islanders, which were not recorded in CDC surveillance data (Figure 5).

We also compared our forecast with other projections for the diabetic population in 2050. According to an analysis from the CDC (22), the number of Americans with diabetes will reach from 1 in 5 to 1 in 3 by 2050 if the incidence rate continues to rise. This analysis projected a diabetic population of 72.1 million (1 in 5) to 120.2 million (1 in 3) in 2050. We projected 71.3 million people with diabetes in 2050, which was close to the 72.1 million (1 in 5) forecast by the CDC analysis.

Moreover, our model considered the gender-, race-, and ethnicity- specific population as the transition probability between disease states was dependent on all these factors, as indicated by the available data (3). Additionally, we were aware of the declining share of White people, growth of minority population, migration to the U.S. and different population changes based on various race and ethnicity groups, thus we included these changes in our projection to avoid any underestimation or overestimation of the diabetic population and associated population with diabetes. Overall, our Markov model provided more accurate projections than previous records (17) and was used for the following risk analysis.

4.1.2 Monte Carlo Simulation

The Monte Carlo method provides a computational device to model complex processes based on repeated random sampling. It is particularly useful to manage complex systems with many uncertainties or randomness, as it can provide multiple possible outcomes, allowing for a large pool of random data scenarios instead of limited historical data. To better understand and accurately forecast the diabetic population in the future, we ran a Monte Carlo simulation with 10,000 trials for the Markov chain model. We checked the input parameters to the Markov chain model in section 4.1.1.2. The most critical parameters were probability of non-diabetes to diabetes, prevalence rate and mortality rate of diabetes, as they affected the final forecast. Considering they varied depending on race, we randomized all these critical parameters within one standard deviation of the mean. Thus, the Monte Carlo simulation showed a wider range of possible outcomes than the following sensitivity analysis in section 5.2 which varied only with the incidence rate.

Using the Monte Carlo simulation, we obtained a clearer picture of the range of diabetic populations we may expect in the future. The simulation results were shown in the following graph (Figure 6):

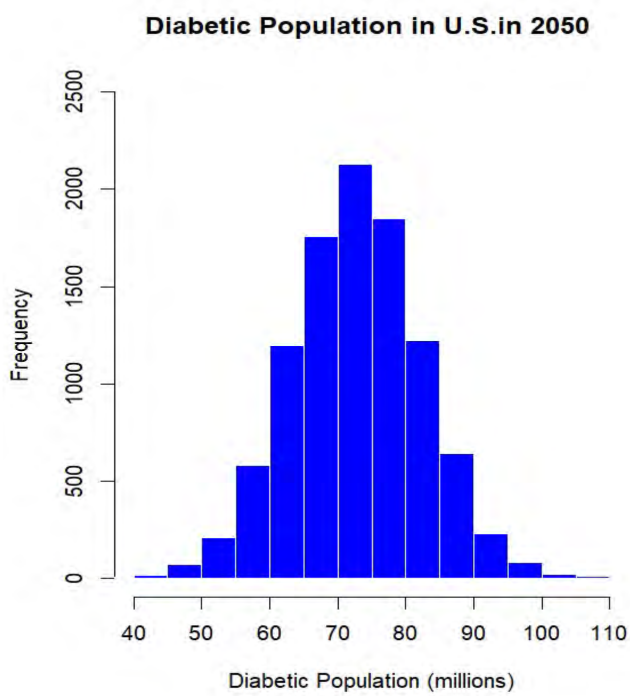

Figure 6: Monte Carlo Simulation of diabetic population (millions) in the year 2050.

Numerical results were summarized in the following table:

Table 4: Monte Carlo Simulation results on diabetic population (millions) in 2050

Projection*	**Total Diabetic Population (millions)**	**Type 1 Diabetic Population (millions)**	**Type 2 Diabetic Population (millions)**
$\mu - \sigma$	63.2	3.7	57.4
μ	72.6	4.2	66.0
$\mu + \sigma$	82.0	4.8	74.5

[*] μ is the mean value and σ is the standard deviation of all results in 10,000 runs

According to the Monte Carlo simulation, the scenario with one standard deviation below the mean yielded about 63.2 million people with diabetes, with 3.7 million for type 1 and 57.4 million for type 2 diabetes, while the scenario with one standard deviation over the mean yielded about 82.0 million people with diabetes, with 4.8 million for type 1 and 74.5 million for type 2 diabetes. Overall, a difference of 18.8 million in the diabetic population was seen between the two estimates (Table 4).

4.2 Model the Medical Costs of Diabetes per Capita in the Future

We examined the historical annual spending for people with diabetes (23), checked the spending for the population without diabetes and quantified the healthcare spending associated with diabetes healthcare.

