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Delaying Onset of Diabetes in Native American Populatons

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DELAYING ONSET OF DIABETES IN NATIVE AMERICAN POPULATIONS

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Abstract

Diabetes is a debilitating disease process caused by the body's inability to control blood glucose levels. With over 30 million diabetics in the United States, and another 85 million prediabetics, the effects of this disease are wide-spread and far-reaching. Native American/Alaska Native populations have a nearly two-fold increase in incidence of diabetes when compared to non-native populations. Risk factors for diabetes in all populations include modifiable risks such as obesity, diet, physical inactivity as well as non-modifiable factors such as age, family history, and ethnicity. Studies have shown that early identification of symptoms, coupled with proper and intentional treatment can delay the onset of diabetes. The purpose of this project is to determine the efficacy of currently recognized best-practice therapies in Native American patients and to identify barriers to successful implementation of such practices in the Native American population. A thorough review of the available literature shows that research of this topic specific to the Native American population is lacking. However, evidence suggests that the broad, general population recommendations made by the American Diabetes Association in their Standards of Medical Care in Diabetes (2018) will be equally effective in the Native American population when applied objectively. It is also recognized that Native Americans face additional barriers in the effort to identify and treat diabetes. These include geographic, economic, and social factors that inhibit treatment efficacy and ultimately lead to increased morbidity in this population.

Keywords: diabetes, prediabetes, American Indian, Native American, diabetes treatment, obesity, glucose, genetic predisposition, pharmacotherapy, ethnicity, insulin, and lifestyle modifications

Introduction

Diabetes is a major factor in the overall health of the U.S. population. It is broadly defined as a fasting plasma glucose of >126mg/dl, a hemoglobin A1c > 6.5%, or a glucose tolerance test of >200mg/dl. According to the Centers for Disease Control (CDC), more than 30 million Americans are diabetic and another 85 million are considered prediabetic, with an A1c of 5.7% - 6.4% or a fasting plasma glucose of 100-125 mg/dl. Over the past 20 years, the number of Americans with diabetes has tripled. This is an alarming rate that carries significant health and financial burdens for those affected, their families, and for the entire nation. Additionally, with nearly one-third of the U.S. population experiencing prediabetic conditions (CDC, 2018), the importance of identification, diagnosis and early treatment is increasingly important.

With an estimated total population of 6.795 million, Native Americans, which include American Indians and Alaska Natives, make up approximately 2% of the total United States population as of 2017 (U.S. Census Bureau, 2018). According to the CDC, the prevalence of diabetes in this population is 16%, which equates to nearly 1.1 million Native American diabetics. When compared to the Caucasian population, a two-fold increase in diabetes prevalence is observed. In fact, when compared to all races, Native Americans exhibit a greater chance of having diabetes than any other racial group.

Diabetes is encountered daily by nearly all clinicians in the rural primary care setting. Because many diabetic patients also present with co-morbid conditions including hypertension and obesity, among other chronic diseases, their treatment plans are often more complex and difficult to manage. In addition to these medical complexities, other issues including financial, geographical, and motivational barriers have been identified as contributory to the current diabetes epidemic within the Native American population.

Social effects are evident as diabetes management requires strict adherence to diet, exercise, and medication regimens, which are time-consuming and tedious. Often, these constraints are not conducive to the lifestyles of their non-diabetic friends and family members, leading to a social isolation for diabetic patients when efforts are made to control their blood sugars through lifestyle modifications. The mental effects of diabetes can also play a devastating role in the overall health of an individual. According to a study by Holt, de Groot and Golden (2014), given the detrimental effects of the disease, diabetic patients are 2 to 3 times more likely to develop depression than those without the disease.

Diabetes continues to be a major health problem in the Native American population. Because of the devastating effects of diabetes on the kidneys, eyes, heart, and other systems, it remains vitally important to identify patients at risk and treat symptoms that are evident prior to its onset. Within the last two decades, major improvements have been made in the management of diabetes, specifically within the Native American community through the Diabetes Prevention Program and the efforts of local tribal entities. However, the disease remains a major cause of morbidity and mortality amongst this population.

Current treatment recommendations from the American Diabetes Association (ADA) include diabetes self-management, education, and support in addition to nutrition therapy, weight management, and physical activity. Although the ADA applies these recommendations to patients of all ethnicities, it also acknowledges social contexts that may require treatment strategies tailored to population-specific needs. Barriers to ideal treatment remain paramount when considering the discordance of diabetes in Native Americans and social contexts must be favorably considered as the healthcare community seeks to reduce the incidence and prevalence of diabetes in this population.

