

REVIEW ARTICLE

Understanding the growing epidemic of type 2 diabetes in the Hispanic population living in the United States

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Summary

The prevalence and incidence of type 2 diabetes (T2D) among the Hispanic population in the United States are higher than the national average. This is partly due to sociocultural factors, such as lower income and decreased access to education and health care, as well as a genetic susceptibility to obesity and higher insulin resistance. This review focuses on understanding the Hispanic population living in the United States from a multidisciplinary approach and underlines the importance of cultural, social, and biological factors in determining the increased risk of T2D in this population. An overview of the acute and chronic complications of T2D upon this population is included, which is of paramount importance to understand the toll that diabetes has upon this population, the health system, and society as a whole. Specific interventions directed to the Hispanic populations are needed to prevent and alleviate some of the burdens of T2D. Different prevention strategies based on medications, lifestyle modifications, and educational programmes are discussed herein. Diabetes self-management education (DSME) is a critical element of care of all people with diabetes and is considered necessary to improve patient outcomes. To be more effective, programmes should take into consideration cultural factors that influence the development and progression of diabetes. These interventions aim to enhance long-term effects by reducing the incidence, morbidity, and mortality of T2D in the Hispanic population of the United States.

KEYWORDS

complications, education, epidemiology, Hispanics, Latinos, pathophysiology, prevention, type 2 diabetes

Hispanics are the largest minority in the United States and have higher rates of diabetes in both adults (80% higher than non-Hispanic whites [NHWs]) and children (fivefold higher than NHW). This conveys a huge cost to society. It was estimated by the American Diabetes Association (ADA) that the economic costs of diabetes in the United States in 2017 had increased by 26% from 2012 because of increased prevalence of diabetes and the increased cost per person with diabetes.¹

Care for people with diabetes accounted for 1 in 4 spent dollars in health in the United States representing \$327 billion when combining direct medical costs and reduced productivity.

It is crucial to understand this phenomenon if it is to be addressed effectively. A combination of unique sociocultural, genetic, and cultural factors likely explains this variation. Herein, we present a systematic review of these factors as well as the complications of type 2 diabetes (T2D) upon this population.

Moreover, we provide an overview of specific interventions directed to the Hispanic populations based on medications, lifestyle

ACRONYMS AND ABBREVIATIONS: MA, Mexican American; NHW, non-Hispanic white; T2D, type 2 diabetes; IGT, impaired glucose tolerance

modifications, and educational programmes. Diabetes self-management education (DSME) is a critical element of care of all people with diabetes and is considered necessary to improve patient outcomes. To be more effective, programmes should take into consideration cultural factors that influence the development and progression of diabetes.

This review aims to provide the theoretical framework to understand this complex population such that effective intervention strategies can be developed and applied for the prevention and treatment of T2D.

1 | DEFINITION AND METHODOLOGY

Although the terms “Hispanic” and “Latino” are often used interchangeably in the medical literature, they are not synonyms. The term “Hispanic”² refers to people born in a country that was “conquered” by Spaniards and for whom Spanish is the primary language. It applies to most countries in Latin America, except Brazil, the Guianas, Belize, and Trinidad and Tobago.

The term “Latino” is a broader term that refers to people born in a country whose language has evolved from Latin (Romance languages).² This term applies to all countries in Latin America and some in Europe, such as Italy, Spain, and France. However, in most cases, both terms refer to people with roots in a Latin American country.

Historically, different ethnicities have contributed to the contemporary Hispanic populations including Spaniards, Blacks, and Native Americans³ making this population very heterogeneous from a biological point of view. Genome-wide analysis among the Hispanic population found that Dominicans and Puerto Ricans showed the highest levels of African ancestry. In contrast, Colombia has wider geographic differences ranging from Caribbean coasts to Andean valleys and mountains, which could explain the enrichment of African ancestry in some individuals and not in others, likely representing the differences in origin within Colombia. Finally, Mexico and Ecuador are two continental countries that had high densities of Native Americans during pre-Columbian times; as expected, the individuals from these two countries show the highest degree of Native American ancestry.⁴

The terms “race” and “ethnicity” also deserve some clarification. “Race” mainly alludes to those physical characteristics that are genetically determined, while “ethnicity” relates to a perceived cultural distinctiveness, expressed in language, music, values, art, styles, literature, family life, religion, ritual, food, naming, public life, and culture.² Thus, Hispanic and Latino are ethnicity-based terms.

Since the Office of Management and Budget (OMB) requires federal agencies to use a minimum of two ethnicities (Hispanic or Latino and not Hispanic or Latino), epidemiological, census, and health data are categorized as NHW, Hispanic, Asian, etc, and this should be taken into account while interpreting these data. It is important to highlight that given that these are ethnicity-based terms, they necessarily imply behaviours determined culturally that will have important effects on health outcomes. This can be viewed both as a limitation and as an opportunity. The main limitation is that it is a heterogeneous group, both biologically and culturally speaking, which limits the

interpretation of some of the studies that do not necessarily represent all the heterogeneity comprised in this group.

However, that there are social and cultural factors that play an important role in these results opens a window of opportunity to intervene and have impactful and long-lasting effects in lowering the incidence and prevalence of T2D in this group.

In this document, we reviewed the literature on MEDLINE through freely accessible PubMed as a search engine for the terms “Hispanic,” “Latino,” “Mexican-American,” and “Diabetes.” Relevant and most significant studies were included. The term Hispanic will be used throughout the review because most of the studies we refer to were done in a population that migrated from a Latin American Spanish-speaking country.

The presented statistics compare Hispanics with NHW since it is the nonminority population in the United States and most clinical studies and policies regarding diabetes are based on studies derived from this group. Although some cited studies also have additional minorities such as African Americans or Asians, for consistency and focus, we decided to limit our comparisons with NHW.

2 | VITAL STATISTICS AND EPIDEMIOLOGY

This section will overview sociological factors that affect access to health care as well as health literacy such as income, insurance, and education specific for the Hispanic population (Table 1). It will also review risk factors such as obesity, impaired fasting glucose (IFG), and glucose tolerance, and it will give a sense of the magnitude that T2D has upon Hispanics.

TABLE 1 Vital statistics and epidemiology of the Hispanic population living in the United States

Variable	Hispanic, %	NHW, %	Reference
High school education	61	90.4	⁵
College education	17.8	29	⁵
Poverty rates	21.4	9.1	^{6,7}
Unemployment	4.9	5	⁷
Lack of health insurance	20	10	^{8,9}
Diabetes	17.9 for men, 18.7 for women	10.2	¹⁰
T2DM in children/y	3.1	0.6	¹¹
Impaired glucose tolerance	20.2	15.3	¹²
Obesity	44 in men, 49.2 in women	37.1	¹³
Obesity in children	21.9	14.7	¹⁴
Extreme obesity	7.6	4.4	¹⁵
Hypertension	26.3 in men, 27.7 in women	29.8 in men, 26.9 in women	¹⁶
Increased total cholesterol	14.2	13.5	¹⁷
Decreased HDL	21.8	17.1	¹⁷
Smoking	10.7	16.6	¹⁸

Abbreviations: HDL, high-density lipoprotein; T2DM, type 2 diabetes mellitus.

2.1 | Income, access to health care, and education

Hispanics comprise the largest US minority group at 17.6%; they are the fastest growing minority group with more than 50 million people and are predicted to comprise 29% of the population by 2050 (Figure 1A).¹⁹ The majority of Hispanic immigrants originate from Mexico,²⁰ followed by Puerto Rico, El Salvador, and Cuba. We have specifically mentioned throughout the review when the cited study was performed on a Mexican American (MA) population so that the reader has this in mind. When not mentioned, studies performed on "Hispanics" might have an overrepresentation of a certain immigration groups depending on where population was chosen within the United States.

From an income point of view, the Hispanic Community Health Study/Study of Latinos (HCHS/SOL) showed that an income lower than \$20 000 was related to a higher prevalence of diabetes (16.9% for men and 18.5% for women) than those with income higher than \$75 000 per year (12.8% for men and 8.3% for women). Hispanics have a lower than average median household income (\$47 675 vs \$59 039),²¹ increased poverty rates (for example, 7.6% vs 5.8% are under 50% of poverty threshold), and lack of health insurance (24.4% of Hispanics vs 14.9% of all other races are not insured) (Figure 1B). This means that the Hispanic population is at higher than the national average risk of not preventing or treating diseases such as diabetes and their complications in a timely manner.

Education plays a key role in the development of T2D with an inverse correlation between diabetes and education.^{22,23} Fifteen percent of adults with less than a high school diploma had diabetes compared with 7% of adults with a bachelor's degree or higher. In 2017, 72% of Hispanics had high school education or more, compared with 93.3% of NHW. About 15.3% of Hispanics had a bachelor's degree or more, compared with 35.6% of NHW²⁴ (Figure 1C).

