

**Health Changes after Diabetes Diagnosis in Middle and Old Age:
Physical, Mental and Cognitive Health Trajectories and Social Stratification**

by

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Dedication

To my family, here and around the world,
in its diversity.
For your dedication, patience, and unconditional love.

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“Nanos gigantum humeris insidentes” (Bernard de Chartres)

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CHAPTER 1

Introduction

BACKGROUND ON DIABETES

Diabetes is described as an aging accelerator. It precipitates decline in several aspects of life, including physical, mental, and cognitive health. Between 1980 and 2011, the number of Americans aged 18 and older with diagnosed diabetes has more than tripled, and by 2050, it is estimated that between 25% and 28% of the U.S. population will live with diabetes (Boyle, Thompson, Gregg, Barker, & Williamson, 2010). Currently 29.1 million Americans live with diabetes (Centers for Disease Control and Prevention, 2014). While mortality from type 2 diabetes has decreased in the past two decades as with cancer, stroke, and heart disease (Centers for Disease Control and Prevention, 2014), an ever increasing number of Americans are being diagnosed with pre-diabetes and diabetes.

Diabetes is unequally distributed in the population, and social groups exhibit differential vulnerability. It is highly prevalent in the older population, in ethnic and racial minorities, and among the poor and less educated segments of the population (Centers for Disease Control and Prevention, 2013). The cost of diabetes is also a major societal concern. According to NHANES (National Health And Nutrition and Examination Survey) data, the cost of caring for diabetics is 2.3 times higher than caring for patients without the condition (Centers for Disease Control and Prevention, 2014). Even more convincing is the study by Dall and colleagues, which showed that

every American, regardless of age and diabetes status, contributes \$700 a year to care for diabetics (Dall et al., 2010). The financial cost of diabetes entails a significant loss of human capital. Diabetes is the seventh leading cause of death. It is also the leading cause of non-traumatic lower-limb amputation, kidney failure, and blindness (Centers for Disease Control and Prevention, 2014). People with diabetes are at higher risk of macro-vascular and micro-vascular complications, nephropathic, and neuropathic complications, which can hinder a person's physical functioning (Chiu & Wray, 2010b; Chiu, Wray, & Ofstedal, 2011; Gregg, Beckles, et al., 2000; Gregg et al., 2002), mental functioning (Anderson, Freedland, Clouse, & Lustman, 2001; Golden et al., 2008; Nouwen et al., 2010), and cognitive functioning (Allen, Frier, & Strachan, 2004; Awad, Gagnon, & Messier, 2007; Biessels, Kerksen, de Haan, & Kappelle, 2007; Cukierman, Gerstein, & Williamson, 2005; Reijmer, van den Berg, Ruis, Kappelle, & Biessels, 2010; Rosebud, Knopman, & Przybelski, 2014; Stewart & Liolitsa, 1999). Finally, diabetes and its management generate a greater need for informal care (Langa et al., 2002), increase the psychological burden upon caregivers, and are associated with job loss and diminished ability to work (Breton et al., 2013).

Age-related outcomes of diabetes, including physical, mental, and cognitive impairments, are important issues for policy and research for several reasons. First, both their prevalence and incidence are increasing in the oldest age groups. Second, the U.S. population is aging at unprecedented rates. Finally, obesity, one of the most important risk factors for diabetes, is also rising in both prevalence and incidence. Therefore the prospect of reduced functional independence, higher healthcare costs, and heightened morbidity in late life, all highlight the need for improved understanding of the link between diabetes and health outcomes in old age.

COMPARATIVE STUDIES OF DIABETES AND HEALTH

Overview of the literature

Medical sociologists, health services researchers, and epidemiologists are interested in the impact of diabetes on health so that they can find new methods of intervention and care. In earlier studies “people with diabetes” were consistently contrasted with “people without diabetes”; and methodologically cross-sectional design or conventional methods of regression over two or three waves of data were favored. However, more recent studies rely on a longitudinal design and perform trajectory analyses, in which age or time (arbitrary study wave) is used to define the levels and rate of health change among people with diabetes. In general, earlier comparative studies found a strong relationship between diabetes, poor health, and health decline with time or age. A brief review of this research is provided below.

Diabetes is linked to higher levels and accelerated decline in physical functional with age (Chou & Chi, 2005; Gregg, Beckles, et al., 2000; Kalyani, Saudek, Brancati, & Selvin, 2010; Maty et al., 2004; Ryerson et al., 2003; Sinclair, Conroy, & Bayer, 2008). It is further linked to persistent difficulties in climbing, taking 10 steps, and walking $\frac{1}{4}$ mile over 3.5 years (Figaro et al., 2006; Gregg, et al., 2002; Wray, Ofstedal, Langa, & Blaum, 2005). Trajectory analyses using study wave as the measure of time agree with these cross-sectional findings. Functional health declines with time in older adults (Chiu & Wray, 2010b; Chiu, et al., 2011).

Related to mental health, clinical and subclinical expressions of depression are higher in people with diabetes than in diabetes-free adults. However, longitudinal examinations of the relationship between diabetes and mental health, and population-based trajectory analyses in particular, are lacking. The few that describe change in mental health among diabetics use non-representative clinical samples, rely on two or three data points, or are interested in the

directionality of the relationship between diabetes and depression. Studies of transitions in and out of depressive states find that depression is highly recurrent over time (Lustman, Griffith, Freedland, & Clouse, 1997; Peyrot & Rubin, 1999). They further find a link between diabetes and mental status over time. Earlier studies reported an increased risk of diabetes-specific depressive symptoms one year after diagnosis (Skinner et al., 2010), a rise in incident depression over a period of 2.5 years (Nefs, Pouwer, Denollet, & Pop, 2012), and a U-shaped relationship between diabetes duration and depression with higher levels in the first 5 years and after 10 years (Egede & Zheng, 2003). These results suggest that among people with diabetes, depressive symptoms are dynamic, and may accelerate over time.

Reviews of case-control (Brands et al., 2007; Chau et al., 2011; van Harten, Oostermn, Muslimovic, van Loon, & Weinstein, 2007), prospective, and longitudinal studies (Elias et al., 1997) of cognitive health among people with diabetes found an average effect size of 0.2 to 0.8 on cognitive health, specifically in memory and executive functioning, and a positive association with cognitive decline (Stewart & Liolitsa, 1999). The effect of diabetes on cognition is stronger with time or age (Bruce et al., 2003; Gregg, Yaffe, et al., 2000; Kanaya, Barrett-Connor, Gildengorin, & Yaffe, 2004; Nooyen, Baan, Spijkerman, & Verschuren, 2010; Okereke et al., 2008; Stewart, Prince, & Mann, 2003; Wu et al., 2003). It is also stronger when diabetes lasts longer (Elias, et al., 1997; Fontbonne, Berr, Ducimetiere, & Alperovitch, 2001; Gregg, Yaffe, et al., 2000), and among those receiving insulin treatment compared with those who are not receiving it (Ott, Stolk, & van Harskamp, 1999). Yet a few studies failed to find a link between cognitive performance and diabetes (Cosway, Strachan, Dougall, Frier, & Deary, 2001; Scott, Kritz-Silverstein, Barrett-Connor, & Wiederholt, 1998). Nevertheless, in general review articles tend to corroborate the finding that people with type 2 diabetes are at increased risk of cognitive

decline or incidence dementia, compared with those who do not have diabetes (Awad, et al., 2007; Biessels, Staekenborg, Brunner, Brayne, & Scheltens, 2006; Cukierman, et al., 2005; Stewart & Liolitsa, 1999). They further suggest that the risk of poor cognition increases with age (Biessels, et al., 2007) and with a longer duration of diabetes (Cosway, et al., 2001; Elias, et al., 1997; Gregg, Yaffe, et al., 2000; Saczynski et al., 2008).

Social stratification in diabetes and health

Stratification in the distribution of physical, mental, and cognitive health among diabetics is well documented. Diabetes widens the racial gap (Kim & Miech, 2009) and the gender gap (Barberger-Gateau, Rainville, Letenneur, & Dartigues, 2000; Gorman & Read, 2006; Liang et al., 2008; Verbrugge, 1989) in functional status, and this gap persists over time (Chiu & Wray, 2010b). However, it does not seem to have a significant effect on functional health among ethnic groups (Chiu & Wray, 2010b), despite persistent inequality or a Hispanic advantage in functional health compared with whites in the general population (Carrasquillo, Lantigua, & Shea, 2000; Liang, et al., 2008). Finally, the adverse effect of diabetes on functional status is greater among those with little education, and this gap widens with time (Chiu & Wray, 2010b). This fact supports the hypothesis that higher education confers a functional advantage upon diabetics who have higher education.

As concerns mental health, trajectory analysis dealing with social variations in depressive symptoms among diabetics is lacking. Analysis of NHIS data using a cross-sectional design failed to show a link between depressive symptoms and race or ethnicity. However, the study included respondents with both type 1 and type 2 diabetes (Egede & Zheng, 2003). Other studies reported a link between black race and higher initial and transient depression in a sample of 246

patients in Baltimore (Peyrot & Rubin, 1999). The same study suggested that sex was associated with initial levels of depressive symptoms, but not with persistent depression (Peyrot & Rubin, 1999). Studies of the link between social position and mental health among diabetics further found that lower education is associated with both higher initial levels of depression and persistent depressive symptoms (Peyrot & Rubin, 1997, 1999) in type 1 and type 2 diabetes (Engum, Mykletun, Midthjell, Holen, & Dahl, 2005). In addition, lack of employment was linked to major depression (Egede & Zheng, 2003).

The negative influence of ascribed and attained social status extends to cognitive health. Compared to whites, being black adversely influences cognitive performance among people with diabetes (Obidi et al., 2008; Reijmer, et al., 2010; Sachs-Ericsson & Blazer, 2005), especially in more complex tasks (Obidi, et al., 2008). As it relates to gender, while in the general population women experience higher levels of cognition at baseline, but faster decline with time (Karlamangla et al., 2009), among diabetics, no gender differences were found in cognition after a 7-year follow-up in a small cohort study (Bruce et al., 2008) and in a community sample of older adults (Okereke, et al., 2008). However, one study found a faster decline in cognitive health among men in gender-stratified analysis (Maggi et al., 2009). Lower education also results in faster cognitive decline in older people (Bruce, et al., 2008), and can adversely influence risk factors for dementia, including diabetes incidence, and medical compliance and treatment (Reijmer, et al., 2010).

In sum, the literature reports that diabetes adversely affects physical, mental, and cognitive health, and this link seems to be socially patterned, with greater vulnerability in women, blacks, Hispanics, and people with lower socioeconomic status (SES).

RESEARCH QUESTIONS

According to the biomedical literature, the natural history of diabetes is characterized by biological, physiological, and health change with longer duration of diabetes (Ramlo-Halsted & Edelman, 2000); these events form a “diabetes trajectory” or “diabetes career” (Figure 1). Several studies modeling trajectories of biomarkers including hemoglobin A1c and fasting plasma glucose support this proposition (Haianza et al., 2012; Schroeder, Bayliss, Newcomer, & Steiner, 2011). However, a person’s location on his or her disease trajectory at any point in time is an important marker of not only metabolic outcomes, but also of health status because of the link between health status, diabetes complications, and the severity of clinical outcomes (Gebregziabher, Egede, Lynch, Echols, & Zhao, 2010; Helgeson et al., 2010; Schroeder, et al., 2011). The time of the onset of diabetes, the patterns of health change after diabetes has been diagnosed, and the social context in which these health changes occur are all important research questions. But comparative studies cannot isolate the net effect of diabetes from that of people’s prior experiences, their location on their diabetes career or location on their life course. At any point in time and at any age in cross-sectional studies and in an age-based or time-based analysis, the group of people with diabetes included is made of diverse of individuals who are at different stages of their disease. Consequently, reported health gaps between older adults with diabetes and those without diabetes are confounded by the dynamic nature of diabetes and the experience of illness; that is, the cumulative damages upon diabetics’ biological, psychological, and social health, and the social, behavioral, and medical interventions implemented to bend the health curve among diabetics.

Yet this dynamic aspect of diabetes is consistently ignored in studies of people’s experience of illness, if diabetes is conceptualized as a time-constant personal attribute.

Assuming that diabetes can create common experiences in people affected according to the natural history of diabetes, the literature on diabetes and health leaves several questions unanswered. First, on average, how does health change after a chronic illness is diagnosed; in other words, how does health change with a longer duration of diabetes? Does it decline exponentially or linearly, or do people recover within the first years after diagnosis? Are these health changes similar for different health outcomes? Second, how does the timing of diabetes; that is, people's location on their life course, affect their health trajectory after diagnosis? Do people of different age groups experience illness similarly or are there differences that can inform clinical decision and policy? How does birth cohort influence health change with diabetes? Do people in younger cohorts have better outcomes than older people with diabetes? Finally, what is the role of social structure on health trajectories after diagnosis? Do individuals in socially disadvantaged groups experience chronic illnesses similarly to their more socioeconomically advantaged counterparts? If so, are health disparities between social groups exacerbated over the course of illness, or do they diminish or remain constant?

As mentioned earlier, demographic and epidemiologic changes are expected to significantly influence the age structure, diabetes prevalence, and the importance of chronic illnesses in the U.S. population. Therefore, expanding our understanding of people's experience of diabetes in middle-age and old age is an imperative research agenda. To address these questions, the existing research could be improved by: 1) focusing on people with diabetes, especially in later adulthood; 2) incorporating elements of the natural history of diabetes into the study of health change associated with diabetes, including the timing and duration of diabetes; 3) assessing the extent to which patients' social and demographic characteristics predict health change with diabetes; and 4) investigating multiple dimensions of health. Addressing these issues

is the main goal of this study, which presents findings from an analysis of a nationally representative sample of U.S. adults aged 50 and older with self-reported incidence of diabetes. The dissertation uses diabetes as the model of chronic illness for several reasons. First, its prevalence is relatively high in the population, and it increases in middle-age and older adulthood (Centers for Disease Control and Prevention, 2014). Second, diabetes in old age generates major health changes that can be easily investigated. Finally, diabetes is beset with health inequalities (Centers for Disease Control and Prevention, 2013), and therefore can permit the study of the role of social position on health change after diagnosis.

THEORETICAL ORIENTATION

In his essay on the sociology of disease, Timmermans argued that since Parson's sickness role model, medical sociologists have invested their efforts in understanding strictly the social aspects of health-related topics. This paradigm shift occurred at the expense of the sociology of disease (Timmermans & Haas, 2008). Rarely is disease at the center of inquiries in modern medical sociology, as can be seen repeatedly in comparative studies of people with diabetes and those without it; these studies consistently treat the disease as time-constant. Consequently medical sociologists are missing an opportunity to understand patients' experience of diabetes, to address what probably matters most to patients and their healthcare providers, and to identify new means of improving the management of diabetes.

The current study attempts to bridge the gap between the biomedical literature and medical sociology by incorporating elements of both schools of thought in the assessment of people's experience of diabetes. It adopts the natural history of diabetes from the medical literature to illustrate the *dynamic nature of the disease* and identifies key time-related variables

necessary to describe the progression of diabetes. It further adopts several elements from the sociology of illness, including the Illness Career Model, the Disablement Process Model, and the theory of social stratification to illustrate the *dynamic nature of the experience of illness* and the influence of the *social context* on this experience. We hypothesize that health changes with time, not just because of the effects of aging, but also because of the progression of diabetes and the medical and social environment in which this progression occurs. The current study aligns the disease, the person, and the social context in which they interact, to elucidate health change with diabetes.

The natural history of diabetes

The natural history of diabetes is not a theory *per se*; rather it illustrates the concept of health change with, and the clinical course of, a chronic illness from the perspective of the disease itself. The natural history of diabetes is used in this research because it supports our concept of diabetes as a dynamic phenomenon.

Originating in the medical literature, the natural history of type 2 diabetes is conceptualized as a series of transitions between successive and non-linear phases (Ramlo-Halsted & Edelman, 2000). Figure 1, which presents a model of the natural history of type 2 diabetes, shows clearly that each phase in this natural history is defined by physiological and metabolic norms. In addition, empirical studies link these phases to the onset of diabetes complications, to the severity of clinical outcomes such as retinopathy, to mortality, and finally to the psychological and behavioral responses to the illness by people affected and by society at large (Gebregziabher, et al., 2010; Helgeson, et al., 2010; Schroeder, et al., 2011). From the natural history of diabetes, we adopt the concept that health change necessarily co-occurs with

the progression of disease. Consequently time should be measured from both the patient and the disease. Although age, age at diagnosis, and birth cohort allow the location of a person on his or her own life trajectory, the onset and duration of diabetes provide the keys to describing the disease and its progression.

Unfortunately the biomedical view of the natural history of diabetes does not explicitly incorporate time-relevant factors—e.g. age, the timing of diabetes, birth cohort—from the patient’s perspective. It further fails to include role of the social determinants of health on the progression of diabetes and to acknowledge the impact of the natural history of diabetes on longer-term outcomes, in particular, on the precursors of loss of independence, including loss of physical, mental, and cognitive functioning.

The Illness Career Model

The Illness Career Model is a sociological model of health and illness rooted in symbolic interactionism. It applies a trajectory perspective to the study of chronic illness, and explores the long-term interconnectedness between chronic illnesses and different dimensions of life. The theory was derived from the social constructionist view centered on labeling and on the definition of the self as presented in Goffman’s description of the “moral career” of mental health patients (Goffman, 1961; Scheff, 1966; Thoits, 1999). The theory has since evolved into a concept that includes any long-term social experiences during an individual’s life (Aneshensel, 1999, 2013). In contrast to the life-course perspective on health and aging, which emphasizes connections among different trajectories including a person’s education, occupation, and family life as he or she ages (Ben-Shlomo & Kuh, 2002; Kuh & Ben-Shlomo, 1997), the career perspective isolates one of these trajectories starting with a life-changing event, and describes its

internal organization. According to Aneshensel, “careers” are “formed around the experience of unusual and unpleasant or unwanted thoughts, feelings, and behaviors.” This model has been successfully used in studies of deviant behaviors (Scheff, 1966), chronic illness (Gerhardt, 1990), caregivers’ health (Aneshensel, Botticello, & Yamamoto-Mitani, 2004), and mental health in youth (Potter, 2013) to describe people’s experiences with these events over time.

Several aspects of the career model are of interest in this research. First, it informs us that the experience of illness is a dynamic process, which starts with the unpleasant feeling of being ill. Second, medical diagnosis is the culminating moment of the career. Finally, it acknowledges that social and medical factors create and maintain the health career, and shape the impact of this career on diabetics and their families. In a sense, and in agreement with our own perspective on diabetes, the career model takes a natural history approach to chronic illness, an approach which postulates that illness and its diagnosis initiate a new trajectory, that illness is dynamic, and is shaped by social factors that also vary with time. Although individual differences in the pathways through this trajectory exist, the model also acknowledges that “cumulative experiences” with a chronic illness “merge into a holistic entity” (Aneshensel, 1999) in which the level and rate of change can be measured.

The Illness Trajectory Model is a clinical variant of the Career Model. It emphasizes the role of medicine and medical professionals in people’s experience of chronic illness (Corbin, 1998; Corbin & Strauss, 1985, 1991; Strauss et al., 1984; Strauss & Glaser, 1975). According to this view too, illness trajectories begin with the onset of an illness; and they are shaped by interactions between the disease, a person’s characteristics, their psychological and behavioral responses to the illness, the actions of healthcare providers, and finally the treatment regimen prescribed. The Illness Trajectory Model also takes into account the involvement of others in

disease management, including a patient's family and support network, as well as the social environment in which they are all embedded. This model also postulates that a patient's position on the disease trajectory determines the effectiveness of disease management and the probability of recovery. The model is therefore highly relevant to diabetes care. For this reason, it is widely used in clinical settings to locate patients on their disease trajectory before the development of end-stage renal failure (Schell & O'Hare, 2013), or in functional decline at the end of life (Lunney, Linn, & Foley, 2003). The model is particularly useful as a means of identifying ways to optimize disease management (Strauss, et al., 1984).

The Disablement Process Model

The third model of interest is the Disablement Process Model (Verbrugge & Jette, 1994), which is also a sociological model of the progression of chronic illness. According to this model, the experience of illness or of an injury evolves from clinically imperceptible physiological changes to functional impairments and disability. The model therefore describes a theoretical pathway linking chronic illnesses to physical functioning; it further places this pathway within a social context. Verbrugge identified three sequential stages in the alteration of physical functioning. *Impairments* occur at the physiological level and can begin even before clinical symptoms are manifest. *Functional limitations*, the second stage, entail restrictions in basic physical and mental activity. Finally, *disability* represents loss or reduction in the ability to perform expected or specified activities associated with assigned social roles for extended periods of time, and as a result of illness or impairment. Disability is situational and depends on the social context.

Several concepts of the Disablement Process Model are pertinent in the current study. First, similar to our concept of the experience of diabetes, Verbrugge defined disablement from the perspective of the ill person, as a dynamic, non-linear, and time-variant process. Second, this model clarifies our definition of physical health, which we operationalize based on the concept of functioning; that is, the extent to which people are able to function normally and carry on their routine daily activities. Functional disability is further conceptualized as the ability to perform self-care, self-maintenance, and physical activities on a daily basis. Third, the model supports our hypothesis that besides aging, disease can initiate a change in health. Finally, the model places the disease process within a social context. We adopt the concept of disability as a social phenomenon, which is contextual and dependent on the social and physical environment. The model proposes that personal characteristics of the ill person (socio-demographic characteristics, lifestyle and behaviors, psychosocial status, and adaptive accommodations), and factors external to the ill person (medical care, social support, physical environment and social environment) can shape people's experience of illness.

Despite the clear identification of disease diagnosis or injury as the starting point of pathological changes, the model is consistently used in conjunction with the life-course perspective on aging with diabetes, a perspective in which the starting point of health trajectories is conceptualized as age or study wave (Chiu & Wray, 2010b). However, although the model is useful in the assessment of the impact of diabetes on health, it does not describe general health changes *after* a diagnosis of diabetes. To the author's knowledge, the Disablement Process Model has never been applied in the context of the Illness Career Model, which is the object of this research.

Theory of social stratification

The theory of social stratification also guides this study. According to this theory, systems of dominance and subordination based on ascribed characteristics such as race or ethnicity (Williams & Collins, 1995), age (Riley, 1987), and gender (Bird & Rieker, 1999; Rieker & Bird, 2000) and partially mediated by socioeconomic status (Robert & House, 2000), create a series of dualisms in established social structures. This dualism leads to a systemically unequal allocation of both resources and risks, which in turn leads to poorer health in disadvantaged groups (House, Lantz, & Herd, 2005; House et al., 1994; Lantz et al., 2001; Link & Phelan, 1995). Lower-status persons have less access to resources that can mitigate risks to health. They are also exposed to higher levels of risk, which can exacerbate the onset and progression of disease.

Empirical research consistently finds evidence of disparities in the determinants of diabetes based on race, ethnicity, gender, and socioeconomic status.

Race – Blacks have lower health literacy (Sentell & Halpin, 2006), weaker adherence to medication regimens (Heisler et al., 2007), poor diabetes control (Heisler, et al., 2007), and low self-efficacy for reducing cardiovascular risk factors (Smedley & Syme, 2001). They also experience poorer patient-provider communication (Saha, Arbelaez, & Cooper, 2003), and worse healthcare access and use (Gary, McGuire, McCauley, & Brancati, 2004; Lanting, Joung, Mackenbach, Lamberts, & Bootsma, 2005; Smedley, Stith, & Nelson, 2003). In addition, they face residential segregation (Williams & Collins, 2001; Sampson, Morenoff, Gannon-Rowley, 2002; Morenoff, 2003; Diez-Roux, 2007) and discriminatory practices that can adversely affect functioning and diabetes management by reducing access to adequate health services, foods, and

healthful environments (Williams, 1995 #181) and by increasing vulnerability to stress (Pearlin, 1989).

Ethnicity – Compared to Caucasians, Hispanics also experience greater diabetes-related distress (Heisler, et al., 2007). They also hold beliefs that can hinder diabetes management (Jezewski & Poss, 2002), and they have behaviors that worsen diabetes management (Nwasuruba, Khan, & Egede, 2007) and diabetes control (Harris, Kovar, Suzman, Kleinman, & Feldman, 1989; Hertz, Unger, & Ferrario, 2006; Quandt et al., 2005). Finally, they have worse patient-physician communication (Lipton, Losey, Giachello, Mendez, & Girotti, 1998). On the favorable side, one study found that Mexican Americans had better controlled diabetes, were more likely to be treated, and to be more aware of diabetes than whites, after controlling for socio-demographic characteristics and access to care (Hertz, et al., 2006).

Gender – Both differential vulnerability and differential access to materials and resources that promote health can lead to gender differences in diabetes outcomes (Bird & Rieker, 1999; Legato et al., 2006; McDonough & Walters, 2001; Rieker & Bird, 2000; Shalev, Chodick, Heymann, & Kokia, 2005; Szalat & Raz, 2007; Verbrugge, 1985). Gender differences in factors relevant to diabetes management and risk factors for diabetes outcomes have been empirically observed. Women experience worse glycemic control and body fat composition, high blood pressure, and more diabetes complications than men (Juutilainen et al., 2004). They report more barriers to the adherence to treatment regimens (Glasgow, McCaul, & Schafer, 1986; Walker et al., 2006), more depressive symptoms (Gucciardi, Wang, DeMelo, Amaral, & Stewart, 2008; Ponzo et al., 2006), weaker perception of family support, and worse diabetes-specific self-efficacy (Brown et al., 2000) (Brown, et al., 2000; Gucciardi, et al., 2008; Ponzo, et al., 2006; Umberson, 1992).

Socioeconomic status – People of lower social status are at a disadvantage compared with others, on important diabetes self-management behaviors, access to healthcare, process of care, and biological processes (Anderson et al., 1995; Baker, Watkins, Wilson, Bazargan, & Flowers, 1998; Beckles et al., 1998; Brown et al., 2004; Fiscella, Goodwin, & Stange, 2002).

Poor understanding of the hemoglobin A1c testing process (Beckles, et al., 1998) and lower health literacy are linked to hypoglycemia (Williams, Baker, Parker, & Nurss, 1998), higher HbA1c levels and the risk of retinopathy, even among those who undergo conventional diabetes education (Schillinger et al., 2002). The education gap in functional status could be reduced if—as studies of managed care organizations have found—inequities in access to healthcare were reduced (Fiscella, et al., 2002).

Finally, the paradigm of intersectionality is used (in Chapter 2) to investigate the combined effects of race and gender on functional trajectories after a diagnosis of diabetes. This sociological paradigm assumes that race, gender, and class mutually construct one other (Mullings & Schulz, 2006; Schulz & Mullings, 2005; Thornton & Zambrana, 2009).

Health disparities in race or ethnicity, on the one hand, and gender, on the other, are well documented. Compared to whites, racial and ethnic minority groups exhibit poorer health and functioning (Hayward & Heron, 1999; Read & Gorman, 2006). Longitudinal studies of disability also found that in old age, each gender within a racial or ethnic group showed different levels of disability. The lowest levels of disability were found in white men, followed by men of racial and ethnic descent, then white women and finally, black and Mexican American women (Warner & Brown, 2011). Recent investigations of the combined role of gender and race using trajectory analysis show that disability trajectories of race and ethnicity by gender vary at initial assessment, with similar rates of change. The exception to this finding was observed in black

women, who exhibited accelerated decline in functioning (Warner & Hayward, 2011). To our knowledge, the intersection of race, ethnicity, gender, and disability has not been studied in the context of late-onset diabetes.

Theoretical framework

Figure 2 provides a visualization of the theoretical framework that guides the current study. From the natural history of diabetes we borrow the concept of diabetes as a time-variant condition on a time continuum, beginning with the diagnosis of diabetes and ending with death. From the Illness Career Model and the Disablement Process Model, we borrow the concept of the experience of diabetes as a dynamic phenomenon, in agreement with our own view. From these theories and the Theory of Social Stratification, we borrow the perspective that links micro-level and macro-level determinants of health disparities. We expect that health will decline as diabetes continues; and that ascribed characteristics including race, ethnicity, gender, and age will directly and indirectly, through their impact on attained social status and diabetes timing, influence the levels and rate of change in physical, mental, and cognitive health as the disease progresses.

NEW PERSPECTIVE: EVENT-BASED APPROACH TO DIABETES AND HEALTH

Based on the sociological and medical concepts of illness and disease, this research is grounded in the belief that the severity of physical, mental, and cognitive health change associated with a chronic illness varies not only with age and time, but also with the progression of the disease. Therefore to quantify the course of diabetes in terms of physical, mental, and cognitive change after a diagnosis of diabetes, we adopt an event-based approach to the study of

diabetes and health. This approach has various conceptual, analytic, and practical advantages over age-based and time-based approaches, which are discussed below.

Conceptual advantages

In an event-based approach, the goal is not to describe health differences with aging among people with diabetes and people without diabetes, as it has been done by comparative studies of diabetes and health. Rather, it is to focus specifically on people with diabetes, and describe how their health changes as their disease progresses. In contrast to age-based and time-based approaches, an event-based approach is a disease-centered perspective. It fits the biomedical model of health and illness, with the conceptualization of diabetes as a dynamic phenomenon. Nevertheless, this approach does not conflict with the sociological view of health and illness, a view which holds that a patient is an active agent in his experience of diabetes; nor does it conflict with the view that health change occurs within a social context. In fact, health change occurs alongside the natural history of diabetes, incorporates measures of change from both the disease (diabetes duration) and the patient's characteristics (cohort, age at diagnosis). Moreover, health change is influenced by social, medical, behavioral, and psychological factors along the way. An event-based approach can therefore provide a better description of the course of diabetes in terms of physical, mental, and cognitive health.

Analytic advantages

Analytically an event-based approach requires that 1) health trajectories begin with the disease itself; 2) that they are defined by the duration of diabetes; and 3) they are modeled as a

function of time-variant and time-invariant social determinants of health change with longer diabetes duration. The distinction between an event-based approach to diabetes and health and an age-based and time-based approach is displayed in Table 1.

In an event-based approach, four measures of time are necessary to accurately capture health change with diabetes. Age- and time-based studies have focused mainly on *age*, which measures the aging process, and at times *birth cohort*, which measures historical and social trends relevant to the experience of diabetes. However, the event-based approach locates patients' position on their life course, which can be interpreted as *age at diagnosis*, and their position on their diabetes career, conceptualized as *diabetes duration*. Both are key elements in the study of diabetes and health change.

The distinction between age, diabetes timing, diabetes duration, and birth cohort as different measures of time is important for ascertaining the social causation of health change with diabetes, and assessing the relative role of each measure of time. This distinction is also important for policy and clinical interventions. If the study is unable to find differences in health with longer diabetes duration across measures of time, medical interventions could be equally applied to everyone with diabetes. On the other hand, the effects of time on the progression of the disease suggest that differential exposure to social risks and benefits are specific to individuals diagnosed at different ages and belonging to different cohorts; and that the experience of diabetes varies for different people. Therefore the management of diabetes will require interventions tailored to the needs of patients at different positions along their disease trajectories.

Earlier studies have routinely incorporated individual measures of time to capture the dynamic nature of diabetes, and their findings are discussed below.

Time-variant chronological age

Time-variant chronological age captures developmental changes in aging (Riley, 1987). As described in the section on the comparative studies of people with diabetes and people without diabetes, older age is a major risk factor for poor health. However, in these studies, age cannot accurately describe the experience of illness, since at any point in time, people of the same age who have diabetes can be at different stages of their illness. For instance, when Chiu and Wray estimated the functional status of a person aged 60 with diabetes, the estimate reflected the functional status of people aged 60 who were diagnosed 20 years earlier (at age 40), and those diagnosed 2 years earlier (at age 58). Depending on the case mix at every age, this estimate could be larger or smaller than the true population parameters of health and health change with diabetes (Chiu & Wray, 2010b).

On the other hand, using the event-based perspective, the physical, mental, and cognitive health of people with diabetes can be more accurately estimated at every age by considering both the duration of diabetes and the age at diagnosis. For instance, we are able to accurately predict the physical, mental, and cognitive health of a patient diagnosed at age 50, when he or she reaches 60 or 70 years of age. Similarly, the health of a person diagnosed at age 70 can be predicted 5 or 10 years later.

In the current study there is no designated indicator of aging; therefore we were unable to determine the extent to which health levels and health change were attributable to diabetes alone, or to the process of aging. But again, our interest is not so much in describing the effect of diabetes on people with the condition compared to those without it, as it is in describing the course of diabetes among middle-aged and old-aged adults with diabetes.

Duration of diabetes

A limited number of studies incorporated duration as a proxy for the natural history of diabetes and as an attempt to capture its dynamic nature. These studies showed that a longer duration of diabetes is a key predictor of functional change because of the adverse effects of the disease on functional status and on the determinants of function (De Gouw et al., 1999; Mitchell, Stern, Haffner, Haduza, & Patterson, 1990; Park et al., 2006). A link also exists between the duration of diabetes and an increased risk of diabetes-related depressive symptoms (Skinner, et al., 2010) and depression (Egede & Zheng, 2003; Nefs, et al., 2012; Thoolen, de Ridder, Bensing, Gorter, & Rutten, 2006), as well as poor cognitive performance (Elias, et al., 1997) and reduced processing speed and executive functioning (Cosway, et al., 2001; Saczynski, et al., 2008; Spauwen, Kohler, Verhey, Stehouwer, & Van Boxtel, 2013).

In addition to its direct effects on health, the duration of diabetes can mediate the link between the disease and health outcomes through poor diabetes control (Benoit, Fleming, Philis-Tsimikas, & Ming, 2005; Blaum, Velez, Hiss, & Halter, 1997) and result in a higher risk of complications from diabetes (Selvin, Coresh, & Brancati, 2006), including retinopathy (Henricsson, Nilsson, Groop, Heijl, & Janzon, 1996) and cataract (Chuang et al., 2006). Finally, longer duration is linked to greater resistance to diabetes medications, despite improved self-care skills (Benoit, et al., 2005; Blaum, et al., 1997; Chiu & Wray, 2010a).

Methodologically studies incorporating the duration of diabetes have additional limitations. First, cross-sectional studies are unable to distinguish between intrapersonal and interpersonal differences in health outcomes. Therefore we do not know how many of the estimates are due to personal differences in health over time or represent true effects of the duration of diabetes. Second, studies relying on two or three time points provide little

information about the underlying growth curve of health change with the duration of diabetes. Yet according to the natural history of diabetes, the disease is defined by transitions between different health phases, which can form an average trajectory (Ramlo-Halsted & Edelman, 2000). Finally, multiple underlying trajectories exist, for patients' physical, mental, and cognitive health status vary at diagnosis and with a longer duration of diabetes, yet are not captured. We conclude that the inclusion of the duration of diabetes as a time-invariant covariate does not capture changes in the different areas of life that can influence health as the disease unfolds. On the contrary, it merely provides a qualitative measure of diabetes without revealing the nature of health change as diabetes progresses.

In sum, earlier studies which provided cross-sectional evidence of the negative link between longer diabetes duration and health do not inform us about the nature of health change after diabetes has been diagnosed, nor do they inform us about the respective roles played by the timing of diabetes, by cohort differences, or by the social context within which health changes occur.

As patients journey through their disease career, diabetics of the same age continue to age simultaneously. We postulate that the duration of diabetes conceived as a time-variant predictor measures more accurately, the time since diabetes was diagnosed. This perspective makes it possible to capture health change as the disease progresses and as people age, and thus to capture the dynamic nature of both the disease and the patient's experience of it. For this reason, the current study uses time-variant diabetes duration as the measure of time in order to define health trajectories after diabetes diagnosis. Estimates of physical, mental, and cognitive health status for a particular patient, with a given diabetes duration, conditional on age at diagnosis, allows us to

depict the average course of diabetes among middle and old-age adults who have incident diabetes.