The goal of this study is to determine the benefits of lifestyle and pharmacologic interventions in pre-diabetic and diabetic Native American patients and to identify barriers that may lead to ineffectiveness of such interventions.

Statement of the Problem

According to McLaughlin (2010), diabetes and other chronic illnesses were virtually non-existent in the Native American population at the turn of the 20th century. Until the early 1970s, diabetes was not in the top 10 causes of death for this population. By 2009, however, diabetes had climbed to number four on this list, and today, more than one in six Native Americans is diagnosed with diabetes.

The benefits of blood glucose management through lifestyle modification therapies are well known and clinically proven (Powers, et al. 2015). According to the ADA's Standards of Medical Care in Diabetes (2018) lifestyle management is a fundamental aspect of diabetes care and includes self-management education and support (DSMES), medical nutrition therapy (MNT), physical activity, smoking cessation counseling, and psychosocial care. These recommendations are strongly supported by evidence from well-conducted, generalizable studies and meta-analyses, earning "A" and "B" ratings from the ADA. Despite the widely known benefits of these interventions, many do not begin until the patient is diagnosed with diabetes, and often not until advanced disease is present. While this is also true in the general population, it appears to be more prevalent in the Native American population. According to Lillie-Blanton and Roubideaux (2005), there is significant evidence to conclude that Native Americans are disadvantaged in the healthcare system due to disparities in healthcare financing, access to care, and quality of care. Because many factors can influence this delayed intervention, the

ramifications for patients are certainly deleterious as damage to delicate tissues such as eyes, kidneys, and other microvasculature may have already progressed. Given the prevalence of diabetes in the Native American population, special attention must be paid to better understand the barriers that exist and ultimately deter patients from receiving optimal care and to determine the most appropriate and clinically sound treatment plans for these patients. Research must be focused on finding opportunities to identify and treat patients before the onset of diabetes.

Research Questions

In Native American patients, can lifestyle and pharmacologic interventions, prior to the onset of diabetes, improve glucose tolerance?

Are there additional benefits of combined therapy with metformin and lifestyle modifications that could improve the quality of life for these patients?

Are there identifiable barriers to successful treatment of prediabetes and diabetes in the Native American population?

Research Methods

For this literature review, CINAHL, Clinical Key, Cochrane, PubMed and ScienceDirect databases, as well as selected articles were searched to provide an overview of current evidence related to the topic of diabetes treatment, both in general as well as within the Native American population. The search included the following key words and MeSH terms: diabetes, prediabetes, American Indian, Native American, diabetes treatment, obesity, glucose, genetic predisposition,

pharmacotherapy, and lifestyle modifications. The initial search included eight years (2010-present) and was expanded to 15 years (2003-present) as a landmark study—the Strong Heart study (and subsequent sub-studies)—was considered critical enough to warrant inclusion. While studies related to prediabetes, diabetes and treatment options were plentiful, those specific to the Native American population were not readily available. Therefore, articles were included if they contained applicable information or data related to the research questions, regardless of ethnic focus. This was not a systematic review of all published articles regarding prediabetes, diabetes and treatment options. The research for this article primarily reviewed current prediabetes and diabetes treatment recommendations, their effects on the health of the participants and translational abilities of such studies to the Native American population.

Literature Review

Review of the literature on lifestyle and pharmacological interventions to reduce the incidence and effects of type II diabetes mellitus (DMII) has shown marked benefits with several specific therapies. These include limited diabetic education, intensive and non-intensive lifestyle modification programs (Powers, et al. 2015), metformin therapy (Ramachandran, et al. 2006), and more recently, newer antidiabetic medications such as DPP-4 inhibitors (Dicker, 2011). While all such interventions have proven beneficial in patients with impaired fasting glucose (IFG) and impaired glucose tolerance (IGT), some are more efficacious than others. Although much of the available literature is not specific to the Native American population, evidence is suggestive of similar benefits in all patients with impaired glucose tolerance. Additionally, genetic, behavioral and socio-economic factors have been implicated in the development of diabetes, despite availability of effective therapies. Given the high prevalence of diabetes in the

Native American population, the results of further study may pay dividends as population-specific approaches to diabetes care are identified and successfully demonstrated.