2.2 | Epidemiology of obesity

Obesity is considered an epidemic in the United States, and it is one of the most important modifiable risk factors for the prevention of T2D.²⁵

This association is maintained among the Hispanic/Latino population. The HCHS/SOL study revealed a linear correlation between body mass index (BMI) and the prevalence of diabetes: 9.8% for those with a BMI lower than 25, 14.25% among overweight men and women (BMI 25-29), and 22.4% in obese individuals (BMI > 29).¹⁰

The prevalence of obesity is higher in Hispanics when compared with NWH. On the basis of the data from National Health and Nutrition Examination Survey (NHANES) 2011 to 2012, the age-adjusted prevalence of obesity for MAs aged 20 years and older was 44% for men and 49.2% for women.¹³ Because of acculturation factors, immigrants who arrive in the United States at younger ages are more likely to be overweight or obese than those who arrive in the United States at later ages.^{26,27}

However, obesity is also an issue in their home countries, as revealed by Mexico's Encuesta Nacional de Salud y Nutrición 2012 (ENSANUT) revealing a prevalence of overweight and obesity of 70% among 20- to 60-year-old men and women,²⁸ revealing

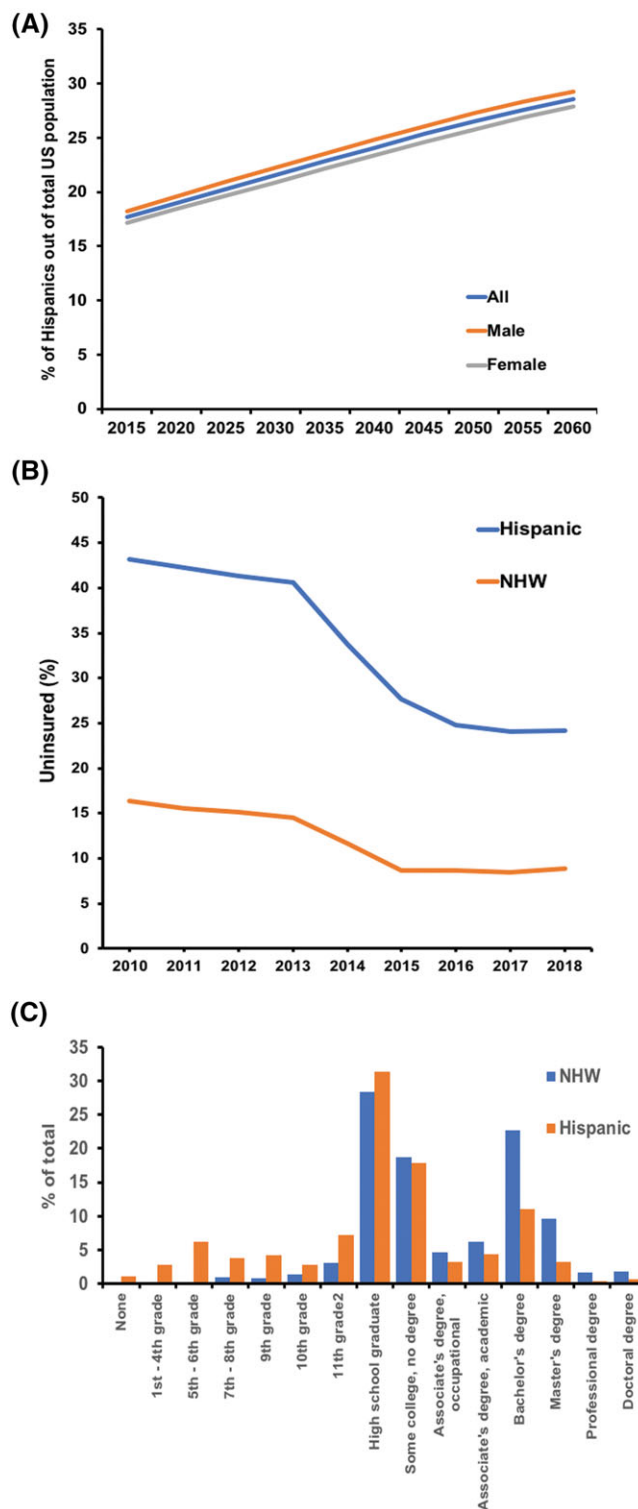


FIGURE 1 Demographics of Hispanics living in the United States. A, Percentage of Hispanics out of the total US population. B, Rates of uninsurance among Hispanics and non-Hispanic white (NHW). C, Comparison of education levels between Hispanics living in the United States and NHW

population-inherent factors that need to be considered and are independent from migration.

Therefore, obesity represents a key area of intervention, since a reduction on its incidence and prevalence among Hispanics would have dramatic effects on T2D.

2.3 | Epidemiology of IFG and impaired glucose tolerance

Hispanics have the highest lifetime risk for T2D.^{29,30} This, in turn, is correlated to higher rates of IFG and impaired glucose tolerance (IGT) among this population.

IFG is defined as a fasting plasma glucose (FPG) level³¹ of 100 to 125 mg/dL. A haemoglobin A1C (HbA_{1c}) level of 5.7 to 6.4% has been included in the definition of IGT.

The presence of IGT increases the risk of developing T2D; according to the San Antonio Heart Study, for individuals who had IGT at baseline, the odds of developing diabetes were twice as high compared with those with normal blood glucose levels.³²

Rates for IFG and IGT are higher in Hispanics than in whites. The age and sex-standardized rates for IFG in people above the age of 20 years in the NHANES III survey were 8.9% in Hispanics and 6.8% in NHW.¹² Rates of IGT among adults aged 40 to 74 years in the same study were also higher for MAs (20.2%) than for NHWs (15.3%).¹²

2.4 | T2D in Hispanics

The incidence of T2D in Hispanics is significantly higher than in NHW.³³

The HCHS/SOL examined the prevalence of diabetes among adults from diverse Hispanic backgrounds¹⁰; results report a prevalence of diabetes of 17.9% for women and 18.7% for men with a Mexican background, 18.2% for Dominicans, 17.7% for Central Americans, 13.4% for Cubans, 18.1% for Puerto Ricans, and 10.2% for South Americans. Since the majority of Hispanics originate from Mexico and Puerto Rico, the overall prevalence of diabetes in the combined Hispanic population is reported to be 16.7 in men and 17.2 in women,³⁴ which is highly influenced by these two populations. Therefore, studies of T2D in Hispanics living in the United States will have an overrepresentation of these two subpopulations unless stated otherwise or specified. This fact should be kept in mind throughout this review.

Going forward, if specific aspects need to be known about Hispanics from different regions, such studies should be designed in such a way that valid representation of subpopulations allows the generation of valid conclusions.

However, the reported differences among Hispanic subgroups are significant, and we believe they are the result of genetic and cultural factors. Genetically, it has been shown by genome-wide analysis that the genetic composition varies greatly among Hispanics from the Caribbean, Mexico and Central America, and Argentina and Chile.

Cultural and lifestyle factors may also play a role in explaining different diabetes rates. For example, the diet of Hispanics from the Caribbean is higher in carbohydrates than that in people from Argentina and Chile. There may also be differences among subgroups based on whether they live in their country of origin or have migrated to the United States.

As mentioned above, even though this heterogeneity might be one of the limitations in studying the Hispanic population in the United States, it is worth noting that 82.9% of Hispanics in the United States is comprised by Mexicans, Puerto Ricans, Central Americans,

and Dominicans, all of which have a similar diabetes prevalence rate of approximately 18%. This should bring some reassurance to the validity of the studies cited in this review.

2.5 | Gestational diabetes

The steady increase of overweight and obesity among women of childbearing age coupled to ethnicity disparity in bodyweight composition has negative repercussions on the increasing rates of gestational diabetes mellitus (GDM). The prevalence of GDM increased from 1.9% in 1989 to 1990 to 4.2% in 2003 to 2004, an increase³⁵ of 122%.

The prevalence of GDM in Hispanics is two to three times higher than the overall average.³⁶

The association between obesity and GDM appears to be twofold higher in obese Hispanics compared with obese NHW women.³⁷ Moreover, approximately 12% of MA women with GDM progress to T2D each year according to a study conducted in Southern California.²

MA women with gestational diabetes have a hazard ratio (HR) of 8 for progressing to T2D according to a recently published study. This is in contrast with an HR of 6.5 in the NHW population.³⁸

A detailed physiological characterization of the development of T2D in Hispanic women with prior gestational diabetes concluded that the latter represents a chronic disease process characterized by failing β -cell compensation for chronic insulin resistance. Weight gain, additional pregnancies, and progestin-only contraception are specific potential modifiable factors that increase diabetes risk in this population,³⁹ besides the known beneficial effects of diet and exercise.

