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Impact of population aging on trends in diabetes prevalence: A meta-regression analysis of 160,000 Japanese adults

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ABSTRACT

Aims/Introduction: To provide age- and sex-specific trends, age-standardized trends, and projections of diabetes prevalence through the year 2030 in the Japanese adult population.

Materials and Methods: In the present meta-regression analysis, we included 161,087 adults from six studies and nine national health surveys carried out between 1988 and 2011 in Japan. We assessed the prevalence of diabetes using a recorded history of diabetes or, for the population of individuals without known diabetes, either a glycated hemoglobin level of ≥6.5% (48 mmol/mol) or the 1999 World Health Organization criteria (i.e., a fasting plasma glucose level of ≥126 mg/dL and/or 2-h glucose level of ≥200 mg/dL in the 75-g oral glucose tolerance test).

Results: For both sexes, prevalence appeared to remain unchanged over the years in all age categories except for men aged 70 years or older, in whom a significant increase in prevalence with time was observed. Age-standardized diabetes prevalence estimates based on the Japanese population of the corresponding year showed marked increasing trends: diabetes prevalence was 6.1% among women (95% confidence interval [CI] 5.5–6.7), 9.9% (95% CI 9.2–10.6) among men, and 7.9% (95% CI 7.5–8.4) among the total population in 2010, and was expected to rise by 2030 to 6.7% (95% CI 5.2–9.2), 13.1% (95% CI 10.9–16.7) and 9.8% (95% CI 8.5–12.0), respectively. In contrast, the age-standardized diabetes prevalence using a fixed population appeared to remain unchanged.

Conclusions: This large-scale meta-regression analysis shows that a substantial increase in diabetes prevalence is expected in Japan during the next few decades, mainly as a result of the aging of the adult population.

INTRODUCTION

Japan's aging rate is currently the highest in the world[1]. Population aging is a major public health concern globally because of the substantial burden that aging-associated diseases place on society. Diabetes mellitus is one of the most common aging-associated diseases affecting the adult population worldwide. Its repercussions on health are numerous: macrovascular and microvascular complications, liver disease, cognitive decline, increased susceptibility to infection, reduced life expectancy, as well as impaired quality of life, among others[2]. A growing body of evidence suggests that diabetes might also be associated with the development of various types of cancer[3–5]. Furthermore, a recent report from the International Diabetes Federation shows

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that approximately 4.5 million deaths in 2011 could be attributed to diabetes, representing more than 8% of global all-cause mortality[6]. Type 2 diabetes, which accounts for most cases of diabetes, is highly dependent on modifiable risk factors, such as unhealthy eating habits, obesity and lack of physical activity. A large proportion of diabetes cases are therefore considered preventable, and controlled trials have confirmed this in Japan and elsewhere[7–9].

The availability of trends data in diabetes prevalence is thus critical to helping policy makers and healthcare providers both measure the extent of the problem and implement appropriate measures to halt its spread[10]. Although global estimates are valuable in alerting the international community to the ongoing diabetes epidemic, they might fail to provide accurate information at the specific country level. Indeed, estimates of the prevalence of diabetes in the Japanese population in recent international studies differ quite substantially[11–14]. This discrepancy could be partly attributed to the diversity of methods and data used to produce them. In 2009, an International Expert Committee recommended the use of glycated hemoglobin (HbA1c) with a threshold of ≥6.5% (48 mmol/mol) to diagnose diabetes[15]. The American Diabetes Association, World Health Organization and Japan Diabetes Society (JDS) used this criterion in 2010, 2011 and 2010, respectively[16–18]. Nevertheless, relatively few studies have reported estimates of diabetes prevalence using this new criterion at a national level[19,20].

In the present study, we aimed to estimate age- and sex-specific trends, and projections of diabetes prevalence through the year 2030 using the most recently adopted diagnostic criteria, and to examine the impact of population aging on trends in diabetes prevalence in Japan, the most rapidly aging society in the world. To accomplish these objectives, we carried out a meta-regression analysis of the results of studies conducted during the past two decades in Japan.

