Diabetes mellitus defined by hemoglobin A1c value: Risk characterization for incidence among Japanese subjects in the JPHC Diabetes Study

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ABSTRACT

Aims/Introduction: Although several risk factors for type 2 diabetes have been identified, most of them have been identified in studies on Western populations, and they should be evaluated in a Japanese population. In 2010, new diagnostic criteria for diabetes mellitus using hemoglobin A1c (HbA_{1c}) were released and its use in epidemiological studies has many advantages. The aim of the present study was to evaluate risk factors for type 2 diabetes defined based on HbA_{1c} values in a Japanese population.

Materials and Methods: A total of 9223 subjects (3076 men and 6147 women) were followed up for 5 years. Diabetes was defined based on self-report or HbA_{1c} value. Risk factors for diabetes were evaluated as odds ratios adjusted for potential confounding factors by logistic regression.

Results: During the 5-year follow-up period, we documented 518 incident cases of diabetes (232 men and 286 women). Of the 518 incident cases, 310 cases were diagnosed by HbA_{1c} alone. Among the men, age, smoking (both past smoking and current smoking) and family history of diabetes significantly increased the risk of diabetes. Among the women, body mass index, family history of diabetes and hypertension significantly increased the risk of diabetes. These results did not change markedly after adjustment for the baseline HbA_{1c} values, and the baseline HbA_{1c} value itself was a significant risk factor for diabetes mellitus.

Conclusions: Known risk factors for diabetes established in Western populations also increased the risk of diabetes in a Japanese population defined on the basis of HbA_{1c} values. (J Diabetes Invest, doi: 10.1111/j.2040-1124.2011.00119.x, 2011)

KEY WORDS: Diabetes mellitus, Hemoglobin A1c, Risk factors

INTRODUCTION

The prevalence of type 2 diabetes has increased, and type 2 diabetes is now one of the main threats to human health[1]. It is known that environmental factors, especially lifestyle, are associated with the risk of diabetes and that adequate lifestyle intervention can reduce the incidence of diabetes[2,3]. Although several risk factors for type 2 diabetes have been identified, most of them were identified on the basis of studies in Western populations. The effect of the risk factors should be evaluated for the Japanese population, because there are genetic and environmental differences between the two populations[4]. In 2010, the Japan Diabetes Society (JDS) released a new diagnostic criteria for diabetes mellitus that included the use of hemoglobin A1c (HbA_{1c}) as a diagnostic tool for diabetes mellitus and a single examination of $HbA_{1c} \geq 6.5\%$ alone being used to define diabetes mellitus in epidemiological studies[5]. Although there are several drawbacks to making a diagnosis of diabetes based on HbA_{1c} values, it is quite appealing for epidemiological studies, because no glucose tolerance test or fasting blood sample is required, detecting chronic hyperglycemia by a single measurement, and there is a low risk of misclassification, which is a result of low variability of HbA_{1c}. The aim of the present study was to evaluate risk factors for type 2 diabetes in a Japanese population. For this purpose, we used the definition of diabetes based on HbA_{1c} value.

MATERIALS AND METHODS

The present study was based on the diabetes research carried out in a large cohort study in Japan, the Japan Public Health Center-based prospective Study (JPHC Study), an ongoing, longitudinal cohort study investigating cancer, cardiovascular diseases and other lifestyle-related diseases. The details of the study design have been described elsewhere[6]. The JPHC study population consists of all registered Japanese inhabitants of the

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public health center areas who were aged 40–59 years in 1990 (cohort I) and 40–69 years in 1993 (cohort II). The JPHC diabetes study, which consisted of the measurement of HbA_{1c}, and an additional questionnaire about diabetes and lifestyle, was carried out at the time of health check-ups and the subjects were the JPHC participants who received a health check-up. Written informed consent to participate in the diabetes study was obtained separately from the informed consent to the JPHC study. The baseline survey of the diabetes study was carried out in 1998–1999 for cohort II and in 2000 for cohort I, and the 5-year follow-up survey was carried out in 2003–2004 and 2005, respectively. As two public health center areas (Katsushika and Kamigoto) were excluded from the analysis in the present study, because different definitions of the study population were used in one area and because the follow-up survey was carried out 6 years after the baseline survey in the other area, the analysis in the present study was carried out on subjects in the remaining eight public health center areas (four in cohort I and four in cohort II). Each participant completed a self-administered questionnaire for the JPHC study that included questions about previously diagnosed medical conditions, medication and lifestyle factors, such as physical activity, alcohol intake and smoking. The separate questionnaire regarding the diabetes study included questions about a detailed past history of diabetes, treatment of diabetes, family history of diabetes, walking and daily physical activity. Of the 24743 subjects (9065 men and 15678 women) who completed the baseline questionnaires, 11601 (3946 men and 7655 women) completed the follow-up questionnaire. We excluded subjects who had any of the following conditions at baseline: cardiovascular disease, chronic liver disease, any type of cancer, or diabetes (n = 1491). We excluded subjects who had diabetes at baseline as subjects of the present study, because it was designed to investigate the incidence of diabetes. In the present study, diabetes was defined based on the self-report or HbA_{1c} value. Individuals who had missing baseline data for any of the exposure parameters described later were also excluded (n = 1154). After the aforementioned exclusions, the remaining cohort consisted of 9223 subjects (3076 men and 6147 women).

