# Diabetes burden among Latinos

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(Preliminary results. Results using the compartment model not shown in this version.)

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## 1 Research Problem

Populations around the world have experienced exceptional increases in the prevalence of diabetes mellitus and even larger increases are expected in the next few decades. The world prevalence of diabetes in adults was estimated in 4.0% in 1995 and it is expected to reach 5.4% in 2025, a proportional increase of 35%. The number of adults with diabetes will increase from 135 million to 300 million during this period. Increases in developing countries will be even more dramatic with prevalence rising from 3.3% to 4.9% - a proportional increase of 48%. In Latin America, the prevalence rates are already higher than average. In 1995, prevalence rate was estimated in 5.7% and it is expected to reach 8.1% in 2025 – a 42% increase. The number of cases in Latin America will rise from 15 million in 1995 to 39 million in 2025 (King et al, 1998), with Brazil and Mexico comprising over 50% of the cases in both years.

There are many explanations to the fast rise of diabetes (and obesity) in less developed countries: rapid economic development, modernization, urbanization, socioeconomic inequality, stress, exposure to environmental toxins, and aging (Fall, 2001; DECODE, 1998). Urbanization and economic development in poor countries are associated higher intake of calories and lower energy consumption. Indeed, there is evidence that in poor countries people tend to get fatter as their incomes increase (Eberwine, 2002) and obesity is demonstrated to be one of the main risk factors to develop diabetes. With modernization, there is also a reduction in the physical activity and again, prevalence of diabetes type 2 is higher among more sedentary people (Fall, 2001). Modernization and urbanization also increase the exposure to toxins that may be a risk factor for diabetes (Yudkin et al, 1999). There is also evidence that some risk factors, such as gestational diabetes, impaired glucose tolerance and genetic predisposition, are more common among Hispanics. Some have in addition linked low birth weight and early malnutrition with obesity later in life. Finally, the 'thrifty gene' theory holds that people in developing countries inherited a tendency toward weight conservation that increased. This predisposition to weight conservation would be responsible for the higher levels of obesity in contexts of higher access to food. Therefore, the already higher prevalence of diabetes in Latin America and its remarkable increase in the next decades can be attributable to

the genetic predisposition within a context of westernization and increase in sedentary life styles.

The relative high incidence and prevalence of diabetes in Latin America and Caribbean imposes high costs for the populations in this region. A recent study conducted by Barceló and colleagues showed that the total annual cost associated with diabetes was estimated in more than US$65 billion. The indirect costs contributed from 82% of the overall costs. Indirect costs are due to a loss of over 330,000 deaths occurring in year 2000 (over 757,000 years of productive life lost) and to approximately 178,000 individuals with permanent disability (over 136,000 years of productive life lost). The direct costs (drugs, consultations and hospitalizations) represented 18% of the overall costs and are estimated at US$703 per capita annually. These values are incredibly high per se, but they are even more striking if we consider that only direct costs represent 19% of the total per capita gross national income in the region. As a result, coherent estimates of diabetes burden in the Latin America are a basic need for policy makers in those countries that lack adequate information to plan interventions that might result in reductions of the disease incidence.

This study has as its main objectives:

1) Describe the main risk factors associated with diabetes mellitus;

2) Systematize the available literature regarding diabetes and Latin America;

3) Explore trends in prevalence rates in Latin America;

4) Analyze the incidence of diabetes among Hispanics and non-Hispanics in the United States;

5) Describe mortality patterns in selected countries in Latin America.

6) Use incidence, prevalence and mortality data as input data in the compartment model.

## 2 Diabetes: definition, risk factors and disease frequency

### 2.1 Definition

Diabetes mellitus is a chronic disease that it can be described as a "metabolic disorder of multiple aetiology characterized by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both" (WHO, 1999: 2). More specifically, diabetes mellitus is recognized as a heterogeneous syndrome that encompasses many diseases and disorders that have in common glucose intolerance and hyperglycemia. Diabetes mellitus is a result of problems in either insulin secretion or impaired of insulin action (Harris and Zimmet, 1992). Those diseases and disorders have distinct pathogenesis, natural history and require distinct prophylactic measures and therapy. Usually, diabetes mellitus is classified in the following distinct types: non-insulin dependent diabetes mellitus (NIDDM), insulin dependent diabetes mellitus (IDDM), malnutrition related diabetes mellitus (MRDM), gestational diabetes (GDM), and other types of diabetes mellitus that are associated with certain syndromes. The most prevalent type is NIDDM, also called Type 2. As suggested by the name, persons that have NIDDM are non-insulin dependent, even though insulin is sometimes prescribed to control hyperglycemia. This type of diabetes has its onset usually at adult ages, generally after age 40. However, NIDDM may occur at all ages (Harris and Zimmet, 1992). Obesity is very common among individuals with NIDDM and usually is treated as a risk factor. Therefore, it is recommended to divide the cases of NIDDM between obese and non-obese. Persons with insulin dependent diabetes mellitus, sometimes called Type 1, need to take insulin to prevent ketosis and sustain life. Most of the cases have its onset at younger ages, but IDDM may occur at any age. Malnutrition related diabetes mellitus is generally divided between two subclasses: fibrocalculous pancreatic diabetes and protein deficient pancreatic diabetes. It was formerly named tropical diabetes because it generally occurs in tropical developing countries. Its occurrence is associated with a past and present nutritional deficiency and its onset is usually before age 35 (Harris and Zimmet, 1992). Individuals are generally underweight and recurrent attacks of abdominal pain frequently extend back to childhood. Gestational diabetes is a type of glucose intolerance that has its onset or recognition during pregnancy. "Other types of diabetes" include a variety of conditions and syndromes that are associated with diabetes: pancreatic disease, drug or

chemical induced, hormonal, certain genetic syndromes and insulin receptor abnormalities. Finally, the classification system incorporates impaired glucose tolerance (IGT) and other types of glucose intolerance. It has been demonstrated that individuals with IGT are at higher risk of developing arteriosclerosis, among others. For some individuals IGT may represent a stage in the development of diabetes.

The clinical diagnosis of diabetes often happens when symptoms (increased thirst, profuse urination, weight loss, among others) become apparent. Individuals with IDDM usually have a sudden onset of severe symptoms that are caused by a lack of insulin due to a diminution of insulin secretor capacity. Given the severity of the symptoms, IDDM cases are more likely to be brought to medical attention and to have a subsequent diagnosis. NIDDM, on the other hand, have a longer course and symptoms to not emerge so severely. Individuals with NIDDM can live for many years without being diagnosed, and in some cases they will never be diagnosed.

WHO suggests that no diagnostic should be made on the basis of a single abnormal glucose value. WHO criteria to diagnose diabetes mellitus are: fasting plasma glucose concentration ≥7.0 mmol/l or 2 hour post glucose load ≥11.1 mmol/l. These criteria should be able to identify the same individuals however, DECODE study group demonstrated individuals identified by the fasting values differ from those identified by 2-hour post glucose load (DECODE study group, 1998). In fact, the probability of disagreement depends on age and body mass index. The fasting criterion is more likely to identify more obese, middle aged patients, while the 2-h criteria is more likely to identify diabetes in lean individuals. The occurrence of disagreement clearly shows that when dealing with chronic diseases, the actual time in which the transition from healthy to a morbid state occurs is much more difficult to be identified.

The American Diabetes Association (1997) suggests three methods to diagnose diabetes:

1) A fasting plasma glucose test with a value of 7 mmol/l (126 mg/dL) or greater;

2) An abnormal oral glucose tolerance test with a 2-hour glucose value of 11.1 mmol/l (200 mg/dL) or greater.

3) A nonfasting plasma glucose value of 11.1 mmol/l (200 mg/dL) or greater for people with symptoms of diabetes.

Other criteria include self-reported use of medications for diabetes, or a self-reported previous physician diagnosis.

Most epidemiological studies will use one of these methods to identify prevalence and incidence of diabetes among the study group. However, epidemiological studies tend to have their samples confined to a particular population, which may limit the generalization of their findings. Population based studies, on the other hand, are more representative, but they tend to rely on the basis of self-report of physician diagnosis. Some limitations emerge when diagnose is based on self-report: for instance, undiagnosed people are not captured, some people with diabetes may not report having diabetes, while others with the condition may not report when questioned. Nevertheless, some studies have demonstrated that self-report of diabetes is a reasonably accurate, valid and reliable assessment method for the diagnosis (Bowling et al, 1996; Stein et al, 1996; Kehoe et al, 1994; Bush et al, 1989). For example, a study in Taiwan, the results showed that a self-reported history of diabetes had the highest sensitivity (66.7%) and specificity (95.2%) (Wu et al, 2000). Therefore, it seems that the main problem with self-reported data is that undiagnosed people are not captured. Indeed, epidemiological surveys show that 30 to 60% of all diabetic individuals are undiagnosed (King et al, 1993).

Another problem in some epidemiological and most population-based studies is the difficulty in distinguishing between the different types of diabetes. Sometimes, studies include information regarding use of insulin as a way to distinguish between types 1 and 2. However, some individuals with type 2 may use insulin to control hyperglycemia. There is no simple way to distinguish between all cases of diabetes. Therefore, the use of age boundaries and body mass index are not sufficient criteria to define cases.

### 2.2 Risk Factors

Diabetes mellitus is generally recognized to be a result of genetic susceptibility and environmental factors. Studies have identified many risk factors that are associated with the development of diabetes 2: obesity, abdominal fat, age, race and ethnicity, socioeconomic

status, sedentary lifestyle, family history, history of diabetes during pregnancy, high blood pressure, high cholesterol and triglyceride levels. Those with impaired glucose tolerance or impaired fasting glucose are also at higher risk of developing diabetes. Other studies have argued that fetal environment, viral infection, dietary macronutrients, inflammation, stress, depression, among others may also be associated with diabetes. Smoking, abnormal lung function and sleep apnea may be related to diabetes, but results are inconclusive (Qiao et al, 1999).

Obesity is probably the most acknowledged risk factor of diabetes and obesity is highly prevalent among people with type 2 diabetes. About 60-90% of NIDDM cases are obese (Harris and Zimmet, 1992). Even crude measures of obesity, such as BMI (Body Mass Index), are powerful predictors of incidence of diabetes. Obese people (BMI>30 $Kg/m^2$) are at much higher risk of developing diabetes. For instance, data from ARIC (Arteriosclerosis Risk in Communities) Study show that incidence rates are two to three times higher among obese adults than among non-obese (Carnethon et al, 2002). Moreover, it has been demonstrated that not only initial BMI is important, but also the weight gain, duration of overweight and obesity. Conversely, weight loss was associated with reduction of incidence of diabetes during the follow-up period (Wannamethee and Shaper, 1999). This higher risk is particularly important in a context in which obesity is on rise. One explanation to the rise of obesity may be that the human organism when exposed to famine tended to develop mechanisms to store calories. However, in a context of increased access to high quantity of food, generally with rich in fat and carbohydrates, the organism may tend to pile up the excess of lipids. The Neel's 'thrifty gene' hypothesis states that populations that had experienced famine are genetically different in their ability to increase insulin secretion from those that did not experienced food shortage (Vadheim and Rotter, 1992). Additionally, obesity is seen as a symbol of wealth and status in Latin America, which contributes to the rise of the obesity among Latinos (Fall, 2000). Finally, obesity is so important as a risk factor, that it is considered one of the factors in the metabolic

syndrome[1] that has been described as an important determinant of diabetes type 2 (Hanson et al, 2002).

Obesity in itself is associated with the onset of diabetes, but it has been demonstrated that body fat distribution is also important (Lundgren et al, 1989; Ohlson et al, 1985). Many studies have demonstrated that abdominal fat, characterized as the "apple body shape" in men and "pear body shape in women, is also associated with the adult onset of diabetes. Individuals with abdominal adiposity tend to have fat accumulated around and in the liver, pancreas and bowel and the excess of internal fat is strongly related to insulin resistance (Carey et al, 1996), hyperinsulinemia and glucose intolerance. Hispanics have higher abdominal obesity, which increases their risk of diabetes (Haffner et al, 1986; Karter et al, 1996). It has also been demonstrated that Black women have a higher waist-to-hip ratio than White women and this measure is frequently used to predict diabetes incidence and prevalence. However, Dowling and Pi-Sunyer (1993) found that the relationship between central obesity, insulin resistance, glucose intolerance and hyperinsulinemia occurred more frequently among White women. Later, Albu and colleagues (1997) showed that Black women had less visceral fat than White women, and that visceral fat were more strongly associated with metabolic problems.