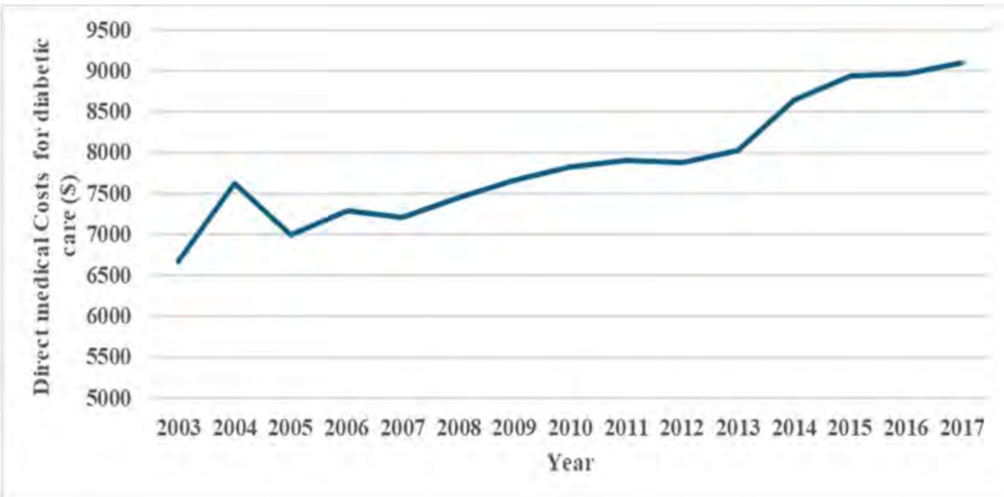

Figure 7: The historical direct medical costs for diabetic care (23).

Using the health spending data during 2003-2017 according to the IMB MarketScan commercial claims and encounter database (Figure 7) (23), we fit the sample data into a linear regression model to predict the direct medical costs in the future from historical data. In our analysis, the direct medical costs for diabetes care per capita followed a specified linear trend which was represented by the equation:

$$C(t) = 1847.7 * \log_{10}(t) + 6388.3 \qquad \text{(equation 4)}$$

with $R^2 = 0.7103$, P-value=$9.12 * 10^{-5}$ for which C(t) is the direct medical costs in dollars per capita at the year t.

Using the above equation, we can project the medical costs until 2050. The historical medical costs data (10-13) allowed us to evaluate the distribution of medical costs for diabetic care. As illustrated by the pie chart below (Figure 8), the top 5 largest costs were spent on hospital inpatient days, other prescription medications, office visits, non-insulin medications, and hospital outpatient visits, followed by other smaller portions of medical costs for various diabetic care.

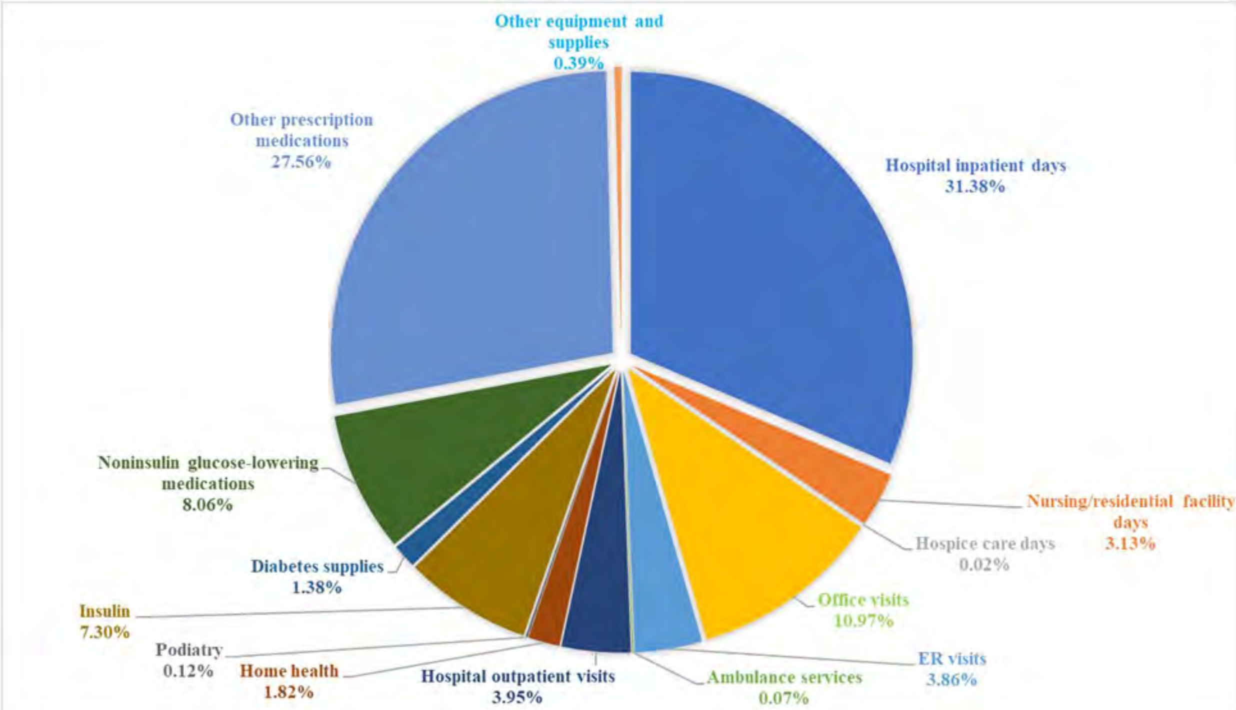

Figure 8: Distribution of direct medical costs components for diabetic care.

Medical costs of diabetic care are usually classified into three main components: institutional care, outpatient care and outpatient medications and supplies. Hospital inpatient days, nursing/residential facility days and hospice care days belong to institutional care. Office visits, ER visits, ambulance services, hospital outpatient visits, home health and podiatry belong to outpatient care. The remaining belong to outpatient medications and supplies (Table 5). Using the distribution of medical costs for diabetic care (Figure 8) and equation 4, we projected the medical costs until 2050 for institutional care, outpatient care and outpatient medications and supplies (Figure 9).