METHODS

Criteria for the Definition of Diabetes

To estimate the frequency of diabetes, the JDS recommends the use of either HbA1c of ≥6.5%[21] (48 mmol/mol[22]) or 2-h plasma glucose of ≥200 mg/dL in a 75-g oral glucose tolerance test (OGTT)[18]. The use of either of these is particularly important in the Japanese population, because screening for a fasting plasma glucose (FPG) level of ≥126 mg/dL alone could miss a substantial proportion of previously undiagnosed cases of diabetes[23]. We therefore included studies that used any of the following standard diagnostic criteria: (i) HbA1c level of ≥6.5% (48 mmol/mol); or (ii) the 1999 World Health Organization criteria (i.e., FPG level of ≥126 mg/dL and/or OGTT 2-h glucose level of ≥200 mg/dL)[24]. Consistent with the JDS recommendations[18], studies that reported a FPG level ≥126 mg/dL, casual glucose level, or self-report of diabetes diagnosis or treatment were also included, provided they also reported the standard HbA1c or 2-h glucose diagnostic criterion. HbA1c values are presented as percentage units, in accordance with the National Glycohemoglobin Standardization Program, and in mmol/mol, as recommended by the International Federation of Clinical Chemistry and Laboratory Medicine[22].

Study Population and Data Collection

We searched the MEDLINE, EMBASE and *Ichushi* (*Japana Centra Revuo Medicina*) databases through March 2013[25]. Two investigators (AG and MG) selected studies that were carried out in the Japanese population, and that evaluated the prevalence of diabetes using either of the aforementioned diagnostic criteria. The MEDLINE search terms were 'Prevalence' (MeSH terms) AND ('diabetes mellitus' [MeSH:noExp] OR 'diabetes mellitus, type 2'[MeSH terms]) AND ('Japan' [MeSH terms] OR 'Japan' [all fields]). Similar search terms were used to search the EMBASE and *Ichushi* databases. The search was limited to studies on adult human subjects with no restriction on language. A manual search was also carried out to identify pertinent data sources from the references of the identified studies. When data necessary for estimating sex- and age-specific (10-year groups) diabetes prevalence estimates were missing, authors were contacted and asked if they could provide the missing information.

Initially, we identified 613 relevant articles. On the basis of the titles and abstracts, 51 articles were considered potentially eligible, and the entire texts of these 51 articles were reviewed. We excluded 20 studies that did not use the standard diagnostic criteria, nine duplicate studies, seven studies that did not report diabetes prevalence and five reviews, editorials or letters to the editor. We further excluded four studies in which sex- and age-specific diabetes prevalence was not available[26–29]. SX (investigator) of the Diabetes Epidemiology: Collaborative analysis of Diagnostic criteria in Asia study[30] coordinated by TN, QQ and JT provided information from three studies (Hisayama Study[31], Funagata Study[32] and Ojika Study[33]). One article[34] provided prevalence estimates for a subset of the study population of the Japan Public Health Center-based Prospective Study Diabetes Study (JPHC Diabetes Study)[35]; MN and ST (investigators) of the JPHC Diabetes Study provided information on the total population for the present study. YH, YA and HS (investigators) of the Toranomon Hospital Health Management Center Study[36], and Machiko Inoue (investigator) of the Yuport Medical Checkup Center Study provided information for the present study[37]. One article[38] provided results from the National Survey on Circulatory Disorders in 1990[39]. Furthermore, we retrieved an additional eight national health surveys[20,40–46]. The study identification process is summarized in Figure S1 of the supplementary material.

For each selected study, we extracted the year of publication, year(s) when data were collected, central year of data collection, definition of diabetes, and the total number of participants and cases of diabetes by 10-year age group and sex. The central year was estimated as the mean between the starting and ending years of data collection. This sometimes resulted in non-integer years, but this did not constitute a problem, as year was

considered a continuous variable in the meta-regression analysis.

Statistical Analysis

In the first step, the sex- and 10-year age-specific diabetes prevalence was estimated by meta-analysis. Prevalence estimates from each study were transformed on the logistic link function (or logit) scale and the corresponding variances were obtained by the Delta method[47]. A random effect meta-analysis was then carried out[48]. The impact of heterogeneity was measured by means of the I^2 statistic, which describes the proportion of total variation in estimates that is as a result of heterogeneity between studies[49]. In the second step, trends in diabetes prevalence were assessed through linear random effect meta-regression[50] of the transformed prevalence estimates using year of assessment as the independent variable. Predicted prevalence estimates for a particular year were obtained on the logit scale by using the estimated parameters of the linear regression model and then transforming back to the prevalence scale using the inverse logistic link (or expit) function. Corresponding variance estimates were computed from the covariance matrix of the model using the Delta method. A sensitivity analysis was carried out by repeating the meta-analysis and meta-regression steps with the exclusion of: (i) studies using both HbA1c and OGTT for diabetes diagnosis; and (ii) studies carried out in a single center.

