2021

INDIVIDUAL PROJECT PROPOSAL

BIA 650: OPTIMIZATION AND PROCESS ANALYSIS

IMPACT OF DIABETES ON FUTURE GENERATIONS AND HOW TO CONTROL IT

BY SHREYA SANDEEP SHINDE

Investigating the Impact of Diabetes on future generations and how to control it

INTRODUCTION:

Despite the known benefits of a healthy lifestyle, many individuals find it hard to maintain such a lifestyle in our modern world, which facilitates sedentary behavior and overeating. Therefore, the prevalence of type 2 diabetes mellitus is predicted to increase dramatically over the coming years. Will developments in treatments be able to counteract the resulting impact on morbidity and mortality? The various lines of research can be grouped into three main categories: technological, biological, and pharmacological.

1. Technological solutions are focused on the delivery of insulin and glucagon via an artificial pancreas, and components of the system are already in use, suggesting this option may well be available within the next 10 years.
2. The biological solutions, pancreas transplants seem unlikely to be used widely, and islet cell transplants have also been hampered by a lack of appropriate donor tissue and graft survival after transplant. However, significant progress has been made in these areas, and additional research suggests manipulating other cell types to replace beta cells may be a viable option in the longer term.
3. The last category, pharmacological research, appears the most promising for significantly reducing the burden of type 2 diabetes mellitus. In recent years, research has concentrated on reducing blood glucose, and the increasing pace of research has been reflected in a growing number of antidiabetic agents.

In the past few years, studies of the complementary approach of protecting cells from the damaging effects of high blood glucose have also been reported, as has research into the control of energy intake and energy expenditure. Evidence from studies of dietary restriction and bariatric surgery suggests it may be possible to reset metabolism to effectively cure diabetes, and research into pharmacological agents that could selectively restore energy balance is currently the most exciting prospect for future treatments for people with type 2 diabetes mellitus.

PROJECT APPROACH:

Before the availability of insulin in the 1920s, hailed not only as the cure for diabetes but also as one of the greatest advances in the treatment of any disease, a person diagnosed with diabetes would have faced death within a few years. Today, diabetes is not the devastating diagnosis it would have been 100 years ago; in fact, it is now a common misconception among the public that diabetes is not a serious disease. The impact of diabetes is so significant that it is affecting overall life expectancy: in the United States (US), life expectancy is falling for the first time since statistics were collected, due to obesity and diabetes [Olshansky et al. 2005] and estimates of diabetes prevalence over the coming years suggest many of us reading this

article will develop diabetes during our lives [Whiting et al. 2011]. The predictions of the increased prevalence of diabetes are rarely accompanied by predictions of improvements in the treatment of diabetes; however, given the impact of diabetes, it has been the focus of intensive research, resulting in major advances in our understanding of diabetes as well as in treatment options. As the centenary of the discovery of insulin approaches, it seems timely to consider how treatment options may look in the 2020s, and the likelihood that the elusive cure for diabetes could be found by that time.
Numerous administration substances including Centers for Disease Control and Prevention (CDC), National foundation of wellbeing (NIH), American diabetes affiliation (ADA) and some other internet-based assets give the genuine information clarifying the momentum circumstance of diabetes in US. For the satisfaction of the task, information will be gathered from these assets and examination will be acted to recognize the different elements. These examinations will incorporate cross arrangement, relapse and so forth considering these elements, methodologies will be figured to convey the assets viably and financially. Examination will be performed on both kind 1 and type 2 diabetes.
The National Diabetes Statistics Report, a periodic publication of the Centers for Disease Control and Prevention (CDC), provides information on the prevalence and incidence of diabetes and prediabetes, risk factors for complications, acute and long-term complications, deaths, and costs. These data can help focus efforts to prevent and control diabetes across the United States. This document is an update of the 2017 National Diabetes Statistics Report and is intended for a scientific audience.
Type 1 and Type 2 diabetes – Type 1 diabetes can be thought as a result of an autoimmune reaction (i.e., body attacks itself, by mistake). This results in obstacle in making insulin. Common Symptoms of type 1 diabetes are often developed quickly. If one has type 1 diabetes, then one will need to take insulin every day to survive. In type 2 diabetes, body doesn't use insulin properly and so it becomes difficult to keep blood sugar at normal levels. It is developed over years and is generally diagnosed in adults. You may or may not notice any symptoms, so it's very important to get blood sugar tested if you think you're at risk.