Age is another powerful predictor of incidence diabetes. For diabetes type 1, many studies have identified two peaks for age at onset. The earlier peak is less pronounced and is located around age 5, the second peak is more prominent and usually coincides with puberty for both males and females (Vadheim and Rotter, 1992). Prevalence rates of NIDDM rapidly increase with age and most of diabetes type 2 occurs in older people. The usual onset of NIDDM is after age 40, but in recent decades there was an increase of incidence at younger ages. Data from NHANES show that the prevalence of diabetes increases with age in the U.S. population (Harris et al, 1998). There is also evidence that lean body mass decreases with age.

[1] The metabolic syndrome is a combination of obesity, insulin resistance, hypertension and dyslipidemia. Even though some studies have shown the predictive power of the metabolic syndrome, others have argued that syndrome traits do not have equal predictive weights for specific outcomes. Indeed, it has been shown that insulinemia, body size and lipid facts significantly predicted diabetes incidence, while blood pressure did not (Hanson et al, 2002).

Ethnic and racial background has been accepted as an independent risk factor of diabetes incidence and prevalence. Diabetes type 1 occurs more frequently among Caucasians, with the highest rates found among those living in northern Europe. Japanese population, on the other hand, has the lowest rates of IDDM (Vadheim and Rotter, 1992). Studies focusing on Aboriginal, African, Latin American and Asian ethnic ancestry populations have found that those groups have higher risk for diabetes. Studies conducted in the United States show that prevalence of diabetes is higher among Hispanics and Blacks (Mokdad et al, 2000) and it is increasing faster among Hispanics (Mokdad et al, 2000).

Sedentary lifestyles are becoming increasingly important to define the diabetes epidemic. Individuals who exercise have lower BMI and physical activity plays an important role in glucose tolerance and insulin sensitivity. Moreover, even among those with impaired glucose tolerance, exercise has shown to reduce BMI and to improve the body fat distribution and, thus, may delay or prevent diabetes type 2 (Liao et al, 2002). Individuals with diabetes are also more likely to exercise less and more likely to have sedentary professions (Thanopoulou et al, 2003).

It has been recognized that genetics have an influential role in the etiology of diabetes, but its precise share is not yet clear because of the heterogeneity of the diabetes syndrome. Different models of inheritance have been developed, but they are controversial. Several studies using twin design approach "have reported a concordance rate of monozygotic twins between 45% and 96%, and for dizygotic twins between 3% and 37%" (Vadheim and Rotter, 1992). This clearly indicates the influence of genetics. More generally, family history seems to be good predictor of incidence of diabetes. Having first-degree relatives with diabetes increases the risk 3 to 10 times (Vadheim and Rotter, 1992; Krolewski et al, 1981; Rotter and Rimoin, 1981). Guerrero-Igea et al (2001) argue that the family history could explain the association between short stature and higher risk and prevalence of type 2 diabetes. However, it is important to point out that environmental influences seem to interact with genetics.

Gestational Diabetes Mellitus (GDM) is carbohydrate intolerance of varying degrees of severity with onset with onset (or recognition) during pregnancy (Metzger and Coustan, 1998). GDM not only brings complications during the pregnancy, but it also increases the risk that a woman who had diabetes during their pregnancy will develop diabetes type 2 later in life,

usually within five to ten years of giving birth (Kim et al, 2002). Conversion rates to diabetes type 2 vary enormously among studies. Kim and colleagues (2002) found that cumulative rates vary from 2.6 to 70%, over a period from 6 weeks to 28 years postpartum. Among Mexican American women there is evidence that those with previous gestational diabetes may be at a higher risk of developing diabetes type 2 later in life (Peters et al, 1996). Finally, children of mothers who had GDM are also at higher risk of being obese and glucose intolerant.

Impaired glucose tolerance (IGT) or impaired fasting glucose (IFG) can precede the development of type 2 diabetes. Individuals with IGT and IFG do not meet the diagnostic criteria for diabetes, but their blood sugar control and reaction to sugar loads are considered to be abnormal. This places them at higher risk of developing diabetes type 2 and cardiovascular disease. Mexican Americans adults have higher rates of impaired glucose tolerance than non-Hispanic whites in the United States (Harris et al, 1998). Insulin levels of Mexican Americans were also higher than in non-Hispanic whites in NHANES III among those who did not have diabetes (Stern and Mitchell, 1995).

Several studies suggest the importance of serum triglyceride levels in people with diabetes (Standl et al, 1988; Fontbonne et al, 1992). Triglyceride levels tend to be raised in diabetic patients and levels of triglycerides appear to be further related to the degree of blood glucose control.

Since Barker's findings in the late 1980s that associated low birth weight and heart disease mortality, a new line of research has been exploring the effects of adverse conditions at womb may be associated with the incidence of chronic conditions later in life (Barker, 1998). After this influential work, studies have shown that normal babies who born with low birth weight (LBW) are more likely to develop diabetes type 2, hypertension, stroke and heart disease (McCance et al, 1994; Eriksson et al, 2001; Rich-Edwards et al, 1997; Huxley et al, 2000). Evidence also exists relating birth length and high blood pressure and cardiovascular disease (Gunnarsdottir et al, 2002). McCance et al (1994) found a U-shape relationship between birth weight and incidence of diabetes type 2, but they argue that the relationship between high birth weight and diabetes later in life is mediated by maternal diabetes during pregnancy. However, it is important to note that most of diabetes cases occur among those born with normal weight.

Diet during pregnancy, stress hormones and improper placental development (Edwards et al, 1993) have been listed as potential factors influencing fetal growth and later development of chronic diseases. However, the use of birth weight, a crude measure of fetal development, as a mark of susceptibility of adult diseases is controversial. Studies have shown that association between LBW and development of chronic diseases is modified by body mass index at childhood and adulthood (Gillman, 2002). The general finding is that individuals born with LBW who became overweight afterward face the highest risks. Moreover, recent studies have explored the hypothesis that there is a common genetic mechanism for fetal growth and later disease (Hattersley et al, 1999; Stern, 2000). So far, understanding of the mechanisms linking fetal experience to chronic diseases remains uncertain (Couzin, 2002).

Some viral infections, such as congenital rubella virus, have been considered risk factors that trigger the development of diabetes type 1 (Dotta, Eisenbarth, 1992). Studies have shown that C-reactive protein (CRP), that is a marker of inflammation in the body, correlates with insulin resistance and hyperinsulinemia. Therefore, CRP may predict development of diabetes. Studies have shown that this association holds for Caucasian whites, but Han and colleagues (2002), using data from Mexico City, have found that inflammation is important in the pathogenesis of diabetes, but only for women. However, the authors point up that the study had more statistical power to detect results among women given the sample size limitations.

Major depression disorders are more prevalent among individuals with diabetes Type 2 than among those without the disease (Gavard et al, 1993; Konen et al, 1996). Some studies have shown that development of depression disorders precedes the diagnosis of diabetes type 2 and that it could be responsible to increase the risk of the developing the disease. However, there is no agreement in the causality path. In other words, it is not clear if physiological changes associated with the onset of depression prompt the development of diabetes or whether depression results from stress associated with the presence of a chronic condition (Talbot and Nouwen, 2000).

It is suggested that individuals exposed to stress are at higher risk of developing diabetes type 2 (Agardh et al, 2003). This possible causality is based on the evidence that psychosocial stress

causes insulin resistance and glucose intolerance, which are associated with the onset of diabetes.

Diabetes, as many other chronic diseases, has a complex etiology, but its causes are not yet clearly defined. However, some factors are strongly associated with diabetes incidence and/or prevalence, which ensure their use as important predictors of the disease distribution.

## 2.3 Disease Frequency in Latin America

Very limited information is available regarding the historical trends of diabetes incidence and prevalence in Latin America. These countries do not have adequate surveillance systems that would be necessary to quantify the burden of the disease in the region. The only available information is generally produced in samples that sometimes are not representative for the whole country. Another problem is that different studies used different methodology, diagnose criteria, and focused in different age groups. Therefore, most of the available data is not comparable.

Without age patterns is also difficult to understand trends in disease frequency particularly because Latin American countries are experiencing fast aging. Another problem with the available statistics is that diabetes tends to be diagnosed late in its development in Latin America (Aschner, 2002) because population has less access to the health care system. It has been shown that individuals present many symptoms of the disease, but they do not identify them as such, which makes the diagnosis more likely to occur later in the course of the illness (Gagliardino et al, 1995). Again, undiagnosed cases are particularly problematic in studies relying on self-report to estimate prevalence rates.

### A. North America

### 2.3.1 Mexico

Mexican population is a mixed race originated by the admixture of American natives and Europeans. This presence of indigenous admixture is considered a risk factor given the evidence that certain indigenous groups, such as PIMA Indians in the United States, present much higher rates of diabetes. Also, obesity and abdominal fat reach high levels among

Mexican-American population (Lindeman et al, 1998). In Mexico, among individuals aged 20 and over, 68% of the individuals have BMI higher than 25 kg/m$^2$ (28% above 30 kg/m$^2$). About 60% of men and 80% of women have abdominal fat distribution (Aguilar-Salinas, 2001). Data from different studies have shown that Mexican Americans have much higher rates of diabetes than non-Hispanic Whites in the United States. Motivated by these factors, a large body of literature has explored the prevalence of diabetes among Mexican Americans in the United States, but less is known about Mexicans residing in Mexico. Prevalence of self-reported diabetes reaches 22% among elderly (65+) Mexican-Americans who live in the Southern United States. No gender, education, marital status or language of interview difference was found (Black et al, 1999). This rate is comparable with the one found using HHANES where the prevalence as estimated in 22.7% for adults aged 65 to 74. However, it was found that rate of diabetes among those aged 85 and older was lower than among those aged 65 to 74.

Rates of diabetes in Mexico vary considerably depending on the social group focused and has been shown to be lower than the ones found among Mexican-Americans. Rodriguez-Saldana et al (2002) estimate in 15% the prevalence of diabetes among elderly (65+) people. Indeed, this rate is considerably lower than the ones found among Mexican-Americans. Among those aged 40 and over, prevalence rates reaches 9% (Aguilar-Salinas et al, 2001), the same rate was found in a previous study in Mexico City (Posadas-Romero et al, 1994). Diabetes was also found to be more common in men than women (Rodriguez-Saldana et al, 2002; Lerman et al, 1998). The lowest prevalence rates of diabetes type 2 were found among the indigenous communities of Durango – 0% (Guerrero-Romero et al, 1996).

In Mexico the estimated percentage of undiagnosed reaches 42% among those aged less than 40, while this percentage is reduced to 26% among those over age 40 (Aguilar-Salinas et al, 2002).

**B. <u>Caribbean</u>**

### 2.3.2 Barbados

Most of the population in Barbados is black and a recent longitudinal survey shows that, as in the United States, in Barbados prevalence rates are also higher among adult black population.

The overall prevalence of diagnosed diabetes in the country reaches 17.5% among those aged 40-84. A clear age pattern is found with diabetes rates increasing from 9.1% among those aged 40-49 to 24% among those 70-79. As in other studies, the older age group (80-84) had lower prevalence rates – 18.1%. These rates are considerably higher than those found by the 'International Collaborative Study on Hypertension in Blacks' that reported prevalence rates of 8.9% among those diagnosed cases aged 25-74 (Cooper et al, 1997). Among the black population diabetes is associated with age, obesity, waist-to-hip ratio and hypertension (Hennis et al, 2002). Prevalence rates are also associated with increases in BMI (Cooper et al, 1997). In addition, women in Barbados seem to have slightly higher prevalence rates than men (Cooper et al, 1997). Most of the individuals diagnosed in Barbados control their diabetes with oral agents (72.5%), and a smaller percentage with insulin (10%), and diet (4.9%). The remaining (12.5%) reported no treatment (Hennis et al, 2002). Cases diagnosed with GHb (glycosylated hemoglobin) represent 10% of the cases and there were no substantial differences by age group (Hennis et al, 2002). This would indicate that 10% of the cases are undiagnosed. However, it is important to mention that GHb is not the current criteria of diagnosis and it is possible that these estimates may be underestimating the true rates and undiagnosed cases.

### 2.3.3 Cuba

Salvador Alvarez and Pérez (1987) found that 4.6% of the adults (aged 40 to 79) in Santiago de Cuba had diabetes.

### 2.3.4 Guadeloupe

Guadeloupe in the Caribbean has relatively low prevalence rates of diabetes (5.8%) when compared to other countries in the region (Moutet et al, 1990). Age and sex standardized rates among the adult population (18 and over) were estimated in 6.6% (Costagliola et al, 1991).

### 2.3.5 Jamaica

Jamaica, as other countries in the Caribbean, presents elevated rates of diabetes prevalence. According to Ragoobirsingh et al (1995) prevalence rates reach 17.9% among individuals aged 15 and over. Undiagnosed cases reach approximately half of the population.

