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Age-Related Trends in the Prevalence of Type 2 Diabetes among Japanese and White and Black American Adults

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Abstract

Aim: To compare the prevalence of poor glycemic control in probability samples of Japanese and American adults, and to determine the association with their somatic phenotypes.

Material and Methods: Blood samples and anthropometric measures were obtained from 382 Japanese, 32-79 years of age, randomly selected to reflect the 23 wards of Tokyo. HA1c values were compared to 1215 Americans, 35-86 years of age, from a national study across the 48 continental states, along with an over-sampling of African-Americans from one city (www.midus.wisc.edu). Body Mass Index (BMI) and Waist-hip ratio (WHR) were also assessed.

Results: Many Japanese now have high HA1c approaching Caucasian-American levels, although elevated HA1c (>6.5%, 48 mmol/mol) is not nearly as prevalent as among African-Americans. Significant age-related trends were evident in both countries, with poor glycemic control occurring at younger ages in males and rarely found until old age in Japanese women. Japanese had higher HA1c levels at BMIs of 23-25, in contrast to Americans with Type 2 diabetes who more typically had a BMI over 30. Central adiposity predicted HA1c levels better than BMI, a relationship also apparent at a smaller WHR in Japan.

Conclusion: The prevalence of high HA1c in Tokyo almost rivals white Americans, but those statistics are dwarfed by the 37% of Afr-Amer adults identified with Type 2 diabetes. Elevated HA1c was more common in men, reflecting central adiposity, but poor glycemic control was also widespread among overweight Afr-Amer women. Type 2 diabetes was higher among older Japanese, when more women succumb. Overall, the findings highlight the societal and clinical challenges posed by demographic trends in both countries.

Keywords: Adiposity; Aging; African-american; Diabetes; Glycosylated hemoglobin, Glycemic control; HA1c; Health disparities; Insulin resistance; Japan

Introduction

The prevalence of Type 2 diabetes continues to increase worldwide reflecting changes in diet, a more sedentary life style,

and the effects of urbanization [1]. In addition to its association with obesity in the United States and many European Union countries [2], the rising incidence of poor glycemic control and insulin resistance has been evident for several decades in Asian countries including Japan [3]. Between 5-14% of older Japanese adults now have Type 2 diabetes, although the rates differ between rural and urban areas, and vary across cities [4,5]. For example, the prevalence is particularly high in Hisayama, a manufacturing city [6], but diagnoses of Type 2 diabetes have also increased in traditionally healthy regions, including Okinawa [7,8].

The current study assessed glycosylated hemoglobin levels (HA1c) across a wide age range of Japanese adults who lived in Tokyo, a city that has not been as systematically surveyed and then compared to other countries. Glucoregulation was considered with respect to a national survey of middle- and older-aged adults in the US, including a city-specific -oversample of African-Americans (Afr-Amer). Although not necessarily reflective of the entire US, these minority participants provided important information about health disparities in a large urban setting where there are prominent racial differences in income and educational attainment. The two datasets derived from the Midlife in Japan, and Midlife in the U.S. (MIDJA and MIDUS, respectively). It is well known that dyslipidemia and poor glycemic control are associated with obesity, which is often assessed by Body Mass Index (BMI). However, among many Asians, the first signs of insulin resistance can emerge at a much lower BMI than 30, the criterion usually considered to be indicative of risk for Americans [9,10]. In fact, many studies suggest a BMI of 25 should be considered high for Japanese adults given the differences in the amount of subcutaneous and visceral fat [11,12]. Therefore, our analyses compared the BMIs of nondiabetics to those with Type 2 diabetes in both countries, as well as population differences in Waist-hip ratios (WHR). Because WHR is a better index of central adiposity, it may be a more sensitive anthropomorphic measure for understanding ethnic and gender differences in glycemic control. The consequences of diet choice and life style accumulate with age, and thus it is not surprising that Type 2 diabetes becomes more common in older adults. However, the influence of ethnicity and race on these age-related trends has not been as well characterized. In addition to comparing Japanese adults to American adults, the analyses compared the prevalence of Type 2 diabetes among white and black Americans. Given the demographic changes taking place in first world countries (with 25.9% of the Japanese population now older than 65 years of age), the societal ramifications and medical costs of extended longevity are significant. Both MIDJA and MIDUS recruited participants across a wide age range, permitting an examination of age trajectories in the prevalence of Type 2 diabetes. Our a priori hypothesis was that Type 2 diabetes would be more prevalent in middle-aged Americans, especially among Afr-Amer participants, whereas Japanese with HA1c high enough to meet criteria for Type 2 diabetes would tend to be older. Finally, we considered the possible influence of educational attainment in both countries. Numerous studies on Americans have found that poor health is both more widespread and evident at a younger age among less educated individuals, but this type of socioeconomic gradient often appears to be less prominent in Japanese society.