Pathophysiology of Type 2 Diabetes

Although there are several recognized disorders under the diabetes umbrella, type 2 diabetes—a complex disease related to the body's ability to produce and utilize insulin—is by far the most commonly diagnosed throughout the world. In type 2 diabetes, patients exhibit an array of dysfunction including resistance to insulin activity, inadequate insulin secretion, and inappropriate glucagon secretion. In healthy individuals, the pancreas produces insulin which is used by the body to allow cells to take up glucose from the blood stream to be used in metabolism and energy production. When adequate energy stores are present, excess glucose from the blood is stored in the liver in the form of glycogen. If energy needs increase or levels fall, and sufficient glucose levels in the blood are not available, the pancreas produces glucagon. This acts to release stored energy, in the form of glycogen, from the liver and into circulation where it can be utilized by peripheral tissues for energy production. When insulin fails to function appropriately—termed insulin resistance—patients can be diagnosed with prediabetes.

In this setting, patients can present with increased blood glucose levels at either fasting or post-tolerance test points. When the body senses increased blood glucose levels, the natural response is to increase the production of insulin from the pancreatic beta cells. Insulin levels will rise in an effort to assist glucose into the cells where it can be utilized for energy production. However, due to insulin resistance, these cells no longer respond to insulin efficiently. Blood glucose levels remain high, which fails to initiate the negative feedback loop on insulin

production. With the increased demand on the pancreatic beta cells, they naturally begin to fail over time, leading to insulin-dependent status for these patients.

Although diabetes is a complex disease process, screening tests for diabetes are simple and primarily focused on glycemia—how much glucose is in the blood. That focus, however, may be too narrow to identify patient-specific disease stages and ultimately limit our ability to treat patients effectively. According to Rosenstock (2007), impaired fasting glucose and impaired glucose tolerance may have different pathophysiological mechanisms. Impaired fasting glucose is thought to be a symptom of insulin resistance in the liver coupled with an insulin deficit while insulin sensitivity in the muscles remains normal. Impaired glucose tolerance, however, can be characterized by insulin secretion deficits in the pancreatic beta cells and a greater insulin resistance in muscles. Essentially, the ability to further break down the pathophysiology of the disease will allow for a refined approach to identification and treatment of type 2 diabetes. Rosenstock believes, for example, that "utilizing b-cell function/insulin secretion and/or insulin resistance to screen and monitor patients would permit more accurate differentiation and better understanding of the effects of preventive treatments on the underlying disease process than does measurement of glycaemia." This approach poses obstacles of its own, including comparative difficulty of testing, cost and lack of wide-spread availability.

Risk Factors of Type 2 Diabetes

According to Lyssenko and Laakso (2013), type 2 diabetes is a complex medical disorder resulting from interactions between genetics and environment, and risk factors to include age, sex, obesity, central obesity, low physical activity, smoking, low fiber diet, high saturated fat diet, ethnicity, family history, history of gestational diabetes, elevated blood pressure,

dyslipidemia, and certain drug treatments such as non-selective beta blockers. Although many independent risk factors are linked to type 2 diabetes, Lyssenko and Laakso also state that there is ample evidence to suggest a strong genetic component to the disease, pointing to a monozygotic twin concordance of 70% compared to a dizygotic twin concordance of 20-30%. Additionally, the lifetime risk of developing diabetes is approximately 40% in the offspring of one parent with type 2 diabetes and nearly 70% in the offspring two affected parents (Lyssenko & Laakso, 2013).

Specific to the Native American population, contributing factors can include genetic, environmental, and behavioral issues. Genetic predisposition to insulin resistance, fetal exposure to hyperglycemia during pregnancy, sedentary lifestyles, obesity as well as social and physical stresses caused by living environments are risk factors specifically identified in an article by McLaughlin (2010). Finally, Alfawaz et al. (2018) identify the manifold correlation between metabolic syndrome and the development of type 2 diabetes. Metabolic syndrome is a group of cardiovascular risk factors including central obesity, hyperglycemia, low HDL cholesterol, hypertriglyceridemia, and elevated blood pressure. Given the high incidence of metabolic syndrome in the Native American population, further study of metabolic syndrome in the setting of diabetes is warranted.

Recent advances in genetic testing have broadened the possibilities for identifying genetic variations that may lead to the development of diabetes, among many other disease processes. For example, since 2007, genome-wide association studies (GWAS) have identified more than 65 genetic variants that increase the risk of type 2 diabetes by 10-30% (McCarthy, 2010). The advances in understanding genetic variants associated with type 2 diabetes will be

advantageous toward the effort of understanding the racial disparity of type 2 diabetes in the Native American population.