Diabetes timing (age at diagnosis)

The timing of diabetes; that is, a patient's age when diabetes was diagnosed, measures patients' position on their life course at the time of diagnosis. The timing of diabetes in middle age and old age is an important aspect of the experience of the disease. Sociological theories acknowledge that illnesses, particularly acute illnesses, disrupt a person's life (Bury, 1982). This disruption arises from a host of physical, psychological, cognitive, and social changes. These changes, in turn, affect a person's experience of the disease. Disruptions in self-perception are characterized by negative self-appraisal of one's life prospects, and by corresponding modifications in relationships with family members and others. Empirical findings suggest that the impact of this disruption on the person's life results from many factors, including the type of illness, the age at which the illness arises, and the medical and social contexts in which it occurs (Faircloth, Boylstein, Rittman, Young, & Gubrium, 2004). A recent study of older adults with chronic illness found that manifestations of biographical disruptions are not only tied to the event itself, but continue throughout the person's life (Larsson & Grassman, 2012). Therefore both the timing of acute or chronic illness and health changes that occur during the illness adversely affect people's lives.

Clinical and epidemiological studies have investigated the effect of diabetes timing upon the health of adult diabetics. Most of these studies found that in contrast to people who received a diagnosis of diabetes when they were older, people diagnosed at younger ages were at heightened risk of diabetes complications (Hillier & Pedula, 2003; Selvin, et al., 2006), and poor

diabetes control (Benoit, et al., 2005; Blaum, et al., 1997; Nichols, Javor, Hillier, & Brown, 2000). For instance, a study of 7,844 Health Management Organization (HMO) enrollees reported that people with early onset diabetes (ages 18-44) are at greater risk of microalbuminuria, macrovascular complications including myocardial infarctus, higher BMI, and worse diabetes control than their older counterparts (Hillier & Pedula, 2003). A similar study by the same authors conducted among 2,437 HMO enrollees with incident diabetes found a greater risk of cardiovascular complications and poor diabetes control among respondents with early onset diabetes (Hillier & Pedula, 2001). A third study further reported an association between diabetes diagnosed before age 40 and poor clinical and cardiovascular risk compared to people diagnosed after age 40 (Hatunic, Burns, Finucane, Mannion, & Nolan, 2005).

Cumulatively these findings suggest that early onset type 2 diabetes may be a more aggressive disease than late onset diabetes. However, none of these studies took into account the duration of diabetes, which is a strong confounder of the link between age at diagnosis and health. Younger age at diagnosis can result in longer diabetes duration in older age, thus can explain the strong link between age at diagnosis and diabetes complications. The two studies that accounted for the role of diabetes duration in the link between age at onset and diabetes complications corroborated earlier studies, with a stronger, independent and negative effect of younger age at diagnosis on retinopathy (Henricsson, et al., 1996; Wong, Moluneaux, Constantino, Twigg, & Yue, 2008). Unfortunately since both studies were limited to retinopathy, they cannot be generalized to the diabetes outcomes of interest in the current study.

One clinical study conducted in several Asian countries investigated the link between age at onset, diabetes duration, and diabetes complications in adults aged 18 and older with type 2 diabetes (Chuang, et al., 2006). This study found that age at diagnosis may confer different levels

of risk depending on the type of complications investigated. After adjusting for diabetes duration, Chuang and colleagues found that the risk of complications increased for every added year of age from onset: by 13% for cataract, 7% for diabetes foot (amputations, absence of foot pulse, or healed ulcer), and 7% for microvascular complications (photocoagulation, retinopathy, or end-stage renal failure). The risk did not differ for macrovascular (myocardial infarct/coronary angioplasty bypass graft/angioplasty, cerebral stroke or peripheral bypass/angioplasty) or neuropathic complications. While these findings are consistent with our assumptions, the study used a clinical sample, with age spanning from young adults to older-aged adults and used cross-sectional analyses relying on mean differences. Therefore this research cannot confirm the role of age at diagnosis on health change in middle age compared to older adulthood.

To our knowledge, only one population study tested the link between age at diagnosis and health in middle-aged compared to older-aged adults (Selvin, et al., 2006). Using a cross-sectional design to analyze 1999-2002 NHANES data, the study found a greater risk of microvascular disease, poor diabetes control, and lower risks of taking glucose-lowering drugs with the onset of diabetes in middle-age compared to its onset in old age. However, the risk of macrovascular disease did not significantly differ between the two groups. Here too, the possible link between diabetes complications and age at diagnosis is confounded by the duration of diabetes, which was not accounted for. Thus the role of diabetes timing on health change with longer diabetes duration in middle-aged and old-aged adults with incident diabetes remains unclear.

On the basis of this literature, and in agreement with Bury's concept of illness as a biographical disruption (Bury, 1982) and Larsson's finding that the disruption in people's life trajectory due to chronic illness persists over time (Larsson & Grassman, 2012), we hypothesize

that the timing of diabetes is an important correlate of diabetes complications and diabetes control.

Birth cohort

Birth cohort or time-constant chronological age assesses cohort differences in health and health change. Cohort effects represent social changes and reflect the impact of exogenous social factors on health change as opposed to developmental and aging processes or disease progression. According to Ryder (1965), cohort effects are surrogates for common experiences among individuals of different age groups. Therefore as with social class, cohort membership can result in social variations in health. For diabetes, educational changes between cohorts, changes in the diagnostic criteria and in treatment modalities can influence patients' experience of diabetes (American Diabetes Association, 2014).

Studies of cohort differences in depressive symptoms generally found improvement with successive cohorts, attributed to better education (Clarke, Marshall, House, & Lantz, 2011) and to improved socioeconomic and marital status (Yang, 2007). These results are mirrored by reports of improved cognitive health with each cohort (Dodge, Zhu, Lee, Chang, & Ganguli, 2013; Karlamangla, et al., 2009; Salthouse, 2013) coupled with a slower decline in younger cohorts, also partly due to higher education (Dodge, et al., 2013). Similar trends were reported for physical health, with a decline in more recent cohorts, and among the oldest old in particular (Seeman, Merkin, Crimmins, & Karmalanga, 2010). These trends were also attributed to improved education, medical care, and to assistive and mainstream technologies (Schoeni, Freedman, & Martin, 2008).

However, findings from two seminal studies suggest that functional status did not decline in younger cohorts of peri-retirement populations aged 60-69 (Seeman, et al., 2010) and 50-64 (Martin, Freedman, Schoeni, & Andreski, 2010). These studies of the general population contrast with Chiu & Wray's (2010b) analysis of Health and Retirement Study data, which supports the view that older cohorts of people with diabetes show greater physical disability and faster decline over time. However, since the authors did not account for diabetes duration or age at diagnosis, their reported cohort effects are inconclusive.

Similar studies among older adults with diabetes are lacking for mental and cognitive health. Nevertheless, changes related to diabetes diagnosis, diabetes management, and risky behaviors all support the hypothesis that there is a positive link between younger cohort and improved health among people with diabetes. First, expansion of the diagnostic criteria for diabetes (Koopman, Mainous, Diaz, & Geesey, 2005) can lead to diagnosis at a younger age, and healthier individuals in more recent cohorts. Second, changes in the recommendations for diabetes management reduce the burden of treating diabetes in older adults. For instance, the American Diabetes Association recommends lower glycemic cutoff values among older adults with high frailty, lower life expectancy, and severe comorbid conditions (American Diabetes Association, 2014). While research on the effects of such recommendations on adherence to treatment and to diabetes outcomes in older adults are still forthcoming, it is likely that the recommendations will have a positive impact on both adherence and outcomes. Finally, improvement in behaviors, such as cessation of smoking and steps to minimize cardiovascular risk, also have a positive effect on the health of people with diabetes (Schoeni, et al., 2008). Therefore although the extent to which cohort membership may influence older adults' experience of diabetes has been very little studied, it is reasonable to assume that the physical,

mental, and cognitive health of older adults with incident diabetes also improves with successive cohorts.

Practical applications

Currently, comparative studies are unable to describe health change over the clinical course of diabetes. Conceptualizing health change along the diabetes career addresses this issue; for it puts all patients on an equal footing with regard to their disease, allowing people with the same disease history to age together. Therefore it is possible to accurately predict physical, mental, and cognitive levels of health at every point along a person's diabetes career, depending on the person's age when the disease was diagnosed. The study can further describe and predict social variations in the clinical course of diabetes, thereby allowing the creation of individualized diabetes management plans. Individualized management plans are important for at least three reasons.

First, from a clinical point of view, heterogeneity among patients poses a serious barrier to high-quality diabetes management. At any given age people with diabetes comprise a diversity of individuals with prevalent or incident diabetes, with variable levels of diabetes complications, physical disability, and with a diversity of social backgrounds—all of which can influence diabetes outcomes and management. As a consequence, clinical recommendations for older adults with diabetes are non-specific (American Diabetes Association, 2014; American Geriatrics Society Expert Panel on the Care of Older Adults with Diabetes Mellitus, 2013; International Diabetes Federation, 2010; Sinclair et al., 2011). Nevertheless, one common concern is the need for an individualized approach to diabetes care and management. This individualized plan allows to compare patients' clinical and functional statuses, comorbid

conditions, and life expectancies, against the time frame within which benefits are expected from different treatment options for clinical decision. The current study can help clinicians identify each patient's location on the clinical course of diabetes, thereby minimizing the effect of patients' heterogeneity at clinical presentation.

Second, the literature supports the view that shared decision-making regarding diabetes management between clinicians and patients is important for successful diabetes care (Kirkman et al., 2012). Yet lack of agreement between clinicians and patients on treatment goals for diabetes has been documented (Huang, Gorawara-Bhat, & Chin, 2005). For physicians, clinical improvement is the most important outcome of diabetes care. But for patients, functional status and functional independence are the most important treatment goals (Huang, et al., 2005). Furthermore, older patients with diabetes perceive diabetes treatment as having an adverse impact on their quality of life; an adverse impact similar to that of diabetes complications (Huang, Brown, Ewigman, Foley, & Meltzer, 2007). Disagreement on treatment goals between clinicians and patients as well as patients' perception that medical treatment poses a burden, may result in minimal adherence to recommended lifestyle changes and medical regimens. The results from the current study could improve patient-physician agreement on the goals for diabetes management in two ways. To a clinician receiving a patient newly diagnosed, visualization of the clinical course not in terms of biomedical and physiological markers, but in terms of outcomes most important to the patient may offer an opportunity to highlight the importance of medical care and treatment adherence for functional independence. On the other hand, for patients newly diagnosed with diabetes, being able to understand, foresee and visualize the clinical course they are likely to experience, starting with diabetes diagnosis, may be of much greater interest than linking their functional health and diabetes status to their age or to randomly assessed time. With

visual graphs of health change over the clinical course of diabetes from the study estimates, clinicians may gain patients' trust and thereby their willingness to adhere to a prescribed medical regimen.

Finally, the study's findings can be useful to policy makers interested in projecting the clinical course of diabetes at a population level in order to plan for the allocation of resources and for the development of medical and behavioral management plans to prevent and slow down health decline with diabetes in middle-aged and older-aged adults.

HYPOTHESES AND OUTLINE OF THE DISSERTATION

Four main hypotheses are tested, and are spelled out in greater detail in the appropriate Chapters. First, we expect that health trajectories will decline with longer diabetes duration as complications arise and the demands of diabetes management increase. Second, older age at diagnosis will result in worse health trajectories with longer diabetes duration because diabetes and its progression increase people's vulnerability in old age. Third, due to general improvements in education, in physical, mental, and cognitive health, and in diabetes diagnosis and management in recent years, people in recent cohorts will have better health trajectories as diabetes lasts longer. Finally, health trajectories over the course of diabetes will be worse among socially disadvantaged groups due to significant sociocultural and medical disadvantages in diabetes management.

The study consists of three empirical analyses of HRS data, a representative biennial panel survey of Americans aged 50 and older, beginning in 1992 (Juster & Suzman, 1995). It uses Hierarchical Linear Modeling to estimate the levels and growth in physical, mental, and cognitive health trajectories, beginning with the diagnosis of diabetes and for every subsequent

year following diagnosis (Raudenbush & Bryk, 2002). This technique is most appropriate for the HRS data for several reasons. First, it allows both interpersonal and intrapersonal variations in health over time to be estimated, thus accounting for the hierarchical structure of the data. Second, it allows estimation of the effect of both time-constant and time-variant covariates on the levels and rate of change in the outcome. Finally, it provides estimates of both the fixed effects of diabetes duration and other covariates on health trajectories, and random variations related to individual variability at baseline, and over time.

The first study models the change in ADL/IADL and mobility disability beginning with a diagnosis of diabetes at age 50 and older (Chapter 2). It further assesses time-related and social variations within these estimates. The second study investigates similar research questions for depressive symptoms (Chapter 3). The third and final study estimates cognitive changes after late-onset diabetes among individuals aged 65 and older. Policy and research implications are discussed in the last chapter (Chapter 5).

RELEVANCE

Earlier studies, using diabetes as a time-invariant personal attribute, found that diabetes generally increases the risk of poor health over time or with age. However, these studies did not describe the trajectories of health changes with longer diabetes duration. On the other hand, studies that included diabetes duration and age at diagnosis to capture the dynamic nature of the disease from the patient's perspective treated these measures as if they were cross-sectional. These studies were therefore unable to separate the respective roles of diabetes duration and diabetes timing from that of aging and cohort in the levels and nature of physical, mental, and

cognitive health trajectories. Therefore the temporal effects of diabetes on physical, mental, and cognitive health after diabetes is diagnosed in middle-age or older age, remains unknown.

The current study contributes to this literature by 1) conceptualizing the experience of diabetes as a dynamic phenomenon that manifests as a trajectory or career, beginning with the diagnosis of diabetes; 2) aligning health change, disease progression, and the social context in which they interact; and 3) disentangling the role of diabetes duration from that of diabetes timing (age at diagnosis) and cohort differences in the experience of diabetes.

Methodologically the study uses analytic techniques which take into account both interpersonal and intrapersonal differences in health with longer diabetes duration. It provides quantitative estimates of the level at diagnosis and rate of change in physical, mental, and cognitive health as individuals journey through their illness careers, and the effects of time-related factors on both. Finally, it estimates the growth parameters of health trajectories after diagnosis across social groups over an extended period of time and uses a nationally representative sample of older adults with self-identified diabetes. Cumulatively these elements of our approach provide a more accurate account of the experience of diabetes among older adults.

Understanding the natural course of type 2 diabetes has three advantages: 1) It can guide healthcare providers in formulating effective treatment regimens that address health change over the course of diabetes, and for specific social groups. 2) It provides a means for clinicians and their patients to formulate identical treatment goals. 3) It can inform policy makers by allowing a more accurate prediction of the health and healthcare needs of people with incident diabetes in middle age and old age.

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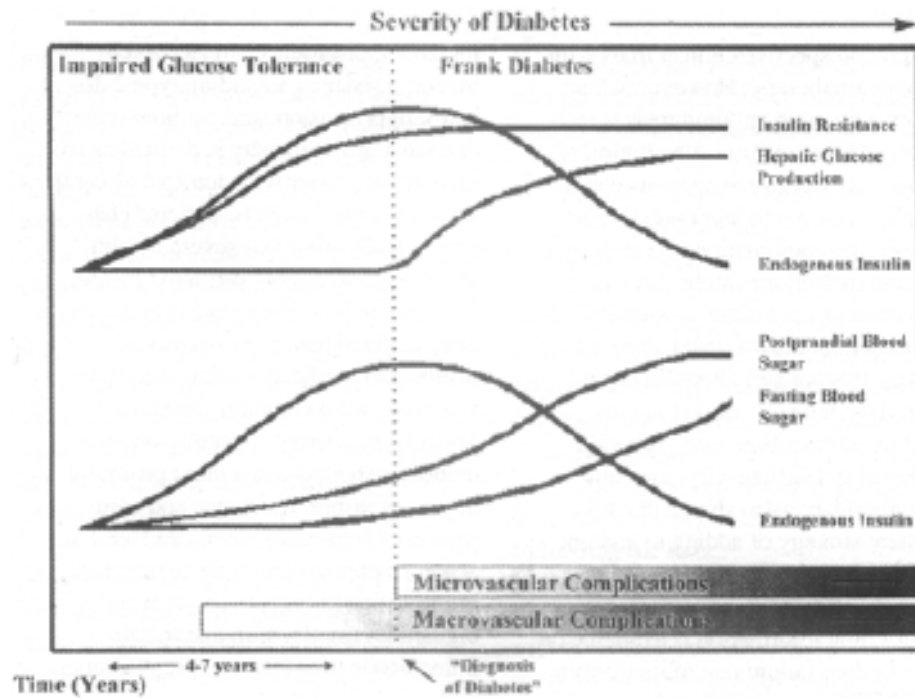
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Figure 1: Natural History of Type 2 Diabetes

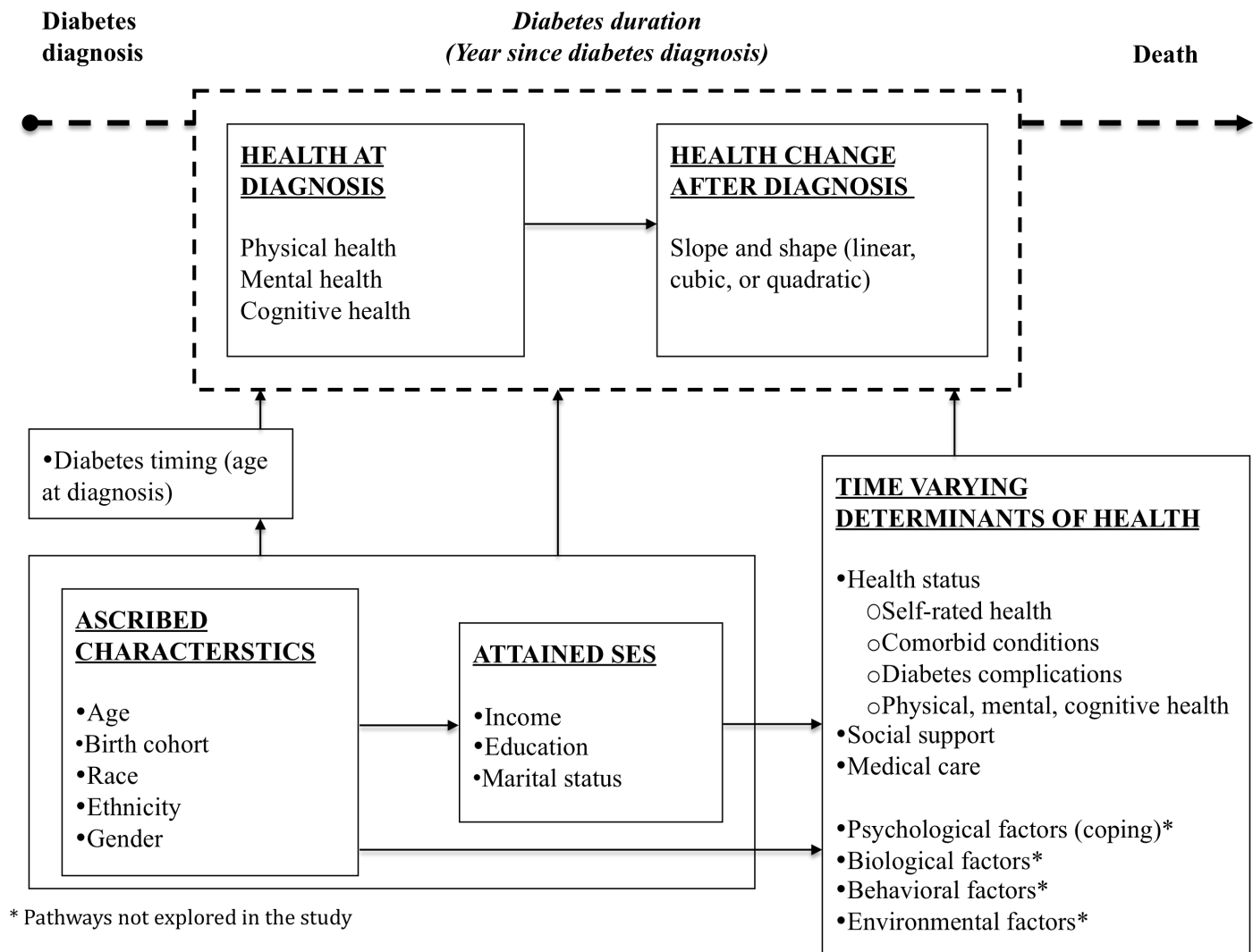


Ramlo-Halsted, B. A., & Edelman, S. V. (2000). The natural history of type 2 diabetes: Practical points to consider in developing prevention and treatment strategies. *American Diabetes Association, 18*(2), 1-10. Used with permission.

Table 1: Distinctive characteristics of an event-based and an age- or time-based approach to diabetes and health

	Event-based approach	Age or time-based approach
Approach	<ul style="list-style-type: none"> • Disease-centered • Patient-centered 	<ul style="list-style-type: none"> • Patient-centered
Subjects under investigation	<ul style="list-style-type: none"> • People with incident diabetes only 	<ul style="list-style-type: none"> • People with both incident and prevalent diabetes • People without diabetes
Research goal	<ul style="list-style-type: none"> • Describes health change with longer diabetes duration, along the natural history of diabetes 	<ul style="list-style-type: none"> • Describes differences in health between people with diabetes and people without diabetes at every age
Starting point of health trajectories (baseline)	<ul style="list-style-type: none"> • Diabetes diagnosis (year since diabetes diagnosis=0) 	<ul style="list-style-type: none"> • Arbitrary age (e.g. age 50) • Arbitrary study wave (e.g. 1994)
Measure of time defining health trajectories	<ul style="list-style-type: none"> • Diabetes duration, measured as year since diabetes diagnosis 	<ul style="list-style-type: none"> • Time since baseline age or time since first study wave
Other measures of time	<ul style="list-style-type: none"> • Diabetes duration (defines health trajectory) • Age at diagnosis • Birth cohort • Age (not explicitly measured; can be deducted from age at diagnosis & diabetes duration) 	<ul style="list-style-type: none"> • Age or study wave (defines health trajectory) • Birth cohort
Characteristics of people with diabetes	<ul style="list-style-type: none"> • All diabetics are at the same stage on their disease trajectory at any point in time (same diabetes duration) • Age differences are controlled at diagnosis • Cohort differences are controlled at diagnosis 	<ul style="list-style-type: none"> • Mixture of people with diabetes at any point in time and at any wave • Diabetics are at different stage on their disease trajectory (diabetes duration) • Cohort difference are controlled at diagnosis

Figure 2: Theoretical Framework



CHAPTER 2

Disability Trajectories after Diabetes Diagnosis in Middle and Old Age:

Do Diabetes Timing and Social Position Matter?

INTRODUCTION

Background

The prevalence of diabetes is rising, particularly in older adults, making it a major public health concern. About one in four U.S. residents aged 65 and older lives with diabetes (Centers for Disease Control and Prevention, 2014). And between 1980 and 2010 the increase among those aged 65-74 was 11 times higher than that of people aged 45 and younger (20.7% versus 1.8%; CDC Data Trends December 27, 2011c). Longitudinal studies of diabetes and functional status (Blaum, Ofstegal, Langa, & Wray, 2003; Figaro et al., 2006; Gregg et al., 2002; Park et al., 2006) found that diabetes doubles the prevalence and risk of developing limitations in instrumental activities of daily living (IADL), mobility, muscle strength and quality of life. Findings concerning activities of daily living (ADL) are less conclusive, but the effects reported are generally similar to those reported on other functional measures (Bruce, Davis, & Davis, 2005; Chou & Chi, 2005; Wray, Ofstedal, Langa, & Blaum, 2005). Recent comparative studies, which model functional change in older adults with and without diabetes, find that diabetes increases the level and rate of functional decline with age (Chiu & Wray, 2010; Chiu, Wray, &

Ofstedal, 2011). These studies further report wider, yet persistent racial and gender gaps, and increasing educational inequalities with time.

Earlier studies conceptualized diabetes as an individual attribute; which does not vary with time. As a consequence, the impact of diabetes on functional status was estimated by comparing individuals with diabetes to those without diabetes. This method overlooked the fact that diabetes itself has a natural history characterized by biochemical (Ramlo-Halsted & Edelman, 2000), psychological (Nouwen et al., 2011), behavioral, and social changes with time (Fischer, 2006; Tunceli et al., 2005); and these changes can in turn alter the progression of the disease. Moreover, the changes can affect the link between diabetes and disability, the development of complications, and the quality of diabetes management (Benoit, Fleming, Philis-Tsimikas, & Ming, 2005; Blaum, et al., 2003; Selvin, Coresh, & Brancati, 2006). To date, the dynamics of health change after a diagnosis of diabetes remains unknown and is the object of this study.

Theoretical framework

In agreement with the concept of the *natural history of diabetes*, which stipulates that diabetes is characterized by biomedical, physiological and clinical changes with longer diabetes duration, we postulate that health changes not only because of chronological age or arbitrary time (study wave), but also because of the clinical course of illness (Ramlo-Halsted & Edelman, 2000). We view diabetes as a dynamic phenomenon. Therefore estimates from earlier studies which used diabetes status as a time-constant measure and as an individual attribute for each respondent were confounded by the dynamic nature of the disease; that is, cumulative changes to

biological, psychological, and social health, as well as the cumulative effects of social, behavioral, and medical interventions devised to address health change resulting from diabetes.

Four theoretical models of health change also inform this study. The *Illness Career Model* and its more clinical variant, the *Illness Trajectory Model*, is a sociological model of the experience of illness from the patient's perspective, which also affords a dynamic view of chronic illness in line with the natural history of diabetes (Aneshensel, 2013; Corbin, 1998; Corbin & Strauss, 1991; Goffman, 1961; Ramlo-Halsted & Edelman, 2000; Strauss et al., 1984). Both models regard illness and its diagnosis as the starting point of a new trajectory, which “forms around the experience of unusual, unpleasant, or unwanted thoughts, feelings, and behaviors” (Aneshensel, 1999). Therefore health change is best portrayed as an “illness career,” emphasizing the dynamic characteristics of the disease, of the ill person, and of the medical and social environments.

Another model being used in the study is Verbrugge's *Disablement Process Model*, which specifically applies to functional change (Verbrugge & Jette, 1994). This model identifies chronic and acute conditions as the precursors of functional change and the starting point of disablement. According to this model, the course of the experience of illness and its impact on health begins with the onset of the illness or with its diagnosis, and varies—in the case of diabetes—with the duration of the illness and with the social environment in which it progresses. The model further identifies personal and environmental factors as determinants of health change after the onset of an illness. This model has been widely used in conjunction with the life-course perspective on aging and health (Chiu & Wray, 2010); however, to the author's knowledge, it has never been applied in the context of the illness career.

The *Social Stratification Theory* is the third model used in the study. It proposes that race, ethnicity, gender, and age, through their effect on attained social status (education, income, marital status) can unequally distribute risks as well as resources that could mitigate the effects of disease, resulting in poor health in socially disadvantaged groups (Bird & Rieker, 1999; House, Lantz, & Herd, 2005; Lantz et al., 2001; Link & Phelan, 1995; Rieker & Bird, 2000; Riley, 1987; Williams & Jackson, 2005). The literature finds strong evidence for social disparities in the experience of diabetes. Blacks, Hispanics, and women bear a greater burden of diabetes, and face more barriers to self-management, to healthcare and to a satisfactory quality of healthcare. In addition, their control of the disease is inadequate, and they experience worse psychological outcomes such as depressive symptoms, diabetes-specific distress, and more comorbidities, as well as weak family support and inadequate diabetes-specific self-efficacy (Brown et al., 2000; Glasgow, McCaul, & Schafer, 1986; Gucciardi, Wang, DeMelo, Amaral, & Stewart, 2008; Heisler et al., 2007; Jezewski & Poss, 2002; Lanting, Joung, Mackenbach, Lamberts, & Bootsma, 2005; Ponzio et al., 2006; Quandt et al., 2005; Sentell & Halpin, 2006; Szalat & Raz, 2007; Walker et al., 2006).

Finally, the paradigm of *intersectionality* at the crossroads of social stratification and gender studies assumes that race, gender, and class interact and mutually construct one another, to produce social disparities (Mullings & Schulz, 2006; Thornton & Zambrana, 2009). This perspective allows us to investigate how structures of power and domination such as sexism and racism have an impact on diabetes outcomes.

From these theories we may infer that health will decline with longer diabetes duration, and that ascribed characteristics such as race, ethnicity, gender, and age will directly and

indirectly, through their impact on attained social status and diabetes timing, influence the levels and rate of change in physical, mental, and cognitive health.

EVENT-BASED APPROACH TO THE STUDY OF DIABETES AND HEALTH

The study is grounded in the assumption that the severity of physical, mental, and cognitive health change associated with diabetes varies not only with age or time, but also with progression of the disease. We therefore propose an event-based approach to diabetes and health, an approach in which the impact of diabetes on physical, mental, and cognitive health is conceptualized as an experience shared by all affected persons, beginning with the diagnosis of diabetes. Health change resulting from diabetes can therefore be quantified and modeled as a trajectory or “diabetes career,” which links the experience of the illness with 1) disease progression (diabetes duration); 2) measures of time which locate patients on their life course, including actual age, birth cohort, and age at diagnosis, and 3) the social, medical, and psychological contexts within which these changes occur.

In categorizing diabetes as an illness career, we model disability trajectories only for patients who have been newly diagnosed with the condition, and begin the trajectories from the time of diagnosis onward. Within this framework we are particularly interested in how diabetes duration shapes functional trajectories, and how age at diagnosis, birth cohort, and agents of social stratification influence functional change with longer diabetes duration. Four measures of time are important to our inquiry.

Chronological age

Time-variant chronological age measures developmental changes in health resulting from aging. Being older correlates with greater functional impairment and accelerated decline in both the general population (Liang et al., 2008) and among diabetics (Chiu & Wray, 2010; Chiu, et al., 2011). However, age alone cannot accurately describe the experience of illness; for at any point in time, people of the same age are at varying stages of their illness depending on their age at the time the illness was diagnosed. The event-based approach places every individual on his or her disease trajectory, and is able to project average health change at any specific time after diagnosis. However, a designated indicator of time-variant chronological age was not included in the study, because the study focuses on the experience of illness according to the progression of the disease.

Diabetes duration

A few studies captured the dynamic nature of diabetes by incorporating the duration of diabetes as a main predictor or a covariate. These studies showed that longer diabetes duration is a key predictor of functional health due to its adverse effects on functional status and its determinants (De Gauw et al., 1999; Mitchell, Stern, Haffner, Haduza, & Patterson, 1990). Longer duration correlates with increasing limitations in functioning of the lower and upper extremities, and with diminished muscle strength (Park, et al., 2006). It also correlates with an increase in the risk of complications of the disease (Selvin, et al., 2006), and with worsened diabetes control (Benoit, et al., 2005). However, the inclusion of diabetes duration as a time-invariant covariate is problematic for several reasons. First, cross-sectional studies are unable to distinguish between intrapersonal and interpersonal differences in health outcomes. Second,

studies relying on two or three time points provide little information on the underlying growth curve of health change with the duration of diabetes (Ramlo-Halsted & Edelman, 2000). Finally, several underlying trajectories exist, because among patients the level of functioning varies both at diagnosis and over time, yet these trajectories are not captured in conventional methods of analysis.

In sum, earlier studies which provide cross-sectional evidence of the link between diabetes duration and physical health do not inform us of the course of physical health change with diabetes, nor do they inform us of the role of diabetes timing, cohort differences, or social context on these health changes. On the other hand, conceptualizing diabetes duration as a time-variant predictor can allow us to depict the growth curve of physical health over the course of diabetes and identify time-constant and time-invariant predictors of the curve. The current study thus uses diabetes duration as the measure of time for defining the growth curve of physical health after diabetes has been diagnosed.

Diabetes timing (age at diagnosis)

According to the biographical disruption theory, the event of illness and its timing can significantly alter people's life trajectory, as well as generate and maintain new life trajectories (Bury, 1982; Faircloth, Boylstein, Rittman, Young, & Gubrium, 2004; Larsson & Grassman, 2012). Empirical studies identify age at diagnosis as a risk factor for both diabetes complications and poor diabetes control. Clinical and epidemiological studies suggest that early onset type 2 diabetes may be more aggressive than late onset diabetes, manifesting a higher risk of complications and poor diabetes control when the disease is diagnosed at a younger age (Benoit, et al., 2005; Blaum, Velez, Hiss, & Halter, 1997; Hatunic, Burns, Finucane, Mannion, & Nolan,

2005; Hillier & Pedula, 2001; Hillier & Pedula, 2003; Nichols, Javor, Hillier, & Brown, 2000). However, these studies did not account for the role of diabetes duration or compare young adults to middle-aged and older-aged adults. The only study that did include diabetes duration as a covariate found a greater risk of complications in later onset diabetes; but here too, the age range of the sample, which included younger adults, limits its generalizing capability in older adulthood (Chuang et al., 2006). This research cannot confirm the impact of diabetes timing on health. We contend that our approach, along with the findings of Chuang and colleagues (Chuang, et al., 2006), allows us to hypothesize that an older age at diagnosis will correlate with a worse clinical course of diabetes, measured as worsened physical health if the duration of diabetes is longer.

Birth cohort

According to Ryder, birth cohort can result in variations in health due to differential exposure to health risks and benefits among people born at the same time, and with a shared history. Studies of physical health between cohorts found improvement in younger cohorts, but little or no improvement in peri-retirement populations (Martin, Freedman, Schoeni, & Andreski, 2010; Schoeni, Freedman, & Martin, 2008; Seeman, Merkin, Crimmins, & Karmalanga, 2010). Among adults with diabetes, improvement in education and behaviors such as lower rates of smoking, changes in diagnostic criteria, and improvement in treatment modalities can positively influence patients' experience of diabetes in younger cohorts (American Diabetes Association, 2014; Koopman, Mainous, Diaz, & Geesey, 2005; Schoeni, et al., 2008). We therefore expect that younger cohorts of people with diabetes will have better physical health trajectories than their older counterparts.

Hypotheses

We hypothesize that the longer the time since diabetes has been diagnosed, the greater the physical disability in middle-aged and older adults with diabetes (Hypothesis 1). In addition, given the higher risk of complications reported with older age at diagnosis and the strong link between physical disability and old age, older age at diagnosis will be associated with higher physical disability at diagnosis, and with accelerated increase with longer duration compared to people diagnosed at a younger age (Hypothesis 2). Given recent ameliorations in behaviors, diabetes diagnosis and therapies in younger cohorts of older adults, we hypothesize that older birth cohort will be tied to worse physical health trajectories with longer diabetes duration compared to younger birth cohorts (Hypothesis 3). Exposure to risks before and during the course of diabetes among vulnerable social groups will result in functional disparities at the time of diagnosis, and the disparities will become greater over time. Therefore women (but not men), blacks and Hispanics (but not whites) and individuals of lower socioeconomic status (but not those of higher socioeconomic status) will experience greater physical disability as the duration of diabetes lasts longer (Hypothesis 4). Finally, compared to white men, minority women will experience greater physical disability at diagnosis, and a faster decline in health thereafter (Hypothesis 5).

METHODS

Data and sample

Data were obtained from the Health and Retirement Study (HRS), a biennial panel survey of Americans aged 50 and older, which began in 1992 (Juster & Suzman, 1995). Respondents

were included in our study if they were interviewed between 1995 or 1996 and 2010.¹ The analysis is limited to respondents aged 50 years and older who reported being diagnosed with diabetes during the study period. Given the relatively late age at diagnosis, we infer from the data that this subsample represents individuals aged 50 years and older in the U.S. with type 2 diabetes (Kenny, Aubert, & Geiss, 1995). Similarly, while the HRS does not include institutionalized adults at study entry, it does follow and interviews respondents as they move in and out of institutional setting.²

Diabetes status was assessed by means of a question regarding whether or not a doctor had told the respondent he or she had a series of conditions, including diabetes (1=yes, 0=no). Respondents with self-reported incident diabetes documented by consecutive negative and positive responses to the diabetes question were included in the analyses. Conflicting answers to the diabetes question (88 total) were addressed by recoding diabetes status to positive if respondents reported taking diabetes medication or insulin (Liang, Quinones, Bennett, & Ye, 2011).