Material and Methods

The 382 Japanese participants were a subset (37%) from a larger number of randomly selected middle- and older-aged adults recruited in 2008 to reflect the age and gender composition of the 23 residential wards of Tokyo. All MIDJA respondents completed demographic and psychological questionnaires, and the biomarker subsample also provided blood specimens at a medical clinic near the University of Tokyo. Mean age was 54.2 years (+/-14.1 years, 32-79 years of age), and 73% were married. Age, gender composition, marital status, and education attainment did not differ significantly between the biomarker and survey participants. Comparison data were generated from MIDUS, which began in 1995-1996 as a national probability sample of 7108 American adults (www.midus.wisc.edu). They had been recruited from the 48 continental states via random -digit telephone dialing procedures. A follow-up assessment of 5900 was initiated in 2004 when they were 35 -86 years of age (MIDUS II), during which a subset of 965 participated in biomedical assessments at one of three Clinical and Translational Research Centers. Those providing blood were similar to the larger study sample with respect to age, gender, and marital status, but likely to be more educated (although 25% still had attained only a high school degree, and 50% had not completed college) [13]. To increase the representation of Afr-Amer participants during the second phase of MIDUS, a city-specific sample was recruited from Milwaukee, WI (N=225). Specimen collections and analyses were approved by the Health Sciences Institutional Review Board at the University of Wisconsin-Madison, as well as by IRBs at UCLA and Georgetown University. A comparable review at the University of Tokyo approved the MIDJA protocols. All participants provided informed consent Both MIDJA and MIDUS data are available in the public domain (Inter-University Consortium for Political and Social Research; http://www.icpsr.umich.edu/icpsrweb/NACDA/).

Demographic Variables

Age, gender, race, and years of education were determined for all participants. Educational attainment was subsequently merged into 3 categories: 1) high school, 2) some college, and 3) college-educated/professional school.

Anthropometric Measures

Height and weight were recorded to calculate Body Mass Index (BMI, weight/height^2, kg/m^2). Waist and hip measurements were obtained to compute the Waist-hip Ratio (WHR).

Blood Collection

Whole blood was collected to determine HA1c, an integrated metric used to capture variation in glucose levels over the prior several weeks [14]. For American participants, fasted blood was obtained between 0500-0700, with a modal time of 0605. All blood was shipped cool via overnight carrier and analyzed at one diagnostic laboratory via turbidmetric immunoinhibition assay (Meriter Labs, Madison, WI). Prior to the current analyses, the shipping protocol was validated by serially testing the same blood samples repeatedly across one week, verifying that HA1c remains stable in refrigerated blood for 4-7 days after collection. Blood collected from Japanese participants was analyzed in Tokyo (Syowa Medical Science). To directly compare MIDUS and MIDJA values, 10 fresh blood samples were collected from both American and Japanese adults in Tokyo, transported to the US by overnight carrier, and analyzed simultaneously in both laboratories. The results from the two testing labs were highly correlated, and a linear algorithm was generated to adjust values from Japan so they scaled identically to the HA1c testing at the American clinical laboratory.