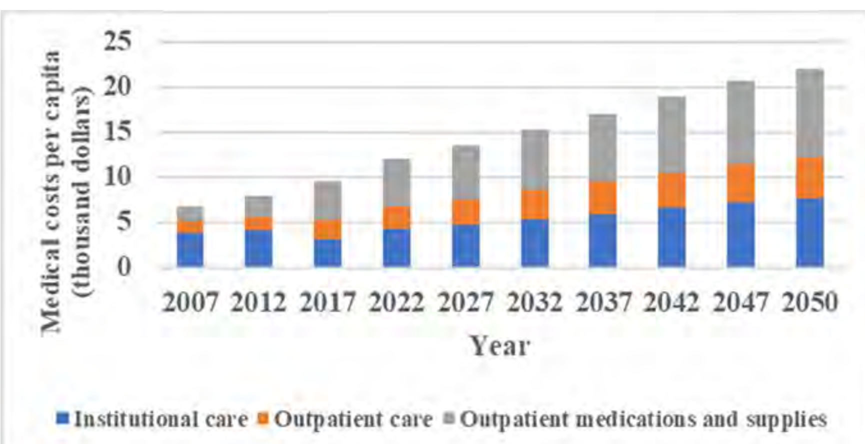

Figure 9: Projected medical costs until 2050 summed for institutional care, outpatient care and outpatient medications and supplies.

Furthermore, the itemized medical costs based on our forecast model were summarized in Table 5.

Table 5: Medical costs of diabetic care in 2050	
cost component (adjusted for age and sex)	
Institutional care	
Hospital inpatient days	$6,920
Nursing/residential facility days	$689
Hospice care days	$3
Subtotal	$7,614
Outpatient care	
Office visits	$2,420
ER visits	$851
Ambulance services	$14
Hospital outpatient visits	$871
Home health	$401
Podiatry	$25
Subtotal	$4,586
Outpatient medications and supplies	
Insulin	$1,610
Diabetes supplies	$304
Noninsulin glucose-lowering medications	$1,777
Other prescription medications	$6,078
Other equipment and supplies	$86
Subtotal	$9,858
Total	$22,057

In total, the medical costs of diabetic care were estimated to be about $22,057 per capita in 2050 (Table 5).

4.3 Evaluate the High-Risk Factors for Diabetes

The multilayer perceptron neural networks model is frequently used for deep learning because of its power in pattern classification, recognition, and prediction (24). It consists of three types of layers: the input layer, output layer and hidden layer. Herein, we used multilayer perceptron neural networks to evaluate the high-risk factors for diabetes. The BRFSS data were fitted to the multilayer perceptron neural networks model. Variables in BRFSS data in section 3.1 were included in the input layer of the model. The number of hidden layers was 1. The hidden layer activation function was a hyperbolic tangent, the output layer activation function was the softmax and the number of output layer units was 2.

Type 1 diabetes was likely caused by genetics and exposure to viruses and other environmental factors (25). In contrast, type 2 diabetes was usually associated with risk factors and can be managed through a healthy diet, physical activities, and medication.

To understand the most important contributors to type 2 diabetes, we divided the risk factors by the maximum indicator value yields and generated the normalized importance order. The top twelve risk factors were GeneralHealth, BMI, HighBP (High blood pressure), HeavyAlcoholConsump, HighChol (High cholesterol), MentalHealth, DiffcultWalk (difficulty in walking may be caused by diabetes or other conditions which reduce mobility), PhysicalHealth, Smoker, PhysicalActivity, Veggies and Fruits. The normalized importance of risk factors was presented in the following (Figure 10):

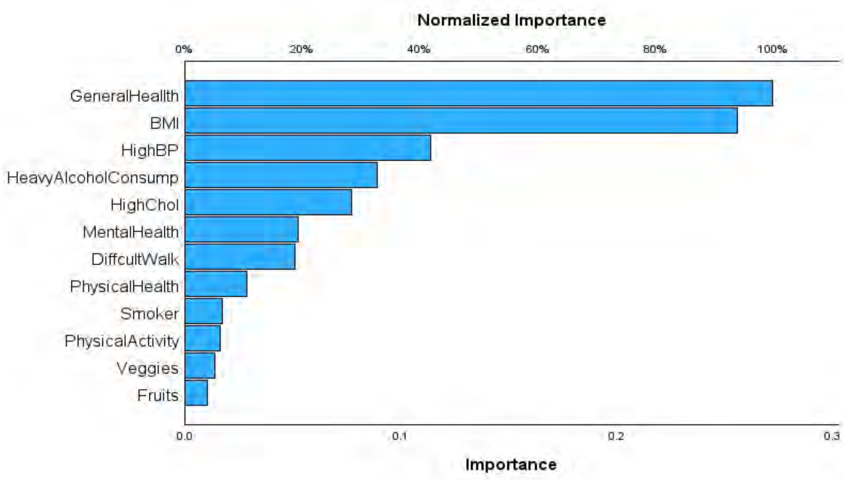

Figure 10: The importance of risk factors for type 2 diabetes. BMI, unhealthy diet and physical inactivity are most important contributors to type 2 diabetes.