The data were stacked starting with the year diabetes was reported for the first time (year of diagnosis) between 1995 and 2010, yielding a total of 3,307 observations at baseline. Time since the diagnosis of diabetes was recorded every wave thereafter.

¹ Baseline years are 1996 for HRS and 1995 for AHEAD because the functional limitation questions for HRS did not include difficulties using a toilet in the prior waves (1992 and 1994). The wording, structure and coding of the questions were also different. Beginning in 1996, however, the question measuring functional limitations was consistent in both wording and coding. In addition, responses to the diabetes question in the years 1994 HRS and 1993 AHEAD were used to confirm that respondents reported being diabetes free prior to the initial assessment in 1996 HRS and 1995 AHEAD.

² <http://hrsonline.isr.umich.edu/sitedocs/sampleresponse.pdf>

Measures

Physical disability – Limitations in mobility and the ability to perform activities of daily living were assessed with the disability index, which combines Katz's Activities of Daily Living (ADL) index and Lawton & Brody's Instrumental Activities of Daily Living index; it has been widely used (Katz, Ford, Moskowitz, Jackson, & Jaffe, 1963; Lawton & Brody, 1969). This combined index measures difficulties in dressing, bathing, eating, transferring, walking across the room, and toileting. It also measures the ability to perform more advanced tasks, including preparing a hot meal, shopping, making telephone calls, taking medications, and managing money (1=yes; 0=no). Positive answers to these questions were summed. Higher scores represent greater disability (range 0-11). The validity and hierarchy of this index have been previously discussed (Spector & Fleischman, 1998). In addition, separate analyses for ADL and IADL measures yielded similar results; therefore the two measures were combined.

Mobility disability was measured as difficulty walking one block and climbing one flight of stairs (Rosow & Breslau, 1966), walking several blocks, climbing several flights of stairs (Nagi, 1976), and walking across the room (Katz, et al., 1963). A summary score was computed with a range of 0 to 5; higher scores reflected greater impairment.

Chiu and Wray (Chiu & Wray, 2010; Chiu, et al., 2011) combined measures of ADL/IADL, mobility disability, and muscle strength because of the hierarchical structure of functional status, whereby mobility disability predicts future ADL limitations (Bruce, et al., 2005). However, in diabetes, the pathways connecting diabetes to these dimensions of functioning vary (Bruce, et al., 2005; Gill, Williams, & Tinetti, 1995). Age is closely associated with both functional and mobility disability. But while diabetes complications and degenerative diseases are predictors of impaired mobility, health behaviors (smoking) and more severe

cardiovascular diseases (e.g. stroke), are predictors of ADL/IADL disability. We therefore studied functional change separately for these outcomes.

Time measure (diabetes duration) – Diabetes duration was operationalized as time since a diagnosis of diabetes was assessed, after aligning the data so that the baseline for all respondents was the year diabetes was reported for the first time. Seven waves, based on the year since diabetes was diagnosed, were generated every two years from the baseline (0-14).

Other measures of time – Diabetes timing was operationalized as a respondent's age at diagnosis and measured interpersonal age differences in physical health over the course of diabetes. Birth cohort, on the other hand, was measured by age in 1995. It assessed intergenerational age differences due to historical changes in risks and benefits to physical health. Both were included as time-constant covariates.

Measures of social stratification – Race and ethnicity (1=non-Hispanic white, 2=non-Hispanic black, 3=Hispanic, 4=other), gender (1=female, 0=male), and education (1=less than high school, 2=high school graduate, 3=college graduate) were included as time-constant covariates.

Time-variant covariates – Comorbid conditions are important risk factors for functional decline in both diabetic and non-diabetic populations (Chiu & Wray, 2010). People's self-rated health status, obesity, and depression are also powerful correlates of functional impairment and diabetes (Anderson, Freedland, Clouse, & Lustman, 2001; Egede, Zheng, & Simpson, 2002; Katon et al., 2004). The complexity of the treatment regimen for diabetes is further tied to its severity (Benoit, et al., 2005); however, being married has a positive effect on diabetes management (Van Dam et al., 2005). Finally, while the mediating, moderating, or independent role of social status on health is still debated, the literature shows that social status widens the

functional gap between diabetics and non-diabetics with age (Chiu & Wray, 2010). To account for these potential confounders, *marital status* (1=married, 0=not married), *self-rated health* on a 5-point Likert scale (1=very good health, 5=very poor health), *mean number of comorbidities* (range 0-11) including kidney problems or proteins in urine, stroke, heart problems, trouble with eye sight, trouble with hearing, heart disease, hypertension, cancer, arthritis, lung problems, psychiatric problems, and incontinence, *depressive symptoms* assessed with the Center for Epidemiologic Studies Depression rating scale – CESD (Radloff, 1977), and *treatment burden* (1=no treatment; 2=oral; 3=insulin injection; 4=oral and insulin injection) (Benoit, et al., 2005) were all included in the multivariate analyses. *BMI* (body mass index in kilograms per squared meter) was also included in the mobility disability models because of the strong association between increased weight and impaired mobility. Continuous covariates were centered on their grand mean.

Mortality and attrition at any point in the study were addressed by including two time-constant indicators in the models (death: 1=yes, 0=no; attrition: 1=yes, 0=no). A time-variant indicator of proxy interview status was included to account for the differential effects of responses obtained from proxy individuals.

Data analyses

Hierarchical Linear Modeling (HLM) was used to estimate average functional trajectories with longer diabetes duration (Raudenbush & Bryk, 2002). This technique allows both fixed and random effects to be estimated; the technique thus models dependence and unobserved heterogeneity stemming from the longitudinal nature of the data. The level 1 model estimates intrapersonal differences in physical disability for each respondent every year after diagnosis.

For each person, this model provides estimates of physical disability levels at baseline (intercept) and the linear and non-linear slopes with every added year after diagnosis. Time-variant covariates can be included at this level to assess the expected outcome at any given point in time for every change in value of the time-variant covariate.

For both ADL/IADL and mobility disability, a linear, quadratic, and cubic model was used to test for both linear and non-linear increase in the outcome. Nested models were compared using the log-likelihood ratio test in order to select the curvature that best described the data. In addition, Akaike Information Criteria (AIC) and Bayesian Information Criteria (BIC) were used in the selection process. The level of statistical significance of the estimates was also included to obtain the most parsimonious model. In the end, the data best fit the quadratic model. This was therefore used in subsequent analyses.

The level 2 models, on the other hand, assess interpersonal differences in the intercept, linear, and quadratic slopes. They allow estimation of the effects of time-constant covariates on the intercept and on the linear and quadratic estimates obtained from the level 1 model.

A model was first estimated with only diabetes duration and its squared value, followed by a model accounting for death, attrition, and the use of a proxy respondent (Model 1). Consecutive models estimated the effect of time-constant and time-variant covariates in this order: age at diagnosis (Model 2), socio-demographic characteristics (Model 3), education (Model 4), and marital and health status (Model 5). These nested models were also compared using the Likelihood Ratio Test and penalty-driven criteria, including AIC and BIC. The level 1 and level 2 models are described below.

$$PHYSDISAB_{ti} = \pi_{0i} + \pi_{1i} * (\text{diabetes duration}) + \pi_{2i} * (\text{diabetes duration}_{ti})^2 + \sum \pi_{ki} * X_{kti} + e_{ti}$$

$PHYSDISAB_{ti}$ is the level of physical disability for each individual i at time t ; π_{0i} is the level of physical disability for each individual at time of diagnosis; π_{1i} and π_{2i} are the linear and quadratic rates of change in physical disability for each individual; $diabetes\ duration_{ti}$ is the year since diabetes diagnosis, and $diabetes\ duration_{ti}^2$ its squared value; π_{ki} are the effects of the k th time-variant covariates X_k for individual i on the trajectory; X_{kti} are the k th time-variant covariates in the model.

$$\pi_{0i} = \beta_{00} + \sum \beta_{01q} * X_{qi} + r_{0i}$$

$$\pi_{1i} = \beta_{10} + \sum \beta_{11q} * X_{qi} + r_{1i}$$

$$\pi_{2i} = \beta_{20} + \sum \beta_{21q} * X_{qi} + r_{2i}$$

$$\pi_{ki} = \beta_{k0}$$

π_{0i} , π_{1i} , π_{2i} , and π_{ki} are the same as above; β_{00} , β_{10} , β_{20} , and β_{k0} are the fixed effects or expected count of physical disability in a year at mean diabetes duration, and expected linear and quadratic growth and the effect of time-variant covariates; β_{01q} , β_{11q} , and β_{21q} are the effects of the q th time-constant covariates X for each i on the intercept, linear, and the quadratic slope; X_{qi} is the q th time-constant covariate for each i ; r_{0i} and r_{1i} , and r_{2i} are random outcome variations at the intercept and linear and quadratic slope.

To address missing items, the data were imputed using the multiple imputation procedure in Stata® assuming that the data were missing at random (Little & Rubin, 2002; Rabe-Hesketh & Skrondal, 2008). Five imputed data sets were generated and the modeling approach described above was then applied to the imputed data sets. All analyses were conducted using Stata® software (Version 12).

RESULTS

The majority of the 3,307 respondents were females (52%) and white (68%); 17% were black and 12% Hispanic (results not shown). Most respondents had at least a high school degree (67.8%), with a mean age of 68.96 years at diagnosis and a mean age of 60.67 years in 1995. The mortality and attrition rates were 27.15% and 16.07%, respectively. A total of 39% of the sample reported no mobility disability at the time diabetes was diagnosed, while 70% of the sample reported no ADL/IADL disability. On average, respondents had lived with diabetes for 3.56 years during the period of observation. Table 2 presents a statistical description of the sample.

Trajectories of physical disability with longer diabetes duration in middle and old age

In agreement with our first hypothesis, ADL/IADL disability increased after diabetes was diagnosed according to a quadratic function with longer diabetes duration (intercept=0.824, $p<0.001$; linear slope=0.110, $p<0.001$; quadratic slope=0.006; $p<0.001$; M1 in Table 3). Mobility disability also increased quadratically (intercept=1.482, $p<0.001$; linear slope=0.087, $p<0.001$; quadratic slope=0.003; $p<0.01$; M1 in Table 4). For both outcomes, the fixed parameters associated with the intercept and linear slope were reduced in magnitude after time-constant and time-variant covariates (M5 in Tables 3 & 4) were included. In particular, in the third models, controlling for race, ethnicity, and gender variations significantly reduced the intercept.

The model fit improved with each subsequent model, as demonstrated by significant log likelihood statistics. This improvement was observed even after penalties were applied for the increasing number of parameters, with decreasing AICs and BICs.

The results also show a significant unexplained variability in the intercept (1.906; $p<0.001$), linear (0.237; $p<0.001$), and quadratic coefficients (0.028; $p<0.001$) for ADL/IADL

disability, and in the intercept (1.247; $p < 0.001$) and linear slope for mobility disability (0.111; $p < 0.001$). This variability remained robust to the inclusion of social and health variables.

Diabetes timing (age at diagnosis)

Our findings also lend support for the second hypothesis, that older age at diagnosis is associated with worse disability trajectories. We found higher ADL/IADL disability and greater linear increase with older age at diagnosis (intercept=0.064, $p < 0.001$; linear slope=0.008; $p < 0.001$; M2 in Table 3). We also found a modest acceleration in the quadratic slope with older age at diagnosis (quadratic slope=0.0001; $p < 0.05$). For individuals diagnosed at age 50, after adjusting for mortality, attrition, proxy interview, age at diagnosis and age in 1995 (results not shown), ADL/IADL disability increased from 0.652 to 3.578 in 14 years, whereas for someone aged 60 at diagnosis, disability levels increased from 1.292 to 5.534 (Figure 3). These results were replicated in the models for mobility limitations, which suggest a robust effect on disability trajectories of diabetes duration and age at diagnosis (Figure 4).

The inclusion of age at diagnosis in the level 2 models for the intercept and slope reduced the level of disability at diagnosis by 20.9% (from 0.824 to 0.652) and 6.3% (from 1.482 to 1.389) and the linear slope of disability trajectories by 11.8% (from 0.110 to 0.097) and 3.7% (from 0.081 to 0.078) for ADL/IADL and mobility disability, respectively (M2, Tables 3 and 4).

Birth cohort

We found that being from an older cohort (older age at diagnosis), raised disability levels by 0.049 ($p < 0.001$) at baseline. The increase was further tied to a 0.008 ($p < 0.001$) increase in the linear slope, and 0.001 ($p < 0.001$) increase in the quadratic term (results not shown). However,

after age at diagnosis was added in the model, the cohort effects were reversed: People from younger cohorts had a 0.049 lower risk of physical disability at diagnosis (-0.049 ; $p < 0.001$), and the risk remained largely unchanged with longer diabetes duration (0.001 , $p > 0.5$ for the linear slope, and 0.001 , $p < 0.10$ for the quadratic slope). These trends remained in the final models after the health measures were included, with -0.052 ($p < 0.001$) at baseline, and -0.002 ($p > 0.05$) and 0.001 ($p < 0.10$) for the linear and quadratic slopes, respectively. Therefore our third hypothesis, that younger cohorts would manifest less physical disability, was not substantiated.

Social stratification

Our fourth hypothesis postulated that gender and racial differences in functional status, as evident at diagnosis, would increase with longer duration of diabetes. The results, however, suggested that, although significant racial and gender gaps in physical disability existed at the time of diabetes diagnosis, these differences remained stable over time. However, our hypothesis was supported when Hispanics were compared to whites: Hispanics were the only social group that experienced accelerated physical disability trajectories with longer diabetes duration (intercept= 0.445 , $p < 0.001$; linear slope= 0.058 ; $p < 0.001$; Table 3, M3); and this ethnic difference in the rate of functional decline was fully explained by education (M5).

Social differences in the trajectory of mobility disability were not nearly as noticeable, with the exception of a persistent gender gap (intercept= 0.678 ; $p < 0.001$; linear slope= 0.003 ; $p > 0.05$, M3, Table 4).

Although there were no racial differences in the trajectories for mobility disability, ethnic differences were nevertheless harder to disentangle as covariates were added to the model. The analysis of race and ethnicity by gender provided more details on the combined effects of race

and ethnicity, on the one hand, and gender on the other, on functional status. Although gender and racial differences in physical disability trajectories were duplicated, ADL/IADL and mobility disability accelerated faster for Hispanic men (ADL/IADL: linear slope=0.100, $p<0.01$; Mobility: linear slope=0.049, $p<0.05$, Figures 5 & 6), followed by Hispanic women, who experienced a more modest increase (ADL/IADL: linear slope=0.054, $p<0.05$). Heterogeneity in education accounts in large measure for racial and ethnic gaps at diagnosis among men, and over time for Hispanic women. Education did not explain the functional decline for Hispanic men. However, higher education was the only socio-demographic characteristic to positively affect the slope of the mobility disability trajectory.

DISCUSSION

Building upon the Illness Career Model and the Disablement Process Model, and relying on the event-based approach in the study of diabetes and health, this study is the first to demonstrate that the clinical course of diabetes is characterized by a quadratic acceleration in ADL/IADL and mobility disability with longer diabetes duration among middle-aged and old-aged adults with incident diabetes. Earlier reports using diabetes as a personal attribute found that being diabetic can increase the risk of functional limitation over time (Chiu & Wray, 2010; Chiu, et al., 2011). Rather than focusing on age or arbitrary time, which provides a cross-sectional view of people's experience of diabetes from the disease perspective, the event-based approach mirrors the clinical course of diabetes. It is therefore more useful to clinicians and patients but also to policy makers interested in understanding the course of diabetes after diagnosis.

Conceptually and methodologically, the current study's strength lies in 1) its conceptualization of diabetes as a career, which allows for aligning functional change with disease progression; 3) its incorporation of several measures of time relevant to both the disease (diabetes duration) and to the patient (age at diagnosis and cohort); 2) its use of a national representative sample of middle-aged and older adults with self-identified incident diabetes and their physical disability over an extended period of time; 4) its statistical technique, which allows differentiation of the respective roles of intrapersonal and interpersonal variations on physical health change in diabetes; and 5) its ability to quantify social differences in the experience of diabetes among different social groups.

Trajectories of physical disability with longer diabetes duration

The study results confirm our first two hypotheses, that among middle-aged and older adults, diabetes is a dynamic aging accelerator in that physical disability, conceptualized as ADL/IADL and mobility disability, increases quadratically after diagnosis, and this increase accelerates with older age at diagnosis. The findings confirm a long-held assumption from cross-sectional and age-based or time-based studies that longer diabetes duration is associated with worsening physical health (De Gauw, et al., 1999; Mitchell, et al., 1990; Park, et al., 2006). However, the study goes one step further by estimating the shape of this relationship. We confirm that the relationship between diabetes duration and physical disability is not time-invariant; rather, it changes with time, in that disabling effects are stronger with longer diabetes duration. On average, and after adjusting for age at diagnosis and cohort effects, there is a 25% loss in people's ability to function physically every year following a diagnosis of diabetes, and a

2.17% quadratic increase with every additional year from an initial level of 0.415 limitations at diagnosis (results not shown).

Socio-demographic and health status differences over the course of diabetes, including the burden of diabetes treatment, explained some of the levels as well as the rate of change in the physical health trajectories, but overall, these remained significant. These results highlight the need for further investigation of the reasons for the remaining levels and increase in physical disability with longer diabetes duration. In addition, substantial interpersonal variability in the disability trajectories at baseline and in the slopes further suggests the need to investigate population heterogeneity in the experience of diabetes, and to identify factors that potentially could set people with healthy trajectories apart from those with relatively unhealthy trajectories.

Diabetes timing (age at diagnosis)

Contrary to studies reporting a greater clinical burden of diabetes among people with younger age at onset compared to their older counterparts (Hatunic, et al., 2005; Hillier & Pedula, 2001; Hillier & Pedula, 2003; Selvin, et al., 2006; Wong, Moluneaux, Constantino, Twigg, & Yue, 2008), we found that individuals who were of older age at diagnosis are at greatest risk of losing physical functioning once diabetes has been diagnosed. This finding is one of the most important contributions of the study. Age at diagnosis is a significant risk factor for not only the levels of physical disability, but also the rate of change with longer diabetes duration. Therefore it may be clinically erroneous, from the perspective of functional prognosis, to treat people identically, if they are of different ages at diagnosis, even if they are of the same age at the time of clinical presentation. Thus identical treatment of older people with incident

diabetes diagnosed at different ages may contribute to greater functional disparities among older people with diabetes.

That there are age differences in health at diagnosis is not surprising, because old age has negative effects on health. However, that physical and mental health decline faster among people diagnosed at older age can be due to clinical vulnerability, psychosocial vulnerability, or to delays in diabetes diagnosis. For instance, varying experiences with diabetes may stem either from a different pathogenesis of diabetes by a person's age at the time when diabetes was diagnosed (Stewart & Liolitsa, 1999) or from greater vulnerability to diabetes in older age (Biessels, Deary, & Ryan, 2008). It is further possible that psychosocial pathways, including social isolation and involuntary role exit—both of which are reported in the literature (Blazer, Bruce, Service, & George, 1991; Mirowsky & Ross, 1992)—increase the burden and management of diabetes (Nicklett & Liang, 2010), especially when it occurs in older age. Finally, delayed diagnosis among people with older age at diagnosis may also explain our findings, for 26.9% of older adults with diabetes go undetected, and may have entered the study at a later stage of diabetes (Centers for Disease Control and Prevention, 2011). In sum, our study supports the need for different treatment goals according to a person's age at diagnosis, because of the greater risk of physical disability when the disease is diagnosed later among middle-aged and older adults.

Birth cohort

The current study does not support our third hypothesis of worse disability trajectories with older cohorts; to the contrary, disability trajectories show evidence for persistent inequality with longer duration, with fewer ADL/IADL limitations at baseline among people in older

cohorts. These findings could be explained by recent research suggesting that while functional health has improved in almost all age groups, there were no functional gains in the middle-aged group with recent cohorts (Seeman, et al., 2010). The results may therefore reflect general trends in the U.S. population, which place middle-aged adults in recent cohorts at a functional disadvantage compared to their counterparts from older cohorts. Alternatively, the cohort gap in the disability trajectory may stem from lifestyle differences, which can affect functional status – including sedentary lifestyle, lack of physical activity, and obesity. Higher obesity rates with more recent cohorts (Reynolds & Himes, 2007) are reported in the literature. Yet the inclusion of BMI along with other measures of health status and diabetes comorbidities in the mobility disability models did not fully explain the gap in the disability trajectories by cohort. Therefore although BMI may explain some of the reasons why younger cohorts are at greater risk of physical disability with diabetes, its contribution may be marginal. The impact of other measures of lifestyle should be investigated in subsequent studies.

Social stratification

The study contributes to the literature on the relationship between social stratification and diabetes by showing that socio-demographic predictors explained over half of observed physical disability at diagnosis, but explained little of the overall increase. It also highlights important differences in how various social groups experience diabetes. Overall, the disability trajectory of diabetics is best described in terms of persistent inequality among most social groups (Figures 5 & 6) with the exception of Hispanics. For Hispanics (especially Hispanic men) both ADL/IADL and mobility disability trajectories diverged from those of white men, due to low education and declining health. These findings are significant, for previous studies generally found support for

persistent inequality in functional status between Hispanics and non-Hispanic whites with age, or a Hispanic advantage, in the general population (Carrasquillo, Lantigua, & Shea, 2000; Liang, et al., 2008), and in diabetics (Chiu & Wray, 2010). Future studies are therefore needed to confirm these results. In addition, since education fully mediated the effect of ethnicity on functional change, there is also a need to identify the aspects of education that put Hispanics at greater risk of functional decline after a diagnosis of diabetes.

The fact that these results are consistent across different functional measures only strengthens the argument for a functional disadvantage for Hispanics over the course of diabetes.

Study limitations

First, the use of self-reported year of diabetes diagnosis can introduce bias due to possible inaccuracies and to uneven distribution of diagnosis services in the population. A recent analysis of the Women's Health Initiative data reported false-positive self-reported diabetes cases in only 5.5% of the sample (Jackson et al., 2013), suggesting that self-reports are robust measures of diabetes status for those with diabetes. Nevertheless, about 28% of diabetes cases in the population are believed to be undiagnosed (Centers for Disease Control and Prevention, 2014), hence are not included in the study. It is likely that these individuals are healthier than the sample, or have greater difficulties accessing diagnosis services; therefore our estimates may be larger than the "true" parameters of trajectories representing the population of older diabetics. Second, people assigned a diagnosis year could have been diagnosed any time between two consecutive observation periods, leading to potentially greater levels of physical disability at baseline. There is, however, no reason to suspect a systematic bias toward specific social groups. Third, as mentioned above, factors related to functional change and social stratification,

including social, behavioral, biological, and psychological determinants, could partially explain our findings; therefore our models may suffer from omitted variable bias. Further analyses should attempt to assess the impact of these covariates on the disability trajectories. Finally, one important limitation is related to the assumptions for the use of a linear model. Preliminary analyses show that both the linearity and collinearity assumptions between the outcome and the predictors are met at level-1. However, the distribution of the level-1 residuals did not meet the normality requirement; consequently, homoskedasticity assumptions were also violated. Therefore, while our estimates are unbiased, the standard errors may be less efficient. Poisson analyses for negative binomial distribution reveals that the overall story did not significantly change, with two exceptions. 1) The quadratic acceleration was weaker and became statistically marginal. 2) The acceleration in the trajectory among Hispanics began strong, but became smaller with longer diabetes duration, a fact which suggests that the Hispanic disadvantage is stronger earlier in the diabetes career (Appendix A). However, the necessity of testing for linearity assumptions in multilevel models when large samples are used is debated (Gelman & Hill, 2007). In addition, most published studies using the ADL/IADL measure adopt a linear model. Therefore to facilitate comparability of our results to the existing research, we presented the results from the ordinary least square models.

Policy implications

From policy and clinical perspectives, efforts to limit physical disability in late-onset diabetes should be undertaken in conjunction with broader policies for early detection of diabetes and early prevention of functional decline during the illness. The study supports the importance of strategies implemented early in the illness career to prevent increasing physical disability and

disparities over the course of diabetes. But once diabetes is diagnosed, interventions to maintain and improve physical health are the most suitable options to bend the disability curve in middle-aged and older adults.

Incorporate measures of disability as an integral part of patient monitoring – Overall, the study highlights the necessity to include measures of physical disability as an integral part of any comprehensive diabetes management plan as a secondary preventive measure. People with diabetes experience increased physical disability with every added year. While physical health is often included either as a criterion for treatment or as a legitimate outcome to address (American Diabetes Association, 2014; American Geriatrics Society Expert Panel on the Care of Older Adults with Diabetes Mellitus, 2013), the recommendations are limited to the point of care. Given the relatively large rate of change in physical disability on an annual basis, and the link between functional decline, mental health, cognitive health, diabetes outcomes, and diabetes management (Ciechanowski, Katon, & Russo, 2000; Feil et al., 2009; Feil, Zhu, & Sultzer, 2012; Okura, Heisler, & Langa, 2009; Rosen et al., 2003), more sensitive tools and more frequent monitoring at home could help prevent poor diabetes outcomes. These measures could be undertaken by incorporating self-screening tools into electronic devices including smart phones, tablets, e-readers, and the internet with e-mail reminders, and by involving family caregivers and case managers who may be more likely to catch subtle changes in physical functioning.

Develop visual graphs of the course of diabetes in terms of physical disability – The study can potentially improve the quality of care by addressing the lack of congruence between patients' goals for diabetes treatment and those of their treating clinicians. So far, a patient's goal of functional independence (Huang, Gorawara-Bhat, & Chin, 2005) has never been incorporated into the natural history of diabetes. With the current study estimates, visual graphs of the course

of diabetes in measures important to patients can be developed and used as promotional tools and supporting material during diabetes assessment and follow-up visits. They can offer an opportunity for clinicians to discuss the implications of life-style changes, medical treatment, and metabolic outcomes, on functional independence, and possibly on the timing of institutionalization. Physicians and patients can therefore "speak the same language" and share a common goal in diabetes treatment. Future studies can determine the effectiveness of such steps in ensuring patient-physician congruence in setting goals for diabetes management.

Incorporate age at diagnosis as a criterion for diabetes care and management – Diabetes duration and chronological age are consistently used as criteria for diabetes care, but age at diagnosis is not seen as a risk factor for poor diabetes outcome in any of the published recommendations. Therefore the study contributes to clinical care and policy by demonstrating that age at diagnosis is an important criterion for diabetes care. According to our results, a 70-year-old person recently diagnosed with diabetes is not just at greater risk of physical disability at diagnosis, but she or he is also at greater risk of increased physical disability compared to a 70-year-old with longer diabetes duration, who was diagnosed 5 or 10 years earlier; and this difference needs to be taken into account in clinical decisions.

Address the upcoming cohorts of older adults with increasing diabetes – The finding that people in older cohorts have lower physical disability over the course of diabetes underscores the risk that future cohorts of older adults with diabetes may suffer greater physical disability. The prospect of unhealthy older adults, in light of the aging of the population and increased incidence of diabetes, paints a bleak picture for future generations. If the trends in diabetes and related physical disability are not addressed, we can expect an overload of the U.S. health system, including Medicare and Medicaid, as well as a proliferation of families left to care for large

numbers of disabled older adults with diabetes. Ultimately the economic impact of diabetes in middle-aged and older adults can be great, because of an expected higher demand for care and reduced ability to contribute to the labor force and thus to the national and local tax bases.

Primary prevention – In addition to monitoring and addressing the increasing disability trajectory over the course of diabetes, primary intervention to prevent diabetes itself is a preferred policy option, and it has been adopted worldwide. Empirical studies have found that lifestyle intervention programs such as the Diabetes Prevention Program can prevent and delay type 2 diabetes (Diabetes Prevention Program Research Group, 2009). About 500 such programs have already been implemented throughout the U.S. Therefore funding and expanding these evidence-based programs in communities seem to be adequate policy options (American Diabetes Association, 2014). For instance, expanding these programs to local lifestyle programs including gyms, yoga clubs, Weightwatchers®, and Curves® can connect middle-aged and older adults to diabetes prevention and screening. Funding could come from a public-private sector combination involving insurers, Medicare and Medicaid, the Department of Defense, and businesses that have a stake in ensuring the public health of the population for security, political, and economic reasons.

Addressing health inequalities early in the life-course – An additional policy implication of the study findings is that overall, childhood and early adulthood strategies to reduce social inequalities implemented before a diagnosis of diabetes stand the best chance of reducing disparities in physical disability over the course of diabetes. Education was the only modifiable determinant with a continuous effect before and after diabetes diagnosis and it further influenced the link between other social determinants of health—a finding that accords with the observation that socioeconomic status is a fundamental cause of health inequalities (Link & Phelan, 1995).

According to a recent comprehensive report on health inequalities in the U.S., racial differences in health are not observed within neighborhoods with people of similar education and income, which suggests that social conditions, not individual characteristics, may be the most important drivers of health disparities (Bleich, Jarlenski, Bell, & LaVeist, 2012, 2013). Therefore policies to address health inequalities in the general population, and consequently among older adults with diabetes should focus on mutable factors such as income inequalities and residential segregation, which jointly affect educational opportunities and thereby determine life prospects (LaVeist, Gaskin, & Richard, 2009).

Research implications

Several new observations are highlighted by the study. First, research is needed to confirm and explain how and why lower education and income result in greater Hispanic disadvantage with longer diabetes duration. Moreover, the heterogeneity among older people with diabetes poses one of the most difficult challenges for diabetes prevention, management, and care (Kirkman et al., 2012). The study's finding of significant variation in the random component variances requires further investigation to identify individual trajectories of people with successful or pathological aging (Rowe & Kahn, 1997) and to link these trajectories to individual characteristics, including behavioral, psychological and socioeconomic predictors and outcomes, as well as to the availability and use of health services.

CONCLUSION

The event-based approach to the study of diabetes and health change adopted in the current study provides a new way to look at patients' experience of diabetes. While disability

trajectories accelerate after diagnosis for all, people's experience of diabetes varies significantly by age at diagnosis, by cohort, and by social group. Therefore efforts to limit functional decline in late-onset diabetes should be undertaken in conjunction with broader policies for early detection of diabetes and early prevention of functional decline. These policies also need to address the Hispanic disadvantage with longer diabetes duration, and also address the respective roles of race, ethnicity, and gender in functional status before the onset of diabetes. Further research is needed to explain how and why age at diagnosis and education affect disability trajectories with longer diabetes duration. A broader research agenda challenges gerontologists to incorporate the natural history of chronic illnesses into studies of aging.

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Table 2: Descriptive Statistics for the sample

	Mean or %	SD
Measures of time and main outcomes		
Average diabetes duration (years)	3.561	2.315
ADL/IADL disability (0-11)	1.229	1.665
Mobility disability (0-5)	1.745	3.484
Level 1: Time varying covariates at baseline (<i>n</i> =10,883)		
Married (%)	61.551	-
Self-rated health	3.353	1.050
Comorbidities (excluding diabetes)	1.412	0.611
CESD	1.903	2.156
Treatment burden	1.939	0.602
BMI	29.880	5.871
Proxy (%)	9.749	-
Level 2: Time constant variables (<i>n</i> =3307)		
Age at diabetes diagnosis	68.960	9.166
Birth cohort (age in 1995)	60.667	9.647
Non-Hispanic white men (%)	34.624	-
Non-Hispanic black men (%)	6.955	-
Hispanic men (%)	4.929	-
Men of other race (%)	1.331	-
Non-Hispanic white women (%)	33.353	-
Non-Hispanic black women (%)	10.463	-
Hispanic women (%)	6.774	-
Women of other race (%)	1.572	-
Education (%)		
Less than high school (%)	32.156	-
High school graduate (%)	34.333	-
Graduate school (%)	33.511	-
Death at any point in time (%)	27.155	-
Attrition at any point in time (%)	16.208	-

Table 3: Trajectory of ADL/IADL Disability with longer diabetes duration

	M1		M2		M3		M4		M5	
	Est.	Sig	Est.	Sig	Est.	Sig	Est.	Sig	Est.	Sig
<u>Fixed effects</u>										
For intercept										
Intercept	0.824	***	0.652	***	-0.054		0.426	***	0.458	***
Age at diagnosis			0.064	***	0.110	***	0.114	***	0.102	***
Birth cohort (age in 1995)					-0.052	***	-0.060	***	-0.052	***
Female					0.565	***	0.533	***	0.345	***
Non-Hispanic black					0.536	***	0.407	***	0.372	***
Hispanic					0.445	***	0.161		0.033	
Other race					0.177		0.143		0.099	
High school graduate							-0.608	***	-0.339	***
College graduate							-0.595	***	-0.178	*
For linear slope										
Intercept	0.110	***	0.097	***	0.081	***	0.113	***	0.075	***
Age at diagnosis			0.008	***	0.008	**	0.008	**	0.008	***
Birth cohort (age in 1995)					0.001		0.000		-0.002	
Female					0.009		0.005		0.013	
Non-Hispanic black					0.031	+	0.022		0.027	
Hispanic					0.058	**	0.039	+	0.037	+
Other race					-0.028		-0.031		0.001	
High school graduate							-0.041	*	-0.046	**
College graduate							-0.041	*	-0.048	**
For quadratic slope										
Intercept	0.006	***	0.008	***	0.009	***	0.009	***	0.008	***
Age at diagnosis			0.0001	*	0.0001		0.0001		-0.001	
Birth cohort (age in 1995)					0.001	+	0.001	+	0.001	+

Time variant variables

Married								0.004	
Self-rated health								0.279	***
Comorbidities								0.223	***
CESD								0.209	***
Treatment burden								0.143	***

Survey status

Death	1.335	***	1.053	***	1.300	***	1.252	***	0.862	***
Attrition	-0.192	*	-0.125		-0.124		-0.140		-0.158	*
Proxy (time variant)	2.585	***	2.473	***	2.505	***	2.486	***	2.205	***

Random effect

Variance

Intercept	1.906	***	1.884	***	1.834	***	1.822	***	1.571	***
Linear slope	0.237	***	0.223	***	0.221	***	0.221	***	0.202	***
Quadratic slope	0.028	***	0.027	***	0.028	***	0.028	***	0.025	***

Covariance

Intercept x linear slope	0.341	***	0.371	***	0.346	***	0.344	***	0.336	***
Intercept x quadratic slope	-0.455	***	-0.437	***	-0.478	***	-0.498	***	-0.594	***
Linear x quadratic slope	-0.310	***	-0.359	***	-0.352	***	-0.366	***	-0.414	***

Level 1 residual

	1.157	***	1.155	***	1.156	***	1.155	***	1.141	***
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Model statistics

Observations	10883		10883		10883		10883		10883	
Groups	3307		3307		3307		3307		3307	
AIC	139649		139427		139316		139288		136725	
BIC	139764		139569		139556		139564		137045	
Log likelihood	-69811		-69697		-69631		-69613		-68326	
-2ΔLog Likelihood statistic	-		227	***	132.7	***	36.3	***	2573.2	***

Table 4: Trajectory of mobility disability with longer diabetes duration

	M1		M2		M3		M4		M5	
	Est.	Sig	Est.	Sig	Est.	Sig	Est.	Sig	Est.	Sig
<u>Fixed effects</u>										
For intercept										
Intercept	1.482	***	1.389	***	0.862	***	1.260	***	1.304	***
Age at diagnosis			0.035	***	0.058	***	0.061	***	0.053	***
Birth cohort (age in 1995)					-0.028	***	-0.035	***	-0.021	**
Female					0.678	***	0.634	***	0.450	***
Non-Hispanic black					0.020		-0.064		-0.076	
Hispanic					0.076		-0.147	+	-0.242	***
Other race					0.118		0.004		-0.028	
High school graduate							-0.381	***	-0.143	**
College graduate							-0.584	***	-0.188	**
For linear slope										
Linear slope	0.081	***	0.078	***	0.087	***	0.077	***	0.043	***
Age at diagnosis			0.003	***	0.001		0.001		0.001	
Birth cohort (age in 1995)					0.003	+	0.003	+	0.002	
Female					-0.001		-0.002		0.006	
Non-Hispanic black					0.002		0.001		0.007	
Hispanic					-0.002		0.030	*	0.026	*
Other race					-0.005		-0.058	*	-0.028	
High school graduate							0.010		0.002	
College graduate							0.014		0.004	
For quadratic slope										
Quadratic slope	0.003	**	0.004	***	0.003	*	0.003	**	0.002	*
Age at diagnosis			-0.00003		0.00002		-0.00002		-0.0001	
Birth cohort (age in 1995)			0.0002		0.0002		0.0002		0.0002	