Statistical Analyses

Descriptive statistics were generated for all variables. Chi square analyses were conducted to compare differences in the prevalence of Type 2 diabetes. Univariate analyses of variance were then employed to assess differences in HA1c levels between countries, and across race and gender. Post hoc contrasts were performed with the Scheffe test. Age was considered both as a continuous and categorical factor with 3 levels (i.e., <49, 50-65, >66 years of age). Using a HA1c criterion of 6.5% (48 mmol/mol), participants were classified as being nondiabetic or having Type 2 diabetes. Then, differences in age, BMI, WHR, and educational attainment were compared. Associations between anthropometric variables and HA1c levels were evaluated with the Pearson test. The strength of BMI and WHR as predictors of HA1c was compared with the Steiger z test [15]. Statistical significance was set at alpha < 0.05.

Results

Mean HA1c levels were significantly higher for Americans than for Japanese participants (6.09% vs 5.84%, 43 vs 40 mmol/mol, $F[1,1568]=15.31$, $p<.001$). However, when race of Americans was considered, the difference was accounted for primarily by the much higher HA1c levels in Afr-Amer participants (Table 1). As expected, Americans also had significantly larger BMIs (29.7 vs 22.5, $F[1,1568]=405.47$, $p<.001$) and WHRs (0.89 vs 0.83, $F[1,1568=236.44$, $p<.001$). Overall, American participants were more likely to have attended and/or completed college than the Japanese, although this difference was more evident for Cau-Amer (Table 1). On average, educational attainment was lowest among the Afr-Amer participants.

		Japanese	Cau-Amer	Afr-Amer	Sig
N	Female	214	523	150	-
	Male	168	442	75	-
HA1c[1]	%	5.84 (.02)	5.96 (.03)	6.66 (.15)	*race, p<.001
	mmol/mol	40 (1)	42 (1)	49 (2)	
BMI	Female	21.6 (.2)	28.6 (.3)	34.0 (.7)	*race, p<.001
	Male	23.7 (.2)	29.5 (.2)	30.2 (.8)	*gender, p<.001
WHR	Female	.78 (.004)	.83 (.003)	.87 (.007)	*race, p<.001
	Male	89 (.005)	.97 (.004)	.95 (.009)	*gender, p<.001
Education[2]	Female	1.79 (.05)	2.18 (.04)	1.76 (.09)	*race, p<.001
	Male	2.13 (.07)	2.30 (.04)	1 .72 (.09)	*gender, p<.001
[1]HA1c shown in traditional percentage values and also as mmol/mol units					
[2]Educational attainment was categorized on a 1-3 scale (1-high school, 2-some college, 3-college graduate).					

Table 1: Mean (+SE) values for the primary parameters used to compare Japanese participants in MIDJA to the Caucasian and African-American participants in the MIDUS project.

Type 2 Diabetes

Significantly more Americans had HA1c levels over 6.5% (48 mmol/mol), self-reported a prior diagnosis of Type 2 diabetes, or were taking diabetic medications (Figure 1) ($X^2 = 97.5$, $p<.001$). In addition to the MIDUS participants with high HA1c levels that met criterion for diabetes, there were 31 other Americans taking diabetic medications who had better glycemic control. Ten MIDJA participants were also prescribed medication for diabetes, but all had HA1c above 6.5%. The difference in the prevalence of Type 2 diabetes between MIDUS and MIDJA was driven by the especially high percent of Afr-Amer with Type 2 diabetes (37%). However, in keeping with concerns about the prevalence of Type 2 diabetes in Japan, 7% of participants were found to have HA1c values over 6.5% (>48 mmol/mol). A gender difference was evident, with poorer glycemic control among male Japanese and Cau-Amer participants. In contrast, the more common obesity among Afr-Amer females was associated with a high prevalence of Type 2 diabetes similar to that of Afr-Amer males. Thus, there was also a significant difference in the prevalence of Type 2 diabetes by gender and race across the two countries (($X^2 = 129.7$, $p<.001$) (Figure 1).