Sex-specific age-standardized estimates of the prevalence of diabetes in the adult Japanese population (age 20 years or older) for a given year were obtained using the direct standardization method. We estimated the age-standardized estimates using the Japanese population distribution of the corresponding year, year 2010[51,52] and year 2030[53], and the world population distribution of the corresponding year, year 2010 and year 2030[54] as standardization populations. We computed the sum of the 10-year age-specific prevalence estimates weighted by the proportion of the population in the corresponding age category. Confidence intervals of the predicted age-standardized prevalence estimates were obtained by simulation. More precisely, we constructed an empirical diabetes prevalence distribution for each year of interest by sampling 20,000 times from the distribution of the model parameters and calculating the corresponding age-standardized prevalence estimates. Confidence intervals were then obtained by taking the 2.5 and 97.5 percentiles of the resulting empirical diabetes prevalence distribution. The estimated number of cases of diabetes was obtained by multiplying the age-standardized prevalence values by the adult Japanese population estimates.

Projections of the sex- and age-specific prevalence of diabetes until 2030 were calculated using population distribution projections[53,54] under the assumption that the trends in prevalence identified in the meta-regression would remain the same in the next decades. The aforementioned procedure was used to compute projected sex-specific age-standardized diabetes prevalence as well as the corresponding confidence intervals. It should be noted that these confidence intervals do not take into account the uncertainty in projected population estimates.

All analyses were carried out with R statistical software version 2.15.0 (R Foundation for Statistical Computing, Vienna, Austria)[55].

RESULTS

In the present analysis, we included a total of six studies and nine national health surveys providing diabetes prevalence estimates for 161,087 individuals (75,250 men and 85,837 women) from 1988 to 2011. Four studies were population-based[31–33,35], two were carried out at single centers[36,37] and nine were national health surveys[20,39–46]. Three studies defined diabetes using OGTT[31–33], whereas 12 used HbA1c[20,35–37,39–46]. Ignoring the effect of age and year of assessment, the overall observed prevalence was 11.5% (8,681 cases) for men and 6.9% (5,925 cases) for women. Details of the studies' characteristics are summarized in Table 1.

Age- and sex-specific estimates showed that the prevalence of diabetes increased with age for both sexes and was higher among men than women in all age categories between 1990 and 2010 (Table 2, Figure S2–S3). For both sexes, the prevalence of diabetes appeared to remain unchanged over the years in all age categories, except for men aged 70 years or older, in whom a significantly increasing trend in diabetes prevalence over time was observed (Tables 2 and S1). Trends in the age-standardized prevalence using the Japanese population of the corresponding year as a standardization population showed an increase among both sexes, which was slightly greater among men (22%) than women (14%), from 1990 to 2010. Diabetes prevalence was 8.1% among men, 5.3% among women and 6.6% among the total population in 1990, and rose to 9.9, 6.1 and 7.9% in 2010, respectively (Table 3). In contrast, the age-standardized prevalence using a fixed population (2010 Japanese, 2010 world, 2030 Japanese or 2030 world population) appeared to remain unchanged over the years, suggesting that population aging is the main factor influencing trends in diabetes prevalence in the Japanese adult population. The age-standardized diabetes prevalence using the 2010 Japanese population as a standardization population was 9.3% among men, 6.6% among women and 7.9% among the total population in 1990, and 9.9, 6.1 and 7.9% in 2010, respectively (Table 3).

Projected age- and sex-specific estimates showed that the prevalence of diabetes might increase with age among men and women, and should be higher among men than women in all age categories between 2015 and 2030 (Table 4). In both sexes, there appeared to be slight decreasing trends in the projected age- and sex-specific diabetes prevalence for individuals in the first four younger age categories (Table 4); however, these decreasing trends were not statistically significant (Table S1). For men aged 70 years or older, it is projected that there should be a significant increasing trend in diabetes prevalence with time (Table 4, Table S1). A further increase in the age-