Time variant variables

Married								-0.032	
Self-rated health								0.364	***
Comorbidities								0.217	***
CESD								0.123	***
Treatment burden								0.083	***
BMI								0.037	***

Survey status

Death	1.052	***	0.876	***	1.058	***	1.000	***	0.619	***
Attrition	0.004		0.048		0.070		0.047		0.023	
Proxy (time variant)	0.882	***	0.810	***	0.846	***	0.822	***	0.614	***

Random effect

Variance

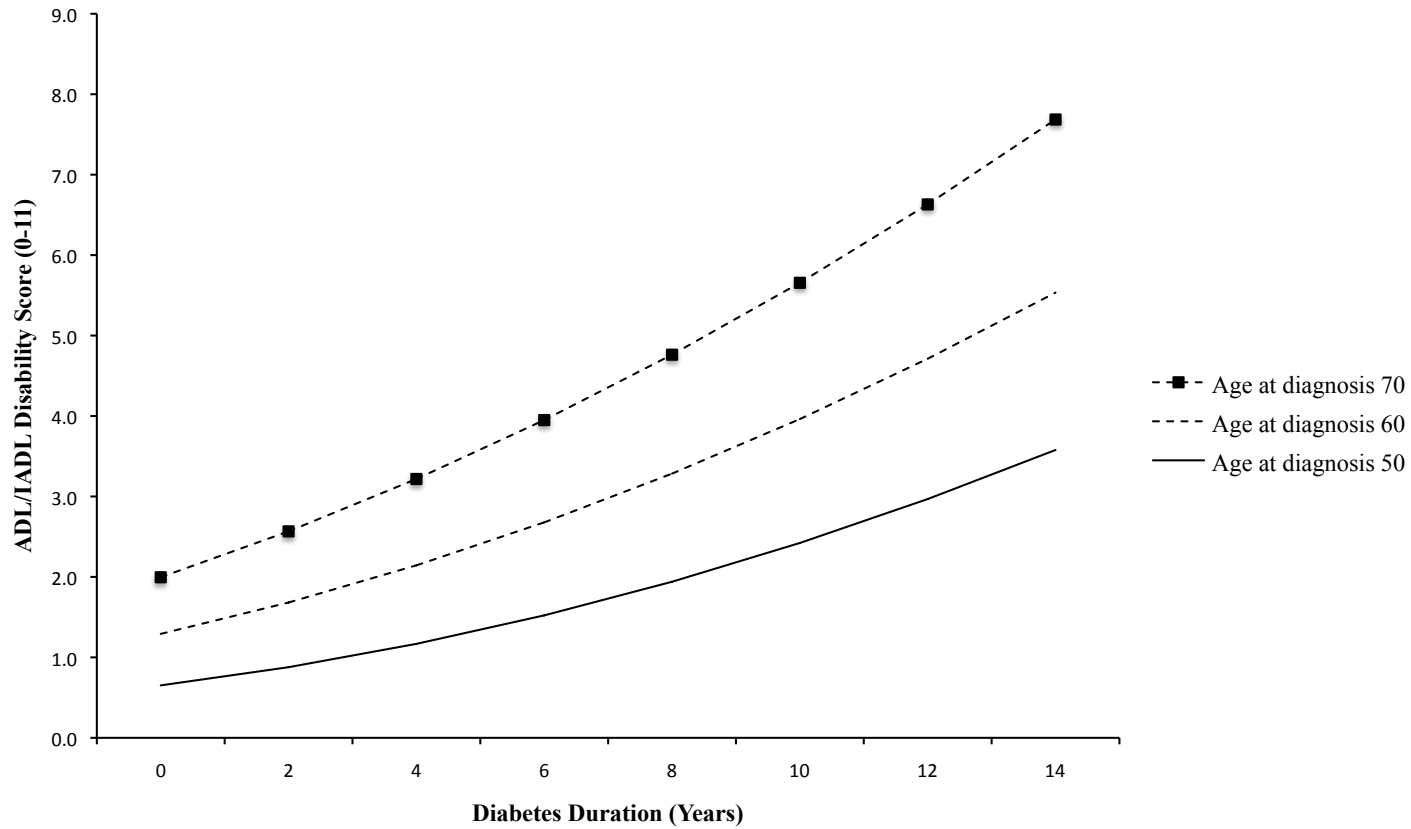
Intercept	1.247	***	1.230	***	1.174	***	1.153	***	0.836	***
Linear slope	0.111	***	0.103	***	0.103	***	0.102	***	0.078	***
Quadratic slope	0.000		0.000		0.000		0.000		0.000	
Level 1 residual	0.945	***	0.944	***	0.945	***	0.945	***	0.931	***

Model statistics

Observations	10883		10883		10883		10883		10883	
Groups	3307		3307		3307		3307		3307	
AIC	130331		130168		130005		129934		124700	
BIC	130420		130283		130219		130183		125002	
Log likelihood	-65156		-65071		-64979		-64939		-62316	
-2ΔLog Likelihood statistic	-		169	***	184	***	79	***	5246	***
Degrees of freedom	-		3		15		4		6	

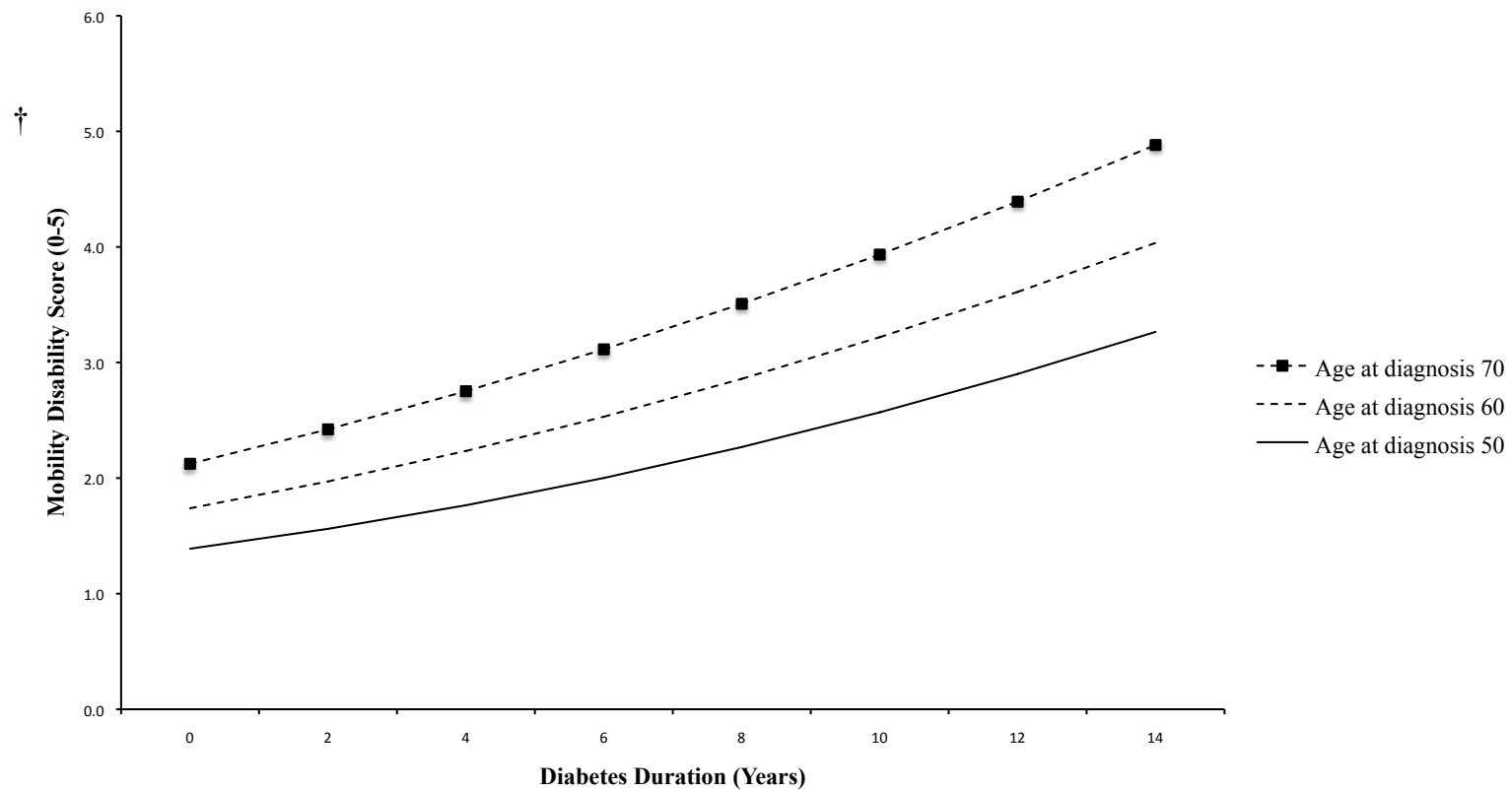
*** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$; + $p < 0.10$; AIC: Akaike Information Criteria; BIC: Bayesian Information Criteria; Log Likelihood Ratio Test tests nested models 2 vs 1, 3 vs 2, 4 vs 3, and 5 vs 4, respectively.

Figure 3: Average trajectory of ADL/IADL disability with longer diabetes duration at different age at diagnosis



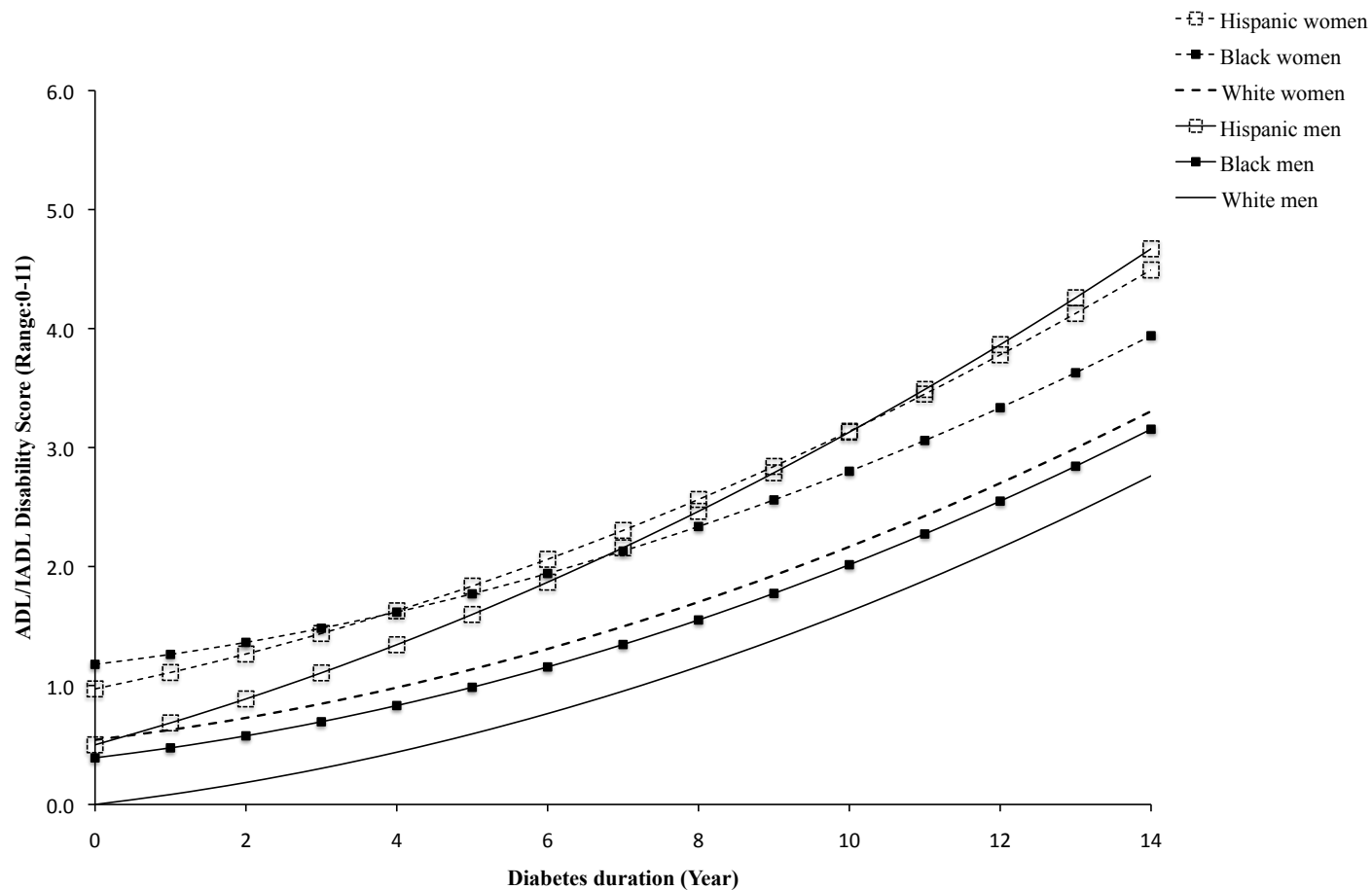
† Model controls for death (=0), attrition (=0), and proxy interview (=0 in each wave); outcome is truncated to improve visualization.

Figure 4: Average trajectory of mobility disability with longer diabetes duration at different age at diagnosis†



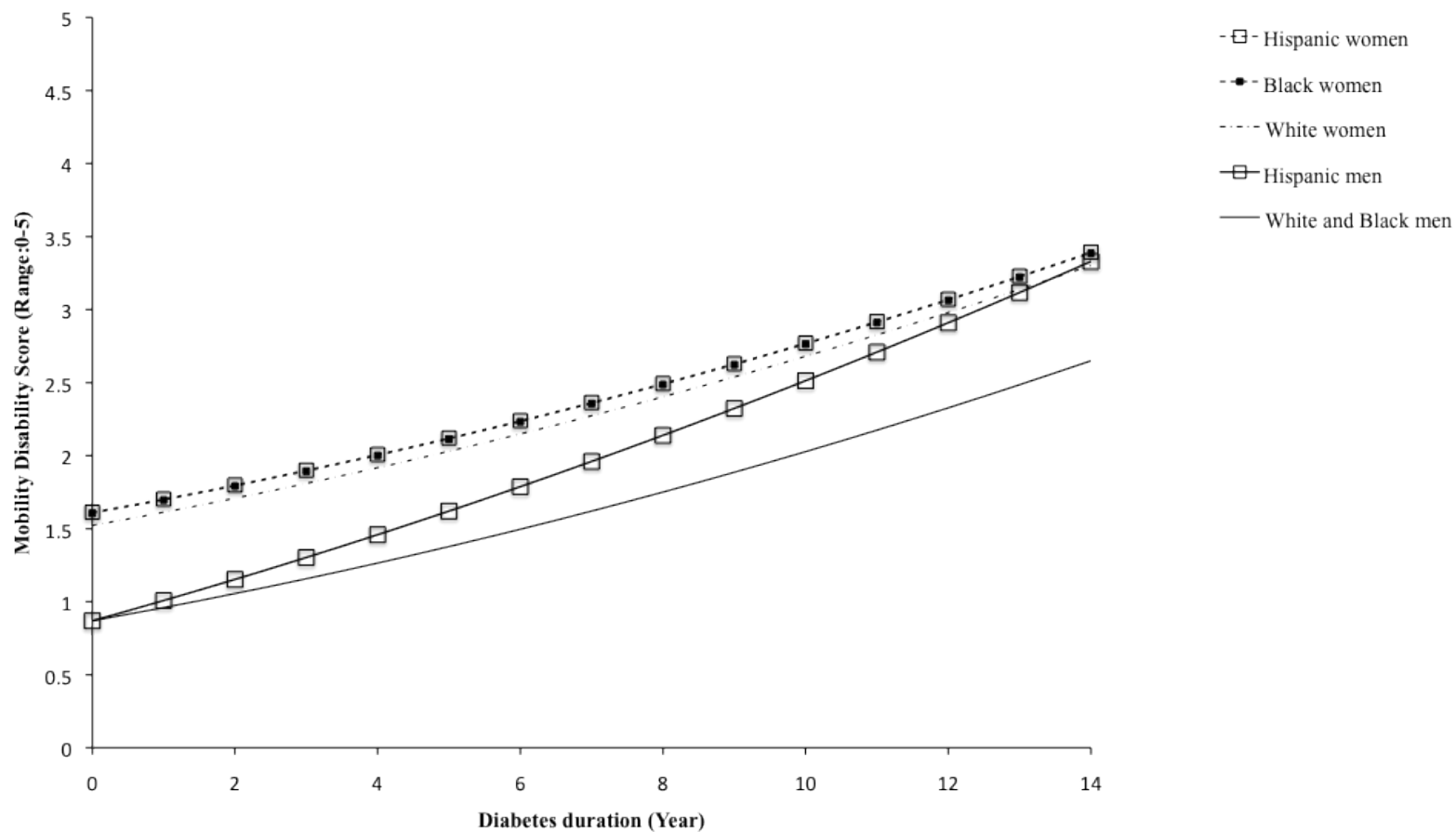
Model controls for death (=0), attrition (=0), and proxy interview (=0 in each wave)

Figure 5: Average trajectory of ADL/IADL disability with longer diabetes duration by race/ethnicity and gender†



†Model controls for death (=0), attrition (=0), proxy interview (=0 at each wave), diabetes timing (mean age at diagnosis) and birth cohort (mean age in 1995); outcome is truncated to improve visualization.

Figure 6: Average trajectory of mobility disability with longer diabetes duration by race/ethnicity and gender†



† Model controls for death (=0), attrition (=0), proxy interview (=0), diabetes timing (mean age at diagnosis) and birth cohort (mean age in 1995).

CHAPTER 3

Depressive Symptoms Trajectory After Diabetes Diagnosis in Middle-Age and Older Adulthood: Age and Social Variations

INTRODUCTION

Studies of diabetes and depressive symptoms

The prevalence of diabetes is expected to rise in the general population and at faster rates in older adults compared with younger adults (Centers for Disease Control and Prevention, 2014). Depressive symptoms, which co-vary with diabetes, also increase after middle adulthood (Clarke, Marshall, House, & Lantz, 2011; Mirowsky & Ross, 1992; Wu, Schimmele, & Chapell, 2012; Xu, Liang, Bennett, Quinones, & Ye, 2010), especially in more recent cohorts (Clarke, et al., 2011; Yang, 2007).

Among diabetics, depression and its symptoms have both policy and clinical relevance. Depressive symptoms exacerbate the negative effects of diabetes on health through biological mechanisms, and by inhibiting self-management behaviors (Chiu, Wray, Beverly, & Dominic, 2010). They also have societal implications, due to their association with increased use of health services, lost productivity, reduced functioning, and diminished quality of life (Egede, Zheng, & Simpson, 2002; Markowitz, Gonzalez, Wilkinson, & Safren, 2011).

Cross-sectional studies of people with and without diabetes find higher levels of depressive symptoms and depression among people with diabetes compared to diabetes-free

adults (Anderson, Freedland, Clouse, & Lustman, 2001; Egede, et al., 2002; Engum, Mykletun, Midthjell, Holen, & Dahl, 2005). A recent meta-analysis reported a 24% increased risk of incident depression among people with type 2 diabetes compared to people without diabetes (Nouwen et al., 2010).

The literature further provides evidence for significant stratification in the link between diabetes and health. Some studies have found no link between depressive symptoms and race or ethnicity (Egede & Zheng, 2003), but others have found higher initial and transient depression among blacks (Peyrot & Rubin, 1999). Sex differences in initial levels of depressive symptoms have also been described (Peyrot & Rubin, 1999). Lower education is linked to both higher initial levels of depression and persistent depressive symptoms (Peyrot & Rubin, 1997, 1999) in patients with type 1 and type 2 diabetes (Engum, et al., 2005). Lack of employment is also associated with major depression (Egede & Zheng, 2003).

Overall, the existing literature is effective in describing the association between diabetes and mental health. It is, however, limited by small, clinical, and ethnically homogeneous samples, and by the use of only one to three observation periods. Longitudinal studies of the effect of diabetes and mental health are lacking, and the few published reports largely focus on exploring the directionality of the relationship between diabetes and depression (Engum, et al., 2005; Golden et al., 2008; Palinkas, Lee, & Barrett-Connor, 2004; Pan et al., 2010).

Furthermore, conceptually these studies use diabetes as a time-invariant personal attribute, meaning that patients are classified as “having diabetes” or “not having diabetes.” This approach can be problematic because the biomedical literature reports that the natural history of diabetes is characterized by biological, physiological, and health change over time (Ramlo-Halsted & Edelman, 2000). Therefore at any point in time “people with diabetes” of the same

age comprise individuals at different stages of their disease. As a consequence, the estimated link between diabetes and mental health is confounded by the natural history of diabetes.

Theoretical framework

We argue that a person's location on his or her disease career at any point in time, and the social context in which this career is formed and maintained, are important markers of mental health status. Therefore the timing of diabetes, the patterns of health change after diagnosis, and the social context in which these health changes occur are all important research questions. Yet because medical sociologists, health services researchers, and epidemiologists are often interested in the impact of diabetes on mental health, diabetes is consistently conceptualized as a time-invariant and individual attribute. What happens to mental health after diabetes has been diagnosed is therefore unknown, and the experiences may well be unique to this population. If they are, this knowledge can inform clinical decisions and policy. The goal of this study is to fill this void in research.

We propose that health changes with time, not only because of the effects of aging, but also because of disease progression and the social environment in which this progression occurs. The current study bridges the gap between the medical and the sociological research by incorporating elements of both clinical medicine and medical sociology in assessing people's experience of diabetes. In addition to taking into account the natural history of diabetes, in which the illness is manifested as a dynamic phenomenon, the current study utilizes the Illness Career Model and the theory of social stratification to describe and estimate health change after a diagnosis of diabetes.

Natural history of diabetes – The natural history of diabetes allows us to conceptualize the disease as a dynamic phenomenon. Accordingly we hypothesize that health change occurs simultaneously with disease progression; therefore time should be measured from the perspective of both the disease and the patient. Age, age at diagnosis, and birth cohort allow us to locate people on their life trajectory, while diabetes onset and diabetes duration provide keys to describe the disease.

Illness Career Model – The Illness Career Model (Aneshensel, 1999, 2013) and its clinical variant the Illness Trajectory Model (Corbin, 1998; Corbin & Strauss, 1991; Strauss & Glaser, 1975) is a sociological model of chronic illness which provides a conceptual framework for understanding people's experience of diabetes. The model allows the conceptualization of mental health change with diabetes as a common experience shared by individuals affected by the condition, starting with its diagnosis. The mental health of people with diabetes can therefore be modeled as a trajectory which links the individual, the illness, and the social environment in which these interact. Since we treat diabetes as a career, the trajectory of depressive symptoms with diabetes begins with the year in which a patient was diagnosed with the disease, and continues along the disease career.

Social stratification and depressive symptoms – According to the theory of social stratification, ascribed characteristics such as race and ethnicity (Williams & Jackson, 2005), age (Riley, 1987), and gender (Bird & Rieker, 1999; Rieker & Bird, 2000), all partially mediated by socioeconomic status (Robert & House, 2000), form the foundation of a system of dominance and subordination, which results in several dualistic social structures. Such structures create

systemically unequal allocation of resources and risks, which in turn leads to poorer health in disadvantaged groups (House, Lantz, & Herd, 2005; House et al., 1994; Lantz et al., 2001; Link & Phelan, 1995).

Barriers to self-management, to access to healthcare, poor quality of healthcare, obstacles to diabetes control, less family support, worse psychological outcomes, distress, and comorbidities are consistently found in the research on blacks, individuals of lower socioeconomic status, women, and Hispanics (Brown et al., 2000; Glasgow, McCaul, & Schafer, 1986; Gucciardi, Wang, DeMelo, Amaral, & Stewart, 2008; Heisler et al., 2007; Jezewski & Poss, 2002; Lanting, Joung, Mackenbach, Lamberts, & Bootsma, 2005; Ponzo et al., 2006; Quandt et al., 2005; Sentell & Halpin, 2006; Szalat & Raz, 2007; Walker et al., 2006). Therefore we expect that with longer diabetes duration, people in socially disadvantaged groups will have poorer mental health trajectories at diagnosis and with longer diabetes duration, due to these inequalities.

EVENT-BASED APPROACH TO THE STUDY OF DIABETES AND HEALTH

The main hypothesis in the current study is that beyond the effects of age and time, physical, mental, and cognitive health changes associated with a chronic illness vary with progression of the disease. Therefore to quantify the course of diabetes in terms of physical, mental, and cognitive changes after a diagnosis of diabetes, we adopted the event-based approach to the study of diabetes and health, which postulates that health trajectories 1) begin with the onset of diabetes; 2) are defined by duration of the disease, which is the measure of time; and 3) are modeled as a function of time-variant and time-constant social determinants of health change.

In this framework, the role of four measures of time relevant to the disease (diabetes duration) and the person (age, age at diagnosis, cohort) are necessary to capture health change with longer diabetes duration. The distinction between these measures of time is necessary in order to ascertain the social causes of health change with diabetes and to facilitate medical and policy intervention; for programs must be tailored to the needs of people who are at different points on their disease trajectory and in their life course.

Chronological age

Time-variant chronological age captures changes stemming only from the process of aging (Riley, 1987). An event-based perspective allows for a more accurate estimate of the health of people with diabetes at every age by using a combination of diabetes duration and age at diagnosis. For instance, the mental health of a patient diagnosed at age 50 can be predicted when they reach 60 or 70 years of age. Likewise, that of a person diagnosed at 70 can be predicted 5 or 10 years later. Since our interest is not in describing the effect of diabetes with age, but rather health changes over the clinical course of diabetes, we have not designated a specific measure of the aging process. The current study is therefore unable to distinguish the effect of diabetes from that of aging at any given time after diabetes has been diagnosed.

Diabetes duration

Rather than age or time, in an event-based approach, diabetes duration is conceptualized as a time-variant measure, which describes health trajectories after a diagnosis of diabetes. Diabetes duration makes it possible to capture health change as the disease progresses, and as

people age along with the disease. Estimates of health status for a particular patient at any point in the progression of the disease, and dependent on the age at diagnosis, accurately measures health at every stage of the natural history of diabetes.

A few studies of transition in and out of mental health states feature diabetes duration as a covariate or a predictor, and find that depression regularly recurs. These studies report a link between diabetes duration and increased risk of diabetes-related depressive symptoms one year after diagnosis (Skinner et al., 2010) and increasing risk of incident depression (Egede & Zheng, 2003; Nefs, Pouwer, Denollet, & Pop, 2012; Thoolen, de Ridder, Bensing, Gorter, & Rutten, 2006). However, the studies have several limitations. First, using diabetes duration as a time-constant predictor does not capture changes in the different areas of life that can influence mental health as the disease unfolds. On the other hand, conceptualized as a time-variant predictor, diabetes duration merely provides a qualitative measure of the stage of diabetes without indicating the nature of health change over the course of diabetes, which exists on a time continuum. Second, these studies are limited by their cross-sectional design, which cannot distinguish between intrapersonal and interpersonal differences in health outcomes. Therefore we do not know how much of the estimated effect of diabetes duration is based on personal differences in health over time or on the true effects of diabetes duration. Finally, studies using two or three time points provide little information about the underlying growth curve of health change with diabetes duration. Multiple underlying trajectories exist as people's mental health varies at diagnosis and with longer diabetes duration, and these interpersonal variations at baseline and with diabetes duration are not captured in the studies cited, which use conventional methods of analysis.

Diabetes timing (age at diagnosis)

Diabetes timing conceptualizes people's location on their life course at the time of diabetes diagnosis. Bury's concept of chronic illness as "biographical disruption" suggests that the event of a chronic illness can define new health trajectories, making it a key measure of the experience of illness (Bury, 1982).

Some studies suggest that patients with earlier onset experience a greater clinical burden of diabetes (Hatunic, Burns, Finucane, Mannion, & Nolan, 2005; Hillier & Pedula, 2001; Hillier & Pedula, 2003; Selvin, Coresh, & Brancati, 2006; Wong, Moluneaux, Constantino, Twigg, & Yue, 2008), but they do not include diabetes duration, which is a strong confounder of the link between age at diagnosis and health. One study, which incorporated diabetes duration, found that the risk of complications—including cataract, diabetes foot, and microvascular complications—increased with every year added to the average age at onset. The risk did not differ for macrovascular or neuropathic complications (Chuang et al., 2006). However, the study used a clinical sample of patients aged 18 and older, and a cross-sectional design. Therefore this research does not provide useful information on the role of age at diagnosis on health change in middle age compared to older adulthood. To the author's knowledge, only one population study tested the link between age at diagnosis and health in middle age compared to older age (Selvin, et al., 2006). But here too, diabetes duration was not adjusted for. As a consequence, the role of diabetes timing on health change with longer diabetes duration remains unclear.

Birth cohort

Cohort effects reflect the impact of exogenous social factors on the health of people of similar age group with shared experiences (Ryder, 1965). Studies investigating cohort effects on

depressive symptoms generally found a reduction in depressive symptoms with successive cohorts, in part attributed to higher education (Clarke, et al., 2011) and to improvement in socioeconomic and marital status (Yang, 2007). For diabetes, educational and behavioral improvement (Schoeni, Freedman, & Martin, 2008) between cohorts, changes in the diagnostic criteria (Koopman, Mainous, Diaz, & Geesey, 2005) and in treatment modalities such as the relaxation in management modalities for older adults (American Diabetes Association, 2014) can exert a positive influence on people's experience of diabetes; but these factors have not been investigated. However, it is reasonable to expect that the mental health of older adults with incident diabetes also improves with successive cohorts.

HYPOTHESES

Hypothesis 1: Studies of loss-related stressors, including bereavement, divorce, and retirement, show that people psychologically adapt within a few years of the event (Aneshensel, Botticello, & Yamamoto-Mitani, 2004; Lucas, Georgellis, Clark, & Diener, 2003; Lynch & George, 2002). But because of the pernicious nature of diabetes, its psychological impact and the burden of its management, the negative effects of diabetes on mental health are likely to intensify over the course of the illness. They are also likely to proliferate into several areas of individuals' lives, including their behaviors, their social relationships, and their health. We hypothesize that people do not adapt to diabetes, because its complications and the burden of treating it result in increasingly poorer mental health with longer diabetes duration, and these changes can be modeled as a trajectory.

This view agrees with the "psychological burden hypothesis," according to which the burden of knowing that one has diabetes, having to manage it, and coping with its complications

and treatment can contribute to higher levels of depression over time (Talbot & Nouwen 2000). It is also in agreement with Harris's conceptualization of a psychological pathway linking continuous exposure to stressors over the course of illness to psychological distress among diabetics (Harris, 2003).

Hypothesis 2: In anticipation that the mental health burden of diabetes and its management are exacerbated by increasing complications (Chuang, et al., 2006) and involuntary role exits, which have adverse effects on mental health and diabetes self-care (Blazer, Bruce, Service, & George, 1991; Mirowsky & Ross, 1992; Nicklett & Liang, 2010), we expect that among middle-aged and older adults with incident diabetes, older age at diagnosis will result in poorer mental health at diagnosis and will be associated with a faster mental health decline with longer duration of diabetes.

Hypothesis 3: In middle-aged and older adults with incident diabetes, people in older cohorts will have higher levels of depressive symptoms at diagnosis and faster increase with longer diabetes duration. This hypothesis stems from evidence of improvement in educational, behavioral and medical improvements in recent cohorts.

Hypothesis 4: Based on the literature, barriers to self-management and to access to healthcare, and poor quality of healthcare, along with obstacles to diabetes control, less family support, worse psychological outcomes, and comorbidities should raise the vulnerability of blacks, women, and individuals of lower socioeconomic status over the course of diabetes, and reduce the Hispanic advantage in the years following diagnosis. Therefore we hypothesize that blacks, Hispanics, women, and individuals of lower socioeconomic status will have higher levels of depressive symptoms at diagnosis compared to their counterparts, and faster increase in the number of depressive symptoms with longer diabetes duration.

METHODS

Data and sample

The Health and Retirement Study (HRS) is a biennial multi-sample nationally representative panel survey of uninstitutionalized U.S. adults aged 50 and older (Juster & Suzman, 1995). Respondents interviewed between 1995 AHEAD/1996 HRS and 2010 HRS³ were included in the study if they reported being diagnosed with diabetes for the first time while in the study, and were aged 50 or older. It is assumed that most respondents had type 2 diabetes because of the late age at onset (Kenny, Aubert, & Geiss, 1995), and because only 5% of diabetes cases in adulthood are attributed to type 1 diabetes (Centers for Disease Control and Prevention, 2014).

Self-reported diabetes status was assessed by consecutive negative and positive response to the HRS diabetes question, which asked whether a doctor had told the respondent he or she had a series of conditions, including diabetes (1=yes, 0=no). Cases with conflicting responses (total of 88) were recoded to “diabetic” if respondents reported taking insulin or oral medication for diabetes in any given year (Liang, Quinones, Bennett, & Ye, 2011).

The data were stacked beginning from the year diabetes was reported for the first time (year of diagnosis=0). Time since diabetes diagnosis was recorded for every wave thereafter between 1995/1996 and 2010, for a total of 7 waves (14 years).

³ Baseline years are 1996 for HRS and 1995 for AHEAD because the functional limitation questions for HRS did not include difficulties using a toilet in the prior waves (1992 and 1994). The wording, structure and coding of the questions were also different. Starting in 1996, however, the question measuring functional limitations was consistent in both wording and coding. In addition, responses to the diabetes question in the years 1994 HRS and 1993 AHEAD were used to confirm that respondents reported being diabetes-free before the initial assessment in 1996 HRS and 1995 AHEAD.

Measures

Depressive symptoms – An abbreviated version of the Center for Epidemiologic Studies Depression rating scale (CES-D) was used. It rates the following: feeling depressed, feeling everything was an effort, restless sleep, feeling lonely, sad, happy, enjoying life, could not get going, and having a lot of energy much of the time in the previous week (Radloff, 1977).

Depressive symptoms were measured every other year. The summary score obtained from the items ranged between 0 and 9, and higher scores reflected more negative affect. The scale has acceptable validity and internal consistency with standardized Cronbach's alpha of 0.80 (Davidson, Feldman, & Crawford, 1994; Radloff, 1977).

Time measure (diabetes duration) – In the event-based approach to diabetes and health change, time is conceptualized as diabetes duration, and is operationalized as the year since diabetes was diagnosed. It ranges from 0 to 14 years after diabetes diagnosis, and is assessed after stacking the data, so that the baseline year for all respondents is the year diabetes was reported the first time.

Other measures of time – Age at diagnosis measures interpersonal age differences in the experience of diabetes. Birth cohort operationalized as respondents' age in 1995, measured cohort or inter-generational age differences. They are both centered on their grand means, and birth cohort was included as a continuous measure because of its monotonous relationship with the outcome.

Measures of social stratification – Race and ethnicity (1=non-Hispanic white, 2=non-Hispanic black, 3=Hispanic, 4=other), sex (1=female, 0=male), and educational attainment (1=less than high school, 2=high school graduate, 3=college graduate) were included as time-

constant covariates. Median household income quartile (highest income is in the highest quartile) was also included as a time-variant covariate.

Time-variant covariates – The accumulation of comorbid conditions and diabetes-specific complications over the course of illness is a risk factor for psychological disturbances (de Groot, Anderson, Freedland, Clouse, & Lustman, 2001; Katon et al., 2004; Peyrot & Rubin, 1999; Talbot & Nouwen 2000; Wu, et al., 2012). Health status, including a person's self-rated health, functional limitations, and comorbid conditions, can further influence depressive symptoms in diabetics (Benoit, Fleming, Philis-Tsimikas, & Ming, 2005; Pan, et al., 2010). Self-rated health assessed on a 5-point Likert scale (1=very good health, 5=very poor health) and mean number of comorbidities (range 0-11), including diabetes-related complications and five major conditions⁴ were included. The functional status index (range 0-11) combined the Katz's Activities of Daily Living index (ADL) and Lawton & Brody's Instrumental Activities of Daily Living index (Katz, Ford, Moskowitz, Jackson, & Jaffe, 1963; Lawton & Brody, 1969; Spector & Fleischman, 1998).