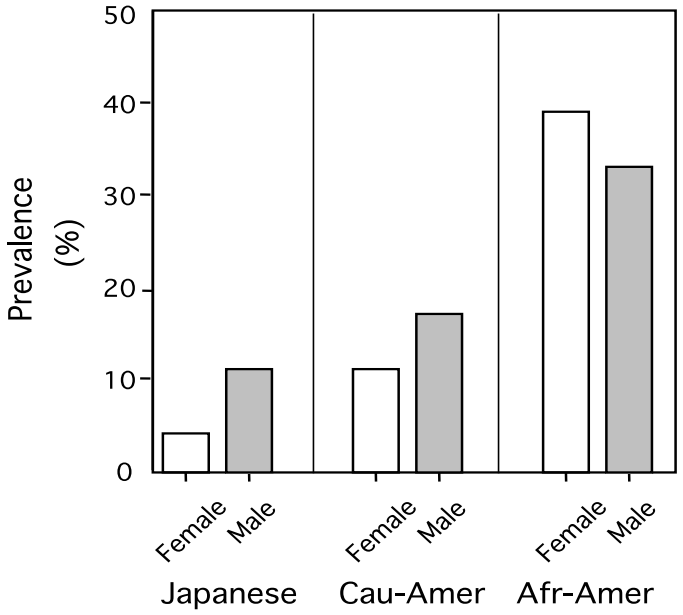

Figure 1: Significant ethnic and racial differences were found in the percent of Japanese and American participants with HA1c exceeding 6.5%, (48 mmol/mol), the level associated with Type 2 diabetes. The significant gender difference evident for Japanese and Cau-Amer participants was not seen in Afr-Amer because of the high percent of women with elevated HA1c.

Effect of Age

HA1c levels increased incrementally with age in both countries, and were significantly higher in adults older than 50 years as well for those past 66 years of age when compared to younger participants below 49 years ($F[2,1568]=10.76$, $p<.001$). This effect of age on glucoregulation was evident in both males and females, although closer inspection of Figure 2 indicates that Japanese women were not likely to have high HA1c of concern until old age. In contrast, many Afr-Amer women already had HA1c levels above 6.5% (48 mmol/mol) by 50 years of age. Males in both countries were more likely than females to have elevated HA1c levels in the prediabetic or diabetic range while still in the 50-65 year range. Only 4% of Japanese women had Type 2 diabetes, and all were older (mean age = 68.9 years, range 62-77 years).

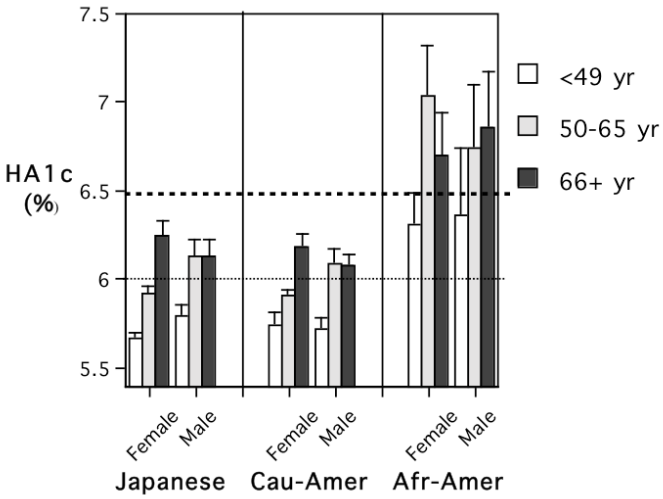

Figure 2: HA1c increased progressively with age in both Japan and the US, but the mean levels did not cross the prediabetic value of 6.0% in Japanese and Cau-Amer women before >66 years of age, whereas that threshold was already commonly exceeded in men by >50 years of age in all 3 races. Many African American adults in the middle age range of 50-65 years old already had elevated HA1c values indicative of Type 2 diabetes.