Evaluating and understanding the high-risk factors was beneficial to bringing recommendations to reduce diabetes risk. BMI and lifestyle have been considered important factors for public health problems in the world and they are the most critical factors in predicting type 2 diabetes (26, 27). Our observation was consistent with the literature (26, 27).

4.4 Strength and Weaknesses

We used the Markov chain model to project the diabetic population in the U.S., modeled the medical costs per capita and quantified the associated financial loss throughout the year 2050. The methodology has unique strengths:

1. The dynamic Markov chain model considered the trend in incidence, prevalence, and demographic composition of the population, thus providing more accurate projections than previous reports (17, 28, 29).
2. The medical costs were projected based on actual health care costs data over 15 years. These were not estimates only but instead presented the reality of medical costs on the diabetic population.
3. This method was simple to utilize to evaluate the feasibility of different prevention strategies from the medical and economic perspective.
4. It provided an approach to estimate the risk and medical costs by type of diabetes and thus strongly supported the following recommendations for mitigation strategies.
5. This method can be useful to provide statistical evidence and offer insight into disease treatment and management approaches.

The methodology has the following weakness:

1. Forecasting diabetes prevalence for the following decades is fraught with a lot of uncertainty. If incidence rates are increased or decreased in the future, the projection will underestimate or overestimate the diabetes prevalence.

2. The model didn't account for unexpected future changes in inflation for medical costs. For example, while the Federal Reserve targeted a 2% inflation rate, in 2022 the U.S. inflation reached 8.5% inflation rate, the largest spike in four decades (30).
3. The estimates didn't account for the indirect costs and other costs not documented in the administrative databases. Therefore, only direct medical costs were projected with potential underestimation, and didn't stand for the total costs due to diabetes.

5. Risk Analysis

5.1 Risk Overview

In 2018, the population in the United States with diagnosed diabetes was 28.1 million. The number of diagnosed diabetics was projected to be 71.3 million in 2050, with 64.8 million type 2 diabetics, 4.1 million type 1 diabetics and the remaining for other type of diabetics. The diabetic population in 2050 has increased by 153% since the year 2018. The fastest growing ethnic group with diabetes is expected to be Hispanic females (354%), followed by Hispanic males (341%), black females (295%) and black males (286%) from the year 2018 to 2050 (Figure 11).

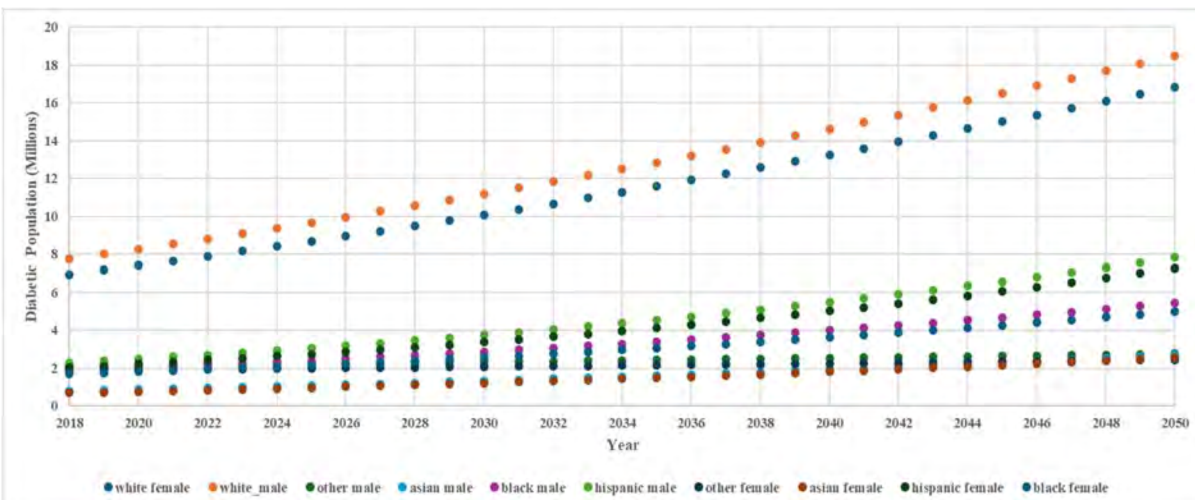

Figure 11: Forecast of diabetic population for each gender and race subgroup in the U.S.

Given the growing diabetic population, diabetes presents a significant constraint on the U.S. healthcare system. For the projected population of diabetes of 71.3 million by 2050, the associated costs of health care will pose significant financial burdens. Therefore, the management and prevention of diabetes remains a health priority in the U.S.

5.2 Sensitivity Analysis

Sensitivity analysis was performed by using the lower and upper incidence rates of diabetes (Figure 12). The "worst" scenario was caused by the upper incidence rate, which could be affected by the high-risk factors such as obesity and unhealthy lifestyles. On the other hand, the "best" scenario occurred when the incidence rate was minimized by reducing obesity, controlling body weight, keeping healthy lifestyles, and implementing effective diabetes prevention strategies. Projections based on low, mean, and upper incidence rates are quite close through the year 2030, differing by only 3.4 million (2.2 million above and 1.2 million below the mean). The projections diverge over time, with an 11.1 million difference in 2050 (7.4 million above and 3.7 million below the mean).