GDM represents another area where interventions can have important impacts in the future epidemiology of T2D. The prenatal environment is increasingly recognized as a risk factor for diabetes showing that GDM increases the risk of obesity and diabetes in the offspring.⁴⁰ Large maternal weight loss from obesity surgery prevents the transmission to children who were followed until adulthood, therefore decreasing their risk of T2D.⁴¹

2.6 | Mortality

There are few studies addressing diabetes-specific mortality rates in the US Hispanic population; however, diabetes is the number one cause of death in Mexico⁴² (Figure 2A) and an important cause of mortality in other Latin American countries (Figure 2B).

The main cause of death among Hispanics with diabetes is cardiovascular disease (CVD). Data from the San Antonio Heart Study showed that estimated age and sex-adjusted rates of all-cause and cardiovascular mortality were higher in US-born MA than in either US-born NHW or Mexico-born MAs. Data from the San Antonio Heart Study were used to compare NHW, US-born MAs, Mexico-born MAs, and Mexico City residents. The age and sex-adjusted HRs, compared with NHW, were 1.77 for US-born MAs and 1.08 for Mexico-born MAs.⁴³

2.7 | Children and adolescents

There has been an increase in the prevalence of overweight in youth, especially among those of Hispanic origin.^{33,44} The results from the

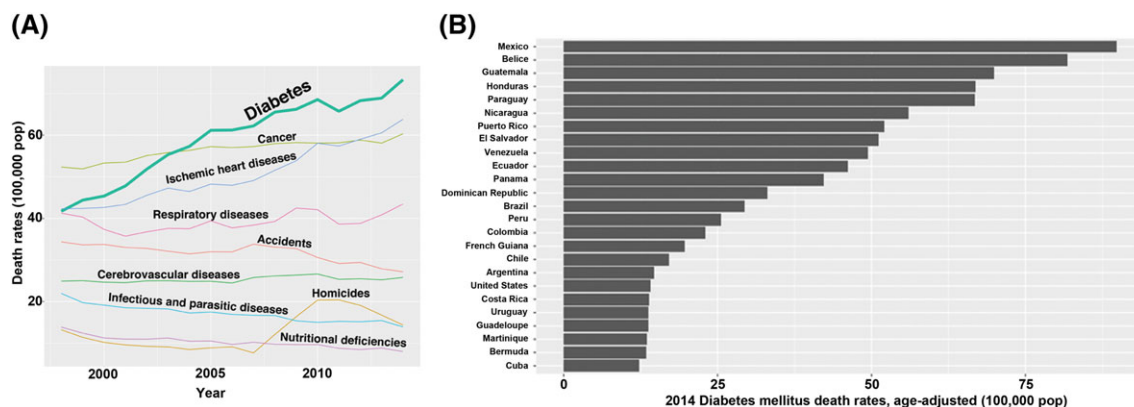


FIGURE 2 Diabetes-related mortality. A, Top causes of mortality in Mexico based on World Health Organization (WHO) data. B, Mortality from type 2 diabetes (T2D) in Latin American countries relative to the United States. Data obtained from WHO

NHANES cross-sectional data indicate that overweight and obesity are a concern for males and females of all age groups, gender, and race/ethnicities considered in this study.⁴⁵ The 6- to 7-year age group had the lowest percentage of overweight and obesity. For the 8- to 9-year age group, MAs had the highest percentages with 21.6% for overweight and 21% for obesity. Females had the highest percentage for overweight. For the 10- to 11-year age group males, MAs had the highest percentages of overweight and obesity with 28.7% and 23.6%, respectively.

The SEARCH (SEARCH for Diabetes in Youth Study) is a U.S. multicenter based study in population with T2D younger than 20 years at onset, predominantly female with an elevated prevalence of high risk minority groups.⁴⁶ SEARCH found T2D to be more common among Hispanics (46.1%) than NHW youth (14%).⁴⁶

In the TODAY (Treatment Options for Type 2 Diabetes in Adolescents and Youth) study, similar results were reported: 64.9% were female with mean age of diagnosis of 14 years; 41.1% of children were Hispanics.⁴⁶

2.8 | Conclusion

The incidence and prevalence of T2D and gestational diabetes are higher in the Hispanic population of across all age groups. As in other ethnic groups, these are accompanied by higher frequency of predisposing factors such as obesity, insulin resistance, and glucose intolerance, all of which can have important environmental causes. There are a number of socio-economic factors that contribute to this phenomenon among Hispanics such as lower income, less access to higher education and health care, and unique cultural perceptions (summarized in Table 1).

3 | PATHOPHYSIOLOGY OF T2D

3.1 | Genetic predisposition

Hispanics are more insulin resistant than NHWs, posing them at greater risk of developing T2D. Although the specific genetic abnormalities conducive to these disturbances in this ethnic group are not clear, their multiple genetic ancestries (Spaniards, Native Indians, and

Africans) might contribute to this phenotype. The thrifty gene hypothesis postulates that in some racial groups, a predisposition to insulin resistance may have protected individuals during long periods of starvation by reducing muscle utilization of glucose and favouring glucose utilization in other organs, like the brain.⁴⁷ These protective genetic changes may have now become deleterious, favouring T2D and other conditions in an environment where food deprivation and constant physical activity are not standard lifestyle characteristics.

Whole-exome sequencing analysis of almost 4000 individuals, both with and without T2D who were Mexican or other from Latin American ancestry, identified sequence variants in two genes: SLC16A11 and HNF1A. The identified SLC16A11 variant had an increased risk of developing diabetes and explains roughly 20% of the increased T2D in Mexico.⁴⁸ This gene is mainly expressed in the liver and controls lipid metabolism, increasing triacylglycerol levels. In a more recent publication, altered fatty acid and lipid metabolism were associated with this genetic variant, suggesting that increasing SLC16A11 function could be therapeutically beneficial for T2D.⁴⁹

In turn, HNF1A is present in 2% of Mexicans with T2D but only in one-tenth among healthy individuals. It carries a fourfold to fivefold increased risk of developing the disease.⁵⁰

Recently, a genetic variant in the IGF2 gene associated with about 20% reduced risk for T2D by comparing individuals with and without T2D of Hispanic descent.⁵¹ A loss of function splice acceptor variant in IGF2 is protective for T2D. The absence of this variant was associated with increased incidence of T2D and increased plasma glycated HbA_{1c} and could be considered as a new therapeutic strategy.

KCNQ1 and CDKN2A/CKN2B are gene variants that have also been identified as increasing diabetes risk among this population (reviewed in previous studies^{52,53}). Interestingly, the CDKN2A encodes P16INK4A, a marker and effector of cellular senescence. This correlation between age and diabetes risk should be kept in mind given that T2D prevalence and incidence increase with age.

Interestingly, a more complex picture to explain genetic predisposition to diabetes in Hispanics arises from a study that suggests that even Spanish admixture may be an important factor in explaining the higher rates for diabetes in this group.⁵⁴ There are various reports about possible genetic abnormalities in Hispanics with obesity, diabetes, and insulin resistance. Among them, a report suggests that the development of the metabolic syndrome may be linked⁵⁵ to the

1q23-q31. A growing number of studies⁵⁶⁻⁶¹ have reported linkage of diabetes or hyperglycaemia to a region on human chromosome 1q21-q25 pointing to chromosome 1 as a key player in determining T2D risk.

Among the genetic susceptibility to obesity among the Hispanic population, several candidate loci, including INSIG2, RGS6, and NGEF, have been associated with increased adipose tissue as determined by computed tomography studies.^{62,63}

Other polymorphisms near SOCS3 have been associated with obesity and glucose homeostasis traits in Hispanic Americans. The SOCS3 gene product participates in the feedback inhibition of a range of cytokine signals and has been shown to inhibit the function of leptin and insulin signalling, thus contributing to insulin resistance.^{64,65}

Also, T2D seemed to develop more frequently in an MA population that had a decrease in the expression of ATP6V1H, which could have an effect on vacuolar-ATPase activity and have subsequent consequences on insulin secretion.⁶⁵

The R230C variant of the ATP-binding cassette transporter A1 (ABCA1) gene has been consistently associated with decreased high-density lipoprotein-cholesterol (HDL-C) concentrations in studies in the Mexican mestizo population.^{66,67}

In the general population, an increased risk of T2D with a single-nucleotide TCF7L2 polymorphism has been described. This single-nucleotide polymorphism (SNP) increases the prospective link by 1.45 in heterozygotes and 2.41 in homozygotes.⁶⁸ This SNP was identified in the Icelandic population and confirmed by the Diabetes Prevention Program (DPP) and the HCHS/SOL genetic study in the Hispanic population.^{53,69} Interestingly, this genotype was associated with decreased insulin secretion pointing at a possible physiological pathway underlying this relationship.

However, since T2D is a polygenic disease, the individual contribution of all of these genetic variants, as well as their interactions and any possible synergisms, remains to be determined. Also, their interaction with known environmental factors that contribute to the development of the disease should be evaluated.