Anthropometric Measures

In both countries, adults with Type 2 diabetes had significantly larger BMIs and WHRs than non-diabetic participants (Figure 3). This difference in BMI for those with Type 2 diabetes was evident in Japanese as well as among Cau-Amer and Afr-Amer adults ($F[1,1568]=38.64$, $p<.001$). However, it was striking that the mean BMI for MIDJA participants with Type 2 diabetes was just 25.4, significantly below the average BMI values for all Americans (mean =29.7). The mean BMI for diabetic Cau-Amer was 31.8, and an even higher 34.6 for diabetic Afr-Amer. Participants with Type 2 diabetes also had significantly larger WHRs than non-diabetics (0.94 vs. 0.87, $F[1,1568]=78.7$, $p<.001$), a difference in central adiposity that was evident in both countries (Figure 3). The statistical conclusions about WHR were more complex, however,

due to significant gender and national differences. WHR was larger in males than females (0.95 vs. 0.83). WHRs also differed by country: larger for Americans than Japanese (0.89 vs. 0.83). In general, WHR was a better predictor than BMI of HA1c levels, although the magnitude of the difference varied by ethnicity and race (Table 2). The obesity that was more common among Afr-Amer women, as well as racial differences in fat distribution, made BMI a less reliable predictor of HA1c levels for Afr-Amer women. Variation in body composition and shape among women of different races has also been reported by others [16].

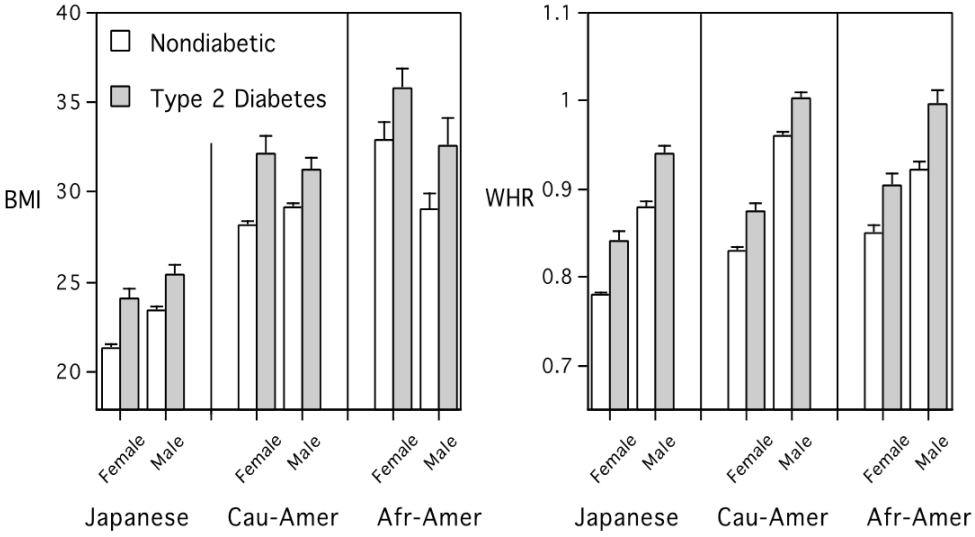

Figure 3: Body Mass Index (BMI) and Waist-hip ratio (WHR) were significantly higher in adults with high HA1c indicative of Type 2 diabetes. However, the analysis indicated that poor glycemic control was evident at a significantly lower BMI and smaller WHR in Japanese adult participants than in American participants.