Table 1 | Characteristics of studies included in the analysis

Study	Year(s) carried out	Source of participants	Definition of diabetes	Men		Women		Age range (years)
				Total *n*	No. cases	Total *n*	No. cases	
Hisayama Study[31]	1988	Population-based, Hisayama Town, Fukuoka	FPG ≥126 mg/dL and/or OGTT 2-h glucose ≥200 mg/dL and/or self-reported diagnosis	1,073	196	1,407	149	≥40
Funagata Study[32]	1990–1992	Population-based, Funagata Town, Yamagata	FPG ≥126 mg/dL and/or OGTT 2-h glucose ≥200 mg/dL and/or self-reported diagnosis	1,160	109	1,485	157	≥40
Ojika Study[33]	1991	Population-based, Ojika Town, Nagasaki	FPG ≥126 mg/dL and/or OGTT 2-h glucose ≥200 mg/dL and/or self-reported diagnosis	554	51	817	48	≥30
JPHC[35]	1998–1999	Population-based, 10 areas in Japan	HbA1c ≥6.5% (48 mmol/mol) and/or FPG ≥126 mg/dL and/or casual glucose ≥200 mg/dL and/or self-reported diagnosis	4,947	654	8,884	640	≥40
	2000			5,338	778	9,095	693	≥50
	2003–2004			4,219	748	6,773	720	≥50
	2005			3,460	539	5,855	599	≥50
Yuport Medical Checkup Center Study[37]	1998–2006	Single center, Tokyo	HbA1c ≥6.5% (48 mmol/mol) and/or FPG ≥126 mg/dL and/or self-reported diagnosis	17,100	1,620	17,200	735	≥20
TOPICS[36]	2002–2007	Single center, Tokyo	HbA1c ≥6.5% (48 mmol/mol) and/or FPG ≥126 mg/dL and/or self-reported diagnosis	19,506	1,682	8,374	292	≥20
National Survey on Circulatory Disorders[39]	1990	Randomly selected from the overall Japanese population	HbA1c ≥6.5% (48 mmol/mol) and/or casual glucose ≥200 mg/dL and/or self-reported diagnosis	3,403	404	4,660	292	≥30
National Diabetes Survey[40]	1997	Randomly selected from the overall Japanese population	HbA1c ≥6.5% (48 mmol/mol) and/or self-reported diabetes treatment	2,403	237	3,656	260	≥20
National Diabetes Survey[41]	2002			2,150	275	3,196	207	20+
NHNS-J[42]	2006	Randomly selected from the overall Japanese population	HbA1c ≥6.5% (48 mmol/mol) and/or self-reported diabetes treatment	1,744	214	2,552	209	≥20
[43]	2007			1,619	247	2,384	173	≥20
[44]	2008			1,813	211	2,621	168	≥20
[45]	2009			1,730	226	2,543	217	≥20
[46]	2010			1,589	264	2,268	208	≥20
[20]	2011			1,442	226	2,067	158	≥20
Total				75,250	8,681	85,837	5,925	

2-h post-load glucose level after oral glucose tolerance test; FPG, fasting plasma glucose level; HbA1c, glycated hemoglobin; JPHC, Japan Public Health Center-based Prospective Study; NHNS-J, National Health and Nutrition Survey in Japan; OGTT 2-hour glucose; TOPICS, the Toranomon Hospital Health Management Center Study; Japan National Diabetes Survey.

Table 2 | Estimated age- and sex-specific diabetes prevalence (%) in the Japanese population 1990–2010

Sex	Year	Age category (years)					
		20–29	30–39	40–49	50–59	60–69	≥70
Men	1990	0.99 (0.15–6.23)	2.87 (1.98–4.14)	7.71 (6.19–9.57)	14.17 (11.84–16.87)	14.62 (12.46–17.09)	14.52 (12.11–17.31)
	1995	0.93 (0.27–3.15)	2.52 (1.97–3.23)	7.11 (6.08–8.30)	13.60 (12.00–15.37)	15.37 (13.77–17.13)	15.79 (13.94–17.84)
	2000	0.87 (0.44–1.71)	2.21 (1.89–2.60)	6.55 (5.77–7.42)	13.05 (11.90–14.29)	16.15 (14.93–17.45)	17.15 (15.74–18.63)
	2005	0.81 (0.46–1.45)	1.94 (1.63–2.32)	6.04 (5.18–7.01)	12.51 (11.27–13.88)	16.96 (15.59–18.42)	18.59 (17.10–20.19)
	2010	0.76 (0.26–2.17)	1.71 (1.29–2.26)	5.56 (4.48–6.87)	12.00 (10.29–13.95)	17.81 (15.79–20.03)	20.13 (17.87–22.60)
Women	1990	0.79 (0.18–3.43)	1.45 (0.63–3.29)	3.51 (2.17–5.62)	7.05 (5.40–9.18)	10.25 (8.14–12.86)	12.30 (10.10–14.91)
	1995	0.74 (0.27–1.98)	1.24 (0.69–2.24)	3.19 (2.26–4.49)	6.64 (5.50–8.01)	10.35 (8.79–12.14)	12.26 (10.67–14.04)
	2000	0.69 (0.37–1.26)	1.06 (0.69–1.63)	2.91 (2.20–3.82)	6.26 (5.43–7.20)	10.45 (9.27–11.77)	12.21 (11.07–13.45)
	2005	0.64 (0.37–1.11)	0.91 (0.59–1.40)	2.64 (1.92–3.62)	5.90 (5.02–6.92)	10.55 (9.26–12.04)	12.17 (10.98–13.46)
	2010	0.59 (0.24–1.46)	0.78 (0.43–1.41)	2.40 (1.55–3.72)	5.56 (4.41–6.98)	10.65 (8.84–12.79)	12.12 (10.46–14.00)

Data are point estimates (95% confidence intervals) of prevalence.