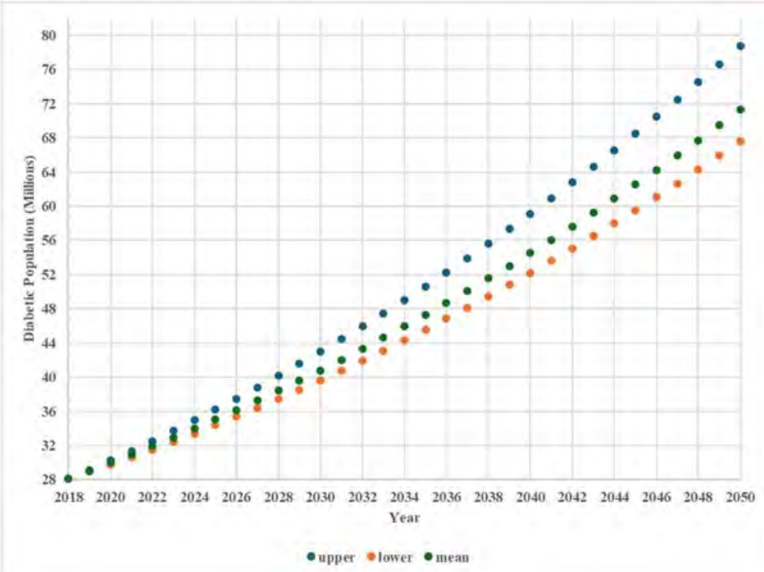

Figure 12: The sensitivity analysis performed using 95% percentile around the mean, lower and upper prevalence.

5.3 Quantify the Total Financial Loss

Using the above equation (3) for total diabetic population D(t) and equation (4) for medical costs per capita C(t), we calculated the total medical costs F(t) at the year t:

$$F(t) = D(t) * C(t) \quad \text{(equation 5)}$$

The medical costs for diabetes in 2050 were estimated to be \$1.572 trillion, with \$0.091 trillion for type 1 diabetic care and \$1.429 trillion for type 2 diabetic care, including the three major components of institutional care, outpatient care and outpatient medications and supplies (Figure 13).

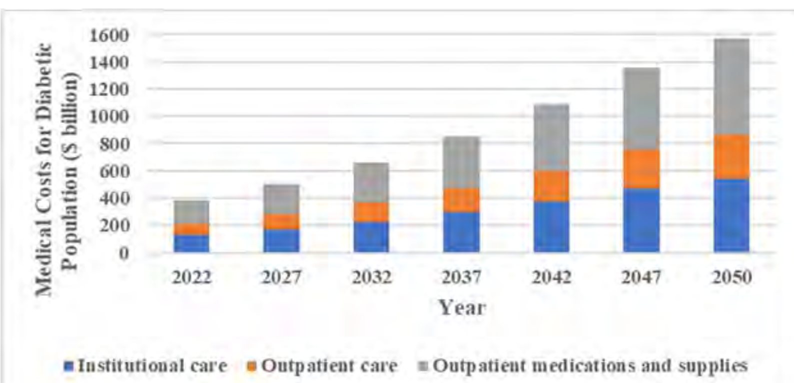

Figure 13: Direct medical costs in $billion for diabetic population with the inflation rate assumed stable at 2%.

The medical costs were projected with the assumption of a stable general inflation rate, as the Federal Reserve maintains the inflation rate at or near 2%. However, in 2022 the U.S. inflation rate reached 8.5%, the largest spike in four decades. Therefore, we tested how the medical costs for diabetic care in 2050 were affected by various inflation rates from 2% to 10% (Figure 14).

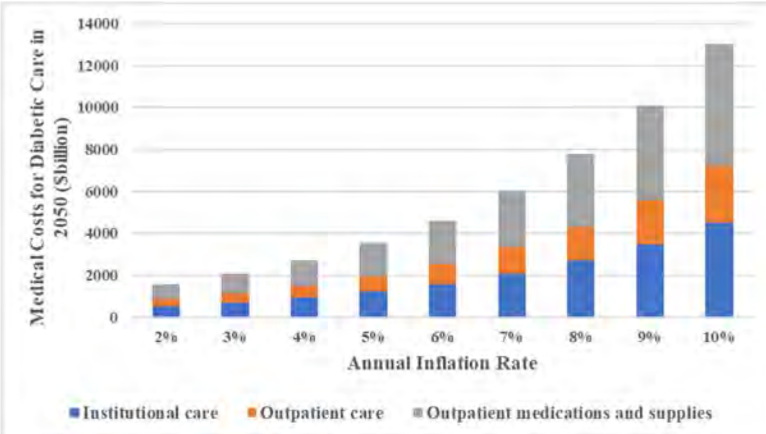

Figure 14: Medical costs in $billion for diabetic care in 2050 are influenced by annual inflation rate between 2% and 10%.

The price of medical services of each component increased when a higher rate of inflation, 3% to 10%, was individually applied. The direct medical costs for diabetic care in 2050 were increased to the range of $0.494 trillion to $11.455 trillion, when the inflation rate reached 3% to 10%.

The result highlighted the large financial loss due to diabetes. Direct medical costs from $0.384 trillion in 2022 to the costs in 2050 showed that the financial loss was increasing (Figure 13) and the loss was amplified when the inflation rate was larger.

5.4 At Risk Groups

The forecast diabetic population in section 4.1 and associated financial loss in section 5.3 were helpful for us to analyze the at risk groups.