Social and spousal support among diabetics is also tied to psychological health because such support facilitates improved self-care (Murphy, Williamson, & Nease, 1994; Rad, Bakht, Feizi, & Mohebi, 2013), improved access to information, and emotional and instrumental support (Van Dam et al., 2005). A dichotomous variable for being married (1= yes, 0=no) was included.

Finally, the complexity of the treatment regimen reflects the severity of the condition (Benoit, et al., 2005) and the burden of treatment, which can predict psychological impairment (Thoolen, et al., 2006). Treatment burden (1=no treatment; 2=oral; 3=insulin injection; 4=oral and insulin injection) controlled for its potentially confounding effect.

⁴ Kidney problems or proteins in urine, trouble with eyesight, trouble with hearing, incontinence, psychiatric problems, lung problems, hypertension, stroke, cancer, arthritis, and heart disease.

Mortality selection and attrition were addressed by including two time-constant indicators in the models (death: 1=yes, 0=no; attrition: 1=yes, 0=no). A time-variant indicator of proxy interview status was also included to account for the responses obtained from proxy individuals.

Diabetes duration and continuous time-variant covariates were centered on their respective means.

Data analyses

Hierarchical Linear Modeling (HLM) allows quantification and depiction of the average trajectory of depressive symptoms from the time of diabetes diagnosis onward (Raudenbush & Bryk, 2002) by modeling intrapersonal (level 1) and interpersonal (level 2) differences in the outcome.

The level 1 model estimates intrapersonal differences in depressive symptoms for each person and for each year after diabetes diagnosis. For every respondent, the model provides estimates of the outcome at baseline (intercept) and the linear and non-linear slopes for each year following diagnosis. Time-variant covariates can be included at this level.

Linear, quadratic, and cubic models were compared using the log likelihood ratio test in order to select the curvature that best described the data. In addition, penalty-driven criteria, including Akaike Information Criteria (AIC) and the Bayesian Information Criteria (BIC), which address the rising number of parameters with each model, were used in selecting the model. The level of significance for the intercept, linear, and quadratic fixed effects were also taken into account and the most parsimonious model was selected. Results from these preliminary analyses show that the data fit the linear model best. Neither the quadratic nor cubic estimates were significant, and compared to the linear model, changes in AIC and BIC were marginal.

The level 2 model estimates intrapersonal or interpersonal differences in depressive symptoms at baseline and over time. It is at this level that the effect of time-constant covariates on the intercept and the linear slope from the level 1 model are estimated.

First, a baseline linear model was estimated accounting for death, attrition, and proxy interview (Model 1). Subsequent models included age at diagnosis (Model 2), birth cohort and socio-demographic characteristics (Model 3), socioeconomic characteristics, including education and income (Model 4), and time-variant covariates, including marital status and health status measures (Model 5). The level 1 and level 2 models are described below:

$$CESD_{ti} = \pi_{0i} + \pi_{1i} * (\text{diabetes duration}) + \sum \pi_{ki} * X_{kti} + e_{ti}$$

$CESD_{ti}$ is the level of depressive symptoms for each individual i at time t ; π_{0i} is the level of depressive symptoms for each individual at time of diagnosis; π_{1i} is the linear rate of change in depressive symptoms for each individual; diabetes duration is the year since diabetes diagnosis and is the time variable; π_{ki} is the effect of the k th time-variant covariates X_k for individual i on the trajectory; X_{kti} are the k th time-variant covariates in the model; and e_{ti} is the measurement error in the outcome.

$$\pi_{0i} = \beta_{00} + \sum \beta_{01q} * X_{qi} + r_{0i}$$

$$\pi_{1i} = \beta_{10} + \sum \beta_{11q} * X_{qi} + r_{1i}$$

$$\pi_{ki} = \beta_{k0}$$

π_{0i} , π_{1i} , and π_{2i} are the same as above; β_{00} , β_{10} , and β_{k0} are the fixed effects or expected depressive symptoms at mean diabetes duration, and expected linear growth; β_{01q} , and β_{11q} are the effects of the q th time-constant covariates X for each individual i on the intercept and linear slope; X_{qi} is the q th time-constant covariate for each individual i ; r_{0i} and r_{1i} , are random outcome variations at the intercept and linear slope.

To address missing items, the data were imputed using the multiple imputation procedure in Stata® (Little & Rubin, 2002; Rabe-Hesketh & Skrondal, 2008; Schafer, 1997). Five imputed data sets were generated. The risk of selection and response bias due to attrition, mortality, and the use of proxy interviews was addressed with the inclusion of time-constant indicators for mortality and attrition (death or attrition at any point in the study; 1=yes, 0=no), and a time-variant indicator for proxy interview. All analyses were conducted using Stata® software (version 12).

RESULTS

From the 3,307 respondents that met the selection criteria, most were female (52.16%) and white (67.97%), 17.41% black and 11.70% Hispanic. Two-thirds of the respondents had at least a high school degree (67.84%). The mean age at diagnosis was 68.96 years, with a mortality and attrition rate of 27.16% and 16.21%, respectively. Overall, the levels of depressive symptoms were relatively low at baseline, with a mean score of 1.903 (sd=2.156; range 0-20). At baseline, 62% of the respondents had at least one depressive symptom, and by year 14, this number rose to 98%. Table 5 presents additional statistics that describe the sample.

Trajectory of depressive symptoms with longer diabetes duration

In agreement with our first hypothesis, on average, while depressive symptoms were relatively low at the time of diagnosis, there is a modest linear increase in the number of depressive symptoms over the course of illness (intercept=1.621, $p<0.001$; linear slope=0.023; $p<0.001$; M1 in Table 6). Figure 7 offers a visualization of the depressive symptoms' trajectory.

Adjusting for time-constant socio-demographic characteristics reduced the levels of depressive symptoms to 1.155 ($p < 0.001$, M3, Table 6), a 28.75% change. It further reduced the fixed parameter associated with the linear slope. Adjusting for education and income fully mediated the effect of time on depressive symptoms and flattened the trajectory (0.023, $p < 0.001$ to -0.015, $p > 0.050$; M3, Table 6). The direction of the trajectory was reversed after the inclusion of health variables and marital status (linear slope = -0.074, $p < 0.010$).

We found a significant unexplained variance in the intercept (1.488, $p < 0.001$) and linear slope (0.110, $p < 0.001$), which remained significant after controlling for time-constant and time-variant covariates. Model fit improved with each model: Values increased for the model BICs and AICs with each subsequent model.

Diabetes timing (age at diagnosis)

In agreement with our second hypothesis, older age at diagnosis was associated with depressive symptoms at baseline (Figure 7). However, the gap did not increase over time (intercept = -0.269; $p < 0.001$; linear slope = -0.006; $p > 0.5$; M2, Table 6). The estimates were not noticeably modified by the inclusion of time-constant or time-variant covariates. We observed, however, that controlling for age in 1995 by itself increased the negative effect of age at diagnosis on the cognitive levels by 25%, from -0.269 to -0.337, $p < 0.001$ (results not shown).

Birth cohort

Contrary to our third hypothesis, younger cohorts did not experience a better depressive symptom trajectory compared to their older counterparts. In fact, after controlling for age

differences at diagnosis, cohort differences at baseline and in the linear slope were very small and non-significant (intercept=0.002, $p<0.005$; linear slope=0.002, $p>0.05$; Table 6, Model 3).

Social stratification

In agreement with our third hypothesis, the study found support for racial, ethnic and gender inequality at the time of diabetes diagnosis. Hispanics showed the highest levels of depressive symptoms, followed by women and blacks. Yet contrary to our expectation of a widening gap over the course of illness, these differences remained constant over time.

Model 3 in Table 6 shows that higher education and higher median household income protect against depressive symptoms at diagnosis. But there was no accumulated advantage for those with higher socioeconomic status over the course of diabetes. In fact, depressive symptoms increased faster among individuals in the top two income quartiles. This is clearly shown in Figure 8, where the levels of depressive symptoms for individuals in the top two quartiles reached those of individuals in the third highest quartile by year 6, and those in the top quartile by year 10. The negative effect of higher income over the course of diabetes was partially mediated by health status (M5, Table 6), but a significant number (about 40%) remained unexplained by the covariates in the models.

Low socioeconomic status accounted for all of the racial differences in depressive symptoms and for about one-third of the Hispanic disadvantage. While lower socioeconomic status reduced the gender gap in depressive symptoms, health and marital status were the strongest predictors of the gender gap over the course of the illness.

DISCUSSION

The key contribution of the study is its conceptualization of diabetes as a dynamic career, which allows the linkage of its 14-year natural history to dynamic changes in depressive symptoms from the time of diagnosis onward. Therefore compared to conventional approaches, which conceptualize diabetes as a time-constant predictor or use an arbitrary baseline year and measure of time, the current study provides a more accurate description of mental health change after diabetes diagnosis in mid to late life.

Trajectory of depressive symptoms with longer diabetes duration

The results corroborate earlier findings of modest levels of depressive symptoms in old age (Wu, et al., 2012; Yang, 2007) and rising incidence over longer duration (Skinner, et al., 2010). But contrary to trajectories of depressive symptoms after bereavement, which show only a transient increase after the event (Aneshensel, et al., 2004; Lucas, et al., 2003; Lynch & George, 2002), and studies of major depression, which show higher risk of depression before 5 years and after 10 years of diabetes duration (Egede & Zheng, 2003), we found that middle-aged and old-aged adults with diabetes do not emotionally adapt to their condition over time. Rather, the progression of diabetes is characterized by modest but persistent depressive symptoms over 14 years after diagnosis, as demonstrated by a linear increase in the trajectory. On average, and after adjusting for age at diagnosis and cohort effects, there is a 1.35% increase in depressive symptoms per year from initial levels of 1.620 at diagnosis. The results also support both the “psychological burden hypothesis” (Talbot & Nouwen 2000) and Harris’s conceptualization of a psychological pathway which links continuous exposure to stressors over the course of illness to psychological distress among diabetics (Harris, 2003).

Adjustment for socioeconomic status and health status reversed the direction of the CES-D growth rate for the overall sample, which changed from an ascending to a descending trajectory. These results mirror earlier reports showing that social status reverses the negative effects of aging on depressive symptoms (Clarke, et al., 2011; Lynch & George, 2002; Mendes de Leon, Barnes, Bienias, Skarupski, & Evans, 2005; Taylor & Lynch, 2011; Xu, et al., 2010; Yang, 2007). They also highlight the need to detect and adequately address the growing psychological needs of middle-aged and older adults with late-onset diabetes all along their disease career. They further substantiate the view that change in depressive symptoms with time is not inherently tied to the stage of diabetes. Rather, education and income synergistically determine the mental health outlook of middle-aged and older adults with diabetes. Therefore future research should elucidate the components of education and socioeconomic status that might be most relevant to diabetes management and outcomes. In addition, given the modest increase in depressive symptoms over time, research is needed to determine the level of depressive symptoms at which self-management behaviors and clinical outcomes begin to be affected in the course of diabetes.

Diabetes timing (age at diagnosis)

Our second hypothesis that older age at diagnosis would result in worse mental health after diabetes diagnosis was substantiated by the findings. The study provides evidence that old age at diagnosis is a key determinant of poor mental health over the course of diabetes, with an increasingly negative influence with longer diabetes duration. Therefore ignoring the timing of diabetes –measured as people’s age at diagnosis– as a risk factor in clinical practice and medical guidelines for diabetes management can contribute to greater disparities in mental health among

older adults with diabetes. The study findings are particularly salient to policy, because the literature reports worse clinical profiles among people with diabetes diagnosed during middle-age compared to those with later-onset diabetes (Hatunic, et al., 2005; Hillier & Pedula, 2001; Hillier & Pedula, 2003; Selvin, et al., 2006). Yet according to our study, these findings are confounded by the natural history of diabetes.

Several features of our study strengthen the validity of its findings and support the quality of the results. First, it used a national representative sample of older adults with self-reported diabetes, which improves its generalizability. Second, it conceptualized time variables important to both the person and the disease and is therefore able to tease out the relative contribution of each. Finally, it employed statistical methods, which took into account the structure in the data, thereby provide more accurate estimates for both interpersonal and intrapersonal differences in health.

The results of the study support Bury's concept of the timing of illness as a biographical disruption (Bury, 1982) in the sense that late age at diagnosis sets older adults with incident diabetes on a trajectory of worse depressive symptoms, with longer diabetes duration. Older age is also tied to a series of social events which can negatively impact mental health and the experience of diabetes. For instance, involuntary role exits, including retirement and widowhood, and declining social support, physical functioning, sense of control, and income in old age are well documented, and these can negatively affect mental health (Blazer, et al., 1991; Mirowsky & Ross, 1992) and diabetes self-care (Nicklett & Liang, 2010). It is therefore not surprising that diabetes diagnosis results in greater disparities in mental health by age at diagnosis.

Birth cohort

Our expectation that socio-economic, behavioral, and medical improvements would result in improved mental health trajectories in younger cohorts of diabetics was not substantiated by our findings (Hypothesis 3). There was no evidence that within 14 years after a diagnosis of diabetes, people in younger cohorts might be better off compared to older cohorts. Therefore among middle-aged and old-aged adults with incident diabetes, social and economic gains observed in the general population do not translate into better mental health with younger cohort. In light of these results, earlier findings that younger cohorts have better mental health in the general population may not accurately depict the link between cohort and health with late-onset diabetes (Clarke, et al., 2011; Yang, 2007).

Economic and social gains in younger cohorts may be offset by increases in risk factors tied to diabetes outcomes in our sample. For instance, physiological changes, including higher obesity rates in more recent cohorts (Reynolds & Himes, 2007), coupled with worse functional health in younger cohorts of peri-retirement age (Seeman, Merkin, Crimmins, & Karmalanga, 2010) are documented. Although functional limitations were included in the current study and did contribute to the overall trends (along with other measures of health status), obesity was not; therefore future studies may need to investigate its impact on cohort differences with late-onset diabetes.

Social stratification

One additional contribution of the study is its depiction of mental health change in various social groups after diabetes diagnosis. Depressive symptoms after a diagnosis of diabetes are characterized by persistent inequality over the course of diabetes, with more depressive

symptoms in Hispanics, blacks, and women compared to their counterparts. This finding was somewhat unexpected, for we hypothesized widening gaps as diabetes progressed, due to the abundant literature that described a greater burden of diabetes among Hispanics, blacks, and women; and a greater burden of depressive symptoms among Hispanics and blacks (George & Lynch, 2003; Glasgow, et al., 1986; Klein, Shankman, & Rose, 2008; Legato et al., 2006; Szalat & Raz, 2007; Walker, et al., 2006; Walsemann, Gee, & Geronimus, 2009; Xu, et al., 2010; Yang, 2007). Yet our study did not show evidence of these findings.

Our study also revealed the negative effect of higher income on the trajectory of depressive symptoms, in that individuals in the top two quartiles begin with lower levels of depressive symptoms, but converge within the first 6 to 10 years after diagnosis. These results have both clinical and policy implications, because although a few studies have reported a reduction in the advantageous effect of income on mental health with old age (Kim & Durden, 2007; Mirowsky & Ross, 2001), most studies have found that lower social status is tied to faster growth of depressive symptoms (Aneshensel, et al., 2004; Liang, et al., 2011; Lynch & George, 2002; Yang, 2007) and higher levels of major depression (Anderson, et al., 2001; Egede, et al., 2002; Katon, et al., 2004). This counter-intuitive finding may be related to a ceiling effect of the measure of depressive symptoms among people who have less education. Alternatively, people with higher income and more demanding jobs may be more reluctant to consult professionals about their psychological problems, resulting in increased mental health morbidity and poor diabetes outcome. For instance, in a study of several Asia Countries, adults with higher income who have lower rates of depressive symptoms, are also less likely to seek treatment for these symptoms (Fukuda & Hiyoshi, 2012). If similar trends exist among older U.S. adults with

diabetes, these trends may explain the fact that mental health worsens among with higher income over the course of their diabetes.

Limitations

Because of sample selection and the measures we used, the study has several imitations. First, self-reported diabetes could introduce self-selection bias due to differential access to care among social groups; but a recent study found limited cases of false-positive self-reported diabetes (Jackson et al., 2013). Second, the CDC found that about 28% of diabetes cases are undetected; therefore our estimates may be larger than the true estimates due to the exclusion of undiagnosed diabetics. Third, clinical and biological changes in diabetes can start up to 7 years before diagnosis (Ramlo-Halsted & Edelman, 2000). As a consequence, initial levels of depressive symptoms could be inflated at diagnosis. In addition, information during the first two years after diagnosis is not available; at least one study found that increases in psychological distress could start as early as the first year after diagnosis (Skinner, et al., 2010). Therefore subtle changes in mental health might have been overlooked in our study. Nevertheless, the overall message of the study remains unchanged, for we found a steady increase in depressive symptoms over 14 years. Fourth, the effect of income on mental health may be influenced by reverse causation. This issue was addressed with the inclusion of income as time-variant, which also captures change in income over the course of illness. Finally, the effect of aging itself cannot be isolated in the study. But again, comparing people with diabetes to those without diabetes was not the goal of the current study, which was to describe mental health change with diabetes duration.

POLICY IMPLICATIONS

Overall, we found that on average, people do not adapt to their condition after they have been diagnosed with diabetes in middle-age and old age; there is a linear increase in depressive symptoms with longer diabetes duration. But although the decline in mental health is relatively small, even modest changes can result in poor health, an increase in the use of health services, institutionalization, and increased demands on the health system; for these changes can lead to a worsened biological profile, worse diabetes outcomes, and poor diabetes self-management (Bruce, 2000; Chiu, et al., 2010; Chodosh, Miller-Martinez, Aneshensel, Wight, & Karlamangla, 2010).

The study has several major implications for policy. First, it is clear from the results that comprehensive diabetes management should incorporate measures of mental health as an integral part of diabetes monitoring in old age. Several guidelines already recommend mental health assessment in the U.S. (American Diabetes Association, 2014; American Geriatrics Society Expert Panel on the Care of Older Adults with Diabetes Mellitus, 2013) and internationally (International Diabetes Federation, 2010; Sinclair et al., 2011). However, all of these guidelines limit their recommendations to the point of clinical care, in the doctor's office. Yet monitoring mental health at home and in the community is just as important; for subtle changes in mental health between visits can interfere with diet, exercise, diabetes care, and diabetes monitoring (Ciechanowski, Katon, & Russo, 2000; Rosen et al., 2003). The screening and monitoring of changes in mental health should also involve not only the patient but also family caregivers and case managers. This more comprehensive personal involvement could be achieved by developing and incorporating screening tools into electronic devices such as smart phones, tablets, and the

internet with built-in reminders; and in addition, creating efficient systems of referral to mental health services.

A second implication for policy is that the study identified diabetes duration and age at diagnosis as key elements in diabetes management and treatment. Determining age at diagnosis can help predict mental health change in people with late-onset diabetes, reduce the effects of population heterogeneity in health outcomes during clinical care, and achieve better individualized diabetes management. For instance, a 70-year-old recently diagnosed with diabetes is at greater risk of mental health decline after diagnosis than a 70-year-old with longer diabetes duration, who was diagnosed 5 or 10 years earlier. Yet based on current recommendations, which only focus on diabetes duration and age, the level of care and attention might be higher for the 70-year-old whose diabetes was of longer duration.

Regarding social stratification, findings of persistent inequality indicate that childhood and early adulthood may be the best times to intervene in order to reduce mental health disparities with late-onset diabetes. Given the anticipated rise in the size of the Hispanic population, greater diversity in the U.S. population, faster increase in diabetes incidence among socially disadvantaged people, and the increasing longevity among people with diabetes, we can expect an increase in the number of older diabetic adults who suffer from poor mental health. Consequently we can also anticipate a greater need for mental health treatment and diabetes care, as well as for hospitals and nursing homes, and thus a greater strain on caregivers, mainly women, and on younger cohorts of Americans. For the country as a whole, the U.S. may face an increasing financial burden due to loss of productivity and a greater burden on existing social programs, including Medicare, Medicaid, and Supplemental Security Income.

It is important to acknowledge that although these recommendations can reduce the impact of mental health decline on diabetes outcomes, primary interventions remain the first line of intervention. To this effect, existing programs that are effective at reducing risk factors or diabetes onset (Diabetes Prevention Program Research Group, 2009), including poor diet and lack of physical exercise, should be further supported financially in conjunction with a general culture of healthy living.

CONCLUSION

When a social condition is time-variant, its occurrence can explain long-term changes in health, over and beyond the effect of age. This perspective has been recently applied in studies of life events, which model health as a function of time after the event. However, the time-variant nature of diabetes is often overlooked in studies on diabetes. The current study adopted the view that diabetes is dynamic, and found that after diagnosis, middle-aged and older-aged adults experience a moderate but steady increase in depressive symptoms. Our results further highlight that the rise in depressive symptoms after late-onset diabetes is socially patterned, and as such can be addressed through policy. Old age at diagnosis along with socioeconomic status are important factors that should be taken into account, to ensure healthy and equitable mental health with late-onset diabetes. Accordingly, policies that address depressive symptoms with incident diabetes in late adulthood should incorporate broad interventions before diagnosis, in order to reduce economic and health disparities which set women, blacks, Hispanics, and people of lower socioeconomic status on a trajectory of worse depressive symptoms over their illness career. Such policies would have to implement strategies for the early detection of diabetes and depressive symptoms in the oldest population.

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Table 5: Descriptive statistics for the sample

	Mean or %	SD
Measure of time and main outcome		
Diabetes duration (years)	3.561	2.315
CESD (0-9)	1.903	2.156
Level 1: Time varying covariates (<i>n</i> =10,883)		
Married (%)	61.551	-
ADL/IADL disability	1.229	1.665
Self-rated health	3.353	1.050
Comorbidities (excluding diabetes)	1.412	0.611
Treatment burden	1.939	0.602
Proxy (%)	9.749	-
Level 2: Time constant variables (<i>n</i> =3307)		
Age at diagnosis	68.960	9.166
Birth cohort (age in 1995)	60.667	9.647
Female (%)	52.162	-
White (%)	67.978	-
Black (%)	17.418	-
Hispanic (%)	11.702	-
Other race (%)	2.902	-
Education		
Less than high school (%)	32.156	-
High school graduate (%)	34.333	-
Graduate school (%)	33.511	-
Median household income (USD)		
Quartile 1	8,620	3,582
Quartile 2	20,868	4,191
Quartile 3	38,993	6,870
Quartile 4	107,487	101,140
Death at any point in time (%)	27.155	-
Attrition at any point in time (%)	16.208	-

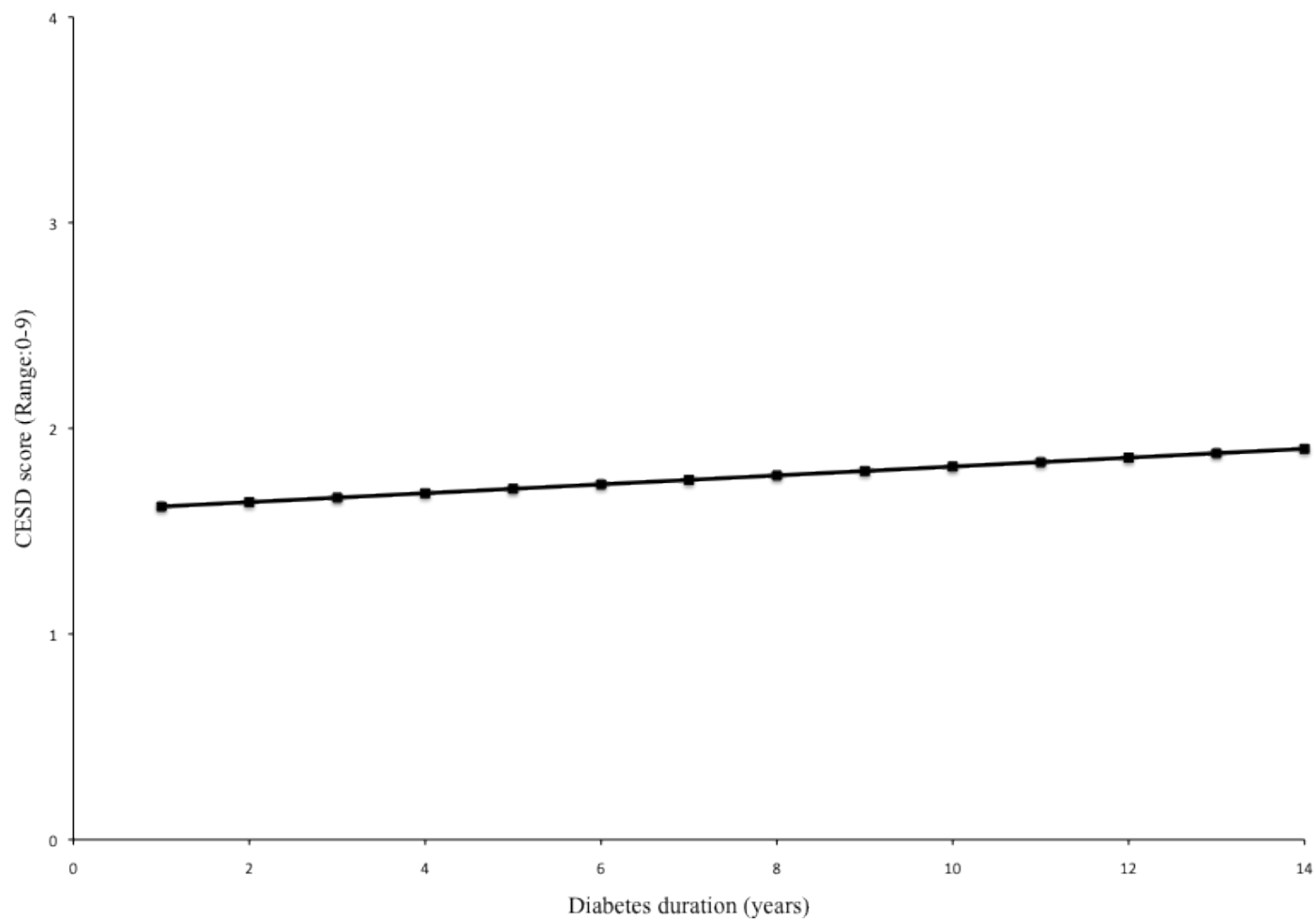
Table 6: Average trajectory of depressive symptoms with longer diabetes duration

	M1		M2		M3		M4		M5	
	Est.	sig.	Est.	sig.	Est.	sig.	Est.	sig.	Est.	sig.
<u>Fixed effects</u>										
For intercept										
Intercept	1.621	***	1.632	***	1.155	***	2.201	***	2.151	***
Age at diagnosis			-0.0004		-0.002		0.001		-0.048	***
Birth cohort (age in 1995)					0.002		-0.011		0.020	*
Female					0.586	***	0.414	***	0.089	+
Black					0.289	**	0.019		-0.039	
Hispanic					0.784	***	0.271	**	0.324	***
Other race					0.191		0.113		0.097	
High school graduate							-0.514	***	-0.261	***
College graduate							-0.756	***	-0.454	***
Income quartile 2							-0.273	***	-0.058	
Income quartile 3							-0.554	***	-0.211	**
Income quartile 4							-0.668	***	-0.204	**
For linear slope										
Linear slope	0.023	***	0.025	***	0.029	**	-0.015		-0.074	**
Age at diagnosis			0.002	*	-0.0001		-0.001		-0.0004	
Birth cohort (age in 1995)					0.002		0.003		0.001	
Female					-0.014		-0.005		-0.008	
Black					0.013		0.025		0.034	*
Hispanic					-0.015		0.005		-0.007	
Other race					-0.050		-0.041		-0.011	
High school graduate							-0.002		0.006	
College graduate							-0.002		0.007	
Income quartile 2							0.024		0.016	
Income quartile 3							0.055	**	0.034	*

Income quartile 4					0.056	**	0.036	*
<i>Time variant variables</i>								
Married							-0.448	***
ADL/IADL disability							0.225	***
Self-rated health							0.327	***
Comorbidities							0.612	***
Treatment burden							0.004	
<i>Survey status</i>								
Death	0.770	***	0.788	***	0.824	***	0.665	***
Attrition	0.071		0.069		0.026		-0.028	
Proxy	1.060	***	1.052	***	1.071	***	1.023	***
<u>Random effect</u>								
Variance								
Intercept	1.488	***	1.490	***	1.431	***	1.346	***
Linear slope	0.110	***	0.108	***	0.107	***	0.107	***
Intercept x linear slope	-0.115	*	-0.112		-0.107		-0.059	*
Level 1 residual	1.435	***	1.435	***	1.435	***	1.437	***
<u>Model statistics</u>								
Observations	10883		10883		10883		10883	
Groups	3307		3307		3307		3307	
AIC	183470		183466		183301		182987	
BIC	183550		183564		183488		183263	
Log likelihood	-91726		-91722		-91629		-91462	
-2Δlog likelihood statistic	-		8	*	185	***	334	***
Degrees of freedom	-		2		10		10	

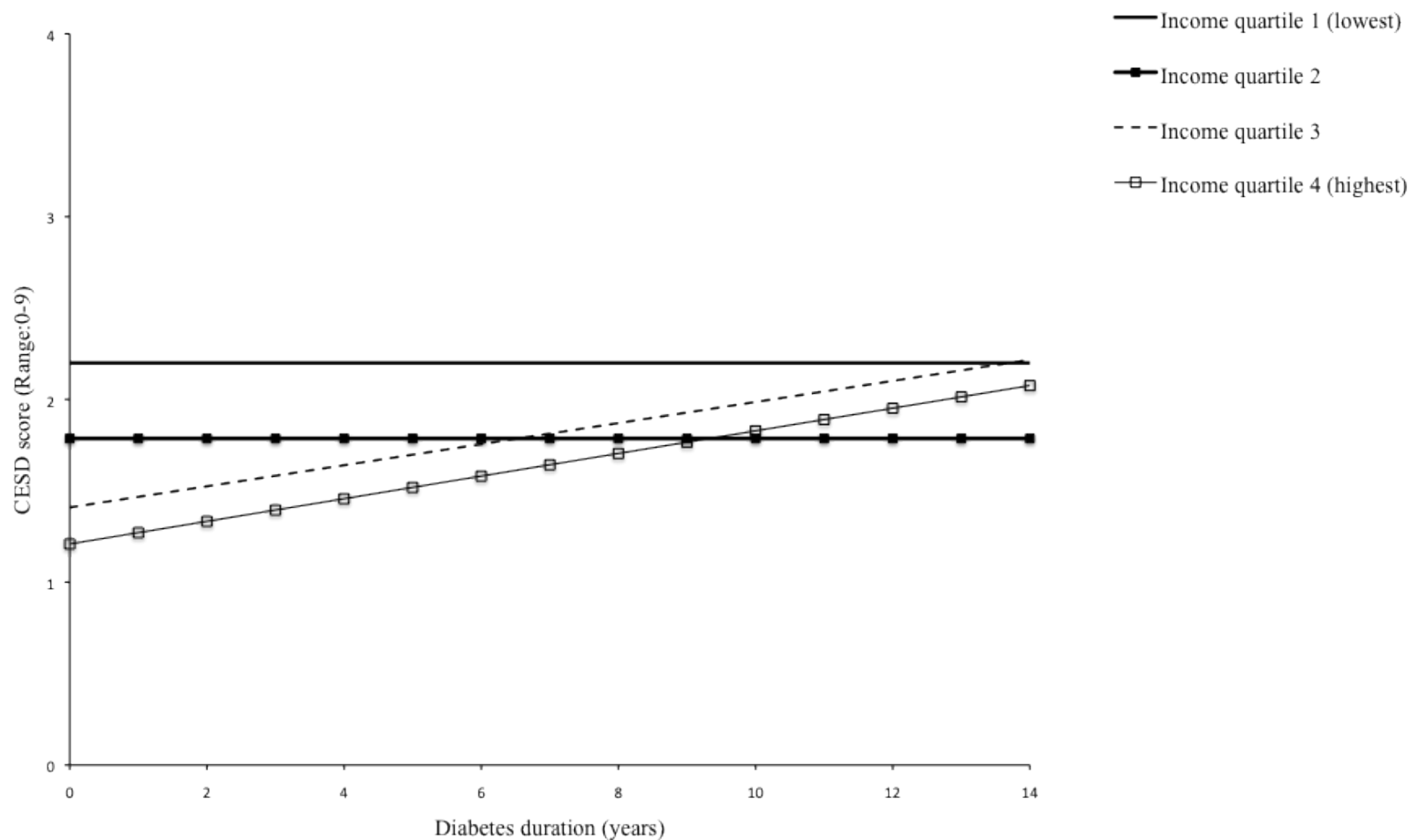
*** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$; + $p < 0.10$; AIC: Akaike Information Criteria; BIC: Bayesian Information Criteria; Log Likelihood Ratio Test tests nested models 2 vs 1, 3 vs 2, 4 vs 3, and 5 vs 4, respectively

Figure 7: Average depressive symptoms trajectory with longer diabetes duration*



† Model controls for death (=0), attrition (=0), proxy interview (=0 in each wave); outcome is truncated to improve visualization

Figure 8: Average depressive symptoms trajectory with longer diabetes duration by income quartile†



*† Model controls for death (=0), attrition (=0), interview (=0), age at diagnosis (mean age at diagnosis), birth cohort (mean age in 1995), race/ethnicity (non-Hispanic white), gender (female), education (graduate school); outcome is truncated to improve visualization

CHAPTER 4

Trajectory of Cognitive Functioning After Diabetes Diagnosis in Middle-age and Later Adulthood

INTRODUCTION

Background

Cognitive impairments increase the risk of dementia (Plassman et al., 2008). They are further linked to reduced functional independence (Dodges, Du, Saxton, & Ganguli, 2006) and to increased healthcare and societal costs (Albert et al., 2011; Chodosh et al., 2004; Lin & Neumann, 2013). In 2002, 22% of adults aged 71 and older had non-dementia related cognitive impairments (Plassman, et al., 2008). A recent empirical study estimated that 4.8 million U.S. adults aged 72 and older developed non-dementia-related cognitive impairments within a period of 5.9 person-years (Plassman et al., 2011).

Cognitive impairments and type 2 diabetes are both degenerative conditions, which increase in prevalence with age. Type 2 diabetes exacerbates poor cognition through mechanisms involving dysglycemia, hypertension, micro- and macro-vascular complications, and depression (Cukierman-Yaffe, 2010; Reijmer, van den Berg, Ruis, Kappelle, & Biessels, 2010). Cross-sectional studies found an effect size of diabetes of 0.2 to 0.8, and a positive association with cognitive decline (Stewart & Liolitsa, 1999). Reviews of longitudinal studies also report a consistent negative change in cognitive function associated with diabetes (Allen, Frier, &

Strachan, 2004; Awad, Gagnon, & Messier, 2007; Cukierman, Gerstein, & Williamson, 2005; Reijmer, et al., 2010; Tilvis et al., 2004). Some studies report a cognitive gap between diabetics and non-diabetics in old age, which although modest (Reijmer, et al., 2010), has significant clinical and economic implications (Lin & Neumann, 2013). Yet the impact of diabetes on health, including cognitive health, has been based on conceptualizing diabetes as a time-constant individual attribute. In other words, individuals under study are classified into two categories: individuals with diabetes and individuals without diabetes.

Theoretical framework

Conceptually, the view of illness as a time-constant attribute directly contradicts the biomedical perspective of the natural history of disease and sociological theories of the experience of illness.