In conclusion, there are different genetic loci and variations that increase the susceptibility of the Hispanic/Latino population. These vary among groups and vary mechanistically, underscoring the complexity of diabetes in this extremely heterogeneous population. Understanding this can aid in the design of more effective and targeted intervention strategies for both the prevention and treatment of diabetes.

3.2 | Insulin resistance

The prevalence of insulin resistance is higher in MAs than in NHWs.⁷⁰ The Insulin Resistance and Atherosclerosis Study found that Hispanics without diabetes have significantly higher prevalence of insulin resistance and higher acute insulin response than whites without diabetes; however, this difference disappears after adjusting for obesity and body fat distribution.⁷¹ These findings would suggest that insulin resistance is primarily the result of obesity in this population. Tumour necrosis factor α (TNF- α) has been suggested to be one of the mediators of obesity-induced insulin resistance. Interestingly, in a multiethnic study, it was shown that TNF- α levels were highest in Hispanics with impaired insulin secretion when compared with other ethnic

groups.⁷² It is worth noting that a limitation of some of these studies is the lack of control for variables that can contribute to insulin resistance status such as socio-economic and education level, length of residence, or any other social determinant of health. While the above-cited studies are very valuable to have an insight into the pathogenesis of diabetes in Hispanics, further studies are needed to clarify whether the described differences persist once socio-economic and educational categories are accounted for. Hopefully, these will be performed in the near future.

There might be other components that contribute to a higher insulin resistance in MA: Studies in children suggest that insulin resistance may have more of a genetic origin, somewhat independent of obesity.⁷³ In a small study in volunteers without diabetes, Hispanics were found to be more insulin resistant than NHW.⁷⁴ Accordingly, a recent study identified several candidate loci that were associated with insulin sensitivity index and insulin disposition index in Hispanic participants. A two-stage genome-wide association study (GWAS) was performed in samples from this population, and several genes were nominally associated with insulin resistance traits. However, replication of these findings in independent cohorts and additional focused analysis of these loci are needed.⁷⁵

Therefore, increased insulin resistance in Hispanics is more likely the result of a combination between genetics and environmental factors such as obesity.

3.3 | β -Cell function and senescence

Higher acute insulin secretion has been reported in MAs compared with NHW.^{71,76} It was found that Hispanics had a higher HOMAIR, Matsuda index, S1Ph OGTT, and S2Ph OGTT than NHWs.⁷⁶

These higher insulin secretory values might be related to the higher insulin resistance levels encountered in this population. This may represent a compensatory response of β -cell function to the degree of insulin resistance that is clearly increased in this population. Eventually, in order to develop T2D, β -cell failure is required. In fact, it is an independent predictive factor for the development of T2D in MAs.^{77,78} Usually, when FPG exceeds 100 to 110 mg/dL, loss of the first phase of insulin secretion is common.⁷⁹ A recent study performed in Latino boys and girls showed that in overweight youth, the compensatory changes in insulin secretion fail as puberty develops, regardless of gender. This is an indication that β -cell function deteriorates during this period, posing this population at risk for early T2D.⁸⁰

As mentioned in regard to insulin resistance, Hispanics could have a higher risk for β -cell dysfunction that fully manifests in the presence of insulin resistance and other metabolic and environmental factors. Although the nature of this abnormality is not well understood, a recent genome-wide association scan for acute insulin response to glucose in Hispanic Americans identified several candidate genes and loci that may be associated with the observed phenotype. The genes identified were involved in phosphorylation and ion transport. Further studies are required to determine their potential contribution to insulin secretion and β -cell function.^{81,82}

A recent study has shown that insulin resistance accelerates β -cell senescence and ageing in mice, leading to insulin secretory defects. Senolytic therapies, which specifically target senescent cells while sparing nonsenescent ones, improve the metabolic profile of different models of rodent insulin resistance and improve β -cell function and gene expression profile.⁸³

Isolated β -cell function studies in the MA population are difficult to perform but are necessary to elucidate mechanisms behind the increased incidence and prevalence of T2D in this population.

3.4 | Obesity

Obesity is a major risk factor for T2D in any population, but differences in prevalence among different ethnic and racial groups have been found.⁸²

The pathogenesis that underlies the relationship between diabetes and T2D is partly addressed by a study performed at the Joslin Diabetes Center and confirmed with the recent results from the SOL Youth study, where plasma markers of endothelial dysfunction, vascular inflammation, and procoagulation were measured in obese Hispanic/Latino children and adolescents with normal glucose tolerance. The results showed that the obese group had higher systolic blood pressure and plasma triglycerides and was significantly more insulin resistant than the lean group. Also, overweight children had higher plasma levels of different circulating inflammation markers such as TNF- α , C-reactive protein (CRP), and tissue plasminogen activator (tPA). All these abnormalities may contribute to the development of T2D and subsequent CVD.^{84,85}

Abdominal or central obesity is particularly relevant in increasing risk for T2D and CVD due to the release of hormones, substrates, and cytokines that promote insulin resistance, endothelial dysfunction, and low-grade chronic inflammation, key abnormalities in the development of both diseases.⁸⁶

Besides a predisposition to visceral adipose accumulation, lifestyle factors, particularly inadequate nutrition and lack of regular physical activity, contribute to obesity. Although this pattern can be adopted anywhere, recent data suggest that the risk of developing obesity significantly increases in Hispanic/Latino immigrants to the United States.

3.5 | Microbiome

In the last decade, the importance of the intestinal microbiome in the development of obesity and T2D has started to become elucidated. An altered gut microbiota has been associated with T2D.⁸⁷ A metagenome-wide association study analysis showed that patients with T2D were characterized by a decrease in butyrate-producing bacteria and an increase in opportunistic pathogens and microbes that were characterized by sulfate reduction and oxidative stress resistance.⁸⁸ The major effectors of the intestinal microbiota are the immune system and diet.⁸⁹ A high-fat diet has been suggested to alter microbiota composition resulting in a proinflammatory state that increases cytokine levels contributing to insulin resistance and glucose intolerance.⁹⁰

Studies suggest that gut microbiomes of urban-industrialized societies are different from those of traditional and could partly explain an increase in the risk of certain diseases (such as T2D) with migration and acculturation.⁹¹ It has been described that the microbiota of US adults is the least diverse when compared with that of other populations (Malawians and Amerindians),⁹² an important factor that could contribute to increased risk of T2D with acculturation of the Hispanic/Latino population. To further support the influences of acculturation, the study of the microbiome of uncontacted Amerindians in South America has revealed the highest diversity of bacteria and genetic functions ever reported in a human group.⁹³ A third study compared the microbiota from hunter-gatherers and traditional agriculturalist communities in Peru and an urban-industrialized community from the United States. They found that *Treponema* is characteristic of gut microbiome,⁹⁴ which interestingly is a known carbohydrate metabolizer, although it is difficult at this point to establish a relationship with T2D.

The unique cultural characteristics of the Hispanic population, their diet, and usage of antibiotics are bound to have profound effects on the composition of their intestinal microbiota, which in turn could explain some of the high susceptibility of this population to the development of T2D. A study done in the Cameron County Hispanic Cohort characterized the gut microbiome of a subset of 63 MAs subjects. In this group, bacterial communities associated with obesity and T2D were enriched. A dominance of butyrate producers was observed, which are often increased in obese individual and depleted in T2D patients.⁹⁵ This prevalent "disease"-related microbiome might set the stage for further mechanistic studies and potential interventions.

Another study sequenced the bacterial microbiome of breast milk and child saliva from low-income MA women and children, finding that the genus *Streptococcus* dominated both milk and salivary microbial communities in most subjects.⁹⁶ These data can be taken into account to further understand the relationship between early life events and subsequent diabetes development.

To date, some interventions to modulate the composition of gut microbiota and improve metabolic status include the use of certain prebiotics and probiotics^{90,97,98} and faecal transplantation.⁹⁹ Indeed, it has recently been demonstrated that faecal transplant from lean donors to obese patients with metabolic syndrome results in transient but marked improvement in insulin sensitivity.¹⁰⁰

In the future, further characterization of the Hispanic microbiota has the potential to increase the understanding of T2D in this subpopulation and enhance the development of specific interventions that could improve their metabolic profiles and reduce the toll of this disease upon Hispanics.

3.6 | Conclusion

The pathogenesis of T2D in Hispanics is complex (Figure 3). There is a definite genetic component that predisposes the Hispanic population to develop T2D and this cannot be changed. However, the other components are subject to interventions, such as obesity and the inflammatory component associated with it, which in turn impacts insulin resistance and β -cell function. If the latter two improve, diabetes development can be prevented.