Diabetes affects the health of people in all race and ethnicity groups. People with obesity and unhealthy lifestyles are at higher risk of diabetes than others. Diabetes usually causes serious health problems and damages human organs. It was the eighth leading cause of death in the United States in 2021. People with diabetes have a shorter life expectancy than those without diabetes. They could lose productivity at work and at home, potentially introducing employment issues, financial problems and other family and social issues. Moreover, since diabetics are usually at high risk of reduced productivity or permanent disability, their absence and disability affect U.S. employers as well.

Financially, diabetes is also the costliest chronic disease in the United States. Total direct costs of diagnosed diabetes were estimated at $227 billion in 2012 and $307 billion in 2022 (3), and the costs were increased from year to year. Our model and analysis showed that health insurance companies pay billions of dollars every year for the treatment of each stage of diabetes. Without any intervention approaches, our model forecasts the economic costs of healthcare for diabetes in 2050 to be $1.572 trillion.

Therefore, we need to develop recommendations to help the at risk groups, manage diabetes problems and mitigate the risks for the future.

6. Recommendations

Based on our projections of diabetic prevalence, we identified three major recommendations for insurance companies, communities and governments to reduce the diabetic population and associated medical costs. The recommendations focus on insurance, behavior changes and modifying outcomes. More specifically, we recommend that insurance companies offer wellness programs, efforts be made towards obesity management and physical activity intervention and the federal government support the development and implementation of the stem cell therapies that are coming to the market for diabetes treatment.

6.1 Insurance

We recommend that insurance companies continue to offer education for wellness programs, as well as working to improve program education and communication to increase participation rates.

For type 1 diabetes, no medication is currently available for prevention yet. However, providing diabetes education is a valuable approach to support and guide diabetics to manage and lower the risk of type 1 diabetes:

- Healthy eating and activity plan.
- Blood sugar testing.
- Monitor feet, skin and eyes to detect problems early.

For type 2 diabetes, lifestyle-related factors such as obesity and physical inactivity are highly risky for diabetes, according to our risk factor analysis. Therefore, keeping a normal weight and healthy lifestyle works best to prevent type 2, the most common type of diabetes, and reduce the healthcare costs for insurance companies.

Insurance companies can offer wellness programs or encourage employers to provide corporate wellness programs, which would be beneficial to both types of diabetes. For example, insurance companies can offer incentivized walking, weight management and healthy lifestyle coaching. According to the CDC, nearly 50% of workplaces in the United States provided wellness programs by 2017 (31), and about 50% of smaller workplaces and 84% of bigger workplaces offered wellness programs by 2019 (32). However, the low usage of wellness programs is still an existing problem. Thus, participation in wellness programs should be increased and we suggest the following strategies to motivate more participants:

- **Understand participants of wellness programs**

  The program should be designed to serve people with high-risk factors of diabetes. It would be useful to survey participants and understand their health needs, interests, and lifestyle, as well as what motivates them to participate in wellness programs.

- **Improve understanding of wellness programs and offerings**

  Communications must be efficient and effective to capture people's attention. Education material, frequent communication, and fun tips should be considered throughout the year to improve understanding of wellness programs.

- **Offer incentives, including both monetary and non-monetary rewards**

  Incentives can motivate more participants, particularly high-risk populations, in wellness programs. Rewards such as small value gift cards, fitness gear, or other types of prizes that match what motivates them can be offered. Additionally, it would be an effective approach to motivate more participants by having employers offer time-off days to encourage people to fully disconnect from work and work on wellness programs.

6.2 Behavior Change

Since lifestyle-related factors, particularly obesity and physical inactivity, are high risk factors for type 2 diabetes, we recommend obesity management and physical activity intervention strategies to prevent type 2 diabetes, lower the direct medical costs and indirect cost due to reduced productivity, lost work and wages.

6.2.1 Obesity Management

We recommend that communities, governments, and healthcare providers offer education and resources for obesity management. According to the National Diabetes Statistics Report on the prevalence and incidence of diabetes and risk factors (3), 89.8% of diabetic adults were overweight or had obesity, with 26.9% overweight, 47.1% obese and 15.7% extremely obese. Based on NHANES (16), the U.S. obesity prevalence was an average 41.9% across all states of the U.S. (Figure 15).

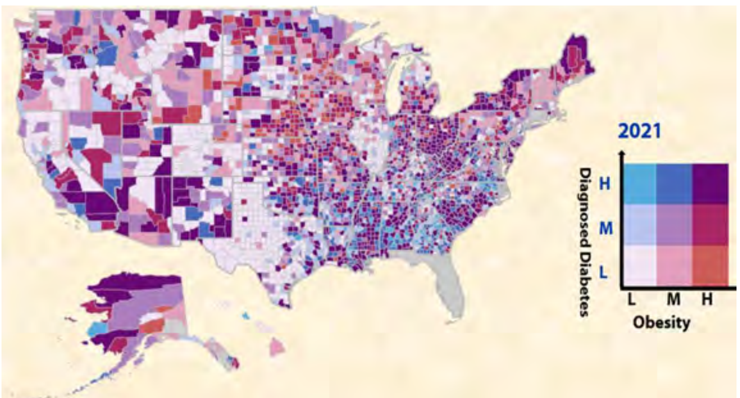

Figure 15: The prevalence of diagnosed diabetes and obesity among adults aged 18 years or older in 2021 in the U.S. map (33). L, M and H stand for lowest, middle, and highest level in each obesity and diagnosed diabetes category respectively.