### 2.3.6 Trinidad and Tobago

Studies have shown that diabetes is associated with lower socioeconomic status, but part of this association is due to the higher prevalence of diabetes among women, people at older ages with longer duration of diabetes and those with Indo-Trinidadian ethnic group (Gulliford and Mahabir, 1998).

## C. South America

### 2.3.7 Argentina

Prevalence of diabetes is relatively low in Argentina compared with other countries in Latin America. A study conducted in Avellaneda in the late 1970s among individuals aged 20-69 showed that 8.1% of the individuals had diabetes (De Sereday et al, 1979). More recently, Hernández et al (1987) estimated in 5.0% the prevalence among those aged 20-74 living in La Plata. Undiagnosed cases reach about half of the cases (Hernández et al, 1987) and among those diagnosed about a third do not control their diabetes by any means and the remaining group presents poor glucose control. Obesity is estimated to inflict 37% of Argentinean population (Hernández et al, 1987).

### 2.3.8 Bolivia

A recent study conducted in four cities in Bolivia estimated in 7.2% the prevalence of diabetes in Bolivia (Barceló et al, 2001). Most of the cases (diagnosed and undiagnosed) were overweight and disease was more common among those with lower education.

### 2.3.9 Brazil

Brazil has a population of about 170 million people according with its 2000 census. Brazilian population is characterized by an intense miscegenation of European, Black and Indigenous populations. The majority of the population self-reported being white (54%), the second largest group is composed by the 'pardos' (39%) that is the mixed category, about 6% reported being Black, and the remaining is composed by indigenous people and those of Asian ancestry. However, part of those reporting being whites and blacks are also mixed. This miscegenation is

particularly important given the evidence that certain racial groups are at increased risk to develop diabetes.

In the late 1980s, Malerbi and colleagues (1992) estimated in 7.6% the prevalence of diabetes among individuals aged 30 to 69 from nine large cities in Brazil. They also report similar rates for men and women: 7.5 and 7.6, respectively. Goldenberg et al (1996) used the same data, but only for the municipality of São Paulo, found a higher prevalence – 9.3%. Regarding socio-economic differentials, Malerbi et al (1992) found that less educated people presented higher rates of diabetes, though this difference disappeared after age was controlled.

There is no agreement regarding racial differences and diabetes incidence and prevalence in Brazil. Malerbi et al (1992) found similar rates among Whites and non-Whites: 7.5 and 7.1, respectively. Brito et al (2001), on the other hand, found that prevalence of diabetes mellitus was significantly higher among women of dark skin (13.3%) compared to women of light skin (7.2%).

In general, there is a clear age pattern in the diabetes prevalence. Malerbi et al (1992) found prevalence rates increasing from 2.7% in the younger age group (30-39) to 17.4% in the older age group (60-69). The same age pattern is present in the self-reported rates, however rates are quite lower: 0.1% in the younger age group and 11.6% in the older. However, it is clear that undiagnosed cases are more common at younger than at older ages.

Sichieri et al (1994) using the cutoff of BMI=30 found that about 5% of men and 12% of women in Brazil were obese. Monteiro et al (1995) reported that the prevalence of obesity is estimated in 9.6% among the adult population (25 to 64 years old) during the 1990s. They also show that obesity was strongly associated with diabetes prevalence. Obese individuals had 11.6% prevalence rate while non-obese, 5.8% (Malerbi et al, 1992).

In a multicenter study, family history was found to be associated with a twofold increase in diabetes prevalence (Malerbi et al, 1992). However, a more recent study, which focused only in normal glucose-tolerant White individuals, found no differences in terms of insulin secretion, insulin sensitivity and hepatic insulin between those with first-degree relatives with diabetes and those without family history (Pimenta et al, 2003).

Levels of undiagnosed diabetes are estimated around 40-50%. Malerbi et al (1992) found that undiagnosed diabetes accounted for 46% of the total prevalence. In this study, glucose tolerance tests were only conducted in those positive screened individuals in the FCG test and some selected negative screenees. Sakata et al (2002) also selected only cases positive screened and found that 42.7% were undiagnosed cases. However, some studies have shown that among selected high-risk populations (obese women), undiagnosed cases can reach 70% (Brito et al, 2001). It has also been found that women are more aware of their disease status than men. Goldenberg et al (1996) report that almost 60% of men in São Paulo constituted undiagnosed cases, while among women the percentage was close to 41%.

Among previously diagnosed cases, 22.3% were not under treatment, 7.9% were on insulin, 40.7% were on oral agents, and 29.1% were on dietary treatment only (Malerbi et al, 1992).

### 2.3.10 Chile

A mixture of European descendants and indigenous groups forms the Chilean population. In the 1992 census, about 10% of the population 14 years and older reported being "Mapuche", the major indigenous group in Chile and other 0.5% being "Aymara" (Uauy et al, 2001). Prevalence rate of diabetes type 2 was estimated in 5.3% in a representative sample of people aged 15 and more from Santiago in the late 70s (Mella et al, 1981). Jadue and colleagues (1999) estimated in 4% the prevalence of diabetes in Valparaiso in 1996. A more recent study conducted in the VII Region in Chile estimated the prevalence of diabetes in 5.4% among those aged 20 and older in the period 1999-2000 (Baechler et al, 2002). Studies focusing only on the indigenous populations of Mapuches and Aymaras found lower prevalence rates (1.0% and 1.5%, respectively) (Larenas et al, 1985; Santos et al, 2001). However, a threefold increase in the prevalence rate has been described among Mapuche indigenous population (Perez-Bravo et al, 2001). Uauy et al (2001) report 4.1% of rural and 9.8% of urban Mapuche classified as diabetics. Baechler et al (2002) found a clear age pattern, in which prevalence in subjects between 20 and 44 years was 1.9%, 10.8% between 45 and 64 years, reaching 11.3% in the age group 65 years or older. In this study, prevalence rate was higher in urban areas (5.8%) compared to rural areas (4.5%), but the difference was not statistically significant. Undiagnosed cases reached 45%, however it was higher in the younger age group (67%), and decreased as

people aged reaching 37.5% in the older age group (Baechler et al, 2002). This is consistent with the fact that older people have more time to develop the disease and to present complications that may trigger medical treatment. Therefore, the finding that undiagnosed cases decrease with age is consistent with the fact that 10 to 40% of individuals have some complication at the time of the diagnosis (Harris et al, 1992; Aschner, 2002).

There is some evidence that prevalence rates have increased in Chile as well as obesity rates. Atalah (1993) reports that 21% of men and 30% of women in Santiago had BMI=27. Albala et al (2002) shows evidence of decreases in malnutrition and rise in obesity levels. They report that one quarter of women are obese (BMI=30) and that obesity is more likely to occur among those of low socio-economic levels. This rise in obesity is a result of "westernization" of life-style and diet and increased sedentarism. Indeed, Chilean population had increased their fat consumption, particularly meat and dairy products, with stable or decreased intake of legumes, grains and other fiver-rich foods (Vio and Albala, 2000; Albala et al., 2001)

### 2.3.11 Colombia

Aschner et al (1993) estimated in 7% the prevalence rate of diabetes in the late 1980s among adults older than 30. As found in other countries in the region, there was no systematic difference between men and women, even though higher levels of impaired glucose tolerance were found among women. Undiagnosed cases reached 40% of men and 30% of women, however all individuals 50 years and older were diagnosed previously. They also found that high BMI in men and advancing age in both sexes were associated with higher levels of glucose intolerance.

### 2.3.12 Paraguay

A recent study among white population in Paraguay estimated in 6.5% the prevalence of diabetes mellitus among those aged 20-74. Age standardized rates indicate that women have higher prevalence rates than men (Jimenez et al, 1998).

# 3 Data and Methods

## 3.1 Prevalence

Many sources of prevalence data are available for recent years in Latin America. Of particular importance are SABE, PNAD 1998 (Brazil) and estimates from WHO. Both sources of data have estimates are based on self-report. Therefore, prevalence of diabetes in the all populations tends to be underestimated by current data sources. In order to deal with this underestimation, I will make use of the available information about the percentage of undiagnosed cases.

SABE (Salud, Bienestar y Envejecimiento en América Latina y el Caribe Proyecto). SABE is a multicenter survey that investigates the health and well being of older people (aged 60 and over) and, in some cases, of their surviving spouse in seven capital/major cities in countries of Latin America and the Caribbean. The questionnaire design was intentionally geared toward the production of information that could be comparable with that retrieved in other countries. In particular, the aim was to include modules and sections modeled after the HRS and the AHEAD. In total 13,023 persons 60+ were selected for the interview and of these 10,906 completed the interview. Information on a medical history of diabetes was obtained during the household interview.

Data from Pesquisa Nacional por Amostra de Domicilios (National Survey of Households). The 1998 PNAD collected information in 112,434 households units and 344,975 individuals in all geographical areas, with exception of rural areas of some states in the North region. Information on self-reported diabetes is used here.

WHO estimates are based on population-based surveys conducted during 1976-1991 of over 150,000 persons from 75 communities in 32 countries that had used current WHO criteria for diagnosis of diabetes (King and Rewers, 1993).

## 3.2 Incidence

Data on incidence rates are available in some prospective studies, but data on Latin America is limited. Therefore, given the availability of the data, I initially explored the Health Retirement Survey (HRS) and Hispanic Established Populations for the Epidemiologic Studies of the

Elderly, 1993-1994 (Hispanic EPESE). Both surveys were conducted in the United States. This is a clear limitation, but the main purpose here is to explore the age pattern of diabetes incidence among individuals of Hispanic origin and compare those with non-Hispanics. HRS provides data on both individuals of Hispanic origin and non-Hispanic, while Hispanic EPESE provides relevant data on different Hispanic groups. Both samples focus on adults and elderly individuals and therefore comprise only individuals who survive from diabetes and other mortality risks.

### 3.2.1 Health Retirement Survey

HRS is a national panel survey conducted in the United States of individuals born between 1931 and 1941, more specifically it comprises individuals aged 51-61 at baseline, and their spouses (regardless of age). The initial panel started with 12,562 respondents. The first wave was conducted in 1992, and the following in 1994, 1996, 1998 and 2000. An important characteristic of HRS is that Hispanics, Blacks, and Florida residents were oversampled, which allow better estimates for those groups. In this study, I use data of the first wave that includes the date of diagnosis among prevalent cases. At Wave 1, 1,390 individuals already had diabetes (11% crude prevalence). Data on diabetes refer to self or proxy reports whether or not a doctor has ever told the respondent he/she had diabetes or high blood sugar. Those responding affirmative were then asked the age at which they were diagnosed. Individuals with missing data on relevant variables (year of birth, diabetes status, date of diagnose and date of interview) were excluded from the analysis. Data was obtained from HRS website.

### 3.2.2 Hispanic Established Populations

The Hispanic EPESE is a survey conducted in the five southwestern states of Arizona, California, Colorado, New Mexico, and Texas among non-institutionalized Mexican-American elderly, aged 65 and older, during the years 1993 and 1994. The main purpose of the study was to provide estimates of the prevalence major health conditions that could be used to compare health status among Mexican Americans and other populations. Data was obtained via ICPSR (Markides, 2000).

Final sample consists in 3,050 individuals. Individuals were asked whether or not a physician has told them that they had diabetes. 690 individuals responded affirmative (yes, definitive) and were considered as having diabetes. Other 155 individuals declared borderline diabetes (impaired glucose tolerance) and were not considered as diabetic in this analysis. Finally, 11 individuals who didn't know their diabetic status were considered non-diabetic. Crude prevalence rate is estimated in 23% among Hispanic elderly individuals. In order to estimate incidence, data on the date at which individuals were diagnosed are used. In 259 cases date on the month of diagnose is missing and the month of June was imputed. Moreover, 52 cases had missing data on year of diagnose and had also data imputed. Face-to-face interviews were completed with 94% of the respondents and the remaining group (too ill or cognitive impaired) had the interview completed by a proxy respondent. Mexicans, Mexican-Americans and Chicanos are contrasted with other Hispanic groups.

### 3.3 Mortality

Data used in this study comes from WHO mortality database. Data is available to mortality by cause, but there is no information on associated causes of death. Registered deaths are listed for 16 countries and availability varies from 1 to 6 years. The period analyzed here extends from 1993 to 2000. Registered deaths were adjusted following WHO recommendations regarding coverage completeness. It was assumed that completeness of diabetes deaths is the same as all deaths. Countries whose coverage was above 100 were not corrected. For most of the 16 countries, WHO database also included the population at risk. For the remaining countries, estimates of the population came from the medium variant of the UN database. Interpolation was used to obtain the necessary estimates for the years of available mortality data.

### 3.4 Methods

#### 3.4.1 Prevalence

Prevalence data provide an indication of the extent of diabetes in those populations; prevalence rates are obtained as the proportion of existing cases of diabetes in a population at a given time. Logistic models are also estimated in order to explore the associations between age, gender and race.