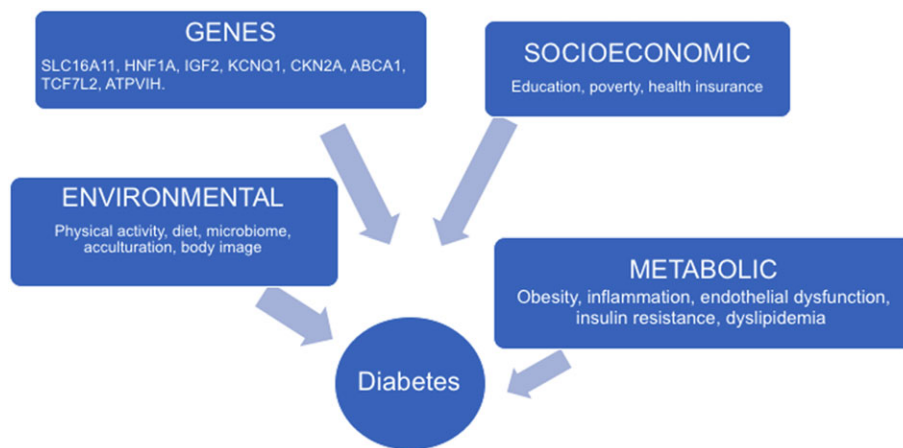


FIGURE 3 Socio-economic and pathophysiological factors contributing to the development of type 2 diabetes in Hispanics living in the United States. Both genetic, metabolic, socio-economic, and environmental factors play a role in the known sequence of pathophysiological events that lead to the development of diabetes in the Hispanic population. Arrows are proven directional events that lead or increase the risk of type 2 diabetes (T2D) development

Further understanding of the role of the microbiome in the development of T2D and interventions targeted at optimizing it are under intense scrutiny and provide an exciting and promising new approach to the disease.

4 | DIABETES COMPLICATIONS

The development of diabetes complications is tightly linked to metabolic control, with a reduction in risk of developing diabetes complications as a result of tight blood glucose control, such as a reduction of 76% of retinopathy, 50% in nephropathy, and 60% of nerve disease as shown by the Diabetes Control and Complications Trial (DCCT) and the UK Prospective Diabetes Study (UKPDS) trial.^{101,102} Its follow-up trial, Epidemiology of Diabetes Interventions and Complications (EDIC), confirmed these results.

In spite of the fact that several large clinical trials (Outcome Reduction with Initial Glargine Intervention [ORIGIN], Action to Control Cardiovascular Risk in Diabetes [ACCORD], and UKPDS) have failed to show a protective effect of tight glucose control on cardiovascular outcomes in T2D^{103,104} (probably because of increased episodes of hypoglycaemia), the consensus is that early control of blood glucose after diagnosis has a significant impact in the prevention of diabetes complications.

There might be a genetic component of the development of complications of diabetes in Hispanics, which are summarized in Table 2.

4.1 | CVD and cerebral vascular disease

CVD remains one of the leading causes of mortality among Hispanics in the United States,^{119,120} and diabetes is a major risk¹²¹ along with hypertension (HTN), hypercholesterolemia, obesity, and smoking. The HCHS/SOL found that among Hispanics, 80% of men and 71% of women have at least one major CVD risk factor.

Approximately two-thirds of all patients with diabetes will die from CVD¹²² since they have more extensive atherosclerosis, a higher incidence of multivessel disease, greater propensity for suffering

cardiovascular sequel, and poorer prognosis after myocardial infarction. In spite of these higher risks, the current therapeutic approach in patients with diabetes is similar to the ones without diabetes.

Moreover, awareness of and prescribed treatment for diabetes and dyslipidaemia occurs less frequently among MA individuals with diabetes.^{123,124}

In spite of these trends, Hispanics have been shown to have a 26% lower incidence of myocardial infarctions compared with NHW and significantly lower rates of stroke and congestive heart disease but higher rates of end-stage renal disease (ESRD).¹²⁵

Willey et al reported that after a 10-year prospective study, Caribbean Hispanics were at lower risk of coronary death and vascular death when compared with NHW. This population consisted mostly of foreign-born Caribbean Hispanics, and therefore, their findings may not be applicable to other Latino populations or to US-born Latinos.¹²⁶ In fact, Hispanics who had been in the United States longer or were born in the United States had a higher probability of having multiple risk factors of CVD and of reporting a history of coronary heart disease.¹²⁷

Hispanics have a lower risk of stroke (1.8%) than the average population (2.9%).¹¹⁹ The BASIC Project following nonimmigrant MAs and NHW in Texas reported a higher cumulative incidence of ischaemic stroke in MAs (RR = 2.04 vs 1.58). They also found that intracerebral haemorrhage was more common in MAs than in NHWs.¹²⁸

4.2 | Nephropathy

Although diabetes is a major risk factor for nephropathy, it is not the only one.

Despite the increased rate of obesity and diabetes in the United States, the incidence of ESRD in NHW has decreased by almost 50% in males and almost 40% in females.^{117,118} Although a decreasing trend is also found in the Hispanic population (8% decrease in males and 25% decrease in females), the incidence of ESRD is 1.5-fold higher in Hispanics than in NHW.^{129,130} In contrast, a study in California reported that with uniform medical coverage, Hispanic patients with

TABLE 2 Genetics of complications of diabetes in Hispanics

Complication	Gene/Chromosome	Correlation with Disease or Susceptibility	Pathway/System/Function	Population/Study	Reference
CVD and nephropathy	ACE-I/D	Yes	Renin-angiotensin	Low-income Mexican Americans with type 2 diabetes from the San Antonio Heart Study	18
	AGT	Yes			
	AT1R	Yes			
	PON2	No	Lipid metabolism	Low-income Mexican Americans regardless of preexisting conditions	105
Nephropathy	Chromosome 2q, near marker D2S427	Yes	—	Low-income Mexican Americans with type 2 diabetes from the San Antonio Heart Study	106
	GREM1	No	Antagonizes bone morphogenic proteins 2, 4, and 7	Low-income Mexican Americans with type 2 diabetes from the San Antonio Heart Study, and first-, second-, and third-degree relatives	107
	ELMO1	No	Phagocytosis, apoptosis, and cell motility	Mexican American ancestry with long-term diabetes from three centres	108
	CNDP1	No	Beta-alanine metabolism		
	HMCN1	Yes	Cell attachments		109
	eNOS	Yes	Nitric oxide production	Low-income Mexican Americans with type 2 diabetes from the San Antonio Heart Study	110
Microalbuminuria	Chromosome 20q12, near marker D20S481	Yes		Low-income Mexican Americans with type 2 diabetes from the San Antonio Heart Study	
Nephropathy	Chromosomes 1q43, 2q13.3, 7q36.1, 8q13.3, 18q23.3	Yes		Mexican American from the FIND study * results for other groups not shown here	111
	PAI-1, 4G/5G variant	Yes	PAI-1	NHW, Blacks, and Hispanics from IRAS	112
CVD	CAV1, SNPs rs926198, rs3807989	Yes	Insulin resistance and hypertension	Hypertensive and normotensive Caucasian and Mexican Americans	113
	CAPN10	Yes	Atherosclerosis, insulin sensitivity, and secretion	Mexican Americans with documented coronary artery disease	114
	LPL, haplotypes 1 and 4	Yes	Insulin sensitivity	Mexican Americans	115
	LPL, haplotypes 2, 3, and 6	Yes	Insulin resistance		
	Chromosome 9p, between markers D9S925 and D9S741	No	HDL-C		116
	LPL polymorphism between HinfIII and PVuII	Yes	Lipid metabolism	Low-income Mexican Americans with type 2 diabetes from the San Antonio Heart Study	117
				Hispanics with and without diabetes and NHW from San Luis Valley Diabetes Study	
	Chromosome 1, 45.3 cM	Any retinopathy		Mexican Americans from Starr County, Texas, with at least two siblings with diabetes	118
	Chromosome 2, 260.6 cM	NPDR-S/PDR			
	Chromosome 3, 9.4 cM	NPDR-S/PDR	Retinal development, venous thrombosis, and retinal interphotoreceptor matrix		
Retinopathy	Chromosome 3, 117 cM	NPDR-S/PDR			
	Chromosome 7, 33.1 cM	Any retinopathy	Adipogenesis, hypertension, obesity, and angiogenesis		
	Chromosome 12, 15.5 cM	Any retinopathy			
	Chromosome 12, 100.5 cM	NPDR-S/PDR	Neovascularization, retinal development, angiogenesis, and arterial endothelium		
	Chromosome 15, 78.4 cM	Any retinopathy			
	Chromosome 15, 108.3 cM	Any retinopathy			

diabetes did not develop albuminuria at a higher rate than NHWs with diabetes,¹³¹ suggesting that differences reported by the CDC may be due to access to health care.

CVD is now recognized as a risk factor for glomerular filtration rate decline, a marker of worsening kidney function.^{132,133} A review of diabetic complications and ethnicity concluded that most of the higher mortality and risk of complications in minorities disappear when factors such as smoking, socio-economic status, income, BMI, and years of education are considered.¹³⁴

While the evidence suggests that the worse outcomes observed in Latin Americans compared with NHWs are not due to genetic factor(s), the disparities in outcome that exist need to be addressed.