Natural history of diabetes – According to the natural history concept, type 2 diabetes is characterized by a series of phases, which are themselves defined by biomedical, physiological, and clinical characteristics and norms (Ramlo-Halsted & Edelman, 2000). On the basis of these characteristics and norms, identification of the phase within which each patient with diabetes falls determines the type and course of care, as well as the prognosis. We therefore adopt the view that diabetes is a dynamic phenomenon. Therefore, estimates of the link between diabetes and cognitive health in earlier longitudinal studies, which used age and arbitrary time (usually study wave) are confounded by the natural history of diabetes; that is, the cumulative damages to a diabetic patient's biological, psychological, and social health, and the social, behavioral, and medical interventions that are implemented to bend the health curve among diabetics. At any

point on the age or time continuum, people with diabetes represent a heterogeneous group in which the natural history of diabetes manifests itself uniquely in each diabetic person.

The Illness Career Model – The Illness Career Model (Aneshensel, 1999; Goffman, 1961) and its clinical version, the Illness Trajectory Model (Corbin, 1998), is a sociological theory of people’s experience of illness. It conceptualizes the experience of illness as dynamic, and views illness (its onset or diagnosis) as the starting point of a new life trajectory characterized by health, behavioral, and social changes. The Illness Career Model portrays health change with diabetes as a common experience, which is influenced by interactions between the ill person and their disease, as well as individual, family, community, medical, and other social factors that impact health. Health change with a chronic illness is therefore more accurately represented as a trajectory or an “illness career,” the shape of which is a function of dynamic factors specific to the disease, the person, and the social environment. While these two theories focus more on psychosocial and behavioral changes due to illness, this concept can apply to any health change following a life event.

Social Stratification Theory – Social Stratification Theory also informs the study. It stipulates that age, race, gender, and ethnicity establish differentiations in social systems which determine one’s life chances. Stratification manifests in unequal distribution of resources and benefits that can mitigate the negative effects of disease, resulting in worse health in socially disadvantaged groups; and socioeconomic status mediates the link between agents of stratification and health outcomes (Bird & Rieker, 1999; House, Lantz, & Herd, 2005; House et al., 1994; Lantz et al., 2001; Link & Phelan, 1995; Rieker & Bird, 2000; Riley, 1987; Robert & House, 2000; Williams & Jackson, 2005).

Cross-sectional studies of people with diabetes found that blacks experience lower cognitive performance and faster cognitive decline in more complex tasks (Obidi et al., 2008); and these differences are attributed to greater susceptibility to diabetes and its complications (Wessels et al., 2011). Older Mexican Americans have lower cognition at baseline, but decline at rates similar to those of whites of similar age (Karlman et al., 2009). To the author's knowledge, this relationship has not been tested among diabetics. Lower socioeconomic status, as assessed by wealth, income (Karlman et al., 2009), or education (Lievre, Alley, & Crimmins, 2008) is an additional risk factor for lower cognition and faster decline in older adults. Gender, on the other hand, is usually not tied to cognition among diabetics (Bruce et al., 2008; Reijmer, et al., 2010). In addition to social inequalities in cognitive functioning, social stratification can potentially influence the progression of diabetes and its impact on cognitive change after diagnosis. Lower socioeconomic status can limit access to healthcare, obstruct compliance with diabetes treatment (Obidi, et al., 2008; Reijmer, et al., 2010; Wessels, et al., 2011), and can induce stress, which in turn has neuro-degenerative consequences (McEwen, 1998; O'Brien, Ames, & Schweitzer, 1993).

Although this research viewed both disease and the experience of disease as dynamic, cognitive health change has not been investigated in the context of dynamic diabetes. As a consequence, several questions remain unanswered. 1) What is the pattern of cognitive change with longer diabetes duration? 2) How does diabetes timing affect cognitive health with longer diabetes duration? 3) Does birth cohort influence cognitive change with longer diabetes duration? 4) Finally, does the experience of diabetes vary among people of different social backgrounds or is it the same? These questions form the basis for the current study.

The study is grounded in the belief that the severity of cognitive decline associated with diabetes varies not only with age and time, but also with progression of the disease. Ascribed characteristics (age, race, ethnicity, cohort, gender) directly, but also indirectly through their impact on attained social status (education, income, marital status), diabetes timing, medical, behavioral, psychosocial, and health status can further influence health change over the course of diabetes.

EVENT-BASED APPROACH TO THE STUDY OF DIABETES AND HEALTH

In agreement with this framework, and to investigate health change as it co-occurs with disease progression, *diabetes duration* is the measure of time that will permit the accurate characterization of cognitive change with diabetes. We further focus on middle-aged and older adults with incident diabetes for several reasons. First, the prevalence of cognitive impairments and diabetes is increasing in the oldest age groups. Second, the U.S. population is aging at unprecedented rates. Finally, obesity, which is one of the most important risk factors for diabetes, is also rising in both prevalence and incidence in older adults. Therefore the prospect of reduced functional independence due to poor cognitive health, higher healthcare costs, and heightened morbidity in late life, all highlight the need for a better understanding of the link between diabetes and cognitive health in old age. The study focuses on middle-aged and older adults newly diagnosed with diabetes, and assesses the extent to which diabetes duration—the progression of diabetes—establishes trajectories of cognitive health beginning with the year diabetes is diagnosed.

The aim of an event-based approach is not to describe health differences over time or with age between people with diabetes and people without diabetes. Rather, it focuses solely on

people with diabetes, and describes how their health changes as their disease progresses. With this approach, measures of time, which describe people's location on their life course (age, cohort, age at diagnosis) and disease progression (diabetes duration), are used to accurately capture health change with the progression of diabetes.

Diabetes duration

Rather than age or time, which were used in earlier studies, diabetes duration (year since diabetes diagnosis), conceptualized as a time-variant predictor, is the measure used in the study to describe health trajectories after diabetes has been diagnosed.

Earlier age-based and time-based studies provided some support for cognitive decline with longer diabetes duration. Longer duration is linked to poor cognitive performance, specifically to lower verbal memory (Elias et al., 1997), and to reduced processing speed and executive functioning (Cosway, Strachan, Dougall, Frier, & Deary, 2001; Saczynski et al., 2008). There is additional circumstantial evidence that the detrimental effects of diabetes on cognition may become stronger as the disease progresses. Longer diabetes duration is linked to increased risk of diabetes complications (Selvin, Coresh, & Brancati, 2006), to poorer diabetes control (Benoit, Fleming, Philis-Tsimikas, & Ming, 2005), to increased risk of diabetes complications, such as vasculopathy, depression (Cosway, et al., 2001; Elias, et al., 1997), and dysglycemia (Reijmer, et al., 2010). Finally, chronic hyperglycemia results in greater cognitive impairments and faster decline over time (Reijmer, et al., 2010). Nevertheless, no research has described health change with longer diabetes duration.

Diabetes timing (age at diagnosis)

The timing of diabetes, measured as age at diagnosis, is an important aspect of the experience of the disease. According to the sociological concept of illness as a “biographical disruption,” the onset of an illness can establish new life trajectories for the people affected (Bury, 1982); and the impact of the disruptive event varies by type of illness, people’s location on their life course, and the medical and social environment in which the illness occurs (Faircloth, Boylstein, Rittman, Young, & Gubrium, 2004). Recent research further suggests that the negative influence of an illness is maintained over time (Faircloth, et al., 2004). We therefore propose that among people with diabetes, older age at diagnosis can be an important risk factor for cognitive impairments for two reasons: 1) Old age is the single most important risk factor for dementia, cognitive impairments (Kloppenborg, van den Berg, Kappelle, & Biessels, 2008), and cognitive decline (Bruce et al., 2003; Tilvis, et al., 2004). 2) People with late-onset diabetes are at greater risk of several diabetes complications, including worsened cognitive function and microvascular complications (Chuang et al., 2006).

Birth cohort

Cohort effects on health change reflect the impact on health and health change of social experiences common to individuals born at the same time (Ryder, 1965). Research shows that cognitive health improves significantly with each cohort (Dodge, Zhu, Lee, Chang, & Ganguli, 2013; Karlamangla, et al., 2009; Salthouse, 2013), and there is slower decline in younger cohorts, partly due to higher education (Dodge, et al., 2013). Although similar studies among diabetics are lacking, gains in education in the last decades, relaxation in the diagnostic criteria, improvement in diabetes treatment, and modifications of the treatment recommendations to

facilitate diabetes management for older adults (American Diabetes Association, 2014) can all exert a positive influence on patients' experience of diabetes, and possibly on their cognitive health also. We can expect improvement in cognitive health with younger cohorts of middle-aged and older adults with diabetes.

Chronological age

Old age is the single most important risk factor for dementia and cognitive impairments (Kloppenborg, et al., 2008) and cognitive decline (Bruce, et al., 2003; Tilvis, et al., 2004); and the effect of diabetes on cognition is stronger with time or age (Bruce, et al., 2003; Gregg et al., 2000; Kanaya, Barrett-Connor, Gildengorin, & Yaffe, 2004; Nooyen, Baan, Spijkerman, & Verschuren, 2010; Okereke et al., 2008; Stewart, Prince, & Mann, 2003; Wu et al., 2003). Review articles corroborate the findings of the negative effect of age on cognitive health (Biessels, Kerssen, de Haan, & Kappelle, 2007).

However, while time-variant chronological age captures developmental changes related to aging (Riley, 1987), it cannot accurately describe the experience of illness, since at any point in time, people with diabetes with the same age can be at varying stages of their illness. No designated indicator of the aging process was included in the current study; therefore we are unable to distinguish how much of the estimated cognitive health levels and cognitive health change are attributable to diabetes itself, and how much is attributable to aging. However, the event-based approach allows us to accurately predict the cognitive health of a given patient diagnosed at age 50, when he or she reaches 60 or 70 years of age. Similarly, health for a person diagnosed at 70 can be predicted in later years.

HYPOTHESES

Hypothesis 1: Given the circumstantial evidence suggesting that longer diabetes duration is tied to poor cognitive health at any age, and that microvascular complications, which are linked to poor cognition, increase with time, we expect that longer diabetes duration will be associated with a decline in the cognitive health trajectory in middle-aged and older adults with incident diabetes.

Hypothesis 2: Viewed within the context of “biographical disruption,” the limited evidence that older age at diagnosis is tied to microvascular complications allows us to speculate that people diagnosed at an older age will experience a greater cognitive burden, as well as higher and faster levels of cognitive decline with longer diabetes duration.

Hypothesis 3: We further expect that improvement in education in recent years along with looser diagnostic criteria for diabetes, and improvement in diabetes treatment for older adults will result in better health trajectories both at diagnosis and with longer diabetes duration among middle-aged and older-aged adults with incident diabetes.

Hypothesis 4: In agreement with the Social Stratification Theory, we expect that exposure to risks before and after diabetes diagnosis among blacks, Hispanics, women, and individuals of lower socioeconomic status will result in worse health trajectories at baseline and with widening gaps with longer diabetes duration.

METHODS

Data and sample

The Health and Retirement Study (HRS) is a biennial representative panel survey of Americans aged 50 and older (Juster & Suzman, 1995). Respondents interviewed between

1995/1996 and 2008 HRS and aged 65 years and older were included if they self-reported that they had been diagnosed with diabetes by their doctor for the first time during the observation period. Age 65 and older was selected due to higher rates of cognitive impairments in later adulthood compared to middle age (Schaie, 1996).

Incident diabetes was documented by consecutive negative and positive responses to the diabetes question. Conflicting answers to the diabetes question (88 total) were addressed using a method previously reported, which involves recoding diabetes status from negative to positive if respondents reported taking diabetes medication or insulin in any given year (Liang, Quinones, Bennett, & Ye, 2011). The selection criteria were met by 2,139 respondents at baseline. Due to the late age at onset, it is assumed that most respondents had type 2 diabetes (Kenny, Aubert, & Geiss, 1995).

The data were stacked starting with the year diabetes was reported for the first time (year of diagnosis) for each respondent. Time since diabetes diagnosis was recorded every wave thereafter, for a total of 7 waves (range: 0-14 years).

Measures

Cognitive functioning – The Total Cognition Score assesses different domains of cognition, including short-term and long-term memory, knowledge of current events, language skills, mathematical skills, and general orientation. The score is a combination of the Total Recall Index (TICS) –which measures episodic memory for immediate and delayed word recall tasks, and items from the Telephone Interview of Cognitive Status – which includes the serial’s 7 subtraction from 100 test, backward counting, or naming test (date, objects, presidents and vice president), and a vocabulary test (Ofstedal, Fisher, & Herzop, 2006). It ranges from 0 to 35, with

higher scores representing greater cognitive functioning. Earlier assessments demonstrate its strong construct and internal validity (Herzog & Wallace, 1997).

Time measure (diabetes duration) – Diabetes duration is operationalized as the number of years since diabetes was reported the first time. Six data waves were generated every two years thereafter (0-12). The data were aligned so that the baseline data for every respondent were obtained from the wave diabetes diagnosis was reported for the first time.

Other time measures – Diabetes timing operationalized as *age at diagnosis*, measured interpersonal age differences in the experience of diabetes. *Birth cohort*, on the other hand, was operationalized as respondents' age in 1995 and measured inter-generational differences. Both were included as continuous variables due to their monotonous relationship with the Total Cognitive Score.

Measures of social stratification – Three measures of social stratification were included as time-constant predictors: race and ethnicity (1=non-Hispanic white, 2=non-Hispanic black, 3=Hispanic, 4=other); gender (1=female, 0=male); education (1=less than high school, 2=high school graduate, 3=college graduate); and median household income (highest income quartile means highest income).

Time-variant covariates – Treatment burden (Ott, Stolk, & van Harskamp, 1999), several diabetes-related macrovascular and microvascular complications (Reijmer, et al., 2010), cardiovascular diseases (Ott, et al., 1999), hypertension (Elias, et al., 1997), loss of functional independence (Njegovan, Man-Son-Hing, Mitchell, & Molnar, 2001) and depressive symptoms (Chodosh, Miller-Martinez, Aneshensel, Wight, & Karlamangla, 2010) negatively influence cognition. Being married can positively influence both diabetes management (Van Dam et al., 2005) and cognitive outcomes (Hakansson et al., 2009). A person's self-rated health (Montiahu

et al., 2011), and overweight and obesity status (Raji et al., 2010; Smith, Hay, Campbell, & Trollor, 2011) are also powerful correlates of cognitive functioning in old age.

We therefore used self-rated health (1=very good health, 5=very poor health); mean number of comorbidities (range 0-11) including diabetes-related complications and non-diabetes related conditions; marital status (1= yes, 0=no); treatment burden (1=no treatment; 2=oral; 3=insulin injection; 4=oral and insulin injection); the Center for Epidemiologic Studies Depression Scale (CES-D, range 0-9) (Radloff, 1977); body mass index; and a functional status index (range 0-11), which combined Katz's Activities of Daily Living (ADL) and Lawton & Brody's Instrumental Activities of Daily Living (Katz, Ford, Moskowitz, Jackson, & Jaffe, 1963; Lawton & Brody, 1969; Spector & Fleischman, 1998).

Selection and response bias due to attrition, mortality, and the use of proxy interviews were addressed by the inclusion of indicators for each variable. All analyses were conducted using Stata® (version 12).

Data analyses

Hierarchical Linear Modeling (HLM) was used to describe the average functional trajectory after diabetes diagnosis (Raudenbush & Bryk, 2002). Preliminary analyses relying on the log likelihood ratio test, the Bayesian Information Criteria (BIC) and the Akaike Information Criteria (AIC) showed that compared to models with second and third order polynomials of age, the data best fit the model with a first order polynomial. Results from these models are presented in the results sections.

The level 1 model estimates intrapersonal differences within repeated observations every year after diabetes was diagnosed. For each respondent, the model provides estimates of

cognitive levels at baseline (intercept), and the linear change in cognitive functioning with every added year after diagnosis. Time-variant covariates can be included at this level to assess the expected outcome at any given point in time for every change in value of the time-variant covariate.

The level 2 models estimate interpersonal differences in the intercept and slope between respondents. These models also estimate the effects of time-constant covariates on the estimates obtained in level 1.

Time since diabetes diagnosis is centered on its grand mean; so were the continuous time-variant covariates. A baseline model was first estimated with time, accounting for mortality, attrition, and proxy interview (Model 1). Subsequent models estimated the effect of time-constant and time-variant covariates, in the following order: age in 1995 (Model 2), socio-demographic characteristics (Model 3), socioeconomic characteristics (Model 4), and health and marital status (Model 4). These nested models were compared using the Likelihood Ratio Test, and the model fit was confirmed with penalty-driven criteria, including the AIC and BIC. The models are described below:

$$\text{COGTOT}_{ti} = \pi_{0i} + \pi_{1i} * (\text{diabetes duration}) + \sum \pi_{ki} * X_{kti} + e_{ti}$$

COGTOT_{ti} is the total cognition score for each individual *i* at time *t*; π_{0i} is the level of depressive symptoms for each individual at the time of diagnosis; π_{1i} is the linear rate of change in cognitive score for each individual; *diabetes duration* is the year since diabetes diagnosis; π_{ki} is the effects of the *kth* time-variant covariates X_k for individual *i* on the trajectory; X_{kti} are the *kth* time-variant covariates in the model; and e_{ti} is the measurement error in the outcome.

$$\pi_{0i} = \beta_{00} + \sum \beta_{01q} * X_{qi} + r_{0i}$$

$$\pi_{1i} = \beta_{10} + \sum \beta_{11q} * X_{qi} + r_{1i}$$

$$\pi_{ki} = \beta_{k0}$$

π_{0i} , π_{1i} , and π_{2i} are the same as above; β_{00} , β_{10} , and β_{k0} are the fixed effects or expected cognitive score at mean diabetes duration, and expected linear growth for every year of diabetes duration; β_{0q} , and β_{1q} are the effects of the q th time-constant covariates X_q for each i on the intercept and linear slope; X_{qi} is the q th time-variant covariate for each i ; r_{0i} and r_{1i} , are random outcome variations at the intercept and linear slope.

The data were imputed using the multiple imputation procedure in Stata® (Rabe-Hesketh & Skrondal, 2008), assuming the data were missing at random (Little & Rubin, 2002). Five imputed data sets were generated.

Two time-constant indicators were also included to address mortality selection and attrition (death while in the study: 1=yes, 0=no; and attrition while in the study 1=yes, 0=no). A time-variant indicator of proxy interview was included as well. All analyses were conducted using Stata® (Version 12).

RESULTS

The sample had 52.9% female (n=2,139), 71.1% white, 16.2% black, and 10.2% Hispanics (results not shown). About two-thirds had completed high school (65.8%). At baseline, cognitive levels were at 20.50 (sd=5.54; range 0-35), and diminished to 15.63 by year 12. On average, respondents reported 1.11 comorbid conditions, excluding diabetes. The mean number of depressive symptoms and ADL/IADL limitations was 1.80 (sd=2.07; range 0-11) and 1.33 (sd=2.69; range 0-11), respectively. During follow-up, 32.82% of the sample died, while 14.82% missed at least one interview. Table 7 provides additional sample descriptive statistics.

Trajectory of cognitive functioning with longer diabetes duration

After adjusting for death, attrition and proxy interview, it was found that cognitive functioning declines linearly at a rate of approximately one-third of a unit per year from a rate of 21.051 at diagnosis (intercept; $p < 0.001$; linear slope = 0.364; $p < 0.001$; M1, Table 8). Adjusting for demographic characteristics and health covariates reduced the level of cognitive functioning by 14%, most of which was due to socioeconomic variations (adjusted intercept = 17.990; $p < 0.001$; M5, Table 8). It further reduced the fixed parameter associated with the linear slope by 31%, and this change was mostly attributable to increasing disability and being married (adjusted linear slope = -0.251; $p < 0.001$; M5, Table 8).

The model fit improved with each subsequent model, as demonstrated by significant log likelihood statistics and increasing AIC and BIC statistics. The random effects also show a significant unexplained variability in the intercept (0.392; $p < 0.001$) and linear coefficient (3.917; $p < 0.001$), which was reduced by 9% and 41%, by the inclusion of social and health variables in Model 5.

Diabetes timing (age at diagnosis)

In agreement with our second hypothesis, older age at diagnosis was associated with lower cognitive levels at baseline (Figure 9). However, the gap did not increase over time (intercept = -0.269; $p < 0.001$; linear slope = -0.006; $p > 0.5$; M2, Table 8). The estimates were not noticeably modified by the inclusion of time-constant or time-variant covariates. We observed, however, that controlling for cohort by itself increased the negative effect of age at diagnosis on the cognitive levels by 25%, from -0.269 to -0.413, $p < 0.001$ (results not shown).

Birth cohort

Adjusting for age at diagnosis, cohort differences were significant both at diagnosis (intercept=0.122, $p<0.001$), and with longer diabetes duration (linear slope=0.021, $p<0.005$; results not shown). However, similar to age at diagnosis, cohort differences in cognitive functioning were significantly reduced by the inclusion of race, ethnicity, and gender indicators (Model 3, Table 8), suggesting that the demographic composition of the cohorts mediate the link between cohort and cognitive functioning in middle-aged and older adults with incident diabetes.

Social stratification

Model 3 in Table 8 shows great vulnerability among disadvantaged groups compared to their counterparts, with lower cognitive levels at baseline (intercept_{race}=-4.693, $p<0.001$; intercept_{ethnicity}= -3.545, $p<0.001$; intercept_{gender}=0.606; $p<0.005$; range of intercept_{education}=2.674-4.141; range of intercept_{income quartile}=0.816-1.307; $p<0.005$). Yet the race, ethnic, gender, and economic gaps observed at baseline do not increase over time (Model 4). In addition, socio-demographic characteristics account for very little of the cognitive scores and cognitive change with diabetes.

Several additional findings are noteworthy. For instance, compared to men we observed a cognitive advantage among women at baseline in model 4 (intercept=-0.606; $p<0.001$; Table 8). However, this advantage was non-significant in Model 3 due to women's lower socioeconomic status and poor health. Furthermore, health and socioeconomic status reduced the racial and ethnic gap in cognitive health, but did not fully explain either (Model 4 & 5, Table 8). Finally, both physical disability and being married were the only time-variant covariates significantly linked to worse cognitive trajectory (Model 5, Table 8).

DISCUSSION

The current study conceptualizes illness as a trajectory beginning with a diagnosis of diabetes. To our knowledge, this is the first study to assess cognitive change after diabetes diagnosis in middle-aged and older adults. The study results provide useful tools for patients and clinicians alike, to anticipate the clinical course of diabetes in terms of changes in cognitive functioning after diagnosis in middle-aged and older-aged adults. The study ultimately allows providers and policymakers to better predict the healthcare and social needs of people with diabetes along the illness career.

Trajectory of cognitive functioning with longer diabetes duration

Research shows that having diabetes modestly promotes accelerated aging of the brain (Reijmer, et al., 2010). The current study extends this research, and in agreement with our first hypothesis, shows that this cross-sectional effect moderately and linearly intensifies with longer diabetes duration. This finding is salient because even mild cognitive deficits can result in difficulties concentrating and in forgetfulness (Reisberg, Ferris, de Leon, & Crook, 1982), which can adversely affect adherence to medical treatment (Hayes, Larimer, Adami, & Kaye, 2009), as well as self-care and independent living (Njegovan, et al., 2001). Our findings therefore support the view that cognitive impairments will continue to be a major clinical and policy concern, as people live longer, and the prevalence of diabetes is expected to increase.

The study supports the need for interventions implemented before and during the illness career to reduce cognitive impairments and cognitive decline. Socioeconomic status, marital status, and physical functioning were the most important modifiable determinants that appeared to bend the cognitive curve after diabetes diagnosis by as much as 31% (from -0.364 to -0.251 in

Table 8, M1 and M5). Contrary to previous findings of a declining effect of socioeconomic status on cognitive health with older age (Karlman, et al., 2009), our study found that education and income reduced both levels and rate of cognitive decline. Furthermore, previous studies showed that being married improves diabetes management and prevents cognitive decline (Hakansson, et al., 2009; Van Dam, et al., 2005). Yet among diabetics, married individuals experience a worse cognitive trajectory compared to their unmarried counterparts. This finding agrees with reports that some forms of support can be detrimental to health. For instance, spousal over-protective behaviors (Johnson et al., 2014), tempting (Henry, Rook, Stephens, & Franks, 2013), and obstructive behaviors (Mayberry & Osborn, 2014) can undermine adherence to diabetes management, and thus be harmful to both self-care and diabetes control. While it is impossible to speculate about the mechanism through which being married affects the cognitive trajectory of newly diagnosed diabetics, the current study raises important questions regarding the role and importance of spousal involvement in diabetes care.

Diabetes timing (age at diagnosis)

As stated in our second hypothesis, the study results suggest that age at diagnosis is a significant agent of stratification for cognitive health (Bruce, et al., 2003; Kloppenborg, et al., 2008; Tilvis, et al., 2004). This finding contradicts previous studies, which reported a stronger effect of diabetes on cognition in people aged 60 to 80 compared to those 85 and older (Biessels, et al., 2007; Biessels, Staekenborg, Brunner, Brayne, & Scheltens, 2006), and a worse clinical profile in younger adults compared to older adults (Hatunic, Burns, Finucane, Mannion, & Nolan, 2005; Hillier & Pedula, 2001; Hillier & Pedula, 2003; Selvin, et al., 2006). These contradictions could reflect methodological differences (analytic differences, and differences in

how age at diagnosis was measured), or differences in the samples under study. Given the important role of diabetes duration in defining cognitive trajectories as highlighted by the current study, its omission can conflate its impact on cognitive health with that of age at diagnosis. Our study can disentangle these effects: It showed that although longer diabetes duration results in incrementally worse cognitive functioning, older age at diagnosis is independently tied to worse cognitive functioning at any point in the disease trajectory.

To the author's knowledge, only one other study included diabetes duration as a covariate in multivariate analysis, and the results were more in line with those of the current study. In this earlier study, the link between diabetes complications and age at diagnosis varied by outcome, with greater risks of cataract, diabetes foot, and microvascular complications among people with every added year of age at diabetes onset (Chuang, et al., 2006). Chuang's study included a sample from several Asian countries and people from a wide age-range (18 years and older), which limit its comparability to our own study. Nevertheless, our findings are in line with his results. This can be explained by the strong link between microvascular complications and poor cognitive health (Biessels, et al., 2007), which Chuang and colleagues found to be more frequent with older age at diagnosis. It is therefore reasonable to conclude that older age at diagnosis establishes new trajectories characterized by greater vulnerability to diabetes with longer duration.

Our conclusions are further strengthened by indications that older age may represent a critical period for cognitive impairments during which even diabetes may have greater effects. Compared to middle-aged adults, older adults have a greater mental health burden due to the association between involuntary role exits (retirement and widowhood) and declining social support, physical functioning, sense of control, and lower socioeconomic status, and the link

between these factors and poor mental health (Blazer, Bruce, Service, & George, 1991; Mirowsky & Ross, 1992) and poor diabetes self-management. A few authors have suggested that the pathogenesis of diabetes may further vary by age group (Stewart & Liolitsa, 1999). Others have shown that severe forms of cognitive impairments and dementia exist in higher frequency with older age, and milder forms of cognitive impairments in younger age (Biessels, Deary, & Ryan, 2008; Reijmer, et al., 2010). While no empirical proof is available for these claims, our study supports previous results by confirming that cognitive trajectories differ significantly by age at diagnosis: Older-aged adults exhibited worse trajectories than their middle-aged counterparts, with a dose-effect on cognitive functioning of age at diagnosis.

Finally, delayed diagnosis among the oldest adults could explain the wider gaps in the cognitive trajectory by age at diagnosis. It is acknowledged, for instance, that over one-third (26.9%) of older adults with diabetes go undetected (Centers for Disease Control and Prevention, 2011). If delayed diagnosis explains our results, the study shows clearly that the consequences of delayed diagnosis can lead to faster decline in cognitive trajectories after diabetes diagnosis among older adults. These findings strongly support the necessity for policies aimed at early detection of diabetes.

Birth cohort

The study results do not support our hypothesis that younger cohorts of older adults with diabetes will have a better cognitive trajectory compared to their older counterparts. The results also contradict previous age-based studies of the general population, which suggest that educational gains in general have resulted in improved cognitive health with each cohort coupled with a slower decline (Dodge, et al., 2013; Karlamangla, et al., 2009; Salthouse, 2013). After

adjusting for age differences, those in older cohorts experience better cognitive trajectories with higher cognitive functioning at baseline and slower decline with longer diabetes duration. In addition, the rate of change with longer diabetes duration was reduced to non-significance by socio-demographic variations in the sample (race, ethnicity, and gender). Therefore the social composition of younger cohorts increases the impact of diabetes duration on physical and cognitive health.

For policy makers and clinicians, these results call for a new approach in dealing with diabetes, an approach which would take into account not only diabetes duration and age at diagnosis but also cohort differences in the experience of diabetes. As baby boomers have now reached retirement age and are reaching old age in large numbers, and the racial and ethnic diversity of the population is expected to rise, the healthcare needs of younger cohorts of people with diabetes in old age might increase in the near future, as the number of older adults with poor cognitive functioning increases.

Social stratification

The study contributes to the research on social stratification by showing that socio-demographic predictors explain about 14% of cognitive impairments at diagnosis, but have a limited influence on the rate of change (only 5%). The study also showed persistent gender, racial, ethnic, and economic disparities in cognitive functioning after diabetes diagnosis, with worse trajectories among women, blacks, Hispanics and people of lower socioeconomic status. The finding of a constant risk of poor cognitive functioning for blacks and Hispanics over the course of diabetes (about 20% higher), when compared to whites, is consistent with the hypothesis that the risk of cognitive decline in late life among minorities may be more affected

by higher levels of cognitive functioning achieved early in life (Karlmanangla, et al., 2009). We conclude that inequalities in cognitive functioning remain stable with longer diabetes duration after late-onset diabetes in middle-aged and older adults, because cognitive damages may have taken place earlier for socially disadvantaged groups before diagnosis. Nevertheless, although this possibility may explain higher cognitive levels at baseline, it cannot completely explain why cognitive functioning remains unchanged over the course of diabetes—especially because compared with whites, faster cognitive decline with time among blacks, particularly in complex cognitive tasks, is documented (Obidi, et al., 2008). Similarly, a cognitive advantage among women, which declined with age, has also been reported (Karlmanangla, et al., 2009). These findings underscore the difficulties in linking mediators of social inequalities such as social support, access to care, and diabetes management to health outcomes. For instance, while diabetes support, which is socially distributed, is tied to health-promoting activities consistent with good diabetes management, there was no significant link between diabetes support and health decline (Nicklett & Liang, 2010). Future studies need to clarify the possible connection between elements of social stratification, behavioral, psychological, and medical mediators, on the one hand, and health outcomes over the course of diabetes, on the other.

Overall, the event-based approach cautions clinicians and policy makers not to extrapolate evidence of social inequalities in the general population to older adults with incident diabetes. The current study shows that circumstances existing before diagnosis are the most relevant determinants of inequalities in cognitive functioning with diabetes. Blacks, women, Hispanics and people of low socioeconomic status are at risk of poor cognition at diagnosis, and this risk is not mitigated over the course of diabetes. Because of the effects of even slight

changes in cognitive health on diabetes management, self-care and mental health, monitoring cognitive health is necessary to reduce health inequities among social groups.

Limitations

The study results should be interpreted in the light of several limitations. First, about one-third of the general population who meet the biological criteria for diabetes are not clinically diagnosed (Centers for Disease Control and Prevention, 2014). Therefore we can infer from this fact that a similar proportion of undiagnosed eligible diabetics were not included in the study. If these individuals are healthier than their diagnosed counterparts included in the sample, our estimates may be larger than the “true” population estimates. Second, differential access to care among social groups can lead to under-representation of individuals in disadvantaged groups, who also tend to have poorer health status. As a result, social differences may be underestimated in our study. Despite these limitations, self-reported diabetes has proved to be an acceptable measure and has been successfully used in longitudinal population studies in which objective measures are not readily available (Bruce, et al., 2003; Bruce, et al., 2008). Furthermore, tests of reliability have shown self-reports to be robust measures of diabetes status (Jackson et al., 2013). However, the use of diagnosis as the starting point of the cognitive trajectory can be problematic because microvascular complications, which are strongly associated with cognitive impairments can start as early as 7 years before a diagnosis of diabetes (Ramlo-Halsted & Edelman, 2000). Cognitive changes due to diabetes may therefore have begun before the diagnosis of diabetes. This limitation could partly explain the levels of cognitive functioning at baseline. Future studies of cognitive change with diabetes should begin the cognitive trajectory years before diagnosis, if studies are to capture these earlier cognitive changes.

Policy implications

Diabetes presents a challenge to the entire healthcare system and its stakeholders due to its high economic and social costs, along with the complexity and burden of its treatment. The current study is the first to describe the clinical course of diabetes in terms of cognitive health after diagnosis in middle and old age. As such, it can provide patients with a graphic illustration of the general trend in cognitive functioning as their disease progresses. The study can also be useful to clinicians as a tool to illustrate the course of diabetes in terms of correlates of functional independence, which are patients' greatest concern (Huang, Brown, Ewigman, Foley, & Meltzer, 2007).

Overall, the study articulates four general recommendations for intervention; these are primary intervention, a shift in diabetes management, planning for upcoming cohorts with lower cognitive functioning, and finally addressing health inequalities early on in the life course.

Primary prevention at the onset of diabetes should be the first line of intervention. Evidence-based programs such as the Diabetes Prevention Program, have proved effective in motivating diabetic adults to change their diet and to exercise; and these behaviors have proved effective up to 10 years after the intervention (Diabetes Prevention Program Research Group, 2009). Therefore efforts to expand and fund such programs should become policy priorities for diabetic patients in general, and for older diabetic adults in particular, in order to support their cognitive health. As the role of diabetes in the future of the nation is being recognized, several initiatives have emerged and are moving a policy agenda in the right direction. These include the American Medical Association's 2013 Improving Health Outcomes Initiative in collaboration with the YMCA, and the 2015 Prevent Diabetes STAT (Screen, Test, Act—Todaytm)⁴ campaign by the American Medical Association and the Centers for Disease Control and Prevention, a

screening campaign which reaches out to, and educates stakeholders in the treatment of diabetes, including patients, clinicians, medical associations, insurers, employers, community organizations, and the general public.

Secondary prevention, on the other hand, aims to reduce health decline after the onset of diabetes. The results of this study highlight the importance of continuous monitoring of cognitive health to minimize the effects of cognitive health decline on diabetes and its management. The incorporation of measures of cognitive health as an integral part of diabetes monitoring in old age is necessary. Although this monitoring is already implemented in physicians' offices, in European guidelines (International Diabetes Federation, 2010; Sinclair et al., 2011), and U.S. guidelines (American Geriatrics Society Expert Panel on the Care of Older Adults with Diabetes Mellitus, 2013), monitoring cognitive functioning at home is also important, because small changes in cognitive functioning between visits to the doctor can interfere with diet, exercise, diabetes care, and diabetes monitoring (Ciechanowski, Katon, & Russo, 2000; Feil et al., 2009; Feil, Zhu, & Sultzer, 2012; Okura, Heisler, & Langa, 2009; Rosen et al., 2003). Continuous monitoring should involve family members and case managers in order to prevent delays in addressing health decline. Measures of cognitive functioning are relatively easy to self-administer, and studies have shown that validated screening instruments can improve the detection of depression and dementia (Ott, et al., 1999). Incorporating these measures into electronic devices such as apps for iPad®, tablets, smart phones, Fit-bits®, and online assessments, can further promote access to care and allow instant detection of changes in cognitive functioning over the course of diabetes.

The finding that younger cohorts are at increased risk of a poor cognitive trajectory over the course of diabetes, due to demographic variations between cohorts, carries significant policy

implications. The current senior population entering old age may face poor cognitive functioning in greater numbers relative to their elders, and the increase in numbers can place a serious burden on families caring for older adults, on the healthcare system, and on the economy. The study therefore highlights the need for more research, and for policies that address the economic and social impact of reduced cognition in younger cohorts of older adults with diabetes.