### 3.4.2 Incidence

Event here means that an individual is diagnosed with diabetes. It is obvious that this is a simplification since diabetes can be better described as a gradual change rather than a sharp, precisely defined in time, event (Allison, 1984). Individuals with better access to the health care system may be diagnosed at earlier phases of the disease than those with less access. In other cases, severity of the disease may play a role. However, data limitations impose restrictions in the conceptualization of the event and here I will adopt the simplification that event occurs at the date of diagnose. There are no time-varying explanatory variables in the analysis. Sex, race and ethnicity will be considered constant over the period of analysis. Data are censored for persons who were not diagnosed by the date of the interview.

Nonparametric analysis is performed to analyze the functional form of the survival function, hazard and cumulative hazard. The advantage of such approach is that no assumption is made about the functional form of those curves. On the other hand, the analysis is limited to a contrast of few covariates. Kaplan-Meier and Nelson-Aalen estimators are analyzed.

Cox proportional hazard models were also estimated. In the Cox proportional model no parametric form of the survival function is specified, but the effects of covariates are assumed to multiplicatively shift the baseline hazard function. The advantage of this approach is that there is no need to specify a particular form for the hazard function when no external information is available regarding the shape of it. On the other hand, whatever shape is assumed, it is the same for everyone. Tests to assess the proportionality assumption are performed.

The Cox proportional model is represented by:

$$h(t|\mathbf{x}_j) = h_0(t) \exp(\mathbf{x}_j \beta_x)$$

Where:

$h(t|\mathbf{x}_j)$: is the hazard rate for he jth subject;

$h_0$: is the baseline hazard;

$x_j$: set of covariates for the j individual.

Cox model is probably the most widely used model to analyze the effects of covariates in the incidence of diseases. However, the baseline function of the Cox model may assume any shape. This characteristic of the Cox model is particularly important because in some circumstances the behavior of the hazard function is of particular interest. More specifically, it is important to know if incidence rates follow a specific pattern everywhere. The knowledge of the hazard function may also inform about the disease process. Therefore, parametric and flexible parametric models are also estimated.

Parametric models (Exponential, Weibull and Gompertz) are also estimated. Parametric models assume a specific form for the hazard function. Exponential models assume that the baseline hazard is constant:

$$h(t|\mathbf{x}_j) = \exp(\beta_0 + \mathbf{x}_j \beta_x)$$

Weibull regression assumes that the baseline hazard has the form:

$$h_0(t) = pt^{p-1} \exp(\beta_0)$$

The advantage of the Weibull distribution is that it can assume different shapes: monotonically increasing or decreasing. Moreover, when p=1 then the Weibull model reduces to the exponential model.

Gompertz distribution assumes that the baseline hazard has the form:

$$h_0(t) = \exp(\gamma t) \exp(\beta_0)$$

And the proportional hazard model is:

$$h(t|\mathbf{x}_j) = \exp(\gamma t) \exp(\beta_0 + \mathbf{x}_j \beta_x)$$

Finally, I test more flexible parametric models developed by Royston and Parmar (2001) and presented by Royston (2001). Those models use natural cubic splines to model the transformation of the survival function, S(t), a link function g(S(t)). Two approaches are

adopted: 1) assumption of proportional hazards (PH); and 2) assumption of proportional odds (PO). The AIC criterion is used to determine the number of knots.

Statistical analyses are performed using STATA 8.0 software.

### 3.4.3 Compartment Model

Figure 1 shows the possible transitions that represent incidence ($\mu_1(x)$), and mortality rates ($\alpha(x)$, $\beta_1(x,t)$, $\beta_2(x,t)$, $\delta_1(x,t)$, $\delta_2(x,t)$). This diagram represents the compartments and transitions of a stochastic process model of diabetes morbidity and mortality. As indicated by Manton and Stallard (1988) given the specification of the compartment model, cross-sectional survival curves can be obtained using multistate life-tables. The idea here is to compare these survival curves to those that already exist to assess the validity of the model. A good description of this model can be found in Manton and Stallard (1988) and Verdecchia and Capocaccia (1988).

Given the high percentage of undiagnosed, for the cases in which self-report information is used some adjustment will be done in order to bring the estimates closer to the true value. Moreover, a simpler model (Figure 2) will be adopted in order to deal with this issue. Mortality of those healthy due to other causes ($\alpha(x)$) is dependent only on age of the individual, transition from the healthy state to the morbid state – incidence rate, $\mu(x)$ – depends on duration in the prior state and can also be measured in years of age. Transitions $\beta(x,t)$ and $\delta(x,t)$ occur for those who are diabetics. Manton and Stallard (1988) in their analysis of lung cancer assume that $\beta(x,t)$ is only a function of age given the assumption that mortality due to other causes is the same for both healthy subjects and individuals with lung cancer. Finally, transition $\delta(x,t)$ depend only on the duration in the diabetic state.

**Figure 1:**

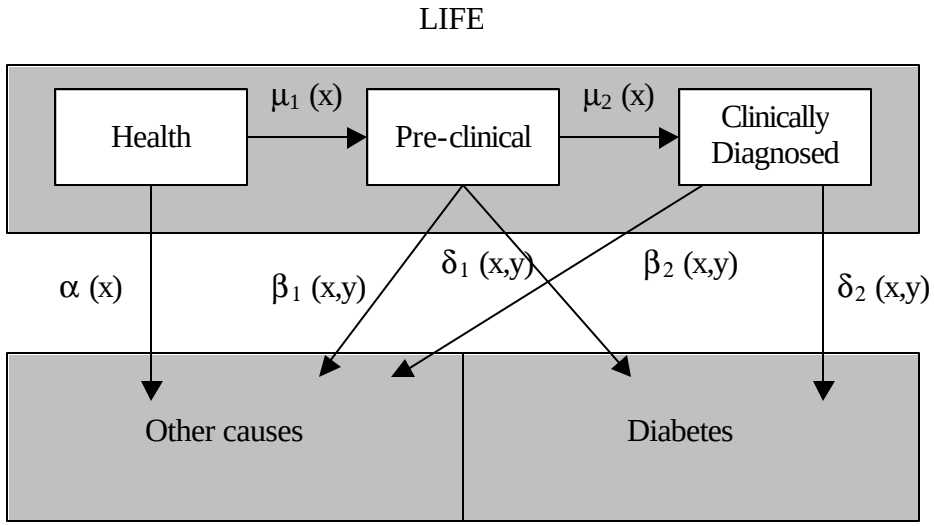
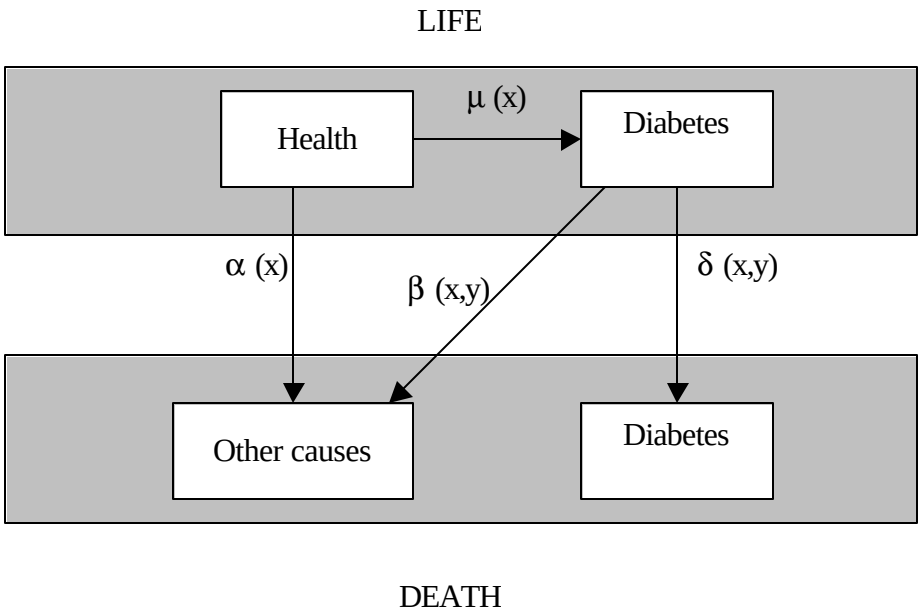



**Figure 2:**




As mentioned above, data on incidence rates ($\mu(x)$) are available in some prospective studies, including some in Latin America. Information on $\alpha(x)$, $\beta(x,t)$, and $\delta(x,t)$ are usually not available. Indeed, information on diabetes mortality is presented for all individuals. It would be

possible to assume that mortality due to 'other causes' would be similar for diabetics and non-diabetics. Manton and Stallard (1988) make this assumption in the lung cancer study. They estimate $\alpha(x)$ and $\beta(x,t)$ using multiple decrement life table (pg. 173). However, it is known that people with diabetes have higher risks of mortality than those without. As a matter fact, diabetic individuals are at higher risk for coronary heart disease, stroke and peripheral vascular disease (WHO, 1999). Those with type 2 have 3.5 times higher mortality and those with type 1 the risks are 7.5 times higher to the general population (Barceló et al, 2003). Here I have to find a way to incorporate this information in the model.

It is clear that I will need to rely on combining information from a multiplicity of sources and studies that are not all necessarily conducted in societies that have similar socioeconomic, environmental conditions or genetic susceptibility close to the ones in Latin America. Moreover, data vary considerably in depth, quality and scope and this will clearly affect the results. Obviously, many assumptions will be necessary over the course of these estimations and the quality of the work will depend on the number of tests to validate those data. The contribution here would be to estimate incidence rates and to check previous estimates of prevalence. Also a discussion of mortality trends will inform the exercise and might contribute to a better understanding of this 'epidemic'.

## 4 Preliminary Results

### 4.1 Prevalence

Table 1 shows the prevalence estimates of diabetes for Latin American cities. Argentina and Chile have the lower prevalence rates, while Barbados and Mexico, the higher. Interesting to note that prevalence rates in those capitals and major cities are higher than the estimates for the respective countries. WHO reports prevalence rates of 7% for São Paulo among those aged 30-64, which indicates that diabetes increases with age in Brazil. There is no clear pattern of diabetes prevalence by gender.

The prevalence by gender and age does not have a common pattern among all countries. There is some evidence that prevalence is lower in the age group 60-64, reaches a maximum in the group 65-74 and decline in the last age group (Table 2).

**Table 1: Prevalence Estimates for Latin American Countries by gender**

| Gender | Estimate | Std. Error | [95% Conf. | Interval] |
|---|---|---|---|---|
| **Buenos Aires (Argentina)** | | | | |
| Female | 0.112 | 0.013 | 0.086 | 0.137 |
| Male | 0.139 | 0.019 | 0.102 | 0.177 |
| **Bridgetown (Barbados)** | | | | |
| Female | 0.247 | 0.013 | 0.221 | 0.272 |
| Male | 0.186 | 0.014 | 0.158 | 0.215 |
| **São Paulo (Brazil)** | | | | |
| Female | 0.187 | 0.012 | 0.162 | 0.211 |
| Male | 0.168 | 0.017 | 0.134 | 0.202 |
| **Santiago (Chile)** | | | | |
| Female | 0.139 | 0.016 | 0.108 | 0.170 |
| Male | 0.119 | 0.021 | 0.079 | 0.159 |
| **Havana (Cuba)** | | | | |
| Female | 0.199 | 0.013 | 0.174 | 0.225 |
| Male | 0.073 | 0.010 | 0.053 | 0.092 |
| **Ciudad de Mexico (Mexico)** | | | | |
| Female | 0.208 | 0.016 | 0.177 | 0.239 |
| Male | 0.223 | 0.020 | 0.184 | 0.263 |
| **Montevideo (Uruguay)** | | | | |
| Female | 0.145 | 0.013 | 0.119 | 0.172 |
| Male | 0.124 | 0.017 | 0.091 | 0.158 |

Source: SABE. Apud:

**Table 2: Prevalence Estimates (%) for Latin American Countries by gender and age**

| | *B. Aires (Argentina)* | *Bridgetown (Barbados)* | *São Paulo (Brazil)* | *Santiago (Chile)* | *Havana (Cuba)* | *Mexico City (Mexico)* | *Montevideo (Uruguay)* |
|---|---|---|---|---|---|---|---|
| Female | | | | | | | |
| 60-64 | 7.4 | 27.1 | 18.3 | 13.9 | 17.0 | 19.7 | 12.9 |
| 65-74 | 13.0 | 24.1 | 19.8 | 16.2 | 19.9 | 21.3 | 16.0 |
| 75+ | 11.5 | 23.9 | 17.0 | 10.8 | 22.4 | 21.3 | 13.2 |
| Total | 11.2 | 24.7 | 18.7 | 13.9 | 19.9 | 20.8 | 14.5 |
| Male | | | | | | | |
| 60-64 | 13.7 | 25.4 | 12.6 | 14.4 | 7.0 | 22.5 | 10.7 |
| 65-74 | 15.2 | 15.7 | 20.6 | 10.1 | 8.7 | 21.4 | 13.6 |
| 75+ | 11.7 | 19.4 | 14.9 | 11.5 | 5.3 | 24.1 | 11.5 |
| Total | 13.9 | 18.6 | 16.8 | 16.8 | 7.3 | 22.3 | 12.4 |

Source: SABE. Apud:

Table 3 shows crude estimates of prevalence for the total population in all countries in Latin America and Caribbean. Among the largest countries, Cuba is the one with the higher

prevalence rates of diabetes and also one that will experience the largest increases. Brazil and Mexico have similar rates of diabetes and changes are expected to follow similar growth in the next three decades. Argentina has a higher prevalence and this may be due to its older age distribution. Prevalence rates for the total population are much lower than the ones for the older population, which suggests a higher incidence at older ages.