Assessing risk in the Native American population will become increasingly important as knowledge of the disease process progresses. Today IFG, IGT, and hemoglobin A1c are used as the primary screening tools for clinicians to determine diabetes status. Equally important is the clinical assessment, as the clinician utilizes information from the history and physical exam to identify other factors that contribute to diabetic or prediabetic states. According to Priya (2018), prediabetes often involves a long asymptomatic period of impaired glucose metabolism. This period offers an opportunity for patients and providers to identify a prediabetic state based on screening tests and to begin treatment with lifestyle modifications and pharmacotherapy before overt diabetes is present and serious complications arise. However, because the patient is asymptomatic, attention must be focused on the risk factors present at each encounter. Clinicians must be knowledgeable of the risk factors related to diabetes, as well as the barriers faced by many in the Native American population in order to successfully exploit the window of opportunity for treatment in the prediabetic state.

Recommended Therapy Options and Efficacies

According to the American Diabetes Association, diabetes was the 7th leading cause of death in the United States in 2015 when over 250,000 death certificates listed diabetes as primary cause of death or a contributing factor. As of 2017, the ADA estimates the total cost of diabetes in the United States to be approximately $327 billion. With diabetes incidence and prevalence rising significantly, and the impacts of the disease readily apparent through both clinical and

economic lenses, the identification of varied therapy options will become exceedingly important as we look to the future of healthcare for these patients.

Numerous studies have looked at the effects of diet and exercise in diabetic and pre-diabetic patients, and many have identified benefits of strategic diet and exercise plans to delay diabetes onset or to improve diabetes symptoms. Today, we recognize the benefits of diet and exercise to the extent that programs such as the National Diabetes Prevention Program are tailored around these interventions. Additionally, the ADA's Standards of Medical Care in Diabetes (2018) highlights the importance of adequate nutrition, weight management and physical activity in delaying the onset of diabetes, as well as in treating those already diagnosed with the disease.

However, the same document also recognizes the need to tailor treatments to social context—something especially important in the Native American population, given their typically rural locations, lower socio-economic status, and other social factors that contribute to the burden of diabetes and other diseases within this population. These factors are important to consider and will be discussed in greater detail throughout this review.

The recommendation of lifestyle modifications including at least 150 minutes of moderate exercise weekly (ADA level of evidence "B") and a decrease of body weight by at least 5% (ADA level of evidence "A") have been proven in several studies. These should be the primary goals for all prediabetic and diabetic patients. Lifestyle modifications were shown to have clearly defined benefits for participants and can be thought of as the standard by which other treatment options for diabetes prevention and treatment should be measured. While metformin has been shown to be beneficial in delaying diabetes in patients with impaired fasting glucose or impaired glucose tolerance and should be considered the first-line

pharmacotherapeutic option, it remains less effective than lifestyle modifications. However, lifestyle modifications are not universally sustainable, according to Srinivasin and Florez (2015). When lifestyle modifications are not possible due to limiting factors such as disability, finances, or lack of resources, pharmacotherapy should be considered in all prediabetic and diabetic patients. According to the ADA, metformin should be considered in all patients with IFG/IGT who have one or more additional risk factors. Metformin, specifically, should be considered in all "pre-diabetic" patients who are unable to attain proper lifestyle modifications (ADA, 2018).

While large-scale generalized studies such as the Diabetes Prevention Program are well-intended and informative, the ability to translate these results to specific populations has not yet been verified. One European study, known as the DE-PLAN study, with publicized results provided by the Health Program of the European Union (2010), sought to determine if group-based, non-intensive dietary counselling would be effective in "real-world" community settings. Through bi-monthly, in-person sessions held in local communities or in places of employment, this study appeared to show that favorable results, specifically related to reduced body mass, reduced triglycerides, and improved 2-hour glucose tolerance were possible in a localized setting.

One DE-PLAN sub-study (Gilis-Januszewska et al., 2018), conducted in Krakow, Poland, showed that interventions are not easily replicated in local settings where limited financial and physical resources are apparent. As many in the Native American population reside in settings where financial and physical resources are often scarce, such interventions may not be successful as found in the DE-PLAN sub-study noted above. Given these limitations, recommendations for implementation in a local setting could not be made without further data to support the approach.