The predicted risk of developing diabetes for the U.S. population in 2050 is 153% greater than that of 2018, corresponding to 43.2 million new cases between 2018 (28.1 million) and 2050 (71.3 million), with approximately 39.3 million being type 2 diabetes (Figure 15). The type 2 diabetic population can be reduced by implementing effective diabetes prevention strategies. If obesity management at a population level was put in place to result in normal body weight, the predicted risk of developing type 2 diabetes would drop by 28.1%, decreasing the number of diabetes cases by 15.7 million (from 71.3 million to 55.6 million) (Figure 16).

Figure 16: Projected diabetic population with obesity management vs. without obesity management in 2050.

The reduced diabetic population saves a significant amount of medical costs (Figure 17). In 2050, the medical costs can be reduced from $1.572 trillion to $1.227 trillion, saving costs of $0.345 trillion, with obesity management. Since diabetes usually causes other health conditions such as heart disease, kidney disease, blindness and neuropathy etc., the actual saved costs could be significantly more than $0.345 trillion in 2050 with the diabetic population reduced. Therefore, obesity and body weight should be managed to prevent and delay progression to diabetes and save medical costs.

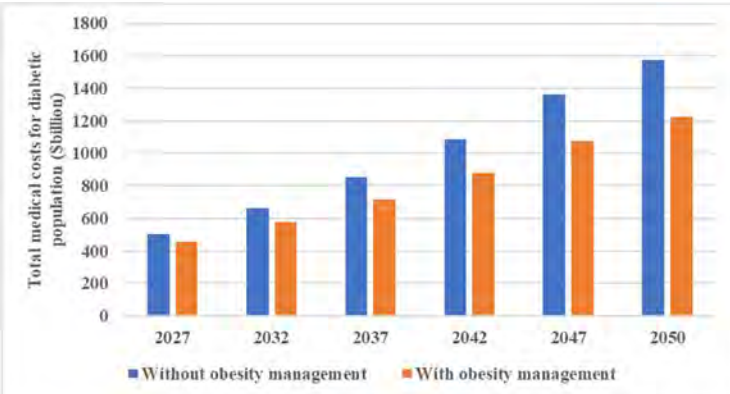

Figure 17: Obesity management reduces medical costs. Blue and orange bars stand for the medical costs of the diabetic population without and with obesity management respectively.

6.2.2 Physical Activity Interventions

We recommend state governments and communities take more efforts to educate and encourage everyone to increase physical activity. Walking, swimming, gym-based activities, or any other types of physical activities are beneficial to reducing type 2 diabetic risks. Moreover, we recommend providing more opportunities for outdoor physical activities. For example, it would be beneficial to provide more biking and hiking trails as these physical activities can reduce diabetic risks and improve individual health conditions.

Though physical activity contributes to significant health benefits, the CDC data 2017-2020 showed that 31.9% of diabetic adults were observed to be physically inactive (3), with no more than 10 minutes a week of moderate or vigorous physical activity in work, leisure time or transportation (3). According to the BRFSS 2017-2020 (15) (Figure 18), the lowest prevalence of inactivity was seen in Colorado with 17.7% and the highest prevalence was in Puerto Rico with 49.4%. Overall, states in the South had the higher prevalence of physical inactivity, followed by the Midwest, Northeast and West.

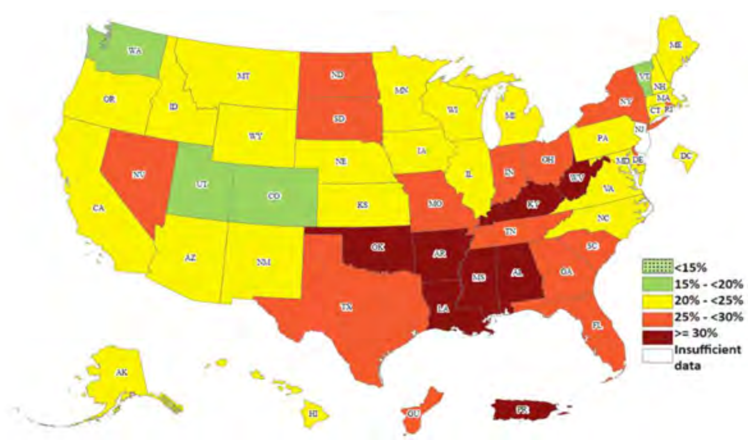

Figure 18: Physical inactivity prevalence by states (34).

Increasing physical activity is important to lower the risk of diabetes prevalence. Epidemiological evidence showed that physical activity may help to reduce 30-50% of diabetic risks (35), since physical activity can improve glucose tolerance and effectively achieve weight loss (36, 37). Therefore, becoming more active can improve well-being, as well as prevent and manage type 2 diabetes.

6.3 Modifying Outcomes

Stem cell therapy is a promising approach to treat and cure both type 1 and type 2 diabetes. We recommend that the federal government provide sufficient support and investment in physical and institutional infrastructure and research to advance the scientific progress of stem cell therapy. Additionally, investment in research translation, research application and clinical trials are required to bring stem cell therapy to the clinical treatment for diabetic patients.