**Table 3: Cases of Diabetes (per thousand), Total population (per thousand), and Prevalence**

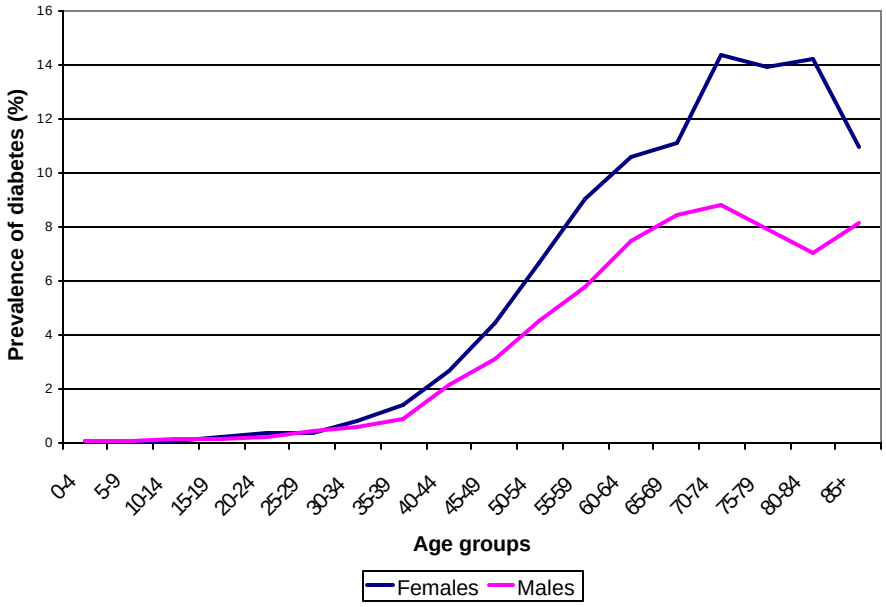
| | Cases of Diabetes | | Total population | | Prevalence | | |
|---|---|---|---|---|---|---|---|
| Country | 2000 | 2030 | 2000 | 2030 | 2000 | 2030 | Change |
| Antigua and Barbuda | 2.9 | 4.8 | 72 | 78 | 4.0 | 6.1 | 2.1 |
| Argentina | 1426.2 | 2457.0 | 37074 | 48611 | 3.8 | 5.1 | 1.2 |
| Bahamas | 11.5 | 26.0 | 303 | 382 | 3.8 | 6.8 | 3.0 |
| Barbados | 11.1 | 22.5 | 267 | 282 | 4.1 | 8.0 | 3.8 |
| Belize | 4.7 | 15.5 | 240 | 373 | 2.0 | 4.2 | 2.2 |
| Bolivia | 206.8 | 554.5 | 8317 | 13275 | 2.5 | 4.2 | 1.7 |
| Brazil | 4553.0 | 11305.5 | 171796 | 222078 | 2.7 | 5.1 | 2.4 |
| Chile | 494.9 | 1047.4 | 15224 | 20311 | 3.3 | 5.2 | 1.9 |
| Colombia | 883.4 | 2410.4 | 42120 | 58157 | 2.1 | 4.1 | 2.0 |
| Costa Rica | 76.5 | 230.5 | 3929 | 5872 | 1.9 | 3.9 | 2.0 |
| Cuba | 479.6 | 875.6 | 11202 | 11338 | 4.3 | 7.7 | 3.4 |
| Dominica | 2.7 | 4.3 | 78 | 80 | 3.5 | 5.4 | 1.9 |
| Dominican Republic | 245.2 | 594.3 | 8353 | 11290 | 2.9 | 5.3 | 2.3 |
| Ecuador | 341.0 | 937.6 | 12420 | 17335 | 2.7 | 5.4 | 2.7 |
| El Salvador | 102.6 | 319.7 | 6209 | 17335 | 1.7 | 1.8 | 0.2 |
| Grenada | 4.2 | 7.2 | 81 | 72 | 5.1 | 9.9 | 4.8 |
| Guatemala | 139.3 | 444.8 | 11423 | 21002 | 1.2 | 2.1 | 0.9 |
| Guyana | 18.5 | 36.5 | 759 | 695 | 2.4 | 5.3 | 2.8 |
| Haiti | 160.6 | 403.2 | 8005 | 11094 | 2.0 | 3.6 | 1.6 |
| Honduras | 81.4 | 279.8 | 6457 | 10715 | 1.3 | 2.6 | 1.4 |
| Jamaica | 80.6 | 197.6 | 2580 | 3380 | 3.1 | 5.8 | 2.7 |
| Mexico | 2178.5 | 6130.2 | 98933 | 133591 | 2.2 | 4.6 | 2.4 |
| Nicaragua | 68.1 | 233.4 | 5073 | 8929 | 1.3 | 2.6 | 1.3 |
| Panama | 59.2 | 153.3 | 2950 | 4514 | 2.0 | 3.4 | 1.4 |
| Paraguay | 102.2 | 324.3 | 5470 | 9890 | 1.9 | 3.3 | 1.4 |
| Peru | 754.1 | 1961.0 | 25952 | 37170 | 2.9 | 5.3 | 2.4 |
| Saint Kitts and Nevis | 1.7 | 2.3 | 42 | 37 | 4.1 | 6.2 | 2.1 |
| Saint Lucia | 5.2 | 11.3 | 146 | 168 | 3.6 | 6.7 | 3.2 |
| Saint Vincent | 5.1 | 8.9 | 118 | 131 | 4.3 | 6.8 | 2.5 |
| Suriname | 9.0 | 23.1 | 425 | 489 | 2.1 | 4.7 | 2.6 |
| Trinidad and Tobago | 60.3 | 124.8 | 1289 | 1327 | 4.7 | 9.4 | 4.7 |
| Uruguay | 154.1 | 223.6 | 3342 | 3958 | 4.6 | 5.6 | 1.0 |
| Venezuela | 582.5 | 1602.1 | 24277 | 36991 | 2.4 | 4.3 | 1.9 |

Note: Cases from WHO database and Population from UN database

More detailed data is available to Brazil and I will explore the associations between age, race, proxy respondent, and access to health care and diabetes prevalence. Proxy respondent is used to check if those reporting themselves have different rates from those having a proxy respondent giving the information. Access to health care is also considering because it is possible that those with more access are more likely to be diagnosed and to report diabetes.

Figure 1 shows that prevalence of diabetes increases substantially with age, with a peak in the age group 70-74, with declines afterwards. Women have in general higher prevalence rates than men. Note that in São Paulo, female prevalence rates are also higher.

**Figure 1: Prevalence of self-reported diabetes in Brazil by age and sex**




Prevalence estimates for the country, obtained from PNAD 1998 (Table 2), are lower than the ones for Sao Paulo obtained from SABE. It is possible that prevalence rates are higher in Sao Paulo given the better access to the health care system, on average, which may increase the awareness about the disease status.

**Table 4: Prevalence estimates, Brazil**

| | Mean | Std. Err. | [95% Conf. Interval] | |
|---|---|---|---|---|
| Female | | | | |
| 60-64 | 0.1086 | 0.0050 | 0.0989 | 0.1183 |
| 65-74 | 0.1293 | 0.0040 | 0.1215 | 0.1371 |
| 75 + | 0.1316 | 0.0054 | 0.1210 | 0.1422 |
| Male | | | | |
| 60-64 | 0.0726 | 0.0045 | 0.0637 | 0.0815 |
| 65-74 | 0.0854 | 0.0037 | 0.0781 | 0.0926 |
| 75 + | 0.0784 | 0.0051 | 0.0683 | 0.0885 |

Source: PNAD 1998

Logistic regression results (Table 5) show that prevalence rates increase with age, males are less likely to have diabetes than women and race was not significant in this sample. As expected, those with higher income, with access to health care and those who live in urban areas have higher probability of reporting diabetes than those with lower income. Those living in the Southeast of the country (most developed region) are also more likely to report having diabetes. Regarding education, those with more schooling are less likely to report having diabetes than those illiterate. Therefore, there is some indication that reporting of diabetes is better among those with more resources to have access to the health care system.

**Table 5: Logistic regression coefficients – Diabetes among adults aged 20 and older in Brazil**

| | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| 25-29 | 0.348** | 0.347** | 0.343** | 0.337** | 0.298** |
| 30-34 | 0.931*** | 0.930*** | 0.922*** | 0.910*** | 0.852*** |
| 35-39 | 1.375*** | 1.373*** | 1.355*** | 1.338*** | 1.273*** |
| 40-44 | 2.118*** | 2.116*** | 2.081*** | 2.060*** | 1.981*** |
| 45-49 | 2.626*** | 2.623*** | 2.574*** | 2.554*** | 2.443*** |
| 50-54 | 3.061*** | 3.059*** | 3.000*** | 2.980*** | 2.844*** |
| 55-59 | 3.318*** | 3.316*** | 3.253*** | 3.231*** | 3.064*** |
| 60-64 | 3.564*** | 3.560*** | 3.491*** | 3.464*** | 3.270*** |
| 65-69 | 3.666*** | 3.663*** | 3.592*** | 3.555*** | 3.339*** |
| 70-74 | 3.866*** | 3.861*** | 3.794*** | 3.760*** | 3.534*** |
| 75-79 | 3.797*** | 3.793*** | 3.733*** | 3.702*** | 3.468*** |
| 80-84 | 3.704*** | 3.699*** | 3.643*** | 3.605*** | 3.345*** |
| 85+ | 3.587*** | 3.584*** | 3.528*** | 3.479*** | 3.267*** |
| Male | -0.412*** | -0.412*** | -0.414*** | -0.395*** | -0.234*** |
| White | | 0.043 | 0.022 | -0.034 | -0.045 |
| 1 to 2 Min. Wages | | | 0.267*** | 0.218** | 0.181** |
| 2 to 3 Min. Wages | | | 0.309*** | 0.234*** | 0.187** |
| 3 to 6 Min. Wages | | | 0.454*** | 0.329*** | 0.272*** |
| More than 6 | | | 0.459*** | 0.308*** | 0.228** |
| 1-4 | | | 0.102*** | 0.05 | 0.025 |
| 5-8 | | | 0.094** | 0.001 | -0.026 |
| High School | | | -0.267*** | -0.348*** | -0.418*** |
| More than HS | | | -0.227*** | -0.309*** | -0.417*** |
| North | | | | -0.173*** | -0.122** |
| Northeast | | | | -0.213*** | -0.191*** |
| Midwest | | | | -0.031 | -0.014 |
| South | | | | -0.253*** | -0.257*** |
| Urban | | | | 0.471*** | 0.405*** |
| Access to health care | | | | | 1.314*** |
| Proxy | | | | | 0.059** |
| Constant | -5.676*** | -5.698*** | -6.017*** | -6.106*** | -6.924*** |
| Observations | 193650 | 193650 | 193650 | 193650 | 193650 |

Source: PNAD 1998

## 4.2 Incidence

Table 6 shows that both surveys have larger numbers of women and that only a small proportion of the cases had answers provided by proxy respondents. At HRS, Hispanics constitute a small group, and at Hispanic EPESE, Mexicans are the majority group (Table 6).