	BMI	r	p	WHR	r	p	Diff	r	for BMI & WHR
Japan	22.6	0.26	**	0.83	0.31	**	+	0.64	**
Male	23.6	0.19	ns	0.89	0.31	**	+	0.6	**
Female	21.6	0.33	**	0.78	0.39	**	#	0.57	**
Cau-Amer	29.0	0.16	**	0.89	0.21	**	0.08	0.35	**
Male	29.5	0.15	*	0.97	0.24	**	+	0.48	**
Female	28.6	0.18	**	0.83	0.27	**	+	0.37	**
Afr-Amer	32.7	0.10	ns	0.9	0.18	*	ns	0.03	ns
Male	30.2	0.34	*	0.27	0.27	*	ns	0.49	**
Female	34.0	0.01	ns	0.19	0.19	*	#	0.006	ns
Pearson's correlations for HA1 with both BMI and WHR. * P < 0.05; ** P <0.001 Diff indicates that the correlation (r value) for WHR was significantly larger than for BMI. + P <.05 with a one-tailed test. # P <.05 with a two-tailed test									

Table 2: BMI and WHR correlations with HA1c levels in Japan and US. In general, WHR was a better predictor of HA1c, except for the Afr-Amer participants. Among African-Americans, the associations seemed to be more generally associated with overall obesity, and a larger BMI appeared to be better tolerated in Afr-American women.

Educational Attainment

Although diabetic Americans were less likely to have attended college than nondiabetic participants, the difference did not reach statistical significance. There also wasn't a substantial influence of educational attainment on HA1c levels in Japan. Across the entire sample in both MIDUS and MIDJA, there was a small, inverse correlation between having more education and a lower HA1c ($r = -0.05$, $p = 0.037$), but it was due primarily to racial differences in educational attainment and obesity in the United States.

Discussion

This survey of middle- and older-aged Japanese and American adults has confirmed concerns about the prevalence of Type 2 diabetes and poor glycemic control in both countries [17]. As many have reported previously, changes in diet and sedentary inactivity, along with a genetic propensity, have increased the likelihood of Type 2 diabetes among older Japanese adults [18,19]. Our estimate of 7% for Japanese adults with Type 2 diabetes concurs with other studies, including the more extensive Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Asia (DECODA) project, which estimated the prevalence to be 7-14% in 4 other Japanese cities [20]. Although indicative of a continuing increase that began after World War II [21,22], the rate is still far below the high prevalence of Type 2 diabetes in the US, especially among Afr-Amer adults. Our estimates from this MIDUS cohort are in keeping with other larger surveys of Americans, including NHANES. One novel finding to highlight is the marked difference in the typical age of onset for Type 2 diabetes between the two countries. Consistent with our hypotheses, few Japanese women evinced poor glycemic control until old age, with the first case of Type 2 diabetes found in this survey at 62 years of age. In contrast, Japanese men followed the pattern of American males with higher HA1c becoming more common by middle age, reflecting an influence of central adiposity (other gender differences in dyslipidemia and hyperglycemia in Japanese adults have also been reported e.g., [23]). Given the expected longevity of Japanese, the trends for Type 2 diabetes later in life indicate there will be many older adults requiring medical attention to lessen the morbidity associated with this chronic health condition.

Our analyses also confirm that poor glucoregulation and insulin resistance occur at a relatively smaller BMI among Japanese adults [24-26]. The mean BMI for MIDJA participants with Type 2 diabetes was 25.4, well below the typical criterion of 30 usually thought to be an indicator of risk among Americans [27]. This difference is believed to reflect racial variation in the amount of subcutaneous and visceral fat [28], as well as genetic differences among Japanese in several critical metabolic pathways involved in glucose control [29,30]. These heritable propensities may also account for why Japanese are more prone to develop dyslipidemia, insulin resistance, and cardiovascular disease after emigrating to other countries and if regularly consuming a westernized diet [31]. The most disturbing finding for the American participants was the extremely high prevalence of Type 2 diabetes among Afr-Amer, including in middle-aged women [32,33]. It likely reflects a common occurrence of obesity, which was evident in both the large BMIs and WHRs. Although the Afr-Amer participants were derived primarily from a city-specific sample in Milwaukee, WI, this profile of diabesity is now common in other American regions, especially in southern states. Based on HA1c levels, the prevalence of Type 2 diabetes in MIDUS was 14% for Cau-Amer and 37% for Afr-Amer participants. Many economic and social factors contribute to the propensity to be overweight and underlie the racial disparities in health in the US. However, using just educational attainment, we were not able to demonstrate its primary effect as the sole mediator. That may reflect a synergism with other psychosocial factors, including racial discrimination, anger and depression, which have all been found to worsen glucoregulation [34]. In addition, there wasn't evidence for a health gradient associated just with educational attainment among the Japanese participants, but that could reflect the benefits of a more effective, universal health care system [35].