Diabetes Prevention Program (DPP) studies have been completed and thoroughly studied in American, Finnish, and Chinese populations. Ramachandran, Snehalatha, Mary, Mukesh, Bhaskar, & Vijay (2006), applied DPP interventions in the Native Asian Indian population to determine its efficacy in patients who were younger, leaner, and more insulin resistant than the previously studied subsets. Using a control group and three intervention groups including a lifestyle modifications group, a metformin group, and a combined lifestyle modification plus metformin group, the study followed over 500 participants for an average of 3 years and found that the results from their study were very similar to those found in previously studied populations. Both lifestyle modifications and metformin groups benefited from their respective therapies with relative risk reductions of 28.5% in the lifestyle modifications group, 26.4% in the metformin alone group, and 28.2% in the lifestyle modification plus metformin group. The results of the study seemed to prove that similar results from these standard interventions can be found in a variety of ethnic backgrounds.

The Finnish Diabetes Prevention Study, according to Rosenstock, showed that even at 3 years after the conclusion of the study, participants maintained a 43% risk reduction for developing diabetes when compared to a placebo group. The cause of this effect is unknown, but whether the effect was based on the continuation of lifestyle changes or a benefit of a physiologic change brought about by the intervention, the result is promising for type 2 diabetics and those with IFG and IGT. Lifestyle interventions, however, can be exceedingly difficult to maintain over the course of a lifetime. This is documented in a study by Middleton, Anton, and Perri (2016) that describes the difficulties of long-term adherence to health behavior changes due to social and behavioral confines, among other barriers. Given the data available regarding risk reduction and symptom improvement with lifestyle interventions, combined with the knowledge

of barriers experienced by many in the Native American population, efforts and resources should be focused on identifying and eliminating obstacles that inhibit implementation and efficacy of these interventions.

Because minimal research has focused on the Native American population, native-focused translational studies such as this will help to guide future work related to the implementation of a robust diabetes prevention program in the Native American community.

Barriers to Success

Many barriers to the implementation of a successful diabetes prevention program exist in the Native American population. Factors including geographical, financial, social, physical and psychological must be considered as the search continues for effective therapies and programs to combat the diabetes epidemic in the Native American communities.

Geography has been identified as a barrier to appropriate healthcare in Native American communities – specifically those on reservation lands, as these areas are typically remote and lack adequate healthcare access through Indian Health Services (IHS) systems (Kruse, Bouffard, Dougherty and Parro, 2016). Additionally, access to specialty care such as cardiovascular and nephrology services, which are often necessary in the setting of diabetes, are typically available in tertiary care facilities which are in larger cities even further removed from reservation land. Related to geography are additional costs of travel, work time lost and peripheral costs such as childcare while seeking medical care. Kruse et al. (2016) claim that travel time for Native Americans seeking specialty care often requires between 2 and 5 hours of travel for a single appointment. With fuel and associated expenses, the patient may incur costs exceeding $200 for travel alone. Travel costs compound the already bleak financial picture for many Native

Americans. According to the Economic Policy Institute, the 2017 American Communities Survey showed that Native American households produce an average annual income of $41,882 – over 30% lower than the national average of $60,336. Although the high cost of healthcare is reality for all populations throughout the United States, those whose financial status is near or below the poverty line are disproportionately affected. According to Zhuo, Zhang, Barker, Albright, Thompson and Gregg (2014), annual medical spending for a diabetic patient in the United States between 2005 and 2008 (the latest data available) was $13,966. This number was observed in the general population and does not account for the known additional costs posed by geography and faced by many Native Americans living on reservation lands.

Another barrier in this population remains access to health insurance. Zuckerman, Haley, Roubideaux & Lillie-Blanton (2004) describe Indian Health Service (IHS) coverage gaps within the Native American population, as only approximately 35% of those who identify as AI/AN are covered by IHS services. While a percentage of Native Americans are covered by employer and private insurances, the number of uninsured in this population outpaces that of other population subsets including Caucasians and Hispanics. Zhuo et al., in their general population study, also identified that diabetics were more likely to be Native American or African American and less educated, but also more likely to be covered by health insurance than people without diabetes. Health insurance coverage tends to improve health outcomes for both chronic and acute conditions. Because this study identified diabetics as being more likely to be covered by health insurance than non-diabetics, it is possible that this is because individuals without health insurance are less likely to seek medical care and therefore less likely to be diagnosed. Additional studies would be needed to consider the unique, and somewhat bizarre result regarding insurance coverage in this study.

Education is a social factor impacting Native Americans in the fight to overcome diabetes. According to the National Indian Education Study (2015), only 49 percent of Native Americans graduate from high school, compared with 86 percent of the general population. Although holding a high school diploma or college degree is not a surrogate for diabetes, the ability to understand the complexity of the disease and the multiple related co-morbidities is more likely in individuals who have displayed the ability to accomplish these milestones of education through dedication and determination.