BUSINESS SOLUTION:

1. Technological solutions

The majority of cases of diabetes are type 2 diabetes mellitus (T2DM), and the predicted rise in diabetes prevalence is expected to be driven by increases in the number of T2DM cases. However, it is likely that significant advances in therapy for T2DM will result from the research in type 1 diabetes mellitus (T1DM), as they are both essentially disorders of glucose management.
In T1DM, the complete lack of endogenous insulin has focused research on ever-more sophisticated ways to deliver insulin, with the eventual goal of developing an 'artificial pancreas'. The elements are already available: a sensor to detect blood glucose readings, a computer to calculate insulin requirements, and a pump to automatically deliver insulin. The feasibility of bringing these elements together has already been demonstrated in clinical trials, with sensor-augmented pump therapy, integrating a sensor and a pump, shown to improve glycemic control compared with a regimen of multiple insulin injections per day [Bergenstal et al. 2010; Hermanides et al. 2011]. A true artificial pancreas would also deliver glucagon to raise blood glucose and prevent severe hypoglycemia, a concept that has already been shown to be feasible [El-Khatib et al. 2010].

Several technological challenges need to be overcome to produce a clinically useful artificial pancreas. First, currently available continuous glucose monitors measure glucose levels in interstitial fluid rather than directly in the blood, resulting in a time lag before changes are measured. As a consequence, accuracy is not sufficiently reliable, with reported error rates of between 12% and 17%. Accuracy is likely to be lowest when blood glucose levels are low; hence, continuous glucose monitoring of interstitial fluid is currently recommended only as an adjunct to standard blood glucose

monitoring [Weinzimer and Tamborlane, 2008]. Insulin pump technology is more advanced; nevertheless, today's pumps deliver insulin subcutaneously, and the delay while insulin is absorbed into the bloodstream limits the ability of software to regulate blood glucose accurately [Renard, 2008]. Catheter complications have prevented intravenous delivery of insulin, and surgically implanted pumps are expensive. It is clear that none of these technological challenges are trivial, but given the pace of developments in technology, we can expect more practical options for patients within the next 10 years. For example, so-called 'smart tattoo' biosensors are capable of detecting glucose levels continuously using a simple infrared detector and providing results in real time. These biosensors, which are based on single-walled carbon nanotubes wrapped in glucose-sensitive polymers that fluoresce in the presence of glucose, are currently being researched in animal models [Barone and Strano, 2009].

2. Biological solutions

Even as technological solutions advance closer and closer to an artificial pancreas, it is unlikely that technology could ever regulate insulin as precisely as beta cells in a healthy pancreas. Research therefore continues into replacing damaged beta cells with functioning cells, or replacing the entire pancreas [Claiborn and Stoffers, 2008; Sachdeva and Stoffers, 2009]. As with the artificial pancreas, most research to date has been conducted in T1DM, but the results will ultimately translate into therapies for T2DM.

Pancreas transplants have been performed since the late 1980s, with more than 30,000 pancreas transplants recorded in the past 25 years [Gruessner, 2011]. In principle, pancreas transplants offer the promise of excellent outcomes for patients with diabetes. Indeed, stricter donor criteria, as well as improvements in surgical techniques and immunosuppression, have led to improved success rates, with the majority of patients no longer needing insulin therapy after the transplant [Gruessner, 2011]. In practice, the vast majority of pancreas transplants are done in patients who have end-stage renal disease and also need a kidney transplant; this is partly due to the shortage of donor organs, but also because the risks of the necessary post-transplant immunosuppressant therapy usually outweigh the health risks of diabetes itself.

A less invasive option that has already been shown to be viable, at least for some patients, is replacing pancreatic beta cells via islet cell transplants [Truong and Shapiro, 2006]. Isolating these cells from a donor pancreas and infusing them into the patient's portal vein has been researched since the 1960s, and a successful protocol using islets from multiple donors, improved cell culture techniques, and reduced toxicity was optimized during the 1990s at the University of Alberta in Edmonton, Canada. Using the Edmonton protocol, initial studies reported success; however, over time transplanted islets lose function and patients still require immunosuppressive drugs, which are known to increase the risk of infections and the incidence of malignancy, as well as being toxic to the islet cells themselves [Alejandro et al. 2008; Shapiro et al. 2000].