Medical evidence showed that diabetic patients usually display multiple immune dysfunctions. Stem cell therapy is a new approach to control or reverse immune dysfunction (38). After being injected into the patient's pancreas, stem cells can regenerate pancreatic cells to replace dysfunctional pancreatic cells that do not produce insulin. It has demonstrated considerable promise in treatment and cure for diabetic patients. Furthermore, it helps to manage diabetes-related complications including diabetic retinopathy, diabetic nephropathy, and diabetic neuropathy. Stem cell therapy is promising as an effective approach to treat type 1 and type 2 diabetes.

For those with type 1 diabetes, the body lacks the function to produce sufficient insulin and thus daily insulin injection is a must. With the successful stem cell therapy, those suffering from type 1 diabetes would no longer need to inject insulin, avoiding large spending on insulin injections and other diabetic care. For those with type 2 diabetes, insulin injection and other diabetes medical care are currently required in the case that a healthy diet and routine exercise are still not sufficient to control blood glucose. Recent stem cell studies have shown the great promise to cure type 2 diabetes. Therefore, new therapeutic strategies with stem cell therapy can significantly reduce diabetes and medical costs associated with diabetes.

However, there have been barriers preventing stem cell therapy from coming to the market for diabetes treatment. There are major limitations to stem cell therapy success. For example, immune rejection, biosafety, cost issues, etc. Therefore, more scientific progress should be developed to overcome the barrier to increase the success rate and minimize the risk of potential treatments for diabetes, and make the stem therapy affordable (39).

The federal government should support the development and implementation of stem cell therapies to make treatments more inclusive and accessible. Since scientific progress in medicine requires sustained support given the long-term research and development process, it may take decades of public and private research to develop successful stem cell therapy to treat diabetes.

Upon the successful implementation of stem cell therapy in the market for diabetes treatment, the incidence rate of diabetes is expected to decrease. Clinical trials using stem cell therapy to restore pancreatic function have shown great promise in treating diabetes and lowering the incidence rate (38-40). Clinical cohort studies have shown the clinical efficacy of stem cell therapies dependent on specific type of diabetic and type of stem cells and there was a clinical cohort study showing as high as 58.9% success rate for type 1 diabetes and lower rate for type 2 diabetes (39). Despite existing technical problems such as determination of the specific stem cells and adverse effects of stem cell therapies, stem cell therapies continue to provide promising opportunity to treat diabetes. Without data of decreased incidence rate of diabetes by the stem cell therapy, we applied a decreased 10% and 50% incidence rate for each year from 2018 and compared the projected diabetic population in 2050.

We observed the reduction in the risk, from a range of 5.4% (with 10% lower incidence rate) to 35.6% (with 50% lower incidence rate) lower diabetic prevalence. Without stem cell therapy, the medical costs will reach $1.572 trillion. However, stem cell therapy can lower diabetic incidence rate, saving $0.081 trillion (from $1.572 to $1.491 trillion) direct medical costs in the case of a 10% lower incidence rate for each year and $0.413 trillion (from $1.572 to $1.159 trillion) direct medical costs in the case of a 50% lower incidence rate for each year (Figure 19).

The saved amount was only focused on direct medical cost for diabetic care. While we consider the medical costs associated with diabetes-related complications and other indirect costs due to the reduced productivity or unemployment for those diabetics, the stem cell therapy approach could have an greatly amplified effect on the mitigation of the total financial loss.

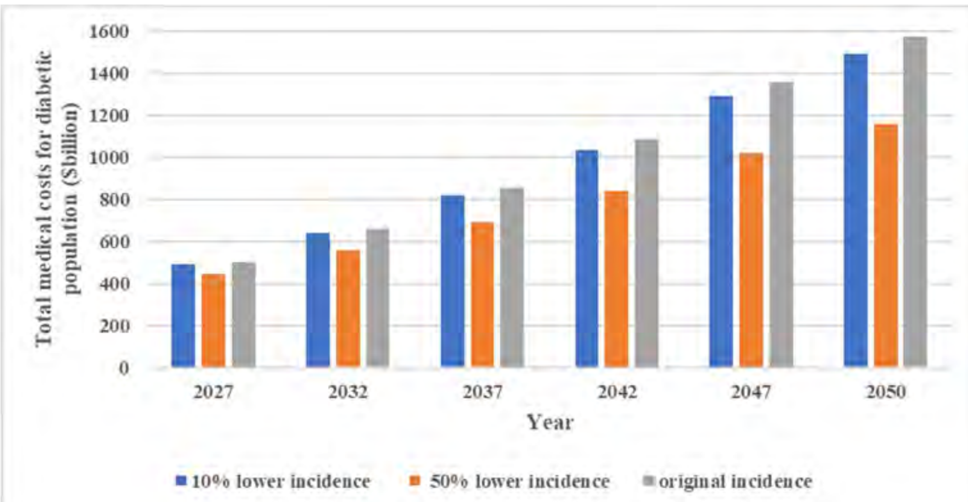

Figure 19: Medical costs are reduced using stem cell therapy. The gray bar stands for the medical costs for the diabetic population without stem cell therapy. The blue bar and orange bar represent the medical costs with stem cell therapy which lead to a 10% incidence (blue bar) or 50% incidence (orange bar) rate decrease respectively.

Therefore, stem cell therapy is a highly promising new approach to effectively reduce the risk of diabetes, and significantly lower the associated medical costs. The federal government should provide more support and investment to develop and implement stem cell therapies, which can come to the market for diabetes treatment soon.

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