Finally, given the importance of cognition on diabetes management, self-care, physical functioning and overall well-being (Sinclair, Conroy, & Bayer, 2008; Sinclair, Girling, & Bayer, 2000), middle-aged and older-aged blacks, Hispanics, women, and people of lower socioeconomic status with incident diabetes will continue to be at a cognitive disadvantage over the course of diabetes. At every stage of their disease, they may require more financial and social resources to deal with their condition. According to the study findings, it is clear that social and other conditions that existed before a diagnosis of diabetes are the most important causes of social variations in the cognitive trajectory of middle-aged and older-aged adults with incident diabetes; and socioeconomic status lies at the center of these variations. And although the protective effect of higher socioeconomic status does not increase over the course of diabetes, it also does not diminish. This fact most likely stems from the positive influence of higher education and better income on access to, and use of health services, to fewer diabetes complications, and to less stress (McEwen, 1998; Obidi, et al., 2008; Reijmer, et al., 2010; Wessels, et al., 2011). Therefore acting on economic conditions in older age to improve the cognitive trajectory of middle-aged and older-aged adults with incident diabetes is a reasonable policy option. A recent comprehensive report on health inequalities in the U.S. makes the strong case that social conditions, specifically education, income and neighborhood, rather than individual characteristics, may be the main drivers of racial inequalities (Bleich, Jarlenski, Bell,

& LaVeist, 2012, 2013). Therefore although the Patient Protection and Affordable Care Act improves access to care by expanding health insurance to almost the entire U.S. population, especially to socially disadvantaged people (Roberts & Rhoades, 2010), any serious policy should address the real sources of inequality, which are income inequalities and residential segregation, which are both influenced by how the school system is financed.

CONCLUSION

The illness career approach to diabetes and cognitive health shows that in middle-age and older adulthood, cognition declines modestly but steadily as diabetes progresses, and the risk of cognitive impairment varies by social group. Older age at diagnosis, younger cohorts, black race, Hispanic ethnicity, low education, and low income increase the risk of cognitive impairments at diagnosis, which remains unabated over the course of diabetes. Women also lose their cognitive advantage over men due to their lower socioeconomic status and poor health. As a consequence, efforts to address cognitive impairments among older adults with late-onset diabetes should focus on prevention and early detection, expand monitoring of cognitive functioning to patients' homes, prepare for greater needs for care and social services with younger cohorts, and address educational and residential inequalities to reduce the socioeconomic gap in cognitive functioning.

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Table 7: Descriptive statistics for the sample

	Mean or %	SD
Measure of time and main outcome		
Diabetes duration (years)	3.011	3.956
Total Cognition Score (0-35)	20.503	5.537
Level 1: Time varying covariates (<i>n</i> =6,234)		
Married (%)	58.200	-
ADL/IADL disability	1.326	2.691
Self-rated health	3.311	1.057
Comorbidities (excluding diabetes)	1.111	0.615
CES-D	1.799	2.072
Treatment burden	1.752	0.647
Proxy (%)	0.118	-
Level 2: Time constant variables (<i>n</i> =2,139)		
Age at diabetes diagnosis	74.139	6.417
Age in 1995	65.284	7.516
Female (%)	52.922	-
White (%)	71.161	-
Black (%)	16.176	-
Hispanic (%)	10.192	-
Other race (%)	2.571	-
Education		
Less than high school (%)	34.222	-
High school graduate (%)	35.512	-
Graduate school (%)	30.266	-
Median household income (USD)		
Quartile 1	8657	-
Quartile 2	18367	-
Quartile 3	33025	-
Quartile 4	91363	-
Death at any point in time (%)	32.819	-
Attrition at any point in time (%)	14.820	-

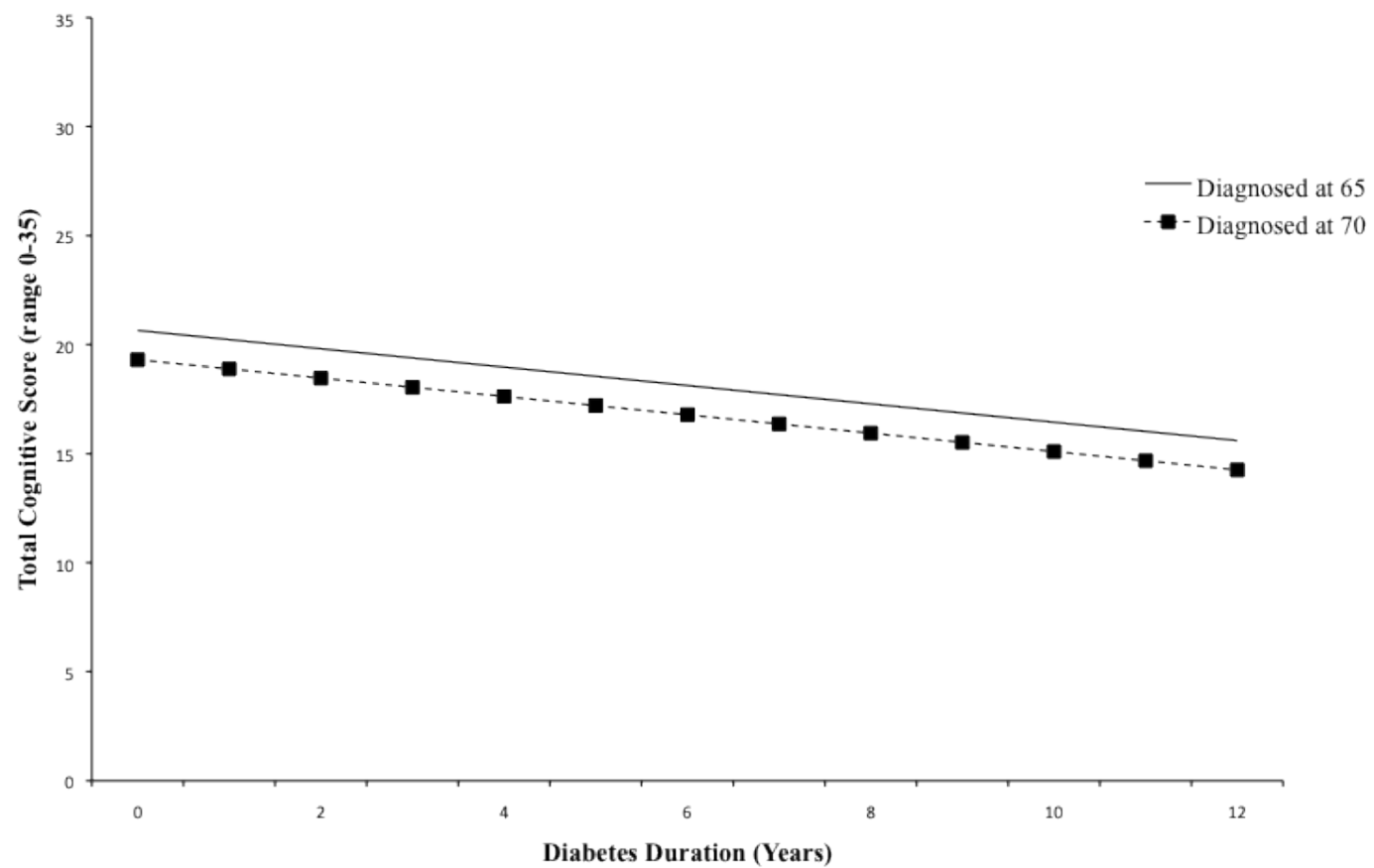
Table 8: Average trajectory of cognitive functioning with longer diabetes duration

	M1		M2		M3		M4		M5	
	Est.	Sig	Est.	Sig	Est.	Sig	Est.	Sig	Est.	Sig
<u>Fixed effects</u>										
For intercept										
Intercept	21.051	***	20.822	***	21.926	***	18.081	***	17.990	***
Age at diagnosis			-0.269	***	-0.336	***	-0.354	***	-0.292	***
Birth cohort (age in 1995)					0.055		0.100	*	0.071	*
Female					0.110		0.606	**	0.739	***
Black					-4.693	***	-3.552	***	-3.383	***
Hispanic					-3.545	***	-1.510	***	-1.462	***
Other race					-1.096	+	-1.111	*	-1.023	*
High school graduate							2.674	***	2.385	***
College graduate							4.141	***	3.838	***
Income quartile 2							0.816	***	0.754	**
Income quartile 3							0.965	***	0.962	***
Income quartile 4							1.307	***	1.210	***
For linear slope										
Linear slope	-0.364	***	-0.401	***	-0.443	***	-0.346	***	-0.251	***
Birth cohort (age in 1995)			-0.006		-0.007		-0.008		-0.008	
Age in 1995					0.002		0.000		0.003	
Female					0.011		0.014		0.012	
Black					0.018		-0.007		-0.002	
Hispanic					0.118		0.058		0.069	
Other race					0.263		0.254		0.217	
High school graduate							-0.031		-0.034	
College graduate							-0.059		-0.061	
Income quartile 2							-0.076		-0.091	
Income quartile 3							-0.096		-0.094	

Income quartile 4 (highest)						-0.043		-0.052		
<i>Time variant variables</i>										
Married								-0.524	*	
ADL/IADL disability								-0.539	***	
Self-rated health								-0.050		
Comorbidities								0.162		
CES-D								-0.082	+	
Treatment burden								-0.281	+	
<i>Survey status</i>										
Death	-3.358	***	-2.211	***	-2.298	***	-1.638	***	-0.907	***
Attrition	-1.098	**	-1.357	***	-0.916	**	-0.680	*	-0.713	*
Proxy	-2.123	***	-1.798	***	-1.794	***	-1.698	***	-0.020	
<u>Random effects</u>										
Variance										
Intercept	0.392	***	0.384	***	0.379	***	0.375	***	0.355	***
Linear slope	3.917	***	3.634	***	3.118	***	2.570	***	2.309	***
Intercept x linear slope	-0.131		-0.116		-0.103		-0.066		-0.211	
Level 1 residual	3.618	***	3.598	***	3.596	***	3.601	***	3.530	***
<u>Model statistics</u>										
Observations	6234		6234		6234		6234		6234	
Groups	2139		2139		2139		2139		2139	
AIC	168828		168462		167976		167437		166527	
BIC	168903		168554		168151		167696		166836	
Log likelihood	-84405		-84220		-83966		-83687		-83226	
-2ΔLog Likelihood statistic	-		370	***	485	***	559	***	922	***
Degrees of freedom	-		2		10		10		6	

*** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$; + $p < 0.10$; AIC: Akaike Information Criteria; BIC: Bayesian Information Criteria; Log Likelihood Ratio Test tests nested models 2 vs 1, 3 vs 2, 4 vs 3, and 5 vs 4, respectively

Figure 9: Trajectory of cognitive functioning with longer diabetes duration at age 65 and 70†



† Model controls for survey status and birth cohort (age in 1995)

CHAPTER 5

Conclusions

The goal of this chapter is to provide an overview of the study by 1) summarizing the results of the three studies and drawing conclusions in the context of the current literature on diabetes and health; 2) laying out the policy implications of the findings; and 3) discussing future investigations that can clarify and expand the current research.

SUMMARY OF FINDINGS WITHIN THE CURRENT RESEARCH ON DIABETES AND HEALTH

Health change with longer diabetes duration

Previous studies have effectively shown that having diabetes results in greater impairments at any point in time and at any age, and that impairments increase with age. In their estimates, however, these studies conflate the effect of diabetes duration and diabetes timing with that of age. The current study addresses these limitations, and takes the concept further in three ways.

First, rather than adopting an age-based or time-base approach, which compares people with diabetes to those without diabetes, it adopts an event-based approach to diabetes and health change, which aligns the natural history of diabetes with patients' experience of the disease. Therefore it bridges the gap between the biomedical (natural history of a disease) and the

sociological (patients' experience of illness as outlined in the Illness Career Model and the Disablement Process Model) literatures.

Second, contrary to previous studies, which included both incident and prevalent cases, the current study focused exclusively on people with incident diabetes in middle-age and old-age. As a result, it describes, for the first time, the true experience of diabetic patients, and quantifies the shape of physical, mental, and cognitive health change with longer diabetes duration. Rather than focusing on age or arbitrary time, this approach also mirrors the clinical course of diabetes by delineating health trajectories that begin with the diagnosis of diabetes, and by using diabetes duration as the measure of time for a common experience. Therefore it is more useful to clinicians and patients, but also to policy makers who want to understand the course of diabetes after diagnosis and to plan for the healthcare needs of diabetic patients.

Finally, it incorporates several measures of time relevant to both the disease (diabetes duration) and the patient (age at diagnosis and cohort); and isolates the respective roles of intrapersonal and interpersonal differences on physical, mental, and cognitive health change with diabetes.

Overall, the study corroborates cross-sectional findings that link diabetes duration with poor health (Park et al., 2006; Skinner et al., 2010; Spauwen, Kohler, Verhey, Stehouwer, & Van Boxtel, 2013). It further provides a longitudinal description of how health changes with longer diabetes duration and supports the assumption that illness is a dynamic event that can be depicted as beginning a trajectory, and that it is shaped by social factors, some of which also change with time. After diabetes is diagnosed in middle age and older adulthood, physical, mental, and cognitive health is characterized by relatively modest decline in health trajectories within the first 14 years. However, a proportionally faster decline in health is observed for physical health

compared to mental and cognitive health. The first chapter demonstrated that functional health among older adults, measured as ADL/IADL, and mobility disability declined according to a quadratic function. The second and third chapters demonstrated a linear increase in depressive symptoms and a decrease in cognitive functioning with longer diabetes duration.

On average, and after adjusting for age at diagnosis and cohort effects, there is a 25% loss in people's ability to function physically every year following a diagnosis of diabetes, and a 2.17% quadratic increase with every additional year from an initial level of 0.415 limitations. These changes correlate with a 2.28% decline in cognitive functioning per year from an average of 20.736, and a decline in mental health of 1.35% per year from initial levels of 1.620 depressive symptoms (Appendix E).

Socio-demographic and health status differences over the course of diabetes, including the differential burden of diabetes care, explained some of the differences and the rate of change in the health trajectories. Socioeconomic status (education and income) completely explained the linear increase in mental health with longer diabetes duration, but the trends reversed after adjustment for differences in health status.

It is important to emphasize that these trends varied from person to person, as demonstrated by significant variations in the random components at baseline and in the slopes for all three outcomes, even after the inclusion of socio-demographic and health-related factors. Future studies should investigate the respective roles of social and medical factors most relevant to the management of diabetes and to the progression of the disease; the latter would include complications, obesity, smoking, physical activity, and alcohol use.

Diabetes timing (age at diagnosis)

Results presented in the three Chapters provide strong evidence that old age at diagnosis is a key determinant of poor health across all outcomes. When middle-aged and older-aged adults are diagnosed at later ages, they begin their diabetes career with higher levels of ADL/IADL disability and lower cognitive functioning. Over the course of the illness, age-related health gaps remain constant for cognitive functioning, meaning that longer diabetes duration does not seem to significantly influence age differences in cognitive health. However, the gaps in the trajectories for ADL/IADL disability and depressive symptoms widen at a constant rate with longer diabetes duration.

An important contribution of the study, therefore, is the strong evidence it provides that during the course of diabetes in middle age and old age, age at diagnosis is an important risk factor for all three precursors of loss of independence. We find persistent inequality in cognitive health trajectories and in the trajectories for ADL/IADL and depressive symptoms by age at diagnosis with longer diabetes duration. Therefore identical clinical treatment of patients who were at different ages when diabetes was diagnosed may contribute to greater functional and mental health disparities among older people with the disease. In addition, adjusting for cohort differences exacerbates these disparities. Thus studies of health change that do not incorporate cohort effects underestimate the negative effect on health of older age at diagnosis and longer duration of diabetes.

The findings are particularly salient to policy, because the literature reports more severe clinical profiles among people with diabetes diagnosed during middle age compared to those with later-onset diabetes (Hatunic, Burns, Finucane, Mannion, & Nolan, 2005; Hillier & Pedula, 2001; Hillier & Pedula, 2003; Selvin, Coresh, & Brancati, 2006). Furthermore, age-based studies

suggest that older cohorts are at risk of faster functional decline over time (Chiu & Wray, 2010). But several methodological and conceptual limitations of these earlier studies, discussed in Chapter 1, can explain the differences between their findings and our own. The consistency of the effects of older age at diagnosis across outcomes, coupled with our nationally representative sample of older adults with self-reported diabetes, our conceptualization of time variables important to both the person and the disease, and our statistical methods, which take into account the structure of the data, all strengthen the validity of our findings and the quality of our results. We can confidently conclude that efforts to ensure successful and equitable aging with diabetes will require addressing the disproportionate risk of poor health both before diagnosis and over the course of illness among older people compared to their younger counterparts.

From a sociological point of view, Bury's conceptualization of the timing of chronic diseases as a biographical disruption and Larsson's finding of a continuous disruption of this biography over the course of chronic illnesses both support our own findings of differential trajectories by age at diagnosis (Bury, 1982; Larsson & Grassman, 2012). Older age at diagnosis delimits new physical and cognitive trajectories characterized by worsening health with longer diabetes duration.

Health gaps by age at diagnosis at baseline may be attributed to age differences in health—a reasonable possibility given the negative effects of old age on health. However, the faster decline in physical and mental health among people diagnosed at older age can be due to differences in clinical vulnerability, psychosocial vulnerability, or to delays in diabetes diagnosis in people of older age at diagnosis.

Several studies on cognitive health suggest that the pathogenesis of diabetes may vary by age (Stewart & Liolitsa, 1999), while others propose that for people with diabetes, older age may

represent a critical period that increases their vulnerability (Biessels, Deary, & Ryan, 2008). The validity of these conclusions would have to be confirmed through empirical studies.

Nevertheless, our study deepens our understanding of the relationship between diabetes and aging by showing that the age at diagnosis plays a crucial role in a patient's experience of the illness.

The concept of diabetes as a "biographical disruption" in old age is further supported by studies, which show that old age can exacerbate risk factors of poor health via psychosocial pathways. Old age is linked to social isolation and involuntary role exits (retirement and widowhood). It is further linked to declining social support, physical functioning, sense of control, and income, which are in turn associated with poor mental health and lower ability to manage diabetes (Blazer, Bruce, Service, & George, 1991; Mirowsky & Ross, 1992). In addition, reduced social support is tied to poor diabetes management (Nicklett & Liang, 2010). Therefore social isolation and weak social support may explain why old age at diagnosis results in worse health trajectories with longer diabetes duration. These observations were explored in Chapter 2, which reported similar depressive symptoms at diagnosis, and a faster increase of these symptoms over the course of diabetes, among people diagnosed in older age.

Finally, delayed diagnosis among the oldest adults could explain the wider health gaps at diagnosis as discussed in Chapters 1 and 3. It is acknowledged, for instance, that over one-third (26.9%) of older adults with diabetes go undetected (Centers for Disease Control and Prevention, 2011). If delays in diagnosis explain our findings, the study might have compared respondents who were at different locations in the natural history of their illness. One way to eliminate this limitation would be to use biomarkers to accurately identify the time at which patients moved from the pre-diabetic to the diabetic phase. From a policy perspective, however, the results of the

study clearly support the probability that if delayed diagnosis in older adults explains our results, the consequences of delayed diagnosis would lead to faster physical and cognitive functional decline with longer diabetes duration, for every year of delay. These findings would be similar to Chuang's results, which showed an increasing risk of complications with every added year of age at diagnosis (Chuang et al., 2006). Therefore, the study results strongly support policies geared towards early prevention and early diabetes detection until the effect of age at diagnosis on precursors of functional loss is better understood.

Birth cohort

The study's contribution extends beyond the effects of age at diagnosis and diabetes duration on the experience of diabetes. It explains the ways in which differences in historical time may influence health change with incident diabetes in middle age and old age. We hypothesized that generational improvements in diabetes care and in the reduction of risky behaviors should translate into better health trajectories among people in younger cohorts. Our findings, however, did not support this hypothesis. Among middle-aged and old-aged adults with incident diabetes, those in older cohorts experience better cognitive trajectories with higher cognitive functioning at baseline and slower decline with longer diabetes duration—evidence of divergent cognitive trajectories (Appendix E). Physical health trajectories showed evidence of persistent inequality with longer duration, with fewer ADL/IADL limitations at baseline in people from older cohorts. No cohort differences were found for depressive symptoms. None of the outcomes studied supported the view that within 14 years after a diagnosis of diabetes, people in younger cohorts might be better off. We conclude that younger cohorts of middle-aged

and older-aged diabetics are at similar risk of poor mental health, but experience persistent and increasingly divergent physical and cognitive health trajectories with longer diabetes duration.

In light of these findings, earlier assumptions, reported by time-based studies, that younger cohorts of diabetics are healthier do not accurately depict the link between cohort and health with late-onset diabetes (Chiu & Wray, 2010). Using an event-based approach, we found that people in younger cohorts have worse physical and cognitive trajectories beginning at diagnosis, and differences in cognitive health among cohorts widen over the course of diabetes. The worsening cognitive trajectories can be explained by socio-demographic variations in the sample (race, ethnicity, gender, and socioeconomic status), but remained significant at baseline. Therefore the social composition of younger cohorts increases the impact of diabetes duration on cognitive trajectories over the course of diabetes.

Several factors may be at play. First, functional health improves in all age groups except the middle-aged (Seeman, Merkin, Crimmins, & Karmalanga, 2010). Our findings may therefore reflect general trends in the U.S. population, at least regarding physical health. Second, increasing sedentary lifestyle, lack of physical activity, and obesity in younger cohorts, with greater frequencies in socially disadvantaged groups, can explain our results. For instance, higher obesity rates in more recent cohorts is well documented (Reynolds & Himes, 2007) along with significant social stratification in BMI trajectories (Botosaneanu & Liang, 201). In the mobility disability, however, the inclusion of BMI along with other measures of health status and of comorbidities of diabetes did not fully explain the physical, mental, and cognitive health gap by cohort, with longer diabetes duration. Therefore although BMI may partially explain why younger cohorts are at risk of poor physical and cognitive trajectories with diabetes, its contribution may be marginal.

Regardless of the explanation, for policy makers and clinicians, dealing with diabetes will necessitate taking into account not only diabetes duration and age at diagnosis, but also cohort differences in the experience of diabetes. Since baby boomers have reached retirement age and are reaching old age in greater numbers, it can be expected that the healthcare needs of people with diabetes in old age will increase in the near future, especially with regard to physical and cognitive health.

Social stratification

The three Chapters also contribute to the research on health disparities. They showed that overall (a few exceptions apply and are discussed below), racial, ethnic, gender, and socioeconomic differences in patients' experience of diabetes are manifested mainly in persistent inequalities the longer the duration of diabetes. These results confirm that social stratification in childhood and adulthood before diagnosis ranks among the most important determinants of physical, mental, and cognitive health among middle-aged and older adults newly diagnosed with diabetes. The important role of early childhood and adulthood life chances on health in old age health is widely acknowledged in developmental and life-course research, which describes how life-course circumstances and events, including social stratification, influence disease susceptibility, illness behaviors, and disease outcomes (Ben-Shlomo & Kuh, 2002; Kuh & Ben-Shlomo, 1997). The research also shows that prenatal and childhood exposure to risks, such as low socioeconomic status and birth weight, along with adulthood factors such as lower socioeconomic status; behavioral factors such as alcohol, smoking, diet, and physical exercise; and psychosocial factors increase the risk of poor health in old age (Lynch & Davey Smith, 2005). These risk factors are unequally distributed in the population. For instance, researchers

have shown a link between chronic disease outcomes and social stratification, including race and ethnicity (Ferraro, Farmer, & Wybraniec, 1997), socioeconomic status (House et al., 1994; Strohschein, 2005), and gender (Zhang & Hayward, 2006).

However, the stability of these social gaps over the course of illness was an unexpected finding, for reports of social differences in diabetes management and outcomes between socially advantaged groups and their disadvantaged counterparts are common in the diabetes literature. Blacks, Hispanics, and women experience more barriers to self-management, less access to and lower quality of healthcare, obstacles to diabetes control, worse psychological outcomes, less family support, and worse diabetes-specific self-efficacy and distress, and more comorbidities (Brown et al., 2000; Glasgow, McCaul, & Schafer, 1986; Gucciardi, Wang, DeMelo, Amaral, & Stewart, 2008; Heisler et al., 2007; Jezewski & Poss, 2002; Lanting, Joung, Mackenbach, Lamberts, & Bootsma, 2005; Ponzio et al., 2006; Quandt et al., 2005; Sentell & Halpin, 2006; Szalat & Raz, 2007; Walker et al., 2006). Similarly, lower socioeconomic status, especially lower educational attainment, hinders important diabetes self-management behaviors (Anderson et al., 1995), and creates barriers to healthcare access (Baker, Watkins, Wilson, Bazargan, & Flowers, 1998; Beckles et al., 1998) and to the process of care (Brown et al., 2004). Given this list of indicators of problematic diabetes management, one key question remains to be answered: Why do socially disadvantaged people not have worse outcomes after a diagnosis of diabetes?

A few exceptions apply to this general observation. As expected, and in agreement with studies reporting significant disadvantage in diabetes management among Hispanics (Hertz, Unger, & Ferrario, 2006; Saha, Arbelaez, & Cooper, 2003), the physical disability trajectory accelerates faster compared to that of whites, especially in Hispanic men (Chapter 1). This finding is significant for two reasons. First, the literature supports either similar physical health

trajectories between Hispanics and whites with time and in the general population (Carrasquillo, Lantigua, & Shea, 2000; Liang et al., 2008), or a Hispanic advantage among diabetics (Chiu & Wray, 2010). It seems, however, from our study that Hispanics are adversely affected by diabetes duration as it relates to physical functioning. Therefore current clinical practice may underestimate the high risk of physical disability among Hispanics with diabetes. Second, our research highlights the urgent need to understand the factors that put Hispanics at high risk of functional decline with longer diabetes duration. Given the demographic transitions occurring in the U.S., with rising numbers of people of Hispanic descent expected in the near future especially in states such as California and Texas (Passel, Cohn, & Lopez, 2011), diabetes can adversely affect healthcare, social, and familial institutions. We also found that the gap in functional trajectory by ethnicity was completely explained by educational differences between Hispanics and whites. General interventions to improve education in minority groups are therefore important for policy. Research is also necessary to identify the specific components of education that can explain the Hispanic disadvantage.

The finding that social gaps do not widen in the trajectories of depressive symptoms (Chapter 2) and cognitive functioning (Chapter 3) is most likely due to small variations in the CES-D and the Total Cognition Score within the study period. Longer-term observations and more culturally sensitive measures may better detect racial and ethnic differences, if any, in the experience of diabetes.

In addition to the Hispanic disadvantage in functional health, the study found that lower socioeconomic status reduced to non-significance the cognitive advantage of women observed in the general population (Karlman et al., 2009) (Chapter 3). This result is consistent with studies of diabetic patients which report either no gender differences in cognitive functioning

(Bruce et al., 2008; Okereke et al., 2008), or a larger negative effect of diabetes in men compared to women (Maggi et al., 2009). We further found that lower socioeconomic status reduces women's cognitive advantage to non-significance. Cognitive health being one of the few health outcomes where women do not suffer greater morbidity in general (Bruce, et al., 2008; Reijmer, van den Berg, Ruis, Kappelle, & Biessels, 2010), the numbers of women needing support to live independently in the future may rise with the increase of incident diabetes in old age.

Finally, the study confirmed research that among middle-aged and older adults with newly diagnosed diabetes, lower socioeconomic status (education and income) is a fundamental cause of health inequalities (Link & Phelan, 1995). Socioeconomic status has a negative influence on health trajectories and a mediating effect in the relationship between components of social stratification (race, ethnicity, and gender) and physical, mental, and cognitive health trajectories (Chapters 1, 2, and 3). Two findings in particular are noteworthy.

First, as reported in Chapter 2, lower socioeconomic status completely explains the increase in depressive symptoms, suggesting that improvement in socioeconomic status among adults with diabetes may result in late-life improvement in mental health. Similar findings have emerged in the general population, in which persistent evidence has shown a reversal of the negative effects of aging on depressive symptoms (Clarke, Marshall, House, & Lantz, 2011; Mendes de Leon, Barnes, Bienias, Skarupski, & Evans, 2005; Taylor & Lynch, 2011; Xu, Liang, Bennett, Quinones, & Ye, 2010; Yang, 2007). Therefore the current study supports the view that depressive symptoms over the course of diabetes is not inherent in the illness; rather, it is lower socioeconomic status that results in poor mental health.

Second, and unexpectedly, the study showed that higher-income individuals as a group are more vulnerable to a faster decline in mental health with longer diabetes duration compared

to lower-income individuals. Although benefiting from lower depressive symptoms at diagnosis, this advantage was reversed as diabetes progressed. Therefore the general expectation of a positive link between socioeconomic status and health may result in unmet health needs among diabetics in the higher socioeconomic class. This counter-intuitive finding may be related to a ceiling effect of the measure of depressive symptoms among people with lower education. Alternatively, people with higher income and more demanding jobs may be more reluctant to consult professionals about their psychological problems, reluctance that may lead to increased mental health morbidity and poor diabetes outcome. Findings from a Japanese study support this observation. Although experiencing lower rates of depressive symptoms, people with higher income also showed lower levels of treatment for depression (Fukuda & Hiyoshi, 2012). If a similar trend exists among older U.S. adults with diabetes, it may explain why mental health worsens among people with higher income.

It is important to note that despite increasing levels of depressive symptoms among older adults in the higher income quartiles, average differences in depressive symptoms between the groups in the top two versus the bottom two income quartiles remained mostly in favor of higher income; and this finding agrees with cross-sectional studies that report a protective effect of higher income among diabetic patients. The current study strengthens this research by showing that the gap in depressive symptoms between individuals in higher income and their counterparts gradually diminishes with a longer duration of diabetes.

Summary

In sum, this study allows an accurate prediction of the clinical course of late-onset diabetes in terms of physical, mental, and cognitive health. It further identifies social factors that

are relevant to diabetes management and policy—factors which, if taken into account, can positively influence health trajectories and ensure equitable and successful aging with diabetes. It finds that overall, health declines after late-onset diabetes, at different rates, and with different outcomes. And although diabetes duration and age have been extensively used to determine the goals of diabetes management, age at diagnosis as well as birth cohort are equally important determinants of health change after late-onset diabetes. In addition, the experience of diabetes is socioeconomically differentiated; differentiation begins in childhood, continues into adulthood, and is carried over to the time of diabetes diagnosis, with little indication that it diminishes over the course of illness.

POLICY IMPLICATIONS

Older adults with type 2 diabetes are a rapidly growing population and account for a great share of healthcare costs in the U.S. They present unique clinical and policy challenges due to their significant socio-demographic diversity, and variations in age at diagnosis, diabetes duration, and clinical presentation (American Diabetes Association, 2014; Kirkman et al., 2012). As a result, physicians must struggle with the incongruence between their own treatment goals and that of their patients (Huang, Brown, Ewigman, Foley, & Meltzer, 2007). Previous studies comparing people with diabetes to people without diabetes have been unable to provide practical tools to clinicians to deal with these issues. In this study we focused solely on people with diabetes and set out to describe physical, mental, and cognitive health changes after a diagnosis of diabetes in middle-aged and older adulthood in ways that are useful to clinical care, to patients, and to policy. The implications of our findings are outlined below.

Health change with longer diabetes duration

Overall, health changes over the course of diabetes are relatively small. However, even modestly incremental changes in physical, mental, and cognitive health can result in poor health, increased use of health services, institutionalization, and increasing demands on the health system as a whole. Every added unit of functional limitation can mean the difference between living independently or needing to live in assisted-living facilities, or in a nursing home. Our results show that for someone diagnosed at age 50 with already 6 functional limitations, it would take only 4 years for the person to need nursing home care; and at 4 functional limitations at diagnosis, by the time the person reaches age 62, the patient is likely to require institutionalization in a nursing home. With these sobering numbers in mind, several strategies can be adopted to reduce the impact of diabetes on physical, mental, and cognitive health in middle age and older adulthood.

Primary intervention – Primary intervention to prevent the onset of diabetes is the first and most effective policy action. Empirical studies have found that it is possible to delay and even prevent type 2 diabetes with lifestyle interventions. For instance, clinical trials of the Diabetes Prevention Program found that the 12-month program increased exercise and reduced weight among adult diabetics, and its effects can last up to 10 years (Diabetes Prevention Program Research Group, 2009). To date, about 500 such programs have already been implemented throughout the U.S. A few other initiatives have also emerged to tackle the diabetes epidemic. The American Medical Association's 2013 Improving Health Outcomes Initiative, in collaboration with the YMCA, aims to increase diabetes screening and referral to community organizations for interventions to effect changes in lifestyle. In March 2015, the American Medical Association with the Centers for Disease Control and Prevention initiated the Prevent

Diabetes STAT: Screen, Test, Act—Today^{tm 5} campaign to reach out to, and educate stakeholders, including clinicians, medical associations, insurers, employers, community organizations, and the general public, about diabetes. It also gives an opportunity for the general public to assess their individual risk factors for diabetes online.

While evidence for the effectiveness of the last two initiatives is not yet available, funding and expansion of Diabetes Prevention Programs to promote physical activity, weight control, and a general culture of healthy eating and exercise in the community at large, seems to be adequate policy options to prevent and delay diabetes and its clinical, and functional complications (American Diabetes Association, 2014). For instance, expanding these programs to local gyms, yoga clubs, or lifestyle programs such as Curves®, which targets middle-aged and older women can link this population to diabetes screening and prevention. Funding could be a public-private sector endeavor, involving insurers, Medicare and Medicaid, the Department of Defense, and businesses that have a stake in ensuring the public health of the population for health, security, political, and economic reasons.

In addition, intervention might also focus on widening the diagnostic criteria for diabetes to identify individuals in the prediagnostic phase. For instance, the ADA guidelines propose screening annually for type 2 diabetes starting at age 45. Adoption of this recommendation, its universal implementation in clinical practice, and reimbursement by third-party payers can reduce delayed diagnosis in old age. Such an initiative would require support from the American Medical Association and other professional medical organizations, and funding from private and public insurance organizations.

⁵ <http://www.ama-assn.org/sub/prevent-diabetes-stat/>

Primary intervention should also focus on creating a general culture of physical activity and healthy diet to improve health in the upcoming cohorts. Such an effort, preferably originating in appropriate U.S. government agencies, should include patient-advocacy organizations, public health experts, clinicians, policy makers, third-party payers, and more importantly, community organizations, the food industry, the media, and urban planners. These key stakeholders in the health of the nation should brainstorm ways to create an environment conducive to healthy living. Financing such an effort would pose a challenge, and resistance from the food industry might also be a roadblock. Earmarked taxation for public health on the processed-food industry might be the equivalent of the taxation on tobacco, which has worked successfully in the past (Chaloupka, Yuekli, & Fong, 2012). Monies raised from these taxes could be used to fund such efforts. Consumer groups could also be encouraged and educated in order to counteract the resistance expected from the processed-food industry.

Secondary prevention – Secondary prevention, on the other hand, aims to reduce health decline after the onset of diabetes. It is clear from our study that for comprehensive diabetes management, it is necessary to incorporate measures of physical, mental, and cognitive health as an integral part of diabetes monitoring in old age. Monitoring of functional health outcomes over the course of the illness (annual check-ups) is not new, as it is included in at least two international guidelines, including the European Diabetes Working Party for Older People⁶ (Sinclair et al., 2011) and the International Diabetes Federation (International Diabetes Federation, 2010). Yet regular assessment of functional status still lags behind in U.S. guidelines,

⁶ 1) Each older patient with type 2 diabetes should have an assessment of their functional status by a multidisciplinary team skilled in evaluation using well-validated assessment tools. This should be at the time of diagnosis and annually thereafter. 2) Each functional assessment must include a measure of the three major domains of function: global/physical, cognitive and affective.

with the exception of mental status assessment⁷ (American Diabetes Association, 2014) and recent recommendations from the American Geriatrics Society Expert Panel (American Geriatrics Society Expert Panel on the Care of Older Adults with Diabetes Mellitus, 2013).⁸

Nevertheless, recommendations, which incorporate the assessment of physical, mental, and cognitive health focus only on monitoring functional status at the point of clinical care. But monitoring functional status at home is just as important because subtle changes in physical, mental, and cognitive status between visits to the doctor can interfere with diet, exercise, diabetes care, and diabetes monitoring (Ciechanowski, Katon, & Russo, 2000; Feil et al., 2009; Feil, Zhu, & Sultzer, 2012; Okura, Heisler, & Langa, 2009; Rosen et al., 2003). Continuous monitoring is therefore necessary, and should involve not only the patient, but also family members and case managers in order to prevent delays in addressing critical health decline, linked to diabetes management. Measures of physical, mental, and cognitive health are relatively easy to self-administer, and studies have shown that validated screening instruments can improve the detection of depression and dementia (Ott, Stolk, & van Harskamp, 1999). The American Geriatrics Society provides a short list of such tests, which could be adapted to the home, the

⁷ 1) It is reasonable to include assessment of the patient's psychological and social situation as an ongoing part of the medical management of diabetes. 2) Psychosocial screening and follow-up may include, but are not limited to, attitudes about the illness, expectations for medical management and outcomes, affect/ mood, general and diabetes-related quality of life, resources (financial, social, and emotional), and psychiatric history. 3) Routinely screen for psychosocial problems such as depression and diabetes-related distress, anxiety, eating disorders, and cognitive impairment.