4.3 | Diabetic eye disease

Diabetic eye diseases are comprised by diabetic retinopathy (DR), diabetic macular oedema, cataract, and glaucoma. Of these, DR is the most common eye complication.

DR is the leading cause of blindness in the United States; it is a progressive disease caused by hyperglycaemia affecting the blood vessels in the retina, causing them to bleed or leak.

The prevalence in US adults with diabetes of DR is high (28.5%), and MAs have an additional 29% higher prevalence.¹³⁵ This implies a rapid decline in the quality of life given the impacts of DR on vision-related daily activities, dependency, and mental health.¹³⁶ The Los Angeles Latino Eye Study reported that the incidence of visual impairment in the Hispanic population was higher than in the overall population and the highest reported in a population-wide study.¹³⁷ The HbA_{1c} was not reported, making it difficult to know whether it is due to worse blood glucose management or genetic factors. However, sociocultural factors could play a big role as suggested by a study that showed MAs are less likely to use eye care services than NHWs.¹³⁸

Hispanics would benefit from prevention, early diagnosis of diabetes, and education in managing HbA_{1c} levels in order to prevent and reduce the progression of diabetic eye complications.

4.4 | Peripheral vascular disease and amputations

Lavery et al found in two different studies that Hispanics had a higher incidence of diabetes-related lower-extremity amputations in comparison with NHW in Texas and California.¹³⁹⁻¹⁴¹

Peripheral vascular disease in MAs with T2D was not different from that of NHWs in the San Antonio Heart Study after correction for prevalence of diabetes. The in-hospital mortality rate from amputations, however, was lower in Hispanics than in NHW.¹⁴¹

4.5 | Conclusion

Hispanics have lower diabetes-related cardiovascular complications than NHW. However, they have higher incidence and prevalence of nephropathy, diabetic eye disease, and higher incidence of diabetes-related amputations. Although some of these complications could have a genetic component (Table 2), they do not seem to correlate

to metabolic control and have been partly attributed to differences in health care.

5 | LIFESTYLE, SOCIAL, AND CULTURAL FACTORS

5.1 | Acculturation

Culture refers to the behaviour patterns, beliefs, arts, and all other products of human work and thought, as expressed in a particular community. *Acculturation* refers to the adoption of some specific elements of one culture by a different cultural group. For immigrants to the United States, it relates to the integration of multiple preferences and behaviours from their mainstream culture. A cross-sectional analysis using the data from the NHANES 2007 to 2010 showed an increased likelihood of diabetes increased with level of acculturation –1.71 (95% CI, 1.31-2.23), 1.63 (95% CI, 1.11-2.39), and 2.05 (95% CI, 1.27-3.29) for score of 1, 2, and 3, respectively—after adjusting for sociodemographic factors.¹⁴²

Culturally appropriate self-management education has been related to significant improvement in glycaemic control and self-management behaviours such as diet and physical activity, as well as diabetes-related knowledge.¹⁴³

5.2 | Nutrition preferences

Lifestyle may ultimately modulate the expression of multiple genes.¹⁴⁴ An unhealthy diet and lack of leisure-time physical activity/exercise are factors associated with an increase of developing diabetes and may contribute to the high prevalence of T2D in Hispanics living in the United States.^{124,145,146}

Dietary patterns have a significant role in the development of obesity and diet-related chronic diseases.¹⁴⁷ The Western diet, characterized by high intake of red and processed meat, white bread, and refined sugars, has been positively associated with weight gain over time and elevated risk of chronic diseases, including CVD and colon cancer, in comparison with diets high in fruit, vegetables, and fibre.¹⁴⁷ Studies on the MA population have suggested that diet quality decreases with nativity and duration of residence in the United States.¹⁴⁷ Findings from nationally representative surveys have consistently demonstrated that higher acculturation is associated with lower diet quality.¹⁴⁸ Data from the NHANES report that MA adults born in Mexico were more likely than adults born in the United States to adhere to dietary guidelines with regard to total fat, saturated fat, fibre, and potassium.¹⁴⁸ Adults born in Mexico had a higher consumption of fruit and vegetables, fruit juices, grains, and legumes and a lower consumption of salty snacks, desserts, and added fats.¹⁴⁸ Two reviews that included results from national,¹⁴⁸⁻¹⁵⁰ regional, and local samples conclude that a higher acculturation was associated with lower fruit and vegetable consumption and a higher intake of sugar and sugar-sweetened beverages and added fats. Similarly, a higher acculturation was associated with eating habits that led to higher intake of solid fat, added sugar, and sodium.¹⁴⁸⁻¹⁵⁰

Some aspects of the Latino culture can make it difficult to maintain a healthy diet. Traditional Hispanic foods can be high in fat and calories. As part of the San Antonio Heart Study, a dietary analysis was conducted and reported that MAs consumed more carbohydrates and saturated fats than NHWs.^{151,152} Moreover, Hispanic family celebrations may involve pressure to overeat. The cultural value *simpatía*, a deferent compliance with others' wishes in order to maintain interpersonal relationships, means that declining food at a social occasion is impolite and socially unacceptable.^{151,152} Another important characteristic is that families often eat meals together at home; so it can be difficult to modify the meal plan for someone with T2D since generally, not everyone in the family welcomes a change in meal patterns.¹⁵³

A series of focus groups were used by the Latino Diabetes Initiative at Joslin Diabetes Center to collect qualitative data from Latino women with T2D.¹⁵⁴ One of the discussed topics was the meal plans for a patient with diabetes; diabetic dietary modification, while requiring training and effort, was described as manageable—a reflection of successful patient education at the Latino Initiative and/or the fact that no one in the group was newly diagnosed.

5.3 | Physical activity

Lack of physical activity is associated with increased risk for obesity, T2D, and CVD among other conditions. The NHANES survey found that 65% of MA men and 74% of MA women reported little or no leisure-time physical activity.^{33,155} Findings from the 2008 National Health Interview Survey (NHIS) show that all Hispanic subgroups had lower levels of leisure-time physical activity than NHW.¹⁵⁶

In the United States, Hispanics are less likely to exercise than NHW. NHIS data from 2004 to 2006 show higher proportions of Hispanic (53.6%) are physically inactive compared with NHW (34.8%).¹⁵⁷ In a cross-sectional analysis of the 1992 Health Retirement Study, the proportion of Hispanics (22%) that never engaged in light or vigorous leisure-time physical activity was higher than the proportion of NHW (8%).^{151,158}

5.4 | Body image

Perception of health and body image is also influenced by Hispanic culture. Physical robustness may be equated with physical health. As a result, Hispanics may be less likely to perceive themselves as overweight.¹⁵¹ A study to assess Latina mothers' health beliefs and attitudes regarding early childhood issues reported that being moderately overweight was not viewed as a problem as long as the child looked and felt good. Mothers frequently reported that a heavier child looked healthiest because her "hair was healthier and shinier" and "her skin was full of life." Additionally, mothers expressed concern that thinness was related to poor health. To immigrant Latinas, thinness was especially worrisome as they considered malnutrition and intestinal infections a greater threat to a child's health than being overweight. They also believed that a little extra weight helps children recover from illnesses and that a thin child is more disease prone.¹⁵⁹

Being robust and slightly overweight can be regarded as a sign of being well nourished and financially successful. Children are often encouraged to "eat well" and finish their entire meal. For some groups, achieving a higher socio-economic status translates into the possibility of eating more, not necessarily eating healthier.¹⁵³

In the same focus groups used by the Latino Diabetes Initiative at Joslin Diabetes Center,¹⁵⁴ women identified a body size ideal larger than the average ideal for NHW women, although not obese; body dissatisfaction was centred on diabetes-induced skin changes and virilization rather than weight.

5.5 | Family integration and support

Hispanics seek encouragement, direction, and advice from a large number of family members. For Hispanics, loyalty to the extended family is more important than the needs of the individual, a concept known as *familismo*. This loyalty may benefit the individual as the family may provide the support needed for disease self-management. At the same time, it may be more difficult for individuals with diabetes to make their own independent decisions. It is common for several members of the family to be involved in the decision-making process related to diabetes treatment, such as a new meal plan, or the use of certain medications.^{33,151,153}

In many Latino families, women are the primary caretakers, and being a wife and mother are considered the most important roles for women. Within the family, women are the most knowledgeable about health care; hence, men often speak to their wives or mothers first for advice about their health concerns.^{33,151,153} In 2011, a study in support and influence in the context of diabetes management examined the sources and frequency of and dietary behavioural responses to health-related social support and control in a racially/ethnically diverse sample of adults with T2D.¹⁶⁰ MAs were significantly more likely to name a spouse or any other family member as a source of support than NHWs. For MAs, all types of health-related social support were associated with good dietary behaviour ($P < 0.001$).¹⁶⁰

5.6 | Education

Latinos are more likely to suffer from serious diabetes complications, due, in part, to inadequate diabetes education and lack of access to preventive health care.¹⁶¹

The symptom interpretation model (SIM) "explains individual reactions to the symptoms experience, and the reasoning and behavioral responses that result. According to the model, when diabetes symptoms occur, an individual with adequate symptom experience, diabetes knowledge, and health literacy will be able to recognize, interpret, and respond to the symptoms interpretation, however, this may also lead individuals to disregard symptoms, self-treat, or delay professional health care."¹⁶¹

Effective diabetes self-management begins with the ability to recognize and understand symptoms, according to the SIM.¹⁶¹ Symptom awareness for Hispanics is sometimes based on culturally defined explanatory models rather than biomedical models. Hispanics tend to explain diabetes based on their symptoms, while NHWs use

biophysical explanations.^{161,162} MAs with T2D may incorrectly interpret symptoms as benign.¹⁶³ Studies suggest¹⁶⁴ that individuals are more likely to seek medical assistance if symptoms are perceived as severe and threaten functional status.