Importantly, the age of newly diagnosed diabetics in the Native American population is increasingly younger. While this trend is concerning given the lifetime of effects, it also provides additional insight into the overall disease process. Type 2 diabetes cannot simply be discounted as a disease of aging but must be considered in patients of all ages. Because of the younger age at diagnosis, patients will often require the assistance of caregivers in their treatment plan. Chambers et al. (2018) identified a direct correlation between successful diabetic treatment and the presence of caregivers who were invested in the care of their youth. In the Native American population, youth and caregivers often share risk-factors for diabetes.

Other social factors that yield barriers to adequate diabetic care include non-diabetic family and friends. Because diabetes treatment is complex and time-consuming, and disease manifestations are often debilitating, the social ramifications of the disease are evident and socially damaging. Proper diabetic care, according to currently recognized standards, must include timely monitoring of blood glucose, dietary restrictions and/or modifications and physical exercise in addition to pharmacological therapy for those that require it. Managing diabetes properly tends to restrict the lifestyle of diabetic patients and further isolates them from their non-diabetic friends and family members.

The demands of the disease are often intrusive to the desired lifestyle of diabetic patients. As the disease progresses, so do the needs of the patient as damage ultimately leads to dialysis, vision loss and loss if limbs, among other co-morbidities. Diabetic patients with fulminant disease often require the assistance of care-takers to attend appointments and even to accomplish activities of daily living. This inconvenient but necessary reliance on others often leads to depression, which acts as a psychosocial barrier to proper care. A study by Li, Ford, Strine and Makdad (2008) reported that despite the benefits of insulin therapy, type 2 diabetics who required insulin regimens were subject to major depression which is likely related to disease severity or progression. Because depression often leads to withdrawal from social activities as the cycle is perpetuated, the disease process worsens and depression increases. This may lead to decreased compliance with therapies, inadequate treatment and follow-up and, ultimately, increased morbidity and mortality as the disease process progresses.

Genetic barriers must be further investigated, given the disparate prevalence of diabetes in the Native American population. Although many of the barriers discussed in this research can be individually significant, none should have the power to account for the nearly two-fold increase in diabetes prevalence in Native Americans. Collectively, it might be argued that these attributes would result in such drastic contrasts when compared to the general population. However, with the data currently available, assumptions would be required to make such a claim, given the widespread nature of diabetes in Native American populations, throughout the generations and across many social and physical confines. If a genetic predisposition to diabetes in this population were identified, it may help to explain the prevalence of the disease. While genetic research is ongoing, one study by Roumen, Blaak, & Corpeleijn (2009) concluded that genetic variation may affect how a person responds to lifestyle interventions based on genotype,

making the question of lifestyle intervention effectiveness circumstantial – which intervention recommendations will be the most effective for individuals based on genetic profiles. One such genotype related to central obesity was identified by Roumen et al. as having a direct correlation with diabetes diagnosis. Although not specific to the Native American population, the trials reviewed in this study showed no difference in progression to diabetes once an impaired glucose tolerance state was identified. Given this information, a genetic involvement predisposing Native Americans to the diabetes appears increasingly plausible.

Recruitment and retention of participants in personal health management continues to be a problem in many population subsets across the United States, especially those with low socioeconomic status. A study by Pratt, Beals, Johnson, Bullock, Manson & Jiang (2018) of 2,901 Native American patients in the Special Diabetes Program for Indians showed an annual assessment completion rate of only 70%. The study was carried out over 4 years and included 3 enrollment years (cohorts) and a follow up period. With only 70% of the study population completing the annual program assessments and other limitations such as the voluntary nature and decreasing participation year over year, the generalizability of the study is limited. However, given the demographic inclusion of Native Americans only, it is important to consider the interpretation and how it may play into the overall efficacy of diabetic treatment options.

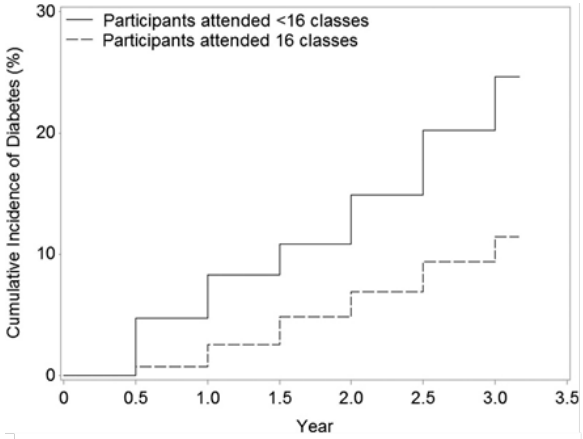
Another study (Jiang, Johnson, Pratte, Beals, Bullock and Manson, 2018), which also utilized the Special Diabetes Program for Indians data, identified the difficulties of reaching male participants for such studies. Although this cohort included over 8,600 participants, over 70% were female, limiting the usefulness of this study in determining the most effective strategies for treating diabetes in the Native American population in general. This does, however, highlight an

additional barrier to proper care – an inability to reach those most-susceptible with the proper information in order to obtain a buy-in for their own medical care and future health.