Several limitations of our analysis should be acknowledged. Most significantly, the estimates of Type 2 diabetes were derived from a single measure--the occurrence of elevated HA1c-- rather than a more complete profiling, including insulin and glucose tolerance testing [36]. However, many have reported that high HA1c is an acceptable proxy [37-39]. For the MIDUS project specifically, it had been demonstrated previously that there is a robust correlation between the HA1c levels and fasted insulin and glucose levels [40]. Only HA1c levels from MIDUS could be compared with the MIDJA data because it was not possible to obtain fasted specimens from Japanese adults who were often commuting long distances to get to work. HA1c levels did accurately capture the MIDJA participants who had received a prior clinical diagnosis of Type 2 diabetes by a physician, including in those using prescription medications. Among the MIDUS participants, 31 reported a prior diagnosis and were using medications for glycemic control, resulting in their having a HA1c value below our cutoff. If included as having Type 2 diabetes, it would increase the prevalence estimates for Americans by 3%. Finally, we did not specifically differentiate a possible diagnosis of Type 1 diabetes, but it was not likely a major contributing factor given its low prevalence: approximately 1.5 per 1000 adults (equivalent to less than 2 participants across both studies by chance). With regard to the participants being nationally representative, for both studies, we verified that the demographic composition of the biomarker participants was mostly concordant with the larger pool of participants who had completed just the questionnaire surveys in terms of their age and gender distribution. For the US sample, the participants who agreed to provide blood

samples did tend to be somewhat more educated and not as likely to be frail or have disabling illnesses [13]. Conclusions about the Afr-Amer participants living in Milwaukee, WI may also not generalize to the whole country, but many other papers have documented similar health and obesity concerns among Afr-Amer adults in other regions of the U.S.

In sum, our findings concur with prior prevalence estimates for Type 2 diabetes in Japan and the US. The National Diabetes Survey in Japan reported that males suspected of having Type 2 diabetes increased from 9.9 to 15.3% between 1997 and 2007, and from 7.1 to 7.3% in women [41]. NHANES estimated the occurrence of undiagnosed and diagnosed diabetes for Americans in 2005-2008 at 11.3% among adults older than 20 years of age, and at 26.9% for adults over 65 years. Importantly, both MIDJA and MIDUS replicated the expected trends for poorer glycemic control with increasing age, although with some ethnic and racial differences. Among Japanese women, who had particularly small BMIs and WHRs, there were few instances of poor glycemic control until old age. The significance of relatively modest weight gains among Japanese was striking, concurring with the propensities for metabolic syndrome and insulin resistance seen among Asian-Americans. Japanese who emigrate from Japan or shift from their traditional lower fat and sugar diet are at increased risk for health problems and increases in several proinflammatory biomarkers associated with poor health [42]. Conversely, for older Japanese with Type 2 diabetes, intervention studies have demonstrated there are therapeutic benefits of including more vegetables and fish in their diets [43]. Finally, MIDUS confirms the widely publicized concerns about obesity among American adults, which was prominent among Afr-Amer women in this survey, even by middle-age. Diet moderation and increased attention to exercise are important public health policy issues for both countries.

Conflicts of Interest

There were no reported conflicts of interest that influenced the research or presented findings.

Author Contributions

All authors contributed to the conceptual design and aims. All reviewed the manuscript and findings. More specifically, CLC oversaw the testing of the HA1c and wrote the first draft. VT and GDL assisted with statistical analyses. NK and MK directed the recruitment of participants in Tokyo. SK and HRM collaborated on the design and MIDJA aims. CJR is the head of both MIDUS and MIDJA and coordinated the team efforts in both countries.

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