Table 3 | Estimated age-standardized diabetes prevalence in the Japanese population 1990–2010

Sex	Year	Standardization population						
		Japanese population of the corresponding year		World population of the corresponding year	2010 Japanese population	2010 world population	2030 Japanese population	2030 world population
			No. cases (×1,000)					
Men	1990	8.06 (7.38–9.31)	3,546	6.25 (5.65–7.96)	9.30 (8.57–10.43)	6.84 (6.22–8.36)	10.32 (9.46–11.50)	7.78 (7.13–9.09)
	1995	8.22 (7.73–8.90)	3,858	6.16 (5.75–6.93)	9.39 (8.85–10.06)	6.69 (6.26–7.42)	10.52 (9.89–11.28)	7.71 (7.25–8.38)
	2000	8.65 (8.29–9.08)	4,222	6.19 (5.90–6.56)	9.51 (9.11–9.95)	6.57 (6.27–6.95)	10.76 (10.29–11.29)	7.66 (7.33–8.05)
	2005	9.21 (8.79–9.67)	4,599	6.31 (6.00–6.68)	9.67 (9.23–10.15)	6.49 (6.17–6.87)	11.05 (10.53–11.61)	7.65 (7.29–8.05)
	2010	9.86 (9.24–10.60)	4,988	6.43 (5.99–7.04)	9.86 (9.24–10.60)	6.43 (5.99–7.04)	11.38 (10.63–12.24)	7.67 (7.17–8.30)
Women	1990	5.31 (4.72–6.26)	2,498	4.05 (3.55–5.09)	6.57 (5.86–7.56)	4.32 (3.80-5.32)	7.53 (6.68–8.65)	5.08 (4.51–6.04)
	1995	5.40 (4.96–5.97)	2,701	3.89 (3.54–4.45)	6.42 (5.91–7.06)	4.15 (3.78–4.70)	7.39 (6.78–8.13)	4.92 (4.51–5.47)
	2000	5.59 (5.25–5.98)	2,913	3.80 (3.55–4.14)	6.29 (5.91–6.73)	3.99 (3.72–4.33)	7.27 (6.82–7.77)	4.76 (4.47–5.13)
	2005	5.81 (5.44–6.24)	3,116	3.75 (3.48–4.08)	6.17 (5.77–6.63)	3.84 (3.57–4.19)	7.15 (6.68–7.69)	4.62 (4.32–5.00)
	2010	6.06 (5.53–6.72)	3,307	3.71 (3.36–4.21)	6.06 (5.53–6.72)	3.71 (3.36–4.21)	7.04 (6.40–7.82)	4.50 (4.09–5.04)
Total	1990	6.64 (6.21–7.45)	6,044	5.14 (4.77–6.17)	7.88 (7.39–8.66)	5.57 (5.19–6.51)	8.86 (8.28–9.70)	6.43 (6.02–7.27)
	1995	6.76 (6.45–7.22)	6,558	5.02 (4.76–5.50)	7.85 (7.49–8.32)	5.41 (5.14–5.88)	8.88 (8.45–9.42)	6.31 (6.01–6.76)
	2000	7.07 (6.83–7.36)	7,135	4.99 (4.80–5.24)	7.84 (7.57–8.15)	5.27 (5.08–5.53)	8.93 (8.61–9.30)	6.21 (5.99–6.48)
	2005	7.45 (7.17–7.77)	7,715	5.02 (4.82–5.27)	7.85 (7.56–8.19)	5.16 (4.95–5.42)	9.01 (8.66–9.40)	6.13 (5.90–6.41)
	2010	7.89 (7.49–8.39)	8,295	5.06 (4.80–5.47)	7.89 (7.49–8.39)	5.06 (4.79–5.47)	9.11 (8.62–9.69)	6.08 (5.76–6.50)

Data are point estimates (95% confidence intervals) of prevalence.

standardized prevalence using the Japanese population of the corresponding year is projected during 2010 to 2030, if the trend observed remains similar, namely an increase of 33% for men and 10% for women (Table 5). In women, it is probable that this trend is mainly a result of the aging of the population, because age-specific prevalence estimates remained constant: the proportion of women aged 70 years or older is expected to increase from 23% in 2010 to 33% in 2030, whereas the proportion of women aged less than 40 years is expected to decrease from 29% in 2010 to 22% in 2030. For men, it appears that the increasing trend in diabetes prevalence is a result of the combined effect of the aging of the population (17% of men aged 70 or older in 2010 vs 26% in 2030) and the increase in the age-specific diabetes prevalence in the older age categories. The overall prevalence of diabetes in the Japanese adult population is expected to rise from 7.9% (representing about 8.3 million people with diabetes) in 2010 to 9.8% (9.7 million people with diabetes) in 2030. In contrast, the projected age-standardized diabetes prevalence using a fixed population (2010 Japanese, 2010 world, 2030 Japanese or 2030 world population) as a standardization population appeared to remain stable between 2015 and 2030 (Table 5).