5.7 | Health literacy

Health literacy is the degree to which individuals have the capacity to obtain, process, and understand the basic information and services they need to make appropriate health decisions.¹⁵³ Low health literacy is defined as inability to read, comprehend, and interpret health-related information and written materials.¹⁶¹ Individuals with diabetes and low health literacy have been associated with inadequate diabetes knowledge, poor glycaemic control, and increased diabetes complications.¹⁶⁵ As many as 62% of Latinos tested in Spanish have been found to have low or marginal health literacy.¹⁵ In another study with 144 adult Latinos with diabetes risk factors, almost half the sample (46.5%) had low literacy, with 12.5% having marginal and 34% inadequate health literacy scores.¹⁶¹ Adequate health literacy can help Latinos understand, interpret, and act on diabetes symptoms. Some studies suggest that adequate health literacy leads to diabetes control as evidenced by lower HbA_{1c} levels.^{161,166} As studies have shown,¹⁶⁷ screening for health literacy could improve the health care given to Latinos and contribute to the development of interventions to improve the quality of care and health outcomes for this population.

5.8 | Judgement and beliefs about diabetes

Every social group shares beliefs about health and illness. A study explored health-related beliefs and experiences of black, Hispanic/Latino, American Indian, and Hmong people (an Asian ethnic group).^{153,168} Results showed that many participants attributed their loss of health to the modern American lifestyle, lack of confidence in the medical system, and the general lack of spirituality in everyday life. Exploring the beliefs about the development and course of diabetes with patients may guide clinicians on important factors to address with the patients and help with their diabetes management.

5.9 | Language

In a clinical and educational encounter, the most obvious "cultural" barrier is the inability to communicate in the same language. It may limit the patient's ability to ask questions, to verbalize important information and concerns, and to establish a natural and spontaneous relationship with the health care provider. Limited English proficiency has been related to disparities in quality of care¹⁶⁷ and has been shown to affect clinician outcomes and may be a serious barrier to effective patient care.^{153,169}

5.10 | Socio-economic status

Poverty influences the development of T2D as well as complications related to diabetes.^{143,150,170,171} Place of birth and length of residence in the United States are factors closely related to socio-economic

status, and these two factors may have a direct effect on specific diseases.¹⁵³

Besides the increase in T2D prevalence,^{170,171} socio-economic challenges can prevent access to optimal health care among Hispanics.¹⁷⁰⁻¹⁷² In a study, 23.9% Latino/Hispanics with diabetes reported that cost was a significant barrier to health care, compared with NHW with diabetes (8.2%).^{172,173} This analysis also reported that a greater proportion of Latino/Hispanics did not have health insurance (20.7% vs 6.4%) and were more worried about the expense of medications for diabetes (71% vs 52%).^{172,173}

Hispanics/Latinos have also reported limited access to transportation, which can be a problem when attending to medical appointments and educational programmes.¹⁷³ Low socio-economic neighbourhoods can hinder diabetes self-management by limiting access to foods, such as fresh fruit and vegetables, as well as limiting opportunities to exercise by a lack of safe places to engage in physical activities.

5.11 | Depression

Depression is extremely common in patients with diabetes. In MAs, it has been identified as an important predictive factor for adverse diabetes-related outcomes.¹⁷⁴ It has also been closely linked with decreased adherence to treatment guidelines. This association may be accountable by many factors such as low socio-economic status, lack of family and social support, and sense of isolation.³³

5.12 | Religion

Religious beliefs play an important role in health care among Hispanic/Latinos. In a survey of 104 Hispanics with diabetes,¹⁷⁵ 78% believed they had diabetes because it was God's will and 81% believed that only God could control their disease. This *fatalismo* (the belief that individuals cannot alter their disease process because it is part of their destiny) may result in Hispanic/Latino patients being less likely to adhere to their recommended treatment plan. But religion can also have a positive effect on T2D management, as a support system, providing strength to cope with the disease, and the ability to face fears, remain positive, and hope that a cure would be provided by God.^{33,176,177}

5.13 | Conclusion

In summary, the development of diabetes in the Hispanic population has a very important cultural component. Awareness of Hispanic values will ensure the design of cost-effective interventions. As an example, targeting Hispanic women in a campaign that promotes nutritional education will be the most impactful because of their central social role within the Hispanic community.

6 | PREVENTION OF T2D

As presented, the Hispanic and Latino population is at high risk of developing T2D and its complications. Prevention strategies are needed to decrease the burden of this epidemic problem on the health

care system. In this section, diabetes prevention programmes that have included (or were designed to study) Hispanics, Latinos, or MAs will be reviewed in order to assess successes and identify potential for new studies.

The DPP is a randomized clinical trial to prevent T2D in persons at high risk. The study population represents different ethnic groups and includes 16% of Hispanics, the majority of which are MAs. The results of the DPP reveal that millions of high-risk people can modify their diet and exercise to lose a small amount of weight to delay or prevent altogether the development of T2D. The DPP also suggests that metformin is effective in delaying the onset of diabetes in younger, heavier people. Participants in the lifestyle intervention group—those receiving intensive counselling on effective diet, exercise, and behaviour modification—reduced their risk of developing diabetes by 58% after an average follow-up¹²⁹ of 2.8 years. This finding was true across all participating ethnic groups and for both men and women. Lifestyle changes worked particularly well for participants aged 60 years and older, reducing their risk by 71%. About 5% of the lifestyle intervention group developed diabetes each year during the study period, compared with 11% in those who did not get the intervention. Researchers believe that weight loss—achieved through better eating habits and exercise—reduces the risk of diabetes by improving the ability of the body to use insulin and process glucose. Participants taking metformin reduced their risk of developing diabetes by 31% compared with the no intervention group. Metformin was effective for both men and women, but it was least effective in people aged 45 years and older. Metformin was most effective in people 25 to 44 years old and in those with a BMI of 35 or higher (at least 60 pounds overweight). About 7.8% of the metformin group developed diabetes each year during the study, compared with 11% of the group receiving the placebo.¹²⁹

The Diabetes Prevention Program Outcomes Study (DPPOS), the 10-year follow-up study to the DPP, has closely followed 88% of the surviving DPP participants who were eligible to join. The DPPOS was designed to examine the longer-term impact of the original treatment interventions, once the interventions had stopped. Results of the DPPOS indicate that the effects of the DPP have persisted for years. The incidence of diabetes in the 10-year follow-up study was reduced by 43% in the lifestyle group and 18% in those taking metformin compared with the placebo group. However, the major problem with lifestyle interventions is the difficulty in maintaining weight loss and increased physical activity. For Hispanic participants, the development of diabetes was reduced by 66% for participants aged 60 years and older; the development of diabetes was reduced by 49% by intensive lifestyle when compared with placebo. After an average of 10-year follow-up, treatment with metformin reduced the rate of developing diabetes by 18% compared with placebo in all ethnic groups.¹³⁰

In the Actos Now for the prevention of diabetes (ACT NOW) trial, pioglitazone was able to decrease the conversion of glucose intolerance to T2D by 72%, while the cessation of thiazolidinedione (TZD) therapy in this group was associated with a return of diabetes incidence similar to those observed in the control group.⁷⁹

The Study to Prevent Non-Insulin Dependent Diabetes Mellitus (STOP-NIDDM) study used acarbose, an α -glucosidase inhibitor, as a strategy to decrease T2D incidence among IGT.¹³¹ This intervention

was effective in preventing diabetes, probably because of a combined effect of inhibition of carbohydrate absorption and enhanced β -cell function since α -glucosidases increase incretin secretion.

Since obesity has been proven to be one of the main risk factors contributing to the development of T2D, strategies that prevent or manage obesity should in theory also have positive preventive potential. This was shown in the XENical in the prevention of diabetes in obese subjects (XENDOS) study where Orlistat, an inhibitor of lipase activity, promoted long-term weight loss and prevented T2D onset in individuals with obesity.¹⁷⁸ This benefit was associated with weight loss, reduced lipid absorption, and decrease of circulating free fatty acids.