**Table 6: Description of the data**

| | HRS | | | Hispanic EPESE | | |
|---|---|---|---|---|---|---|
| Variable | Failure | Total | Time exposed | Failure | Total | Time exposed |
| Male | 700 | 5867 | 330743 | 291 | 1292 | 90775 |
| Female | 690 | 6784 | 360920 | 399 | 1758 | 123321 |
| Hispanic | 184 | 1174 | 63523 | | | |
| Non-Hispanic | 1206 | 11477 | 628140 | | | |
| Mexicans | | | | 658 | 2834 | 198883 |
| Other Hispanic | | | | 32 | 216 | 15212 |
| Proxy | 61 | 647 | 36102 | 91 | 316 | 23368 |
| Non-proxy | 1329 | 12004 | 655561 | 599 | 2734 | 190727 |
| Total | 1390 | 12651 | 691663 | 690 | 3050 | 214095 |

Source: HRS (Wave 1) and Hispanic EPESE

Incidence rates are estimated in 2.01 per thousand person-years in HRS and 3.22 in Hispanic EPESE (Table 7). Men and women show similar rates in both surveys. Interesting to note that rates from Hispanic EPESE are higher than the rates found for Hispanics in HRS. Therefore, the results presented here confirm the general finding that Hispanics who live in the United States have higher morbidity rates associated with diabetes than non-Hispanics. In both samples, men and women have similar incidence rates. No clear pattern emerged for proxy respondents.

**Table 7: Incidence rates by sex, ethnicity and proxy**

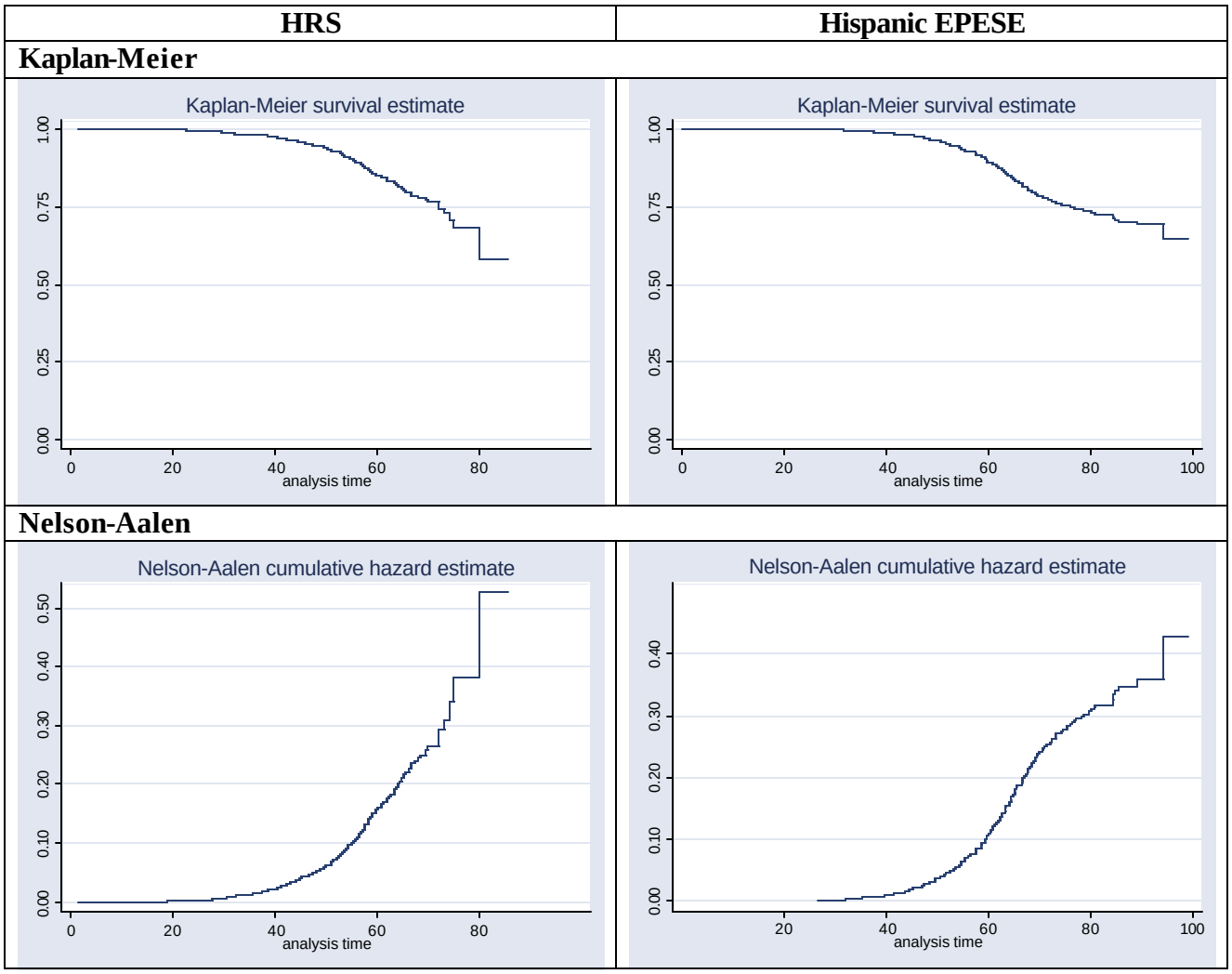
| Variable | HRS | Hispanic EPESE |
|---|---|---|
| Male | 2.09 | 3.21 |
| Female | 1.94 | 3.24 |
| Hispanic | 2.90 | |
| Non-Hispanic | 1.92 | |
| Mexicans | | 3.31 |
| Other Hispanic | | 2.10 |
| Proxy | 1.68 | 3.90 |
| Non-proxy | 2.02 | 3.14 |
| Total | 2.01 | 3.22 |

Source: HRS (Wave 1) and Hispanic EPESE

### 4.2.1 Kaplan-Meier and Nelson-Aalen estimates

Figure 2 shows Kaplan-Meier and Nelson-Aalen estimates for both samples. Mean age at Hispanic EPESE sample is 70.2 years (s.d. 9.6) than mean age at HRS (54.7 years, s.d. 6.9). Mean age at diagnose was 47 years (sd. 10.5) among HRS participants and 59.7 (s.d.10.1) among Hispanic EPESE participants. This could indicate a later onset of the disease among Hispanics. One extra evidence comes from the fact that me minimum recorded age at onset at Hispanic EPESE was 26 years and among Hispanics at HRS 18, which contrasts with non-Hispanics at HRS – 1 year old. Incidence rates seem to impose higher burden past age 40.

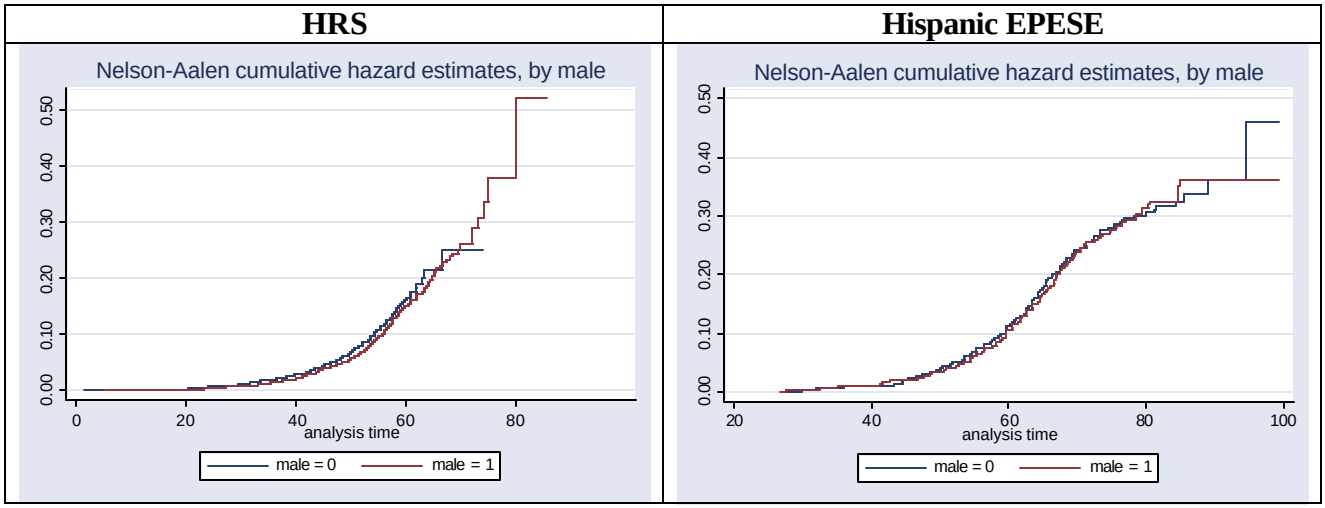
**Figure 2: Kaplan-Meier and Nelson-Aalen**




Source: HRS (Wave 1) and Hispanic EPESE

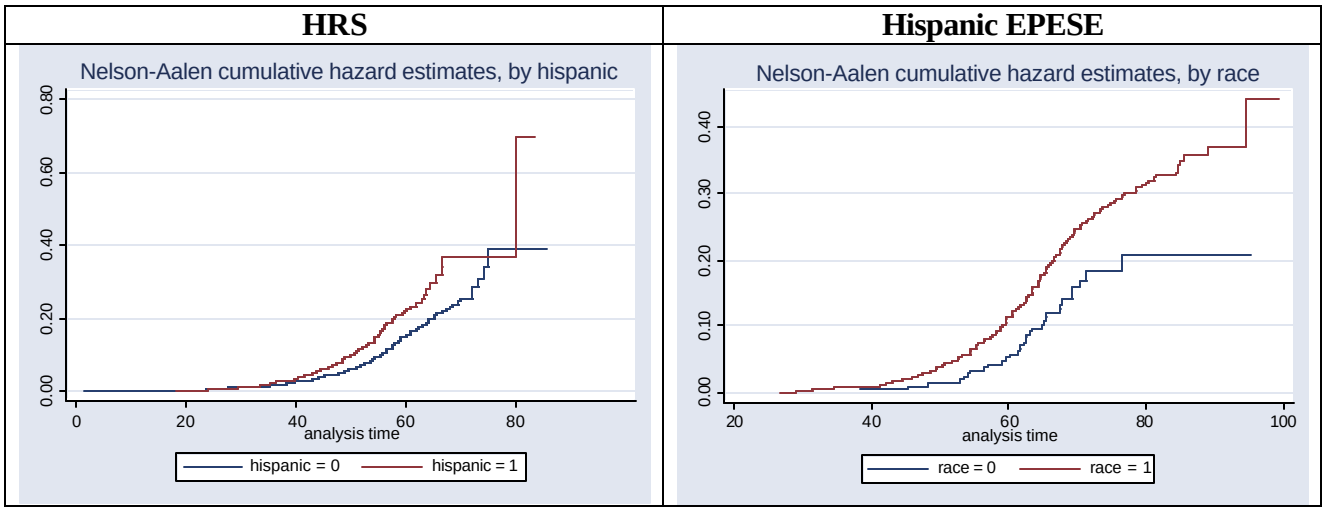
In both samples, cumulative hazard estimates follow the same pattern for both men and women (Figure 3). Ethnicity, on the other hand, is clearly important. In HRS, Hispanics have higher incidence of diabetes than non-Hispanics, and Mexicans have higher rates than other Hispanics at Hispanic EPESE (Figure 4). Reinforcing Table 7, variable proxy does not seem to provide a clear pattern (Figure 5).

**Figure 3: Nelson-Aalen estimates by gender**



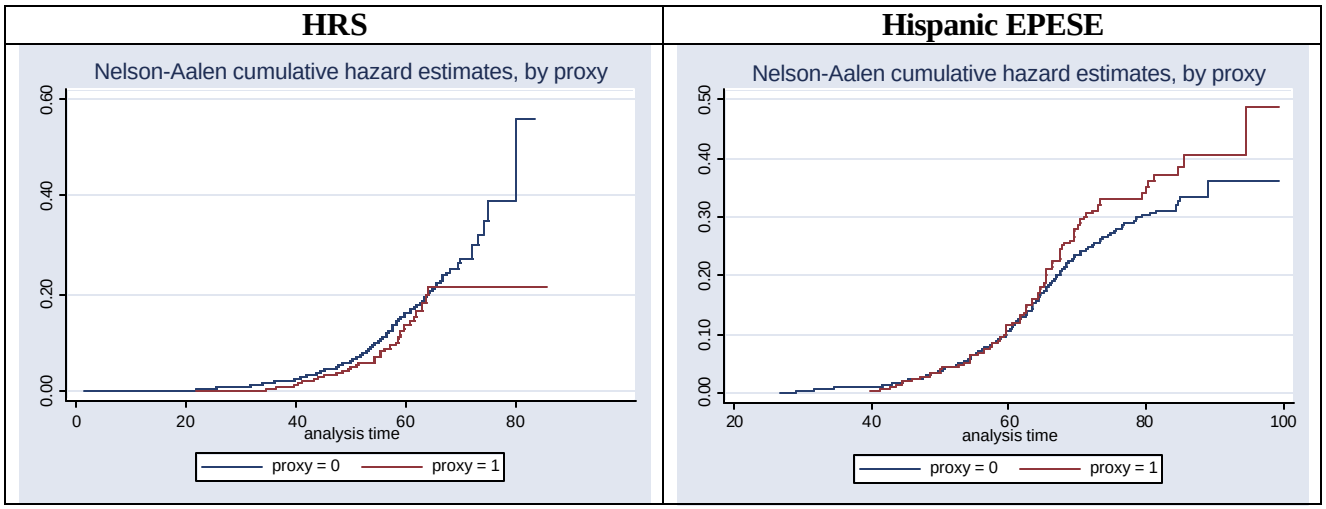

Source: HRS (Wave 1) and Hispanic EPESE

**Figure 4: Nelson-Aalen estimates by Ethnicity**




Source: HRS (Wave 1) and Hispanic EPESE

**Figure 5: Nelson-Aalen by proxy response**




Source: HRS (Wave 1) and Hispanic EPESE

### 4.2.2 Cox, parametric and flexible parametric models

Regression coefficients in Table 9 show that for most models being male is associated with lower incidence of diabetes, but coefficients are significant only for HRS sample and this may be associated with the small sample size of Hispanic EPESE survey. Focusing in HRS, it seems clear that being Hispanic is associated with higher incidence rates. Results from Hispanic EPESE show that among Hispanics, those of Mexican ethnicity have even higher rates than those reporting 'other Hispanic'. At HRS, incidence rates are lower among those who were unable to answer the questionnaire.