Table 4 | Projected age- and sex-specific diabetes prevalence (%) in the Japanese population 2010–2030

Sex	Year	Age category (years)					
		20–29	30–39	40–49	50–59	60–69	≥70
Men	2010	0.76 (0.26–2.17)	1.71 (1.29–2.26)	5.56 (4.48–6.87)	12.00 (10.29–13.95)	17.81 (15.79–20.03)	20.13 (17.87–22.60)
	2015	0.71 (0.13–3.80)	1.50 (0.99–2.25)	5.11 (3.81–6.83)	11.50 (9.26–14.19)	18.68 (15.79–21.98)	21.77 (18.41–25.53)
	2020	0.67 (0.06–6.69)	1.31 (0.76–2.27)	4.71 (3.23–6.82)	11.02 (8.31–14.51)	19.59 (15.71–24.14)	23.50 (18.85–28.90)
	2025	0.63 (0.03–11.53)	1.15 (0.57–2.29)	4.33 (2.71–6.84)	10.56 (7.39–14.85)	20.53 (15.63–26.52)	25.32 (19.31–32.49)
	2030	0.59 (0.01–19.52)	1.01 (0.44–2.32)	3.98 (2.28–6.85)	10.12 (6.59–15.20)	21.51 (15.54–28.95)	27.23 (19.69–36.33)
Women	2010	0.59 (0.24–1.46)	0.78 (0.43–1.41)	2.40 (1.55–3.72)	5.56 (4.41–6.98)	10.65 (8.84–12.79)	12.12 (10.46–14.00)
	2015	0.55 (0.14–2.17)	0.67 (0.29–1.53)	2.18 (1.20–3.94)	5.24 (3.80–7.19)	10.75 (8.28–13.82)	12.08 (9.79–14.78)
	2020	0.52 (0.08–3.28)	0.57 (0.19–1.71)	1.98 (0.92–4.24)	4.93 (3.24–7.45)	10.86 (7.71–15.05)	12.03 (9.15–15.71)
	2025	0.48 (0.04–5.08)	0.49 (0.12–1.91)	1.80 (0.70–4.55)	4.65 (2.76–7.72)	10.96 (7.18–16.37)	11.99 (8.48–16.68)
	2030	0.45 (0.02–7.88)	0.42 (0.08–2.15)	1.64 (0.53–4.94)	4.37 (2.33–8.06)	11.06 (6.65–17.84)	11.95 (7.89–17.74)

Data are point estimates (95% confidence intervals) of prevalence.

Table 5 | Projected age-standardized diabetes prevalence in the Japanese population 2010–2030