The treatment is still considered experimental and is only available to patients with very poor glycemic control and severe hypoglycemic events but, given the benefits of a successful therapy, there is significant drive to overcome the challenges of limited availability of donor tissue and graft survival after transplant. As well as optimizing the yield of islets from donor pancreata, basic science research into cell differentiation has identified possible alternative sources of beta cells, including differentiating stem cells and reprogramming somatic cells [Baiu et al. 2011; Kelly et al. 2011]. Various strategies are also being researched to improve graft survival after transplantation, by

developing immunosuppression regimens that are less toxic to islets and inducing revascularization/reinnervation of the islets [Plesner and Verchere, 2011].

In the longer term, other biological solutions using nonislet cells from the patient themselves are possible options, such as transdifferentiation (mediated by growth factor treatments or gene transfer) of nonislet pancreatic cells or liver cells [Claiborn and Stoffers, 2008; Kojima et al. 2003], and regenerating beta cells and/or expanding beta-cell mass using mediators of beta-cell differentiation and maintenance of adult beta cells [Sachdeva and Stoffers, 2009].

3. Pharmacological solutions

For patients with T1DM, who make no insulin, the only pharmacologic option is replacement insulin. Astonishing progress has been made since replacement insulin first became available, when insulin batches were of variable quality and large, twice-daily injections were needed. Today, it is hard to imagine how difficult it must have been to manage T1DM without disposable needles or patients self-testing glucose. The possibilities for improvement in pharmacological care for these patients should not be underestimated, although most likely they will be essentially improvements in the convenience of insulin delivery.

Dietary restriction is known to increase lifespan in rodents, and can delay or prevent diseases such as cancer, heart disease, and diabetes; however, studies in nonhuman primates have reported conflicting findings, indicating the effects of dietary restriction are likely to be complex [Mattison et al. 2012]. Such studies are hard to replicate in people, but trials showing a severely restricted diet can improve beta-cell function and insulin sensitivity in patients with a relatively short duration of T2DM suggest that humans, like hibernating mammals, have the capacity for recovering from insulin resistance [Lim et al. 2011]. The problem, the study investigators believe, is that few people could maintain such a limited calorie intake, and any successful nonsurgical solution may therefore rely on drugs mimicking the effects of dietary restriction. Given the current and predicted prevalence of obesity, there is already intensive research into agents that decrease appetite or increase satiety. The endocannabinoid system is known to have a role in the regulation of appetite, but cannabinoid receptor antagonists such as rimonabant have been associated with unacceptable side effects [Eckel et al. 2011], although more selective agonists may be an avenue targeted in the future. To date, other therapies developed for the treatment of obesity have also been plagued by safety issues, but there are now several promising molecules in the early stages of development [Eckel et al. 2011].