The next step is to define which model provides the best model for the shape of the incidence curve of diabetes. As mentioned before, good part of the literature uses Cox models because in the absence of knowledge regarding the shape of the incidence curve, the more convenient way is to leave for the model to decide. However, the knowledge of such shape has advantages not only for projecting incidence, but also to better understand the disease process. Given the preference for the Cox model, it is useful to test the proportionality assumption. Results are presented in Table 8 show evidence of proportional hazards for the variables considered in the analysis. Therefore, the use of Cox model seems adequate, but as discussed before it would be important to have a parametric distributional form to fit the incidence of diabetes.

**Table 8: Test of proportional hazards assumption**

| | rho | chi2 | df | Prob>chi2 |
|---|---|---|---|---|
| **HRS** | | | | |
| Male | 0.04629 | 2.96 | 1 | 0.0853 |
| Proxy | 0.03354 | 1.56 | 1 | 0.2110 |
| Hispanic | 0.00437 | 0.03 | 1 | 0.8710 |
| Global test | | 5.16 | 3 | 0.1603 |
| **Hispanic EPESE** | 0.02513 | 0.44 | 1 | 0.5092 |
| Male | 0.04291 | 1.27 | 1 | 0.2603 |
| Proxy | -0.03842 | 1.02 | 1 | 0.3128 |
| Mexican | | | | |
| Global test | | 2.77 | 3 | 0.4288 |

Source: HRS (Wave 1) and Hispanic EPESE

Based on the deviance values presented at Table 9, the Exponential, Weibull, Proportional Hazard and Proportional Odds considerably increased the fit. Additional tests are performed to assess the correct distributional form. But before presenting them, it is interesting to analyze the effects of the covariates. In HRS, males seem to have lower incidence than women, proxy respondents are less likely to report diabetes, and Hispanics seem to be at much higher risk of developing diabetes. In Hispanic EPESE, maybe due to the sample size, the only variable significant was the one identifying Mexicans as a group at a higher risk of developing diabetes.

Figure 6 shows some of the tests suggested by Cox and Oakes (1984) to assess the distributional form. In test 1, I assess if the cumulative hazard is linear in t. The linearity would suggest a constant hazard and a exponential distribution of time (t), however for both HRS and Hispanic EPESE there is no indication that this is the case. Test 2 assesses whether the log of the cumulative hazard is linear on t – linearity would suggest a Gompertz distribution – but again, there is no indication that this is the case. Finally, in test 3 a linear relation between the log of the cumulative hazard and log of the time indicates that the distribution follows a Weibull form. For both datasets, there are indications that Weibull distribution would be more adequate. This is particularly true when ages at diagnosis are between 20 and 80 years in HRS and between ages at diagnosis 40 and around 70 in Hispanic EPESE. The next step is to contrast Cox, Weibull, PH and PO distributions (keeping in mind the form of the Nelson-Aalen distribution in Figure 6). Figure 7 shows that Cox models fit quite well when compared with Nelson-Aalen estimates, for HRS, both PH and PO also confer good fit. Results seem less clear for Hispanic EPESE.

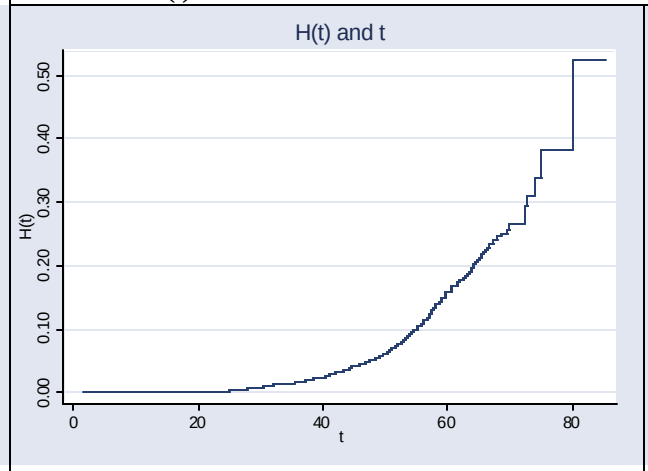
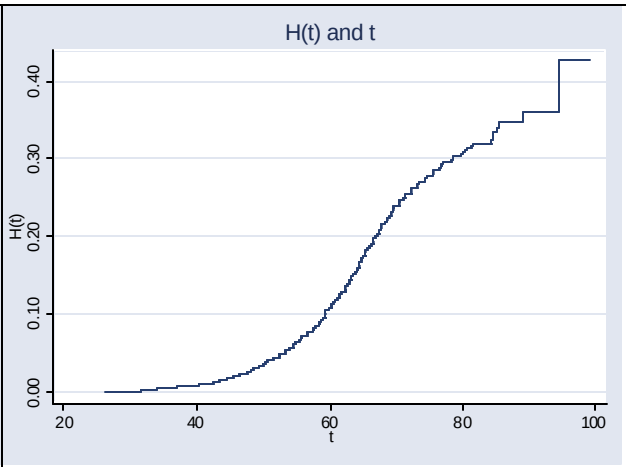
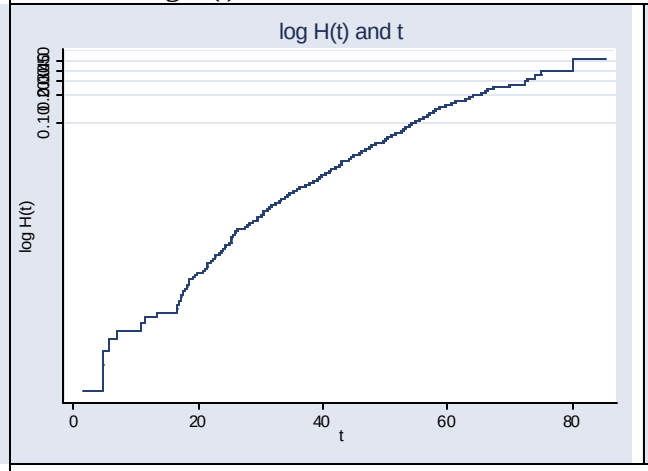
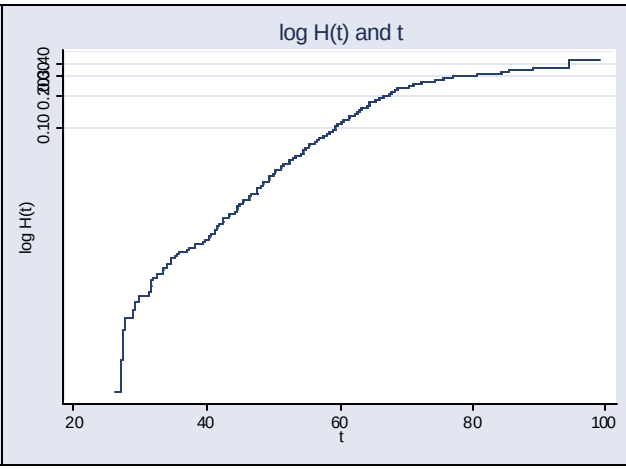
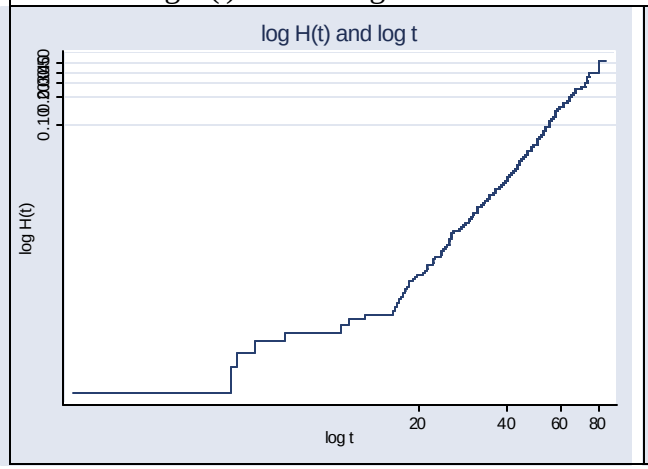
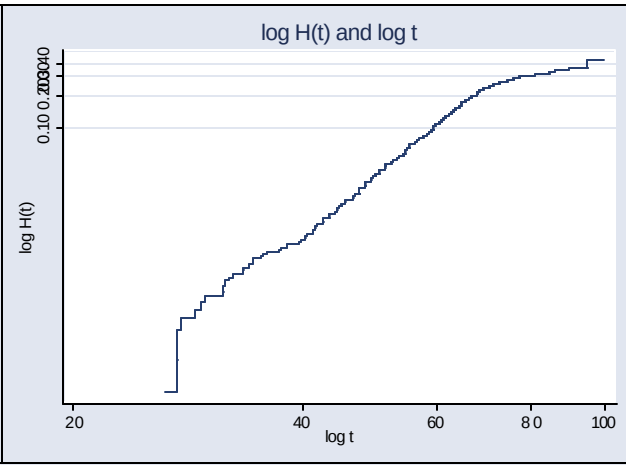
## Table 9: Regression coefficients

| | Cox | Exponential | Gompertz | Weibull | PH | PO |
|---|---|---|---|---|---|---|
| **HRS** | | | | | | |
| Male | -0.10* | 0.09 | -0.16*** | -0.10* | -0.12** | -0.12** |
| Hispanic | 0.44*** | 0.41*** | 0.42*** | 0.43*** | 0.42*** | 0.47*** |
| Proxy | -0.22* | -0.22 | -0.23* | -0.22* | -0.22* | -0.24* |
| S1 const | | | | | 1.14** | 0.85* |
| S2 const | | | | | -0.73*** | -0.84*** |
| Constant | | -6.29*** | -9.554*** | -19.63*** | -11.21*** | -10.64*** |
| Observations | 12651 | 12651 | 12651 | 12651 | 12651 | 12651 |
| Log likelihood | -12468.3 | -4700.3 | -3653.8 | -3649.5 | -3636.0 | -3634.1 |
| Deviance | 24936.6 | 9400.6 | 7307.5 | 7299.0 | 7272.0 | 7268.2 |
| **Hispanic EPESE** | | | | | | |
| Male | -0.02 | -0.01 | -0.01 | -0.01 | -0.02 | -0.03 |
| Mexican | 0.46** | 0.45** | 0.42** | 0.43** | 0.46** | 0.52*** |
| Proxy | 0.16 | 0.213* | -0.08 | -0.02 | 0.16 | 0.17 |
| S1 const | | | | | 5.39*** | 5.19*** |
| S2 const | | | | | -35.70*** | -39.48*** |
| S3 const | | | | | 45.46*** | 49.38*** |
| Constant | | -6.18*** | -9.06*** | -19.84*** | -25.01*** | -24.34*** |
| Observations | 3050 | 3050 | 3050 | 3050 | 3050 | 3050 |
| Log likelihood | -5330.3 | -1833.4 | -1318.7 | -1377.6 | -1241.0 | -1240.9 |
| Deviance | 10660.6 | 3666.9 | 2637.5 | 2755.3 | 2482.0 | 2481.7 |

Source: HRS (Wave 1) and Hispanic EPESE

Note: * significant at 10%; ** significant at 5%; *** significant at 1%. Comparison groups: Female, Respondent, and Non-Hispanic (HRS) and Other Hispanic (Hispanic EPESE)