⁸ Specific geriatric syndromes that have been included and emphasized in the updated 2013 guidelines are depression, polypharmacy, cognitive impairment, urinary incontinence, injurious falls, and persistent pain. Clinical and functional heterogeneities in older adults with DM that were also addressed in the 2013 guidelines are differences in general health status, age and duration of disease at diagnosis, number of years of treatment, comorbidities and underlying chronic conditions, range of complications, degree of frailty, limits in physical or cognitive function, and differences in life expectancy (time horizon for benefit).

nursing home, and community settings (American Geriatrics Society Expert Panel on the Care of Older Adults with Diabetes Mellitus, 2013).

Incorporating these measures into electronic devices such as apps for iPad®, tablets, and smart phones; but also Fit-bits® or even online assessments, can further increase access and allow instant detection of health change over the course of diabetes. These devices often have built-in reminder systems, but emails or postal mail can also be used to remind patients, family members, or case managers to monitor physical, mental, and cognitive health change. Adoption of technology is not significantly hindered by old age. For instance, a 2012 Pew Research Center survey found that more than half of older adults (65 or older) are Internet users. About 59% go online; 86% use email – 48% of them on a daily basis; 47% report having a high-speed broadband connection at home; and 77% have a cell phone. Similar trends are found with tablets and iPads among those who adopt electronic devices as they become an integral part of their life. The feasibility, cost, and effectiveness of this strategy in preventing adverse diabetes outcomes should be investigated, and if the results are conclusive, the measures outlined above could be incorporated into future diabetes guidelines. However, caution is essential, so that unequal access to electronic devices does not result in widening inequalities in health in this population.

An additional contribution of the study is that it provides a tool that could improve patient-physician agreement on the goals of diabetes treatment (Huang, Gorawara-Bhat, & Chin, 2005). Estimates from the models of health change with diabetes duration can be used to develop visual graphs of the course of diabetes in terms of physical, mental, and cognitive trajectories parallel to the metabolic and clinical course of diabetes, including hemoglobin A1c, insulin, and glucose levels. These graphs could be incorporated as promotional tools and supporting materials during diabetes assessment and follow-up visits, to discuss the implications of life-style changes,

medical treatment, and functional and metabolic outcomes on functional independence. Additionally, they could be used to predict the timing of institutionalization given their functional levels at assessment. Future studies can assess the effectiveness of such materials in ensuring patient-physician agreement on the goals of diabetes management and encouraging adherence to diabetes treatment.

Finally, the study highlights the need to develop an effective and efficient referral system to physical, mental, and cognitive health services.

Diabetes timing (age at diagnosis) and birth cohort

Our results regarding age at diagnosis and cohort differences in the experience of diabetes has several policy implications. 1) Both measures of time are important factors to consider during diabetes management. 2) Interventions to address age-related and cohort-related gaps in health trajectories will require both primary and secondary prevention. 3) The burden on society may increase with younger generations of older adults with incident diabetes.

Although the key role of diabetes duration is recognized in several U.S. guidelines for clinical care, age at diagnosis is identified by the current study as a major risk factor for poor health. For instance, the U.S. Department of Veterans Affairs and the U.S. Department of Defense⁹ mention diabetes duration as a criterion for glycemic control and aspirin therapy in the 2010 update of their guidelines. Similarly, the American Diabetes Association's 2014 Standards

⁹ The patient with longer duration diabetes (more than 10 years) or with comorbid conditions and who requires a combination medication regimen including insulin should have an A1C target of <8%; Consider individual evaluation for aspirin therapy for patients age 30 to 40 with type 2 DM, with other cardiovascular risk factors, or with type 1 DM for duration of disease longer than 2 years.

of Medical Care in Diabetes uses diabetes duration as a criterion for diabetes care in old age.¹⁰

Our study highlights the fact that ascertaining cohort and age at diagnosis are just as important in predicting functional change in patients with late-onset diabetes. In fact, they are necessary to account for population heterogeneity in diabetes outcomes. According to our results, a 70-year-old person recently diagnosed with diabetes is at much greater risk of physical and mental health decline after diagnosis than a 70-year-old with longer diabetes duration, diagnosed 5 or 10 years earlier. The focus of care should therefore probably shift to the 70-year-old who has been recently diagnosed, so that an opportunity is not missed for administering equitable and appropriate care.

Finally, the finding that younger cohorts are at increased risk of poor physical and cognitive health trajectories over the course of diabetes has significant policy implications, for the senior population currently entering old age may face functional and cognitive limitations in greater numbers relative to their elders. The increasing burden of disability in middle adulthood and early old age will place a serious strain on the healthcare system, the economy and social institutions, including Social Security, Medicare, and Medicaid. In particular, middle-aged adults will be less likely to participate in the labor market despite their inflated ranks, resulting in lower tax contributions and greater demands on the health system. Greater prevalence of physical and cognitive disability can result in a greater burden on families left to care for diabetic family members, and the burden will be even greater for women, who are more likely to be caregivers (Bird & Rieker, 1999). The study therefore highlights the need for more research, and policy makers should pay attention to the risk of poor cognition and physical health in the upcoming

¹⁰ Perform an annual test to quantitative urine albumin excretion in type 1 diabetic patients with diabetes duration of ≥ 5 years and in all type 2 diabetic patients starting at diagnosis.

cohorts of older diabetics. Here too, aggressive primary interventions (change in culture, early detection, Diabetes Prevention Programs) and secondary interventions (monitoring, behavior change, referral) can reduce the risk of poor health in younger cohorts.

Social stratification

The most important implication of the findings regarding race, ethnicity, gender, and economic disparities is that policies to address physical, mental, and cognitive health inequalities in the general population early in the life course may be the best approach to address physical, mental, and cognitive inequalities with diabetes in middle-aged and older adults. By the time socially disadvantaged older adults are diagnosed, little can be done to bend the health gap compared to their socially advantaged counterparts. Given the anticipated rise in the size of the Hispanic population, along with faster increase in the incidence of diabetes among socially disadvantaged people, and the increasing longevity among people with diabetes, the lack of political action to seriously tackle health inequalities will likely result in increased numbers of older adults with diabetes in socially disadvantaged groups suffering from physical, mental, and cognitive impairments. We can therefore expect greater need for diabetes care, but also for hospital and nursing home care, and an added burden on caregivers, mainly women, and on younger cohorts of Americans. Moreover, an increasing financial burden will be placed upon existing social programs, including Medicare, Medicaid, and Supplemental Security Income.

Health inequalities are unjust and costly. Between 2003 and 2006, about \$1.24 in health costs were attributed to health (LaVeist, Gaskin, & Richard, 2009). Measures to reduce health inequalities have been called for by the public health community for a long time, starting in the

1980s with the Black Report, the Whitehall Report, and the Acheson Report in the UK and Canada.

Empirical studies have found a consistent link between socioeconomic status and poor functional and self-rated health (Lantz et al., 2001) across time, place, and populations (Link & Phelan, 1995), and over the life course (House, et al., 1994). This link occurs through multiple pathways as identified by the fundamental-cause hypothesis (Link & Phelan, 1995), and includes race (Williams & Collins, 1995), gender (Adler & Newman, 2002; Verbrugge, 1985), and ethnicity (Markides & Black, 1996; Markides & Eschbach, 2005). Research has consistently shown that systemically unequal distribution of determinants of good health lead to risk-bearing behaviors, stress, poor neighborhoods, and poor healthcare among socially disadvantaged groups. The unequal burden of obesity (Botosaneanu & Liang, 201), lack of physical exercise, poor nutrition and diet (Coggins, Swanston, & Crombie, 1999; Davey Smith & Brunner, 1997), poor neighborhoods along with residential segregation and their related stressors (Williams & Collins, 2001; Sampson, Morenoff, Gannon-Rowley, 2002; Morenoff, 2003; Diez-Roux, 2007), greater exposure to stress (Pearlin, 1989), and unequal access to adequate and quality care (Smedley, Stith, & Nelson, 2003) in socially disadvantaged populations are all widely documented. In a comprehensive study of population-based data sets in the U.S. and England, Bleich and colleagues confirmed that race, ethnicity, gender, and socioeconomic disparities in life expectancy, risk behaviors, and metabolic indicators have persisted over the past three decades (Bleich, Jarlenski, Bell, & LaVeist, 2012). The same authors further demonstrated that social conditions rather than individual characteristics may be the main drivers of these inequalities (Bleich, et al., 2012; Bleich, Jarlenski, Bell, & LaVeist, 2013). They found no evidence of health disparities in a black and white sample of adults with similar income levels,

and living in the same neighborhoods. Therefore policies to address health inequalities in the general population and consequently among older adults with diabetes could be more efficiently focused on factors such as socioeconomic status and neighborhood conditions.

To date, most policies are geared toward gathering information about health inequalities, developing recommendations, setting priorities to address health or economic disparities, and creating research institutions to document these inequalities.¹¹ However, little *action* has been taken to address health inequalities. The recent enactment of the Patient Protection and Affordable Care Act attempts to address access to care by expanding health insurance to almost the entire population. It can by the same token improve access to healthcare among socially disadvantaged people, who are more likely to be uninsured (Roberts & Rhoades, 2010). So far, the results of the Act are promising. There has been a 4% to 7% reduction in the number of uninsured, and the largest changes are occurring in socially disadvantaged groups, including Hispanics and blacks, but also in adults 18 to 34 years of age (Sommers et al., 2014). Regardless of political will, however, income inequalities and residential segregation, which are linked by the ways in which school systems are financed, will continue to determine life chances and maintain existing health disparities, which begin before birth and continue into old age.

A recent analysis of U.S. school finance data over three years reveals that property taxes play a disproportionate role in inequality in per-student revenues because taxable property wealth is inversely related to poverty rate (Baker & Corcoran, 2012). Therefore districts with higher

¹¹ Social policies including the Supplemental Security Income, Temporary Assistance for Needy Families, the Earned Income Tax Credit, the Supplemental Nutrition Assistance Program (formerly food stamps) attempt to reduce economic inequalities; Agencies and programs created to study health inequalities include the Office of Minority Health, The Indian Health Care Improvement Act, the Special Diabetes Program for Indians, The National Center on Minority Health and Health Disparities. An example of goal setting includes Healthy People 2020 (Bleich et al 2012).

poverty rates receive less from property taxes than districts with lower poverty, despite similar levels of tax effort. While state aid is designed to offset these inequalities, it is often insufficient to compensate for disparities in local resources. Revisiting the school financing system seems to be a viable policy option in efforts to reduce health inequalities in general, and among people with diabetes in particular.

Summary

Improving physical, mental, and cognitive health with late-onset diabetes and related social inequalities will require a paradigm shift, in which both primary and secondary preventions play important roles. Primary prevention entails efforts to improve the health of upcoming cohorts and early diabetes detection. Secondary prevention would incorporate means to closely monitor physical, mental, and cognitive change using innovative technology and an effective and efficient system of referrals to service providers that can prevent or reduce physical, mental, and cognitive health decline with diabetes. Disparities in the experience of illness are best addressed through general social and economic policies that aim to reduce gender, racial, ethnic, and economic gaps in health in the general population. These efforts will require using all the research that is currently available. And while the ACA is a step in the right direction, other policies addressing social factors such as income inequality, neighborhood segregation, and the education system need to be developed.

RESEARCH PRIORITIES AND FUTURE DIRECTIONS

Five major directions can be taken from here. The first direction would improve study methodologies, while the second would address questions unanswered by the current study. The

third direction would identify steps for assessing heterogeneity in health trajectories and its link to health outcomes. The fourth direction would investigate the trajectories of physical, mental, and cognitive health with longer diabetes duration. The final direction would extend the disease-career perspective to other chronic and acute conditions.

Methodological improvements

Self-reported diabetes – Self-reported diagnosis is a reliable proxy of diabetes status (Jackson et al., 2013), but diagnosis itself is problematic, for about one-third of people with diabetes remain undiagnosed (Centers for Disease Control and Prevention, 2014). Selection bias due to differential access to care could be reduced by the use of biomarkers such as Hemoglobin A1c (HbA1c) in several ways. Biomarkers provide accurate estimates of the timing of diabetes onset and health changes in the pre-diabetic stage (Haianza et al., 2012; Ramlo-Halsted & Edelman, 2000); they also address issues raised by differences in the timing of diabetes diagnosis by social group (Koopman, Mainous, Diaz, & Geesey, 2005). Finally, they can be used as time-variant predictors in the form of a trajectory (Haianza, et al., 2012), which can then be linked to health trajectories. Unfortunately, the HRS has only two measures of HbA1c from the same respondents. Blood samples were collected every four years for the first half of the sample in 2006 and 2010; and in 2008 and 2012 for the second half. These data could not be used for the purpose of the current study, but the results highlight the need for such data.

The type of diabetes (type 1 or type 2) was not assessed at baseline. Yet a differential link between diabetes type and mental health progression (Engum, Mykletun, Midthjell, Holen, & Dahl, 2005; Peyrot & Rubin, 1999; Talbot & Nouwen 2000) and cognitive dysfunction (Biessels, Kerssen, de Haan, & Kappelle, 2007; Kodl & Seaquist, 2008; Reijmer, et al., 2010) has been

reported, thus has the potential to introduce a bias in our estimates. However, only about 5% of diabetes cases in adulthood are attributed to type 1 diabetes (Centers for Disease Control and Prevention, 2014), suggesting that most of the study sample falls under the diagnosis of type 2 diabetes. Therefore if there is a case definition bias, it should be negligible given our large sample size.

Censoring – Left censoring, which occurs when people die before having a chance to enter in the study is a threat to the validity of longitudinal studies, for it can influence the representativeness of the sample and generalizability of the results. However, since we included only incident cases, death before study participation was not a major problem over the course of diabetes. On the other hand, right censoring due to mortality or attrition when the respondent is in the study, can be a problem as sicker people are more likely to die or drop out. This problem was handled by incorporating two indicators of mortality and attrition in the statistical models. As expected, both were significant; therefore their inclusion in the analyses was justified.

Study time frame – Another methodological improvement would entail expanding the study time-frame to the time before diabetes was diagnosed. This change in the study time-frame would allow longitudinal assessment of the acute and long-term effects of diabetes on post-event functional, cognitive, and mental health, while controlling for functional change before the diagnosis of diabetes. This approach has been already applied to studies of health changes before and after myocardial infarction (Dhamoon, Moon, Paik, Sacco, & Elkind, 2012) and stroke (Levine et al., 2014).

Address unanswered questions

A significant amount of outcome variance in the slopes remains unexplained in Chapters 1 and 3. There is also a large amount of unexplained variance for the random effects presented in all three Chapters. The explanatory power of the study could therefore be strengthened by the inclusion of variables known to influence diabetes outcomes and tied to the dynamic changes of diabetes. These include behavioral (diet, physical exercise, smoking, treatment adherence), psychological (coping, social support) and physiological factors (HbA1c, lipid profile) (Chiu & Wray, 2011).

Additional questions involve 1) explaining why Hispanics are at risk of greater functional decline (Chapter 1); 2) explaining how socioeconomic status reverses the trajectory of depressive symptoms over the course of illness; 3) identifying the measures of social status most relevant to diabetes management at every stage of diabetes (Chapter 2); 4) explaining why the beneficial effect of income is reversed for those in the top two income quartiles; and 5) explaining why age at diagnosis is a persistent risk factor for poor health, whether it is a consequence of age-related vulnerabilities, delayed diagnosis, or a completely different pathogenesis by age group.

Heterogeneity in the experience of diabetes

Heterogeneity in older people with diabetes is one of the most difficult challenges for diabetes prevention, management, and care (Kirkman, et al., 2012). The findings of significant variation in the random component variances in the current study reflect a high degree of heterogeneity in health trajectories with longer diabetes duration. As spelled out in the career model (Aneshensel, 2013), it is reasonable to expect significant heterogeneity in how people experience diabetes, with some individuals having a relatively stable progression, others

experiencing remission, and still others experiencing a rapid decline in health. This person-centered approach (as opposed to the variable-centered approach adopted in the current study) allows the identification of qualitatively distinct trajectories within the study group (Jones & Nagin, 2007; Jones, Nagin, & Roeder, 2001; Nagin, 2005), and the classification of people with diabetes into those able to achieve successful aging, those with normal aging, and those with pathological aging in the course of diabetes (Rowe & Kahn, 1997). The clinical significance of each of these groups is useful for research and policy as they can be linked to characteristics of the health system, characteristics of the diabetic, including behavioral, psychological, and socioeconomic predictors, and outcomes. In addition, the linkage of each trajectory to death or survival, or to the use of health services and to behaviors such as treatment adherence can be estimated. Ultimately, the effectiveness of medical and policy interventions to ensure successful aging with diabetes can be developed and evaluated using the trajectories identified (Nagin, 2005).

Joint trajectories of physical, mental, and cognitive health with longer diabetes duration

The study found strong evidence that among middle-aged and older adults with incident diabetes, physical, mental, and cognitive health trajectories change over time, and the changes can vary by outcome. Therefore there are co-occurring changes in multiple functional domains, which are not well understood. Xu and colleagues have demonstrated that underlying multisystem processes of health change with age can increase our understanding of overall health change over time (Xu, Liang, Bennett, Botosaneanu, & Allore, 2014). Our fourth direction is therefore to estimate multi-trajectories of physical, mental, and cognitive health and their link to socio-demographic and behavioral characteristics and to the quality of health systems. This type

of research is supported by evidence showing the interconnectedness of physical, mental, and cognitive health. For instance, prevalent and incident depressive symptoms, stroke, and ADL disabilities contribute independently to poorer cognitive functioning in older Americans, although they do not appear to influence rates of cognitive decline (Chodosh, Miller-Martinez, Aneshensel, Wight, & Karlamangla, 2010). A recent longitudinal population study further found that diminished cognitive function was linked to early onset and faster rate of progression of disability after onset (Rajan et al., 2012). Finally, while the directionality of the link between depressive symptoms and disability is complicated by the variety and appropriateness of measures, methods, and samples, available cross-sectional and longitudinal studies generally agree that there is a strong link between depression and disability (Bruce, 2000).

This type of research can help elucidate population heterogeneity in older adults with late onset diabetes. Investigating the simultaneous effect of diabetes duration on physical, mental, and cognitive health can provide a more complete picture of patients' experience of diabetes, and its relationship to the health services that diabetic patients would need. Ultimately a multi-trajectory approach can help fine-tune interventions tailored to older adults with incident diabetes based on a set of morbidities relevant to diabetes progression and diabetes care.

Extend the career perspective to other chronic and acute conditions

Studies of life events have used a variety of technical approaches to investigate health change, before and after a social or medical event. Examples include studies of mental health change among caregivers after bereavement (Aneshensel, Botticello, & Yamamoto-Mitani, 2004), physical and cognitive health change after a stroke (Dhamoon, et al., 2012; Levine, et al., 2014), changes in body mass index before the development of type 2 diabetes (Heianza et al.,

2014), in physical health after a traumatic brain injury (Andelic et al., 2014), in self-rated health with retirement (Curl & Townsend, 2014), and in health before hospice care (Stabenau et al., 2015). These studies confirm that the dynamic effect of life events on health can be documented and is relevant for medical care and policy. Therefore the last future direction involves expanding the career perspective on health change to other chronic and acute conditions, including obesity, stroke, cancer and the identification of behavioral, social, economic, and medical determinants of health trajectories before and after these events.

CONCLUSIONS

It is widely recognized that diabetes increases the risk of poor health at every age and at any point in time. The current study is less interested in the magnitude of the effect of diabetes on health than on describing the pattern of health change after a diagnosis of diabetes, and quantifying patients' experience of the illness. The three Chapters, which comprise this study covered different domains of health, complement each other, and provide a dynamic view of health experiences of diabetes in middle-aged and older adults. They show that health change with diabetes is characterized by a quadratic acceleration in physical disability and a linear decline in mental and cognitive health. People who are older at the time of diagnosis, younger cohorts, women (due to lower socioeconomic status), blacks and Hispanics (partly due to socioeconomic disadvantage and health disparities before diagnosis) are at increased risk of a poor health trajectory over the diabetes career, when compared to their counterparts. Cumulative or persistent socioeconomic disadvantages were found for all outcomes, with worse health trajectories among older adults whose socioeconomic status was lower, with the exception of those in the top two income quartiles, who experienced a faster decline in mental health despite

better scores at diagnosis. The study concludes that diabetes cannot be viewed as a time-constant individual characteristic. Rather, the dynamic nature of chronic illnesses needs to be better understood so that effective healthcare and policy interventions can be devised to ensure successful and equitable aging after a diagnosis of diabetes in middle age and old age.

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APPENDICES

Appendix A: Average ADL/IADL disability trajectory using HLM® negative binomial multilevel poisson regression

	M1		M2		M3		M4		M5	
	ERR	Sig	ERR	Sig	ERR	Sig	ERR	Sig	ERR	Sig
<u>Fixed Effect</u>										
For intercept										
Intercept	0.244	***	0.210	***	0.113	***	0.096	***	0.141	***
Age at diagnosis			1.056	***	1.120	***	1.123	***	1.105	***
Birth cohort (age in 1995)					0.936	***	0.930	***	0.943	***
Female					1.429	***	1.381	***	1.223	**
Non-Hispanic black					1.529	***	1.339	**	1.352	***
Hispanic					1.805	***	1.367	**	1.205	+
Other race					1.049		1.030		1.036	
Less than high school							1.889	***	1.390	***
High school graduate							1.107		0.992	
For linear slope										
Intercept	1.128	***	1.123	***	1.135	***	1.162	***	1.097	***
Age at diagnosis			1.003	***	1.006	*	1.005	*	1.006	*
Birth cohort (age in 1995)					0.997		0.998		0.997	
Female					0.990		0.991		0.998	
Non-Hispanic black					1.004		1.012		1.019	
Hispanic					1.035	+	1.051	*	1.040	+
Other race					0.914	*	0.910	*	0.942	
Less than high school							0.956	*	0.968	+
High school graduate							0.973		0.980	
For quadratic slope										
Intercept	0.997	+	0.998		0.999		0.995		0.999	
Age at diagnosis			1.000		1.000		1.000		1.000	
Birth cohort (age in 1995)					1.000		1.000		1.000	
Female					1.004		1.003		1.001	
Non-Hispanic black					0.998		0.996		0.995	
Hispanic					0.989	*	0.987	*	0.991	+
Other race					1.009		1.010		1.005	
Less than high school							1.008	*	1.006	+

High school graduate							1.005		1.004	
<i>Time variant variables</i>										
Married									1.016	
Self-rated health									1.294	***
Comorbidities									1.265	***
CESD									1.117	***
Treatment burden									1.089	**
<i>Survey status</i>										
Death	4.263	***	3.139	***	4.131	***	1.351	***	2.586	***
Attrition	1.001		1.077		1.078		0.042		1.022	
Proxy (time variant)	2.264	***	2.160	***	2.177	***	0.766	***	1.801	***
<u>Random effect</u>										
Variance	2.863	***	2.721	***	2.508	***	2.465	***	1.652	***
Intercept	0.053	***	0.049	***	0.047	***	0.048	***	0.037	***
Linear slope	0.002	***	0.002	***	0.002	***	0.002	***	0.001	***
Quadratic slope										
Covariance	0.030		0.027		0.016		0.018		0.033	
	-		-		-		-		-	
Intercept x linear slope	0.026		0.025		0.024		0.025		0.021	
	-		-		-		-		-	
Intercept x quadratic slope	0.006		0.005		0.005		0.005		0.004	
Linear x quadratic slope										
Level 1 residual	0.470	***	0.472	***	0.481	***	0.478	***	0.498	***

*** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$; + $p < 0.10$; ERR: Estimated Rate Ratio

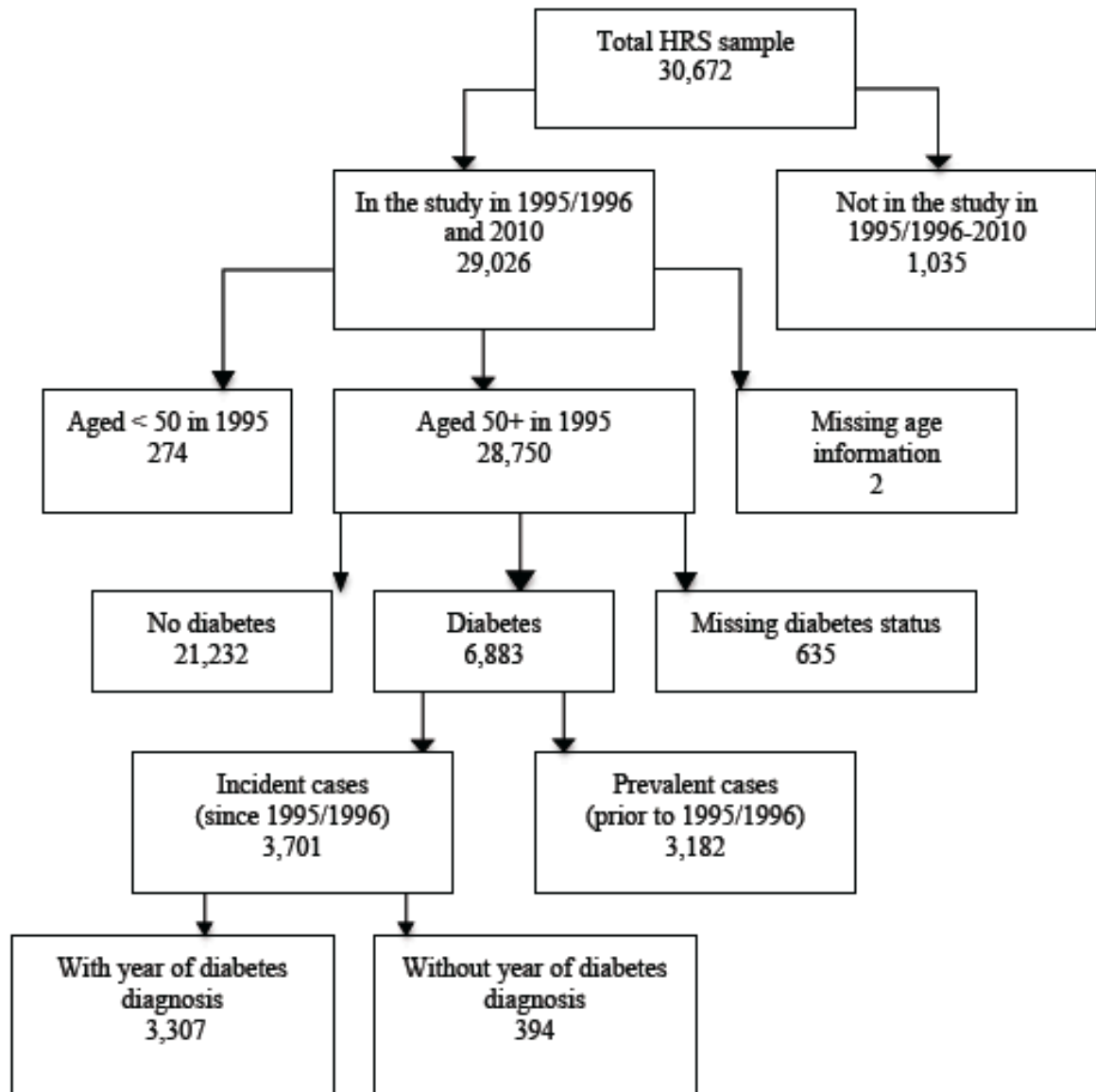
Appendix B: Average mobility disability trajectory using HLM® negative binomial multilevel poisson regression

	M1 ERR	Sig	M2 ERR	Sig	M3 ERR	Sig	M4 ERR	Sig	M5 ERR	Sig
<u>Fixed effects</u>										
For intercept										
Intercept	1.027		0.957		0.625	***	0.537	***	0.740	***
Age at diagnosis			1.026	***	1.051	***	1.053	***	1.043	***
Birth cohort (age in 1995)					0.971	***	0.967	***	0.979	***
Female					1.645	***	1.605	***	1.418	***
Non-Hispanic black					0.981		0.917	+	0.916	*
Hispanic					1.133	*	0.975		0.916	+
Other race					1.057		1.056		1.039	
Less than High school							1.514	***	1.203	***
High school graduate							1.207	***	1.096	*
For linear slope										
Linear slope	1.063	**	1.063	***	1.083	***	1.098	***	1.055	***
Age at diagnosis			1.001	**	1.001		1.001		1.001	
Birth cohort (age in 1995)					1.000		1.001		1.001	
Female					0.977	***	0.978	***	0.988	*
Non-Hispanic black					0.994		1.001		1.004	
Hispanic					1.015	+	1.030	**	1.023	*
Other race					0.963	+	0.962	+	0.983	
Less than High school							0.966	***	0.977	**
High school graduate							0.985	+	0.987	+
For quadratic slope										
Quadratic slope	1.001		1.001	*	1.002	+	1.001		1.002	
Age at diagnosis			1.000		1.000		1.000		1.000	
Birth cohort (age in 1995)					1.000		1.000		1.000	
Female					1.000		1.000		1.000	

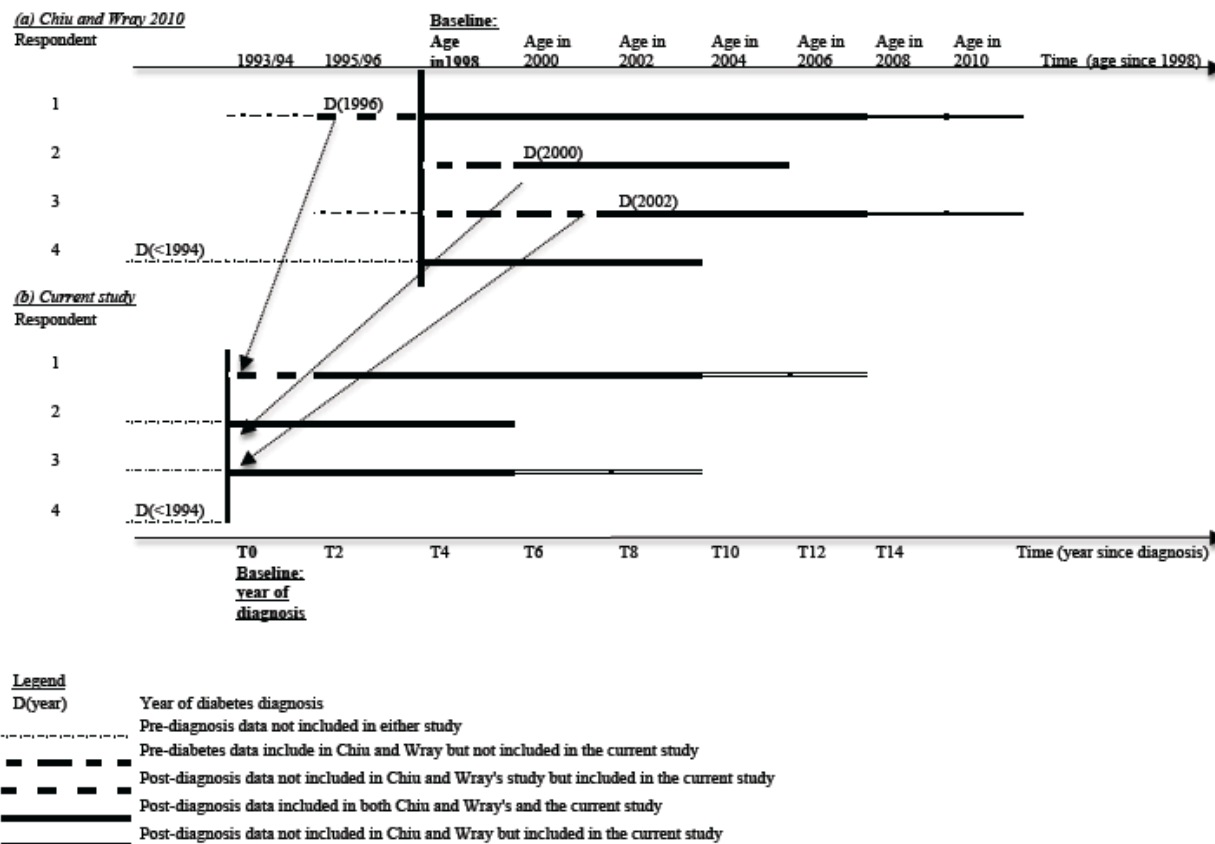
Non-Hispanic black				1.001		1.001		1.000
Hispanic				0.997	+	0.997	*	1.000
Other race				0.995		0.996		1.002
Less than High school						1.002		0.999
High school graduate						1.001		0.996
<i>Time variant variables</i>								
Married								0.972
Self-rated health								1.258 ***
Comorbidities								1.169 ***
CESD								1.053 ***
Treatment burden								1.038 **
BMI								1.021 ***
<i>Survey status</i>								
Death	2.135	***	1.842	***	2.157	***	2.075	***
Attrition	1.040		1.082		1.095	+	1.078	
Proxy (time variant)	1.416	***	1.359	***	1.378	***	1.369	***
<u>Random effect</u>								
Variance								
Intercept	0.895	***	0.895	***	2.157	***	0.753	***
Linear slope	0.005	***	0.005	***	1.095	+	0.005	***
Quadratic slope	0.00002		0.00002		1.378	***	0.00002	***
Covariance								
Intercept x linear slope	-0.019		-0.019		2.157	***	-0.015	
Intercept x quadratic slope	-0.002		-0.002		1.095	+	-0.002	
Linear x quadratic slope	-0.0002		-0.0002		1.378	***	-0.0002	
Linear x quadratic slope	0.583		0.583		0.589	***	0.586	

*** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$; + $p < 0.10$; ERR: Estimated Rate Ratio

Appendix C: Sample selection



Appendix D: Differences in study timelines between Chiu & Wray (2010)¹² and the current study



¹² Chui C., & Wray, L. A. (2010). Physical disability trajectories in older Americans with and without diabetes: The role of age, gender, race or ethnicity, and education. *The Gerontologist*, 51(1), 51-63. doi: 10.1093/geront/gnq06

Appendix E: Fixed effects from the HLM models for diabetes duration, age at diagnosis, and cohort on physical, mental, and cognitive health

Model	ADL/IADL Disability (0-11)			Cognitive function (0-35)		Depressive Symptoms (0-9)	
	At diagnosis	Linear change	Quadratic change	At diagnosis	Linear change	At diagnosis	Linear change
Diabetes duration	0.824***	0.110***	0.006***	21.051***	-0.364***	1.621***	0.023***
Diabetes duration	0.652***	0.097***	0.008***	20.822***	-0.443***	1.632***	0.025***
Age at diagnosis	0.060***	0.008***	0.0001*	-0.269***	-0.007	-0.0004	0.002*
Diabetes duration	0.415***	0.100***	0.009***	20.736***	-0.473***	1.620***	0.022**
Age at diagnosis	0.107***	0.008***	-0.0004	-0.413***	-0.034***	-0.004	-0.0002
Birth cohort	-0.049***	0.001	0.001+	0.122***	0.021**	0.004	0.002

Models adjust for attrition (0=no), death (0=no), and proxy interview (0=no)