As discussed previously, development of gestational diabetes poses women at greater risk to develop T2D later in life. Therefore, specific studies have been designed to address this high-risk population. The Pioglitazone in Prevention of Diabetes (PIPOD) study was conducted to evaluate β -cell function, insulin resistance, and the incidence of diabetes during treatment with pioglitazone in Hispanic women with prior gestational diabetes who had completed participation in the Troglitazone in Prevention of Diabetes (TRIPOD) study.¹⁷⁹ This intervention stabilized β -cell function, and insulin resistance was improved. However, both effects were lost when the administration of the drug was suspended. The diabetes rate dropped to 4.6% in the intervention group from the 12.1% incidence per year observed in the placebo group. In conclusion, these two studies support the role for TZD drugs to modify the natural history of progression to T2D in high-risk Hispanic patients.

Preliminary results of the DPPOS found that nearly 8% of participants with prediabetes in the DPP had DR. Diabetic eye disease was also seen in 12.6% of participants with T2D who developed diabetes during the DPP. These findings suggest that patients with prediabetes or newly diagnosed T2D should be screened for retinopathy.¹³⁰

6.1 | Conclusion

Given the discussed particularities of the Hispanic population and the results of the different prevention trials, life style modifications that reduce weight and metformin are the most impactful interventions to avoid the progression to T2D.

7 | DIABETES SELF-MANAGEMENT PROGRAMMES FOR HISPANIC/LATINOS

DSME is a critical element of care of all people with diabetes and is considered necessary to improve patient outcomes. To be more effective, programmes should take into consideration cultural factors that influence the development and progression of diabetes.¹⁸⁰ Also, the increasing availability of popular diabetes apps should be optimized to meet the needs of Hispanics, both being available in Spanish (only one-third of them are at the moment) and incorporate basic features such as diabetes education, reminders to check blood glucose levels or take medications.¹⁸¹

Following is a brief summary of some of the programmes for diabetes self-management for Hispanics.

7.1 | The Diabetes Assessment, Nursing, Nutrition and Dental Evaluation Project

The *Diabetes Assessment, Nursing, Nutrition and Dental Evaluation Project* evaluated the impact of an intensive, culturally specific diabetes education programme on dietary patterns and nutrient composition in 152 MA men and women with T2D in the border towns of Texas.^{180,182}

The project consisted of 2-hour nutrition education sessions for 8 weeks in groups of 8 to 10 people where they viewed a videotape (bilingual) followed by a group discussion. The topics were nutrition, HTN, eye care, foot care, oral health, and kidney-related complications.^{180,182} Most groups experienced significant weight loss and videos that were specifically tailored to low-literacy Hispanics seemed to contribute positively to the results.

7.2 | Project Dulce

Project Dulce was developed by a health care organization in San Diego, California, to improve the quality of care, quality of life, and health among uninsured, low-income minority patients with diabetes.¹⁸³ This project was culturally appropriate, community-based, with a nurse case management/peer education diabetes care model, which consisted of a clinical care component and a health and education component. This was a bilingual, 12-week programme. Trained peers from the community, *promotoras*, delivered patient education and participated as culturally sensitive community health workers. The intervention group had significant improvements in HbA_{1c}, total cholesterol, low-density lipoprotein (LDL) cholesterol, and diastolic blood pressure, as well as diabetes knowledge, self-efficacy, treatment satisfaction, and cultured-based beliefs.^{180,183} The improvements after 1 year showed a decrease in HbA_{1c} from 11.5 to 8.3% ($P < 0.0001$), total cholesterol from 219 to 181 mg/dL ($P < 0.00001$), systolic blood pressure from 129 to 122 mm Hg ($P < 0.03$), and diastolic blood pressure from 79 to 75 mm Hg ($P < 0.006$).

Other programmes such as the Diabetes Empowerment Education Program and the T2D Self-management Social Support Intervention in the United States-Mexico border have used *promotoras* to improve behavioural skills and glycaemic control.^{184,185}

7.3 | The Starr County Health Initiative

The *Starr County Health Initiative* was designed to address the unique needs of the MA population, culturally appropriate regarding language, diet, family participation, and health beliefs.^{180,186} The programme included 52 contact hours distributed in weekly 2-hour education sessions for 3 months in nutrition, exercise, and self-monitoring of blood glucose and 14 biweekly 2-hour support group sessions to promote behaviour changes and food preparation demonstration.

The intervention group had lower fasting blood glucose and greater knowledge at 12 months compared with the control group, who received usual care provided by their private physicians or local clinics.¹⁸⁶

7.4 | Tomando Control de su Salud

The *Tomando Control de su Salud* programme is the Spanish version of the community-based Chronic Disease Self-management Program, taking into account the Latino culture.^{180,187} The intervention consisted of 14-hour education administered in 2.5-hour sessions over 6 weeks. The topics included in the sessions were fitness, healthy eating, action planning, relaxation, depression, family relationships, and medications.

Of the 319 participants, 67% improved health behaviours, health status, health care use, and self-efficacy.¹⁸⁷

7.5 | Rosal et al

A pilot randomized clinical trial in Boston, Massachusetts, conducted by Rosal et al, examined the efficacy of a self-management intervention in low-income Puerto Ricans with T2D.¹⁸⁸ The intervention was adapted to a low health literacy audience and incorporated relevant characteristics of the Latino culture. It consisted of a 1-hour individual session followed by 10 weekly group sessions of 2.5 to 3 hours, with a 15-minute individual session before the group sessions. The intervention was delivered by a diabetes nurse, a nutritionist, and an assistant; the focus was on diabetes knowledge, attitudes, and self-management skills including physical activity, diet, adherence to medications, and blood glucose monitoring.¹⁸⁸ The intervention group had a greater decline in HbA_{1c} levels compared with the control group and had an increase in physical activity and self-monitoring blood glucose.

7.6 | Tomando Control

Tomando Control (different from *Tomando Control de su Salud* described above) is a programme, tested in a pilot study to assess the feasibility, acceptability, and efficacy of a culturally appropriate and culturally relevant cognitive-behavioural diabetes self-care education programme for Hispanic Americans with T2D.^{180,189} The intervention consisted of 3-hour weekly sessions for 6 weeks at a health centre. The curriculum used for the intervention was the 2001 ADA-accredited *Taking Control* developed by Philadelphia's Health Promotion Council. Over the 6 months of the study, men and women showed an increase in knowledge scores, improvements in lipid profiles, and a reduction in A1C levels.^{180,189}

7.7 | Banister et al

An intervention implemented by Banister et al¹⁹⁰ was conducted in Hispanic and African American individuals with T2D at a community clinic in Texas to assess the effectiveness of a diabetes self-management training programme. The intervention consisted of 4-hour sessions followed by individual sessions with a dietitian and monthly support sessions. A significant reduction in A1C levels (9.75-8.2%) was seen after 12 months, and 61% of the participants experienced positive medication outcomes.^{180,190}

7.8 | El Camino a la Salud

The racial and Ethnic Approaches to Community Health Detroit Partnership's Diabetes Lifestyle Intervention developed a culturally oriented, behavioural change programme for African Americans (*The Journey to Health*) and for Latinos (*El Camino a la Salud*) with T2D.¹⁹¹ The curriculum used the "Strong in Body and Spirit" method as the diabetes lifestyle intervention, which was originally designed and evaluated among Southwest Native Americans with T2D. The educational programme was tailored to meet the specific needs of the Latino and the African American cultures. The intervention consisted of five 2-hour, monthly sessions delivered by community residents, supervised by a registered dietitian. The intervention group had significant improvements in A1C levels, dietary, and physical activity knowledge and behaviours.^{180,191}

7.9 | Rosa's Story/La Historia de Rosa

Rosa's Story/La Historia de Rosa: An Audio-novella for Latinos with Type 2 Diabetes, and their Families,¹⁸⁰ an education tool developed by the Latino Diabetes Initiative at the Joslin Diabetes Center, represents a unique approach to culturally competent diabetes education for Spanish-speaking Latinos at risk and living with T2D. It consists of an audio-novella and a patient booklet.

This educational tool uses short stories to teach individuals about diagnosis, blood glucose control, nutrition, medication, and exercise. This audio-novella is now being tested in a randomized controlled trial.

7.10 | Puentes hacia una mejor vida (Bridges to a Better Life)

Volunteer peer leaders were used to provide support for patients with T2D through telephone contact, in-person, individual, and group sessions. The intervention group (168 participants) showed reductions in HbA_{1c} compared with the control group (168 participants), as well as increase in fruit and vegetable consumption and examination of feet.¹⁹²

7.11 | Conclusion

The development of materials in Spanish that are culturally appropriate and incorporate face-to-face interactions has positive effects on self-management measures of diabetes including nutrition and physical activity. They have shown to have a positive impact on HbA_{1c} and fasting glucose levels.

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CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

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