Sex	Year	Standardization population						
		Japanese population of the corresponding year		World population of the corresponding year	2010 Japanese population	2010 world population	2030 Japanese population	2030 world population
			Number of cases (×1,000)					
Men	2010	9.86 (9.24–10.60)	4,988	6.43 (5.99–7.04)	9.86 (9.24–10.60)	6.43 (5.99–7.04)	11.38 (10.63–12.24)	7.67 (7.17–8.30)
	2015	10.63 (9.71–11.80)	5,354	6.69 (6.09–7.73)	10.10 (9.23–11.21)	6.40 (5.82–7.45)	11.75 (10.68–13.06)	7.71 (7.05–8.74)
	2020	11.41 (10.10–13.21)	5,683	7.05 (6.27–8.73)	10.36 (9.23–12.01)	6.39 (5.67–8.22)	12.16 (10.74–14.06)	7.79 (6.95–9.44)
	2025	12.26 (10.51–14.87)	5,989	7.51 (6.55–10.24)	10.67 (9.25–13.03)	6.40 (5.56–9.57)	12.61 (10.82–15.25)	7.89 (6.88–10.59)
	2030	13.10 (10.91–16.71)	6,228	8.02 (6.82–12.41)	11.00 (9.29–14.39)	6.44 (5.47–11.72)	13.10 (10.91–16.71)	8.02 (6.82–12.41)
Women	2010	6.06 (5.53–6.72)	3,307	3.71 (3.36–4.21)	6.06 (5.53–6.72)	3.71 (3.36–4.21)	7.04 (6.40–7.82)	4.50 (4.09–5.04)
	2015	6.28 (5.52–7.29)	3,423	3.76 (3.30–4.51)	5.96 (5.25–6.92)	3.59 (3.15–4.34)	6.94 (6.07–8.07)	4.38 (3.85–5.17)
	2020	6.43 (5.41–7.86)	3,478	3.85 (3.27–4.93)	5.87 (4.98–7.19)	3.49 (2.96–4.57)	6.85 (5.76–8.38)	4.28 (3.64–5.39)
	2025	6.57 (5.31–8.50)	3,501	3.97 (3.27–5.48)	5.79 (4.73–7.51)	3.39 (2.78–4.94)	6.77 (5.47–8.75)	4.18 (3.44–5.71)
	2030	6.69 (5.19–9.22)	3,486	4.10 (3.26–6.19)	5.72 (4.50–7.95)	3.30 (2.62–5.54)	6.69 (5.19–9.22)	4.10 (3.26–6.19)
Total	2010	7.89 (7.49–8.39)	8,295	5.06 (4.79–5.47)	7.89 (7.49–8.39)	5.06 (4.79–5.47)	9.11 (8.62–9.69)	6.08 (5.76–6.50)
	2015	8.37 (7.79–9.16)	8,777	5.22 (4.86–5.88)	7.95 (7.41–8.70)	4.99 (4.64–5.65)	9.24 (8.57–10.11)	6.04 (5.64–6.71)
	2020	8.81 (8.02–9.98)	9,161	5.44 (4.99–6.49)	8.03 (7.35–9.11)	4.93 (4.52–6.04)	9.38 (8.53–10.62)	6.03 (5.54–7.07)
	2025	9.29 (8.26–10.94)	9,490	5.74 (5.19–7.38)	8.14 (7.30–9.65)	4.89 (4.42–6.76)	9.56 (8.50–11.23)	6.03 (5.45–7.66)
	2030	9.75 (8.50–12.01)	9,714	6.05 (5.39–8.64)	8.26 (7.29–10.37)	4.86 (4.33–7.95)	9.75 (8.50–12.01)	6.05 (5.39–8.64)

Data are point estimates (95% confidence intervals) of prevalence.

We observed moderate heterogeneity among studies, particularly in age categories 40 years or older (Table S2). We therefore carried out a sensitivity analysis by repeating the meta-analysis and meta-regression steps excluding: (i) studies using OGTT for diabetes diagnosis[31–33]; and (ii) studies carried out in a single center[36,37]. Analyses excluding studies using OGTT for diabetes diagnosis (Table S3) and studies carried out in a single center (Table S4) showed similar patterns, with a higher diabetes prevalence in men than women and an increase in prevalence in men aged 70 years or more with time. Furthermore, we also examined sensitivity by including data from the national health surveys only. This resulted in a substantial reduction of heterogeneity and the corresponding trends in prevalence were higher than those estimated when using all studies (Table S5).

DISCUSSION

Here, we present the results of a comprehensive meta-regression analysis of studies carried out among the Japanese population in the past two decades. The present study included

161,087 individuals, allowing us to estimate sex- and age-specific trends in the prevalence of diabetes over the past two decades, and to present prevalence projections from 2010 until 2030. Furthermore, by combining these estimates with sex- and age-specific population distribution estimates, we also calculated age-standardized diabetes prevalence trends as well as expected numbers of adults with diabetes in Japan.

The present findings suggest that diabetes prevalence in Japan will substantially increase in the next two decades, mainly as a result of population aging. The number of cases is expected to rise from 8.3 million in 2010 to 9.7 million in 2030. Thus, rapidly aging societies, such as Japan, Italy and Germany[1], could experience substantial increasing trends in diabetes prevalence during the next decades. Curbing this increase in these societies requires the identification of effective preventive strategies, such as promoting a healthy lifestyle and screening for people at high risk for diabetes[56]. With regard to sex- and age-specific prevalence estimates, we observed a marked difference between men and women: prevalence is expected to remain constant for women regardless of age category, but to steeply increase in older men.

A major strength of the present study was its use of the standard diagnostic criteria provided in the JDS recommendation[18]. This implies that the estimated trends might be attributed to real changes in the prevalence of diabetes in the Japanese population and not merely to changes in the criteria used to define diabetes.