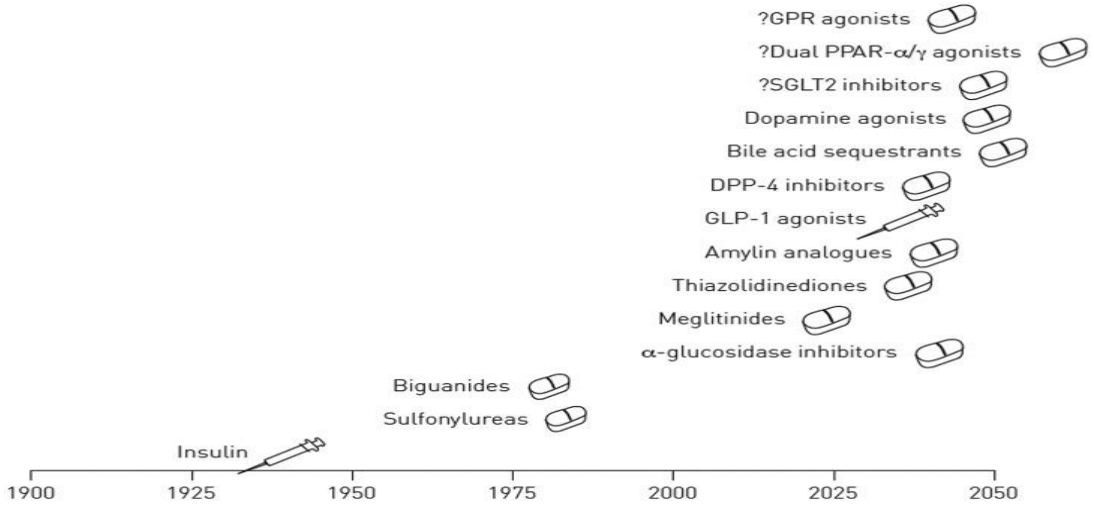


Fig 1: US Food and Drug Administration approval of pharmacological options for type 2 diabetes mellitus.

Among the currently available therapies for T2DM, various classes also promote weight loss. For example, the subcutaneous agent pramlintide is associated with reduced food intake and body weight in obese people with and without diabetes, although it is associated with only modest hemoglobin A1c (HbA1c) reductions and the amount of weight loss induced is also relatively small [Lee et al. 2012]. Pramlintide is a synthetic form of amylin, which is secreted after meals and signals short-term satiety, and may therefore be more useful in combination with other agents. Therapies combining pramlintide with long-term signaling molecules are in the early stages of development, along with other therapies targeting appetite [Powell et al. 2011].

Metformin is also associated with weight loss, although the amount of weight shed is insufficient to meet FDA criteria for a weight loss drug (at least 5% of body weight). Guidelines now recommend physicians consider metformin for preventing or delaying diabetes in individuals with elevated glucose measurements and a body mass index >35 kg/m2 [American Diabetes Association, 2012]. Intriguingly, research has shown that metformin-induced alterations mimic many of the same transcriptional changes in the liver that occur with dietary restriction [Dhahbi et al. 2005]. The effects of metformin are still incompletely understood, but activation of AMP-activated protein kinase (AMPK) appears to play a central role [Zhou et al. 2001]. AMPK is a sensor of energy shortage within cells, acting as a metabolic switch (Box 2). The role of AMPK, and possible activators, are being intensively investigated and, at present, this route appears the most exciting line of enquiry into a possible cure for T2DM.

STAKEHOLDERS AND CLIENTS:

The major stakeholders which are associated with diabetes in some way and may contribute to controlling the diabetes are:

1) The patient itself – the patient is the key stakeholder in the project research because controlling the diabetes in the patient and help them in living a healthy life is also important.
2) The prospects who think they are at the risk of having diabetes – motivating the young and adults to go for health checkup is important because early detection of the diabetes helps to control it from moving it into later stages. Also, early detection helps the patient in living the normal lifestyle.
3) Government entities – Government entities can play important role by providing the equipment for detection and medication for free or discounted price.
4) Medical professionals i.e., doctors, nurses, pharmaceutical companies/outlets – good availability of doctors, nurse and medicines with the reach of average people can open the far better way to control the diabetes.

Components of the clinical management of patients with (or at risk for) diabetes are reviewed. Clinical practice guidelines are key to improving population health; however, for optimal outcomes, diabetes care must be individualized for each patient. The American Diabetes Association highlights the following three themes that clinicians, policymakers, and advocates should keep in mind:

Patient-Centeredness: Practice recommendations, whether based on evidence or expert opinion, are intended to guide an overall approach to care. The science and art of medicine come together when the clinician is faced with making treatment recommendations for a patient who would not have met eligibility criteria for the studies on which guidelines were based. Recognizing that one size does not fit all, these Standards provide guidance for when and how to adapt recommendations. Because patients with diabetes have greatly increased risk for cardiovascular disease, a patient-centered

approach should include a comprehensive plan to reduce cardiovascular risk by addressing blood pressure and lipid control, smoking prevention and cessation, weight management, physical activity, and healthy lifestyle choices.

Diabetes Across the Life Span: An increasing proportion of patients with type 1 diabetes are adults. For less salutary reasons, the incidence of type 2 diabetes is increasing in children and young adults. Patients with type 1 diabetes and those with type 2 diabetes are living well into older age, a stage of life for which there is little evidence from clinical trials to guide therapy. All these demographic changes highlight another challenge to high-quality diabetes care, which is the need to improve coordination between clinical teams as patients transition through different stages of the life span.