Results of these studies demonstrate that the composition of cohorts and their willingness/ability to participate plays a role in the effectiveness of interventions and implicates broader lessons for future studies.

Population-Based Studies

One large-scale study - termed the Special Diabetes Program for Indians (SDPI) – included over 2,900 participants representing 80 tribes and 36 health care programs and has provided the strongest evidence to date regarding translational effectiveness of general population interventions within the Native American population. Based on the Diabetes Prevention Program (DPP) lifestyle interventions, the SDPI was funded by the U.S. Congress to assess the effectiveness of such interventions within a diverse, but wholly Native American cohort. Diversity of the project included rural, urban and reservation-swelling participants from 18 states throughout the U.S. The 16-session Lifestyle Balance Curriculum was offered to all participants and post-curriculum clinical assessments were completed immediately upon completion of the sessions and annually thereafter for 3 years. Clinical measures including diabetes incidence, weight loss and changes in blood pressure were monitored and recorded. The results of the study at three years post-completion showed significant improvements in blood pressure, lipid levels and weight.



Participants who completed all 16 sessions displayed a significantly lower incidence of diabetes at all measured timeframes. Jiang, et al. (2013). Translating the diabetes prevention program into American Indian and Alaska Native communities: Results from the special diabetes program for Indians - diabetes prevention demonstration project. *Diabetes Care.*

According to Jiang et al. (2013), these results were observed immediately following session completion and continued annually thereafter, providing evidence that benefits of such interventions remain long after cessation of intentional efforts such as the 16-session curriculum. Evidence of the long-term benefits of these interventions are reflected in the secondary outcomes of the SDPI study. For example, weight loss was greater than 7% in over one-fifth of the study population at the end of the 16-session program and 17.5% reached that goal by the end of the third year. Additionally, there was a direct correlation with weight loss and diabetes incidence with course completion – diabetes incidence at 3 years post-completion was nearly 25% for participants who had completed less than 16 sessions, while participants who had completed all 16 sessions displayed an 11% incidence (Jiang, 2013). A follow-up study by Jiang, et al. (2018) showed a reduction in diabetes incidence of 64% for those that completed the program.

Results of the SDPI program have demonstrated the effectiveness of utilizing standardized, but intensive therapies to combat the diabetes epidemic in the Native American population. However, barriers continue to exist for widespread and large-scale prevention programs – primarily related to the financial and human-resource needs required for implementation.

Results

Studies of the diagnosis and treatment of prediabetes and diabetes specific to the Native American population are lacking in both quantity and quality in order to make definitive, population-specific recommendations for care. Given this, general and other focused-population studies must be translated and applied to Native American populations in order to understand with greater clarity the potential benefits of therapies in this setting. However, because no

evidence was found through this study to refute the benefits of the American Diabetes Association's 2018 recommendations in Native Americans, healthcare providers should encourage all patients to abide by these guidelines including regular exercise, healthy eating and self-management education.

Importantly, Native Americans face many barriers to proper diabetes care including geographical, financial, and social factors which must be recognized by not only the patient and provider, but also by policymakers, tribal leaders and the healthcare and health insurance industries as efforts are made to reduce the burden of diabetes on individuals and society. Because diabetes is a life-long disease, patients who are diagnosed and treated earlier, and those who can maintain prolonged lifestyle interventions will ultimately experience fewer complications and hospitalizations and will incur lower healthcare costs compared to those who are diagnosed later and who are unable to sustain lifestyle interventions.

Finally, it is paramount that all diabetic patients are treated as individuals, and not as a generalized population. Inherently, however, research studies provide a greater understanding of populations, not individuals. While generalized information is certainly advantageous in observing patterns and identifying possibilities, it must then be applied to the individual in a way that meets patient-specific needs. It is this specificity that will ultimately lead to successful treatment of diabetes and improve the lives of countless individuals diagnosed with, or yet-to-be diagnosed with diabetes.