Our present estimates substantially differ from those of several recent studies that estimated and projected diabetes prevalence worldwide, including the Japanese population[6,11–13]. The International Diabetes Federation provided diabetes prevalence estimates of 7.6% for 2013 and 8.2% for 2035[14], which are slightly lower than those in the present study and show a less pronounced increasing trend. This difference might be partly explained by the fact that data used to derive the International Diabetes Federation estimates used results from a single national health survey carried out in 2007[43]. Furthermore, the International Diabetes Federation estimates are based on a country-specific prevalence function that depends on sex, age and level of urbanization, but does not vary with year of assessment; as a result, these estimates reflect changes in the demographic structure of the country's population (population growth, aging, and urbanization), but take no account of possible trends in diabetes prevalence resulting from changes in the influence of factors, such as unhealthy diet, sedentary lifestyle (though this is partly taken into account through the urbanization variable) or other possibly unexplored societal factors.

A recent article by Danaei *et al.*[11] provided global and country-specific diabetes prevalence estimates up to 2008 using a Bayesian hierarchical modeling procedure that included the year of assessment as an explanatory covariate. Prevalence estimates for Japan were lower than those of the present study, but showed similar trends and differences between men and women (4.9 and 4.2% in 1990, 7.2 and 4.7% in 2008 for men and women respectively). However, the regression models used to calculate these estimates were based on FPG estimates, and the primary outcome was thus derived from studies that used different glycemic metrics from those in our present study.

The observed sex difference in diabetes prevalence in the Japanese population might be partly a result of the higher prevalence of obesity among Japanese men[20,57,58]. This sex difference could also result from a strong influence of lifestyle habits. Indeed, several studies have reported substantial sex differences in alcohol and tobacco consumption, physical activity, and levels of stress[59,60], which could directly or indirectly influence the development of diabetes.

The increase in diabetes prevalence along time in men aged 70 years or older might be partially explained by cohort effects; changes in lifestyle habits between birth cohorts, particularly changes in dietary intake since the Second World War[61], might be responsible for the trend. A possible decrease in mortality among Japanese individuals with diabetes over time might also explain the increasing prevalence in this age category. Alternatively, because of the use of wide age categories, residual confounding by age might also explain the observed trend. In contrast, we observed no evidence for such differences in diabetes prevalence between birth cohorts in women. The reasons for this sex difference are unclear, but the difference might possibly reflect differential shifts in lifestyle habits between men and women[59,60], or the effects of sex hormones on glucose metabolism[62].

The present study had several limitations. First, although the largest studies included in our analysis covered several calendar years, we summarized the diabetes prevalence of the corresponding population for a single point in time, namely the central year, because details about the precise year of diagnosis for each patient were not available. As a consequence, we might not have been able to accurately capture the temporal trend in diabetes prevalence. In particular, results from the sensitivity analysis using only national survey data, which did have year-specific prevalence estimates, showed that we might have substantially underestimated the projected prevalence for both sexes. Second, our use of wide age categories decreased the precision of our estimates of the effect of age on the prevalence of diabetes. However, we consider that this lack of precision is compensated for by the robustness of our estimates. Third, our projections assume that the trends estimated by meta-regression will remain constant during the next decades, which might not be correct. However, given that a sudden change in the incidence of diabetes is not expected, our predictions could appropriately describe what might happen in the absence of specific public health policies aimed at reversing this tendency. Finally, we observed moderate heterogeneity across studies in the prevalence estimates, particularly in age categories 40 years or older. The presence of heterogeneity, while unavoidable, could have altered the results of our meta-regression. In particular, studies carried out in a single center might not be representative of the overall Japanese population. The exclusion of such studies, however, did not materially change prevalence estimates. Fur-

thermore, the restriction of the analysis to data from the national health surveys, which have a very similar design and consequently exhibit much less heterogeneity, showed higher trends in prevalence. However, because participants in the national health surveys tend to be more cooperative and perhaps more health-conscious than the average, despite the random selection procedure used at the time of recruitment, these surveys might fail to encompass the Japanese population in all its diversity. For that reason, we believe that the estimates presented, based on all the studies included, might give a better reflection of the trends in diabetes prevalence in the Japanese population.

In conclusion, this comprehensive meta-regression analysis of the Japanese population shows that diabetes can be expected to substantially increase in the next few decades, and that this increase will be mainly a result of population aging. Because diabetes is preventable through diet and lifestyle modification, our findings support the need for public policies and health systems that promote a healthy diet and lifestyle.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Figure S1 | Flow diagram of the study identification and selection process.
Figure S2 | Prevalence of diabetes mellitus in Japanese men according to year of assessment.
Figure S3 | Prevalence of diabetes mellitus in Japanese women according to year of assessment.
Table S1 | Coefficient associated with time in the linear meta-regression model.
Table S2 | Assessment of heterogeneity across studies.
Table S3 | Sensitivity analysis with exclusion of studies using OGTT for diabets diagnosis.
Table S4 | Sensitivity analysis excluding studies conducted in a single center.
Table S5 | Sensitivity analysis using national surveys only.