Advocacy for Patients with Diabetes: Advocacy can be defined as active support and engagement to advance a cause or policy. Advocacy is needed to improve the lives of patients with (or at risk for) diabetes. Given the tremendous toll that obesity, physical inactivity, and smoking have on the health of patients with diabetes, efforts are needed to address and change the societal determinants at the root of these problems. Within the narrower domain of clinical practice guidelines, the application of evidence level grading to practice recommendations can help to identify areas that require more research (1). Refer to Section 14 “Diabetes Advocacy.”

DATASET:

To conduct my research, I will draw data from the official sites of Centers for Disease Control and Prevention (CDC), American diabetes association (ADA), PMC US National Library of Medicine National Institutes of Health Search database, World Health Organization (WHO), National institution of health (NIH), Center for Medicare and Medicaid services, U.S. census, U.S. department of Labor and Statistics and from some other online resources as well.

After owing all the data, I will perform my analysis based on some most relevant algorithms on most of the data but not all. This data will be included based on the input and output variables taken into consideration.

The variables I will use for my model are:

Output Variables

1. Degree of diabetes after following the healthy diet
2. Number of appointments or visits to clinic
3. Average monthly expenditure for a diabetes patient
4. Average life span of diabetes patients.
5. Degree of diabetes after following the exercise and yoga routine

Input Variables

1. Healthy diet plan
2. Good exercise and yoga plan
3. Gender of the patient
4. Age of the patient
5. Prediabetes awareness

CONCLUSION:

To allow us to cope with periods of famine and feast, humans are adapted to make the most of the energy available to them. What ensured our survival then has become our weakness now, and all predictions indicate the prevalence of T2DM will get worse before it improves. Modern lifestyles allow continual access to food and encourage sedentary behavior, leading to a progressive cycle of overeating and weight gain. Despite efforts at education, lifestyles will likely become yet more sedentary over the next 20 years, facilitated by advances in technology. For example, concepts for controlling the world around us with only our thoughts would have been science fiction 20 years ago but are now actively researched [Hochberg et al. 2006]. There seems little doubt that, without interventions, the prevalence of T2DM will increase.