Clinical Application

Apparent throughout this study was evidence that the Native American population, in general, faces numerous barriers that limit the opportunity for early diagnosis and proper

treatment of diabetes. These barriers lead to an increased prevalence of this disease process within the Native American community and ultimately to higher morbidity and mortality. Further, studies point to identification of risk factors, specifically obesity, in Native American youth. Because of the long-term health impact of diabetes, observation of these risk factors at a younger age must be acknowledged as a significant finding by clinicians in the primary care setting.

Although this review did not produce a defined treatment plan for diabetes specific to the Native American population, several highlights appear to be equally as effective within this population as in the initial respective study population. Specifically, the ADA's Standards of Medical Care in Diabetes 2018 guidelines identify that physical exercise, diet modifications, and diabetes self-education should be implemented in all patients with diabetes and pre-diabetes. Patients with additional risk factors, and those who may be physically unable to undertake adequate exercise may also benefit from the addition of metformin to their treatment plan.

Large-scale programs for the identification of diabetes and risk factors in the Native American population have been only moderately successful, owing their shortcomings to a high attrition rate and lack of generalizability. Until further research can identify best-practice methods by which to successfully identify and treat Native Americans with diabetes, clinicians must take a one-on-one approach to ensure that patients are receiving the best possible care. Suggestions identified in this study include risk-factor screening at every office visit and annual follow-up for those with significant risk factors but not yet diagnosed with diabetes or pre-diabetes. Finally, opportunities for patient education must be capitalized within the office setting. Compliance with any treatment plan remains a personal decision. However, educating patients

on the risk factors, disease process, complications and treatment options remains vital as informed patients can make informed decisions.

Conclusion

Diabetes prevalence in Native Americans is disproportionate to the general population. Native Americans are being diagnosed with diabetes at a younger age and with more co-morbidities than in decades past. This data justifies the focused attention and resources necessary to identify and treat risk factors in this population and throughout the world. Given the ramifications of this disease on lifestyle and overall health, as well as the associated economic and financial burdens, more research is needed to identify specific pathophysiology, risk factors and barriers to proper and effective treatment in this population.

While foundational studies specific to the Native American population are limited, baseline data is available that has identified known barriers to ideal diabetes care and proper healthcare in general. Additionally, general population studies have demonstrated effective treatment options for delaying the onset of diabetes and for treating the disease after diagnosis and translational studies have failed to prove that the current best-practices would be ineffective in the Native American population.

There remains much progress to be made in the effort to fight the diabetes epidemic in the Native American population. Based on currently available research, Native American diabetic patients should be treated using general guidelines such as the ADA's Standards of Medical Care in Diabetes, as research has shown a benefit to lifestyle modifications in all patients, regardless of ethnicity. Additionally, pharmacotherapy with metformin should be

recommended in all patients with IFG/IGT who have additional risk factors, as well as in those who are physically unable to complete appropriate lifestyle modifications.

Barriers addressed in this paper can be directly attributed to patients, providers, caregivers, communities and institutions. To ensure that individual barriers are identified and overcome, and effective therapies are provided, successful treatment of diabetes and prediabetes necessitates active involvement and collaboration of these entities. Future research should be directed at discovering solutions through collaboration and shared resources.

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Appendix

Table 1—ADA evidence-grading system for "Standards of Medical Care in Diabetes"

Level of evidence	Description
A	Clear evidence from well-conducted, generalizable randomized controlled trials that are adequately powered, including • Evidence from a well-conducted multicenter trial • Evidence from a meta-analysis that incorporated quality ratings in the analysis Compelling nonexperimental evidence, i.e., "all or none" rule developed by the Centre for Evidence-Based Medicine at the University of Oxford Supportive evidence from well-conducted randomized controlled trials that are adequately powered, including • Evidence from a well-conducted trial at one or more institutions • Evidence from a meta-analysis that incorporated quality ratings in the analysis
B	Supportive evidence from well-conducted cohort studies • Evidence from a well-conducted prospective cohort study or registry • Evidence from a well-conducted meta-analysis of cohort studies Supportive evidence from a well-conducted case-control study
C	Supportive evidence from poorly controlled or uncontrolled studies • Evidence from randomized clinical trials with one or more major or three or more minor methodological flaws that could invalidate the results • Evidence from observational studies with high potential for bias (such as case series with comparison with historical controls) • Evidence from case series or case reports Conflicting evidence with the weight of evidence supporting the recommendation
E	Expert consensus or clinical experience