**Figure 6: Assessment of distributional form of diabetes incidence**

| HRS | Hispanic EPESE |
|---|---|
| Test 1: Is H(t) linear in t? | |
|  |  |
| Test 2: Is log H(t) linear in t? | |
|  |  |
| Test 3: Is log H(t) linear in log t? | |
|  |  |

Source: HRS (Wave 1) and Hispanic EPESE

**Figure 7: Cox, Weibull, PH and PO distributions**

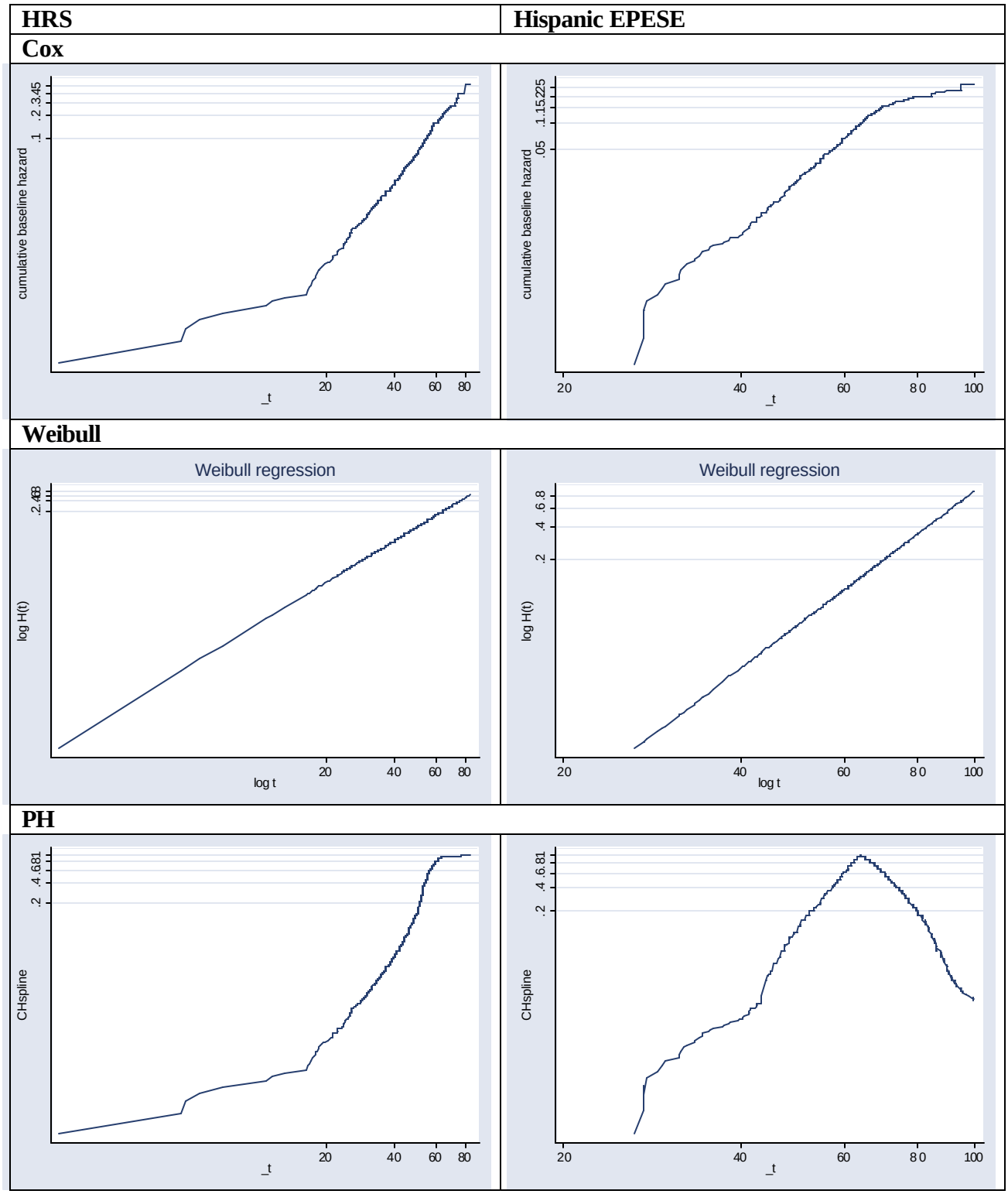
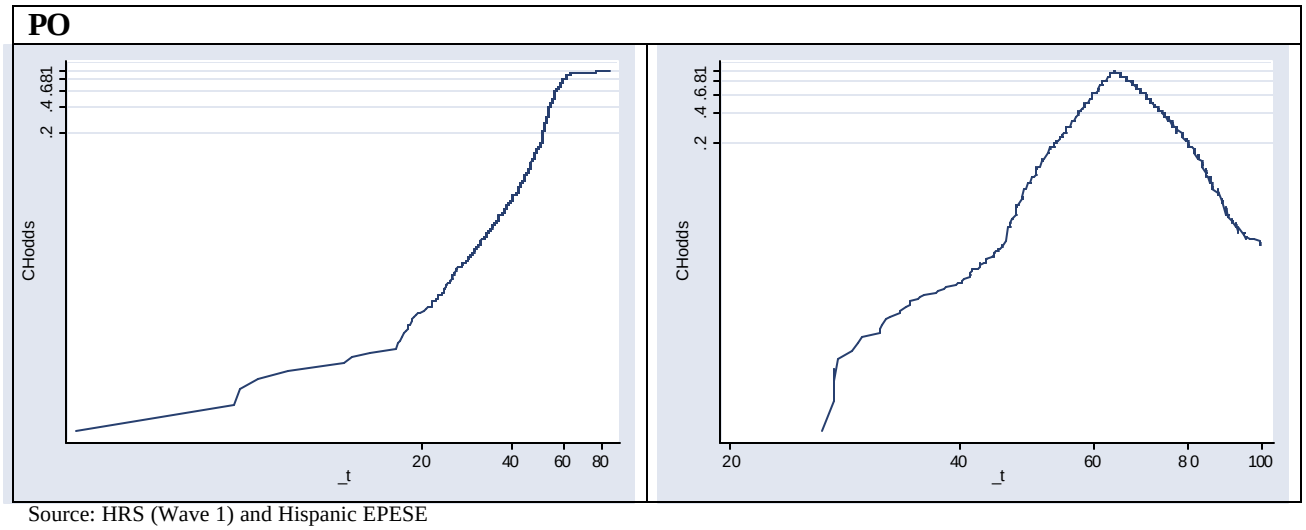


Figure 7: Cox, Weibull, PH and PO distributions (continued)

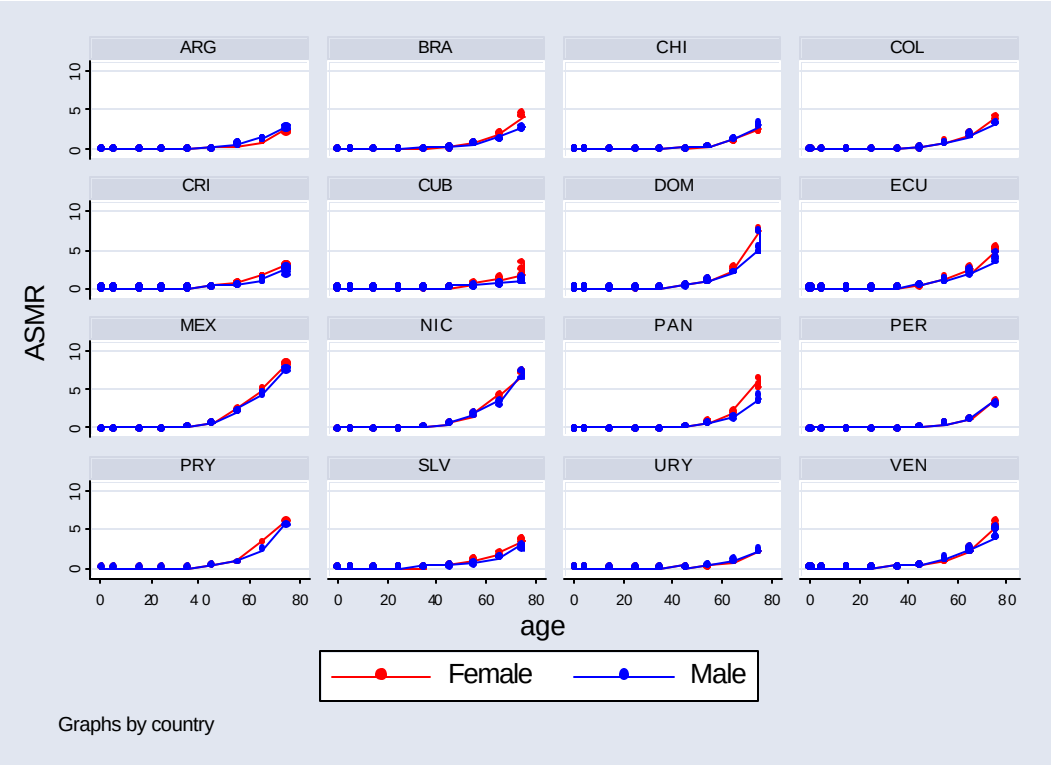



Source: HRS (Wave 1) and Hispanic EPESE

## 4.3 Mortality burden due to diabetes mellitus in Latin America

There is no standardized collection of information on mortality due to diabetes in Latin America. For more recent years, WHO had systematized the data for some countries, but data do not allow the analysis of temporal trends. Figure 8 shows that mortality rates tend to increase with age. Mexico and countries from Central America and Caribbean have higher rates, on average, than South America. However, Cuba has one of the lowest rates (together with Uruguay) in the region. Rates by sex show that in some countries males, while in others females, experience higher burden. Indeed, there is no clear pattern by gender.

**Figure 8: Age-specific mortality rates due to diabetes mellitus for selected countries in Latin America in the last decade (1993-2000)**




Sources: WHO database and UN population estimates.
Note: ARG (Argentina), BRA (Brazil), CHI (Chile), COL (Colombia), CRI (Costa Rica), CUB (Cuba), DOM (Dominican Republic), ECU (Ecuador), MEX (Mexico), NIC (Nicaragua), PAN (Panama), PER (Peru), PRY (Paraguay), SLV (El Salvador), URY (Uruguay) and VEN (Venezuela).

## 5 Discussion

Latin American countries have experienced a fast aging process in the last decades that impacts the prevalence of diabetes in this region. Urbanization and economic growth have changed diet and lifestyles (mainly through lack of exercise) of a considerable part of Latin American population and those changes have impacted the prevalence of diabetes. However, prevalence is a result of incidence and survival (duration). The problem is that expected increases in prevalence can occur due to the aging process, increases in incidence or even reductions in mortality. The limitation to our understanding of the process relies on the fact that available data is confined to prevalence and mortality. Therefore, the factors underlying the increase in incidence of diabetes in Latin America are not clear. Some countries such as Mexico, Jamaica,

Barbados, Trinidad and Tobago, and Cuba have documented excessive prevalence of diabetes. At the same time Mexico, Nicaragua, Panama and El Salvador present high rates of mortality due to diabetes, while Cuba has one of the lowest rates. In general, it seems that Mexico, and some countries from Central America and Caribbean have higher prevalence and higher mortality due to diabetes. Data from Latinos in the United States, particularly Hispanics, show higher incidence of diabetes than among the general population.

This study compiled the available information regarding prevalence and mortality in Latin America. The idea is to pool together the necessary data to model incidence, prevalence and mortality altogether as described by Manton and Stallard (1988) and Verdecchia and Capocaccia (1988). Given the difficulties in obtaining information on incidence of diabetes in Latin America, the strategy was to use largely available datasets that had information on age at diagnosis for Latinos residing in the United States. The idea is to test the hypothesis that there is an age pattern of diabetes incidence that could be common across populations (and that only levels would vary). The main limitation in trying to identify this age pattern is that both studies analyzed here focused on adults and elderly people. In the Hispanic EPESE the lowest age at diagnosis was 20 years and this may be related to three factors: 1) Hispanics have higher rates at which they develop diabetes; 2) Duration of diabetes is smaller among Hispanics (or alternatively, they have higher mortality) and 3) Hispanics are diagnosed at older ages. The ideal would be to follow prospectively those groups. HRS has on following waves information on current status, but there is no information on age or date at diagnosis. Moreover, both datasets are limited to self-reported diabetes. Other datasets will be necessary to explore the patterns of diabetes incidence at younger ages.

The next step will be to collect more information on incidence and test if there is a unique age pattern of diabetes incidence. Second, it will be important to review the assumptions in the projections of diabetes prevalence. Finally, it will be necessary to collect historical data on mortality and to standardize it in order to analyze historical trends.

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