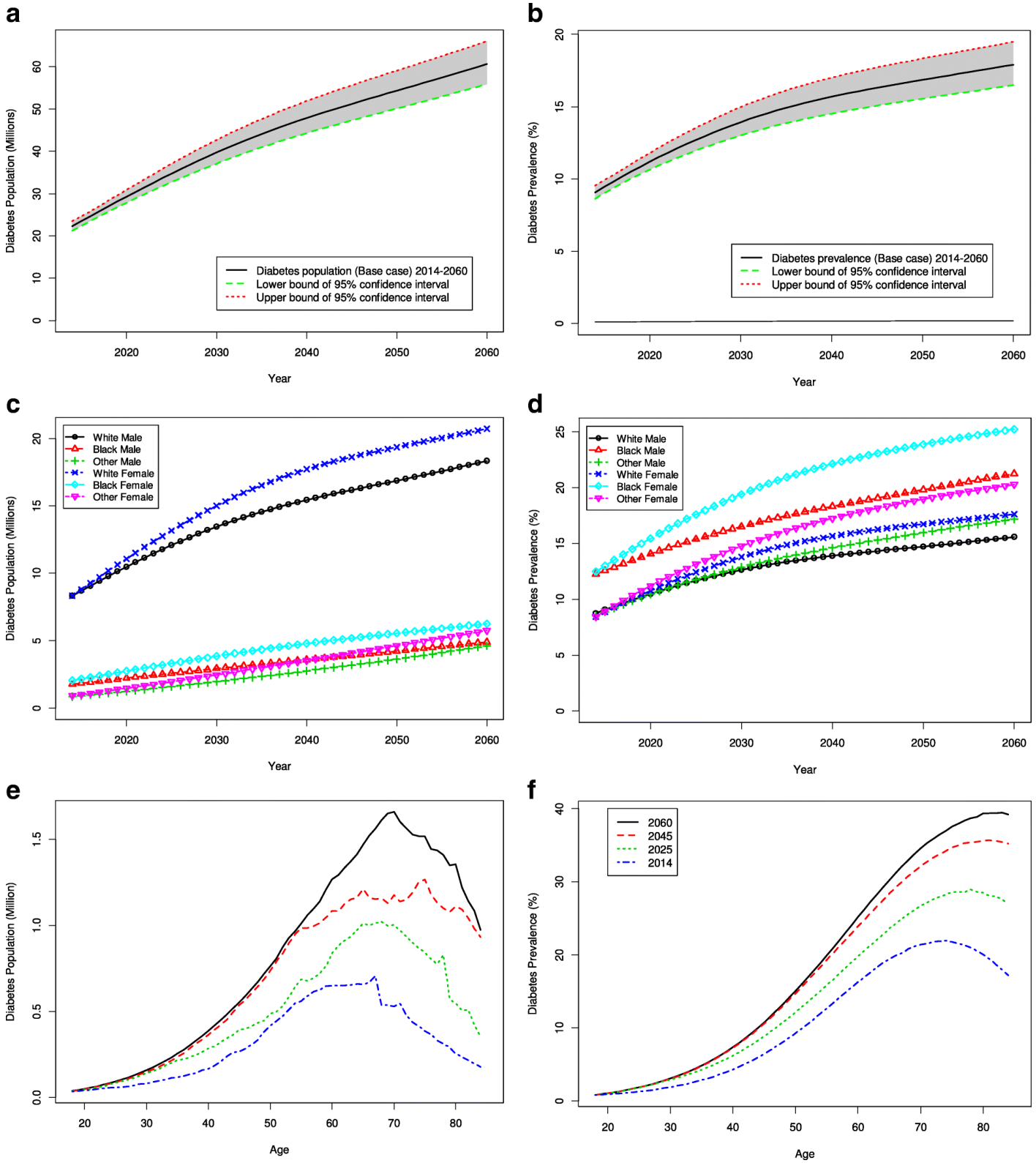
For those who prefer simplistic views, it is easy to blame individuals for having diabetes. Indeed, despite the clear benefits of a healthy lifestyle, changes in long-term behavior and lifestyle are rare. However, as we understand more about our biology, we can appreciate that our environment naturally puts us all at high risk of diabetes. Nowhere is this seen more clearly than in populations that have been exposed to sudden changes in lifestyles as a result of urbanization, such as the Pima Indians in the US, who have far higher rates of T2DM than Pima Indian populations in Mexico [Esparza-Romero et al. 2010].

Is it realistic to ask people to change their lifestyles? The advances in therapy over the past 50 years have provided a remarkable array of options so that treatment can be tailored for each patient, but, even with expert teams of dieticians and diabetes educators, most patients need drug therapy, probably multiple-drug therapy, to achieve recommended HbA1c targets. However, in spite of achieving HbA1c targets, they still retain a residual risk for complications compared with people without diabetes. In the future, we may accept that drugs are needed to allow us to lead modern lifestyles without increasing our risk of diabetes. The scientific community should be applauded for taking the pragmatic approach of searching for interventions that could help individuals, probably the majority, who are unable to maintain healthy lifestyles in the long term. Because our lifestyle means that diabetes will become a normal aspect of life, the research ongoing today is vital to provide tools to counteract the diabetes epidemic.

REFERENCES:

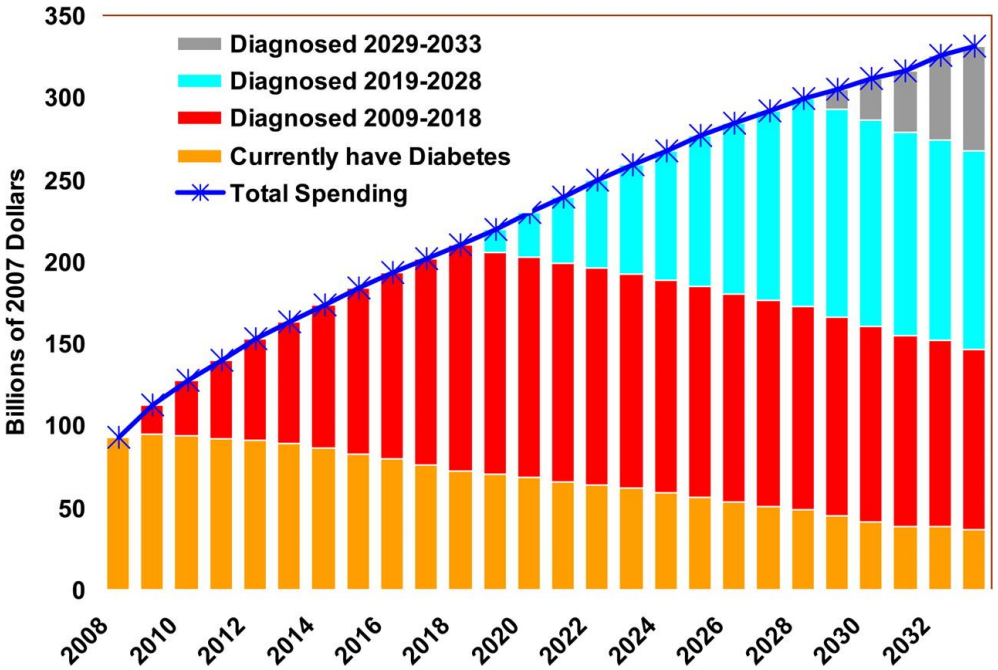
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3498849/
https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6125024/
https://www.cdc.gov/diabetes/prevent-type-2/type-2-kids.html
https://www.who.int/diabetes/actionnow/en/DANbooklet.pdf
https://care.diabetesjournals.org/content/32/12/2225
https://pophealthmetrics.biomedcentral.com/articles/10.1186/s12963-018-0166-4
https://www.who.int/diabetes/actionnow/en/DANbooklet.pdf

APPENDIX I:



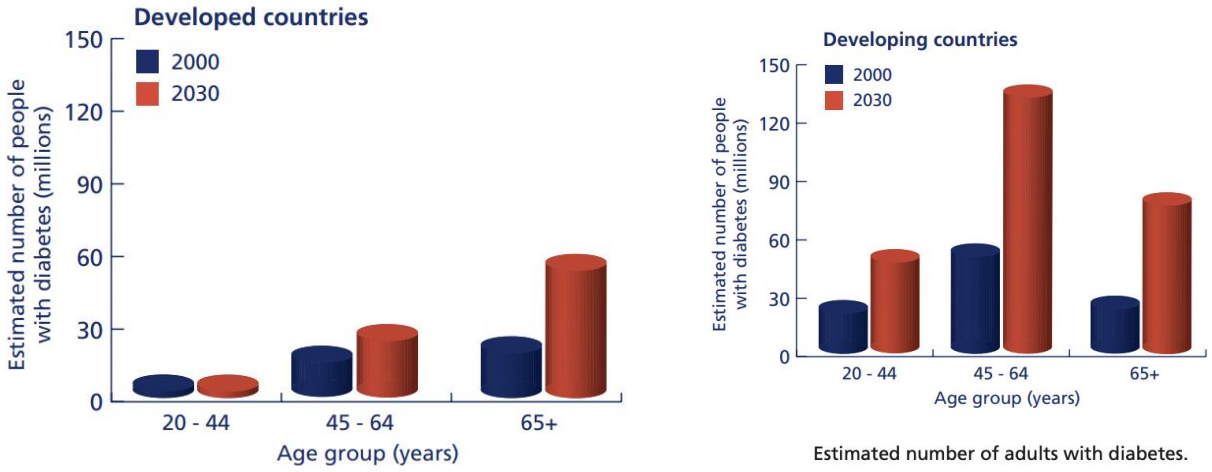
Projection of diagnosed diabetes prevalence in US adults: a overall number, b overall percent, c number by race and sex, d percent by race and sex, e number by age and year, f and percent by age and year

APPENDIX II:



Projected direct spending on diabetes and its complications for different cohorts, 2008–2033

APPENDIX III:



Estimated number of adults with diabetes.

The number of people with diabetes will more than double over the next 25 years, to reach a total of 366 million by 2030. Most of this increase will occur as a result of a 150% rise in developing countries.