Assessment of Diabetes

In the present study, diabetes was defined based on self-report or a HbA_{1c} value of 6.5% or more in National Glycohemoglobin Standardization Program equivalent value (see the 'Supporting Information' for details). Those who did not have diabetes at baseline, but who had diabetes at the time of the 5-year follow-up survey, were defined as incident cases of diabetes.

Assessment of Risk Factors

Coffee intake was assessed based on the consumption of cups of coffee and cans of coffee (canned coffee is popular in Japan) separately by dividing it into the following categories: 1–2 days per week, 3–4 days per week, 5–6 days per week, 1 cup (or can) per day, 2–3 cups (or cans) per day, 4–6 cups (or cans) per day, 7–9 cups (or cans) per day and 10 or more cups (or cans) per day.

Physical activity was assessed on the basis of leisure time physical activity, daily physical activity and walking. Leisure time physical activity was divided into two categories: active (participate in sports at least once a week) and inactive, as in the previous report[7]. Daily physical activity was classified into four levels: light, moderate, slightly heavy and heavy. Walking was classified into the following four categories according to average number of hours walked per day: <0.5, 0.5–0.9, 1–1.9 and 2 h or more.

The details of the assessment of other risk factors have been described elsewhere[7].

Statistical Analysis

All analyses were carried out by using the data from the 9223 individuals (3076 men and 6147 women). We carried out multivariate logistic regression analysis to evaluate the contribution of the risk factors (some of them are beneficial) to diabetes incidence. As the primary objective of the present study was to examine the effect of established (mainly in Western countries) risk factors of diabetes in the Japanese population, the established risk factors for incidence of diabetes were selected as explanatory variables.

Alcohol intake was divided into the following four groups: non-drinker (consume alcoholic beverage less than once a week) and three groups of alcohol drinkers (consume alcoholic beverage one or more times per week) according to tertile of weekly ethanol intake. We included several risk factors, such as coffee intake, waking and daily physical activity, that were not included in the previous study. For each category of coffee intake, an average daily intake was assigned as follows: 0.2 for 1–2 days per week, 0.5 for 3–4 days per week and 0.75 for 5–6 days per week, 1 for 1 per day, 2.5 for 2–3 per day, 5 for 4–6 per day, 8 for 7–9 per day and 10 for 10 or more per day. Total daily coffee intake was calculated by adding average daily intake from cups of coffee and double the average daily intake from cans of coffee based on the estimate that one can of coffee is the equivalent of two cups of coffee. Then, total coffee intake was divided into four categories: less than one cup per day, 1–1.9 cups per day, 2–2.9 cups per day and 3 cups or more per day.

Risk factors of diabetes were evaluated by logistic regression as odds ratios adjusted for potential confounding factors including age (46–55, 56–65 and 66–75 years), body mass index (quartiles), smoking status (never smoker, past smoker or current smoker at <20 or ≥20 cigarettes per day), alcohol intake, family history of diabetes (at least one parent or one sibling with diabetes), leisure time physical activity, walking (<0.5, 0.5–0.9, 1–1.9 and 2 h or more), daily physical activity (light, moderate, slightly heavy and heavy), hypertension (defined as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg or being on medication for hypertension), coffee intake and baseline HbA_{1c} value. All analyses were carried out separately for men and women. We analyzed cohorts I and II together, because the results of separate analysis for cohorts I and II did not differ largely.

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RESULTS

The baseline characteristics of the subjects of the analysis are shown in Table 1. During the 5-year follow-up period, we documented 232 incident cases (7.5%) of diabetes among the men and 286 cases (4.7%) among the women. Of the 518 incident cases of diabetes, 132 were diagnosed by self-report alone, and 310 on the basis of the HbA_{1c} value alone, and 76 cases on the basis of both self-report and HbA_{1c} value.

The multivariate-adjusted odds ratios for the incidences of diabetes mellitus are shown in Table 2. Among the men, age, body mass index, smoking (both past smoking and current smoking) and family history of diabetes significantly increased the risk of diabetes. Among the women, body mass index, family history of diabetes and hypertension significantly increased the risk of diabetes. Although some factors became insignificant and others became significant, the results did not change markedly after being adjusted for the baseline HbA_{1c} values. Walking, daily physical activity (for men) and coffee intake (for women) tended to decrease the risk of diabetes, but the odds ratios were not statistically significant. Baseline HbA_{1c} values significantly increased the risk of diabetes for both men and women. Every 0.1% increase in baseline HbA_{1c} value increased the risk of diabetes by 1.36 among the men and by 1.52 among the women.

Table 1 | Baseline characteristics of the subjects

	Men (*n* = 3076)		Women (*n* = 6147)	
Age (years)	64	58–68	62	56–67
Body mass index (kg/m^2)	23.6	2.9	23.7	3.1
Smoking				
Never	1273	41.4	5953	96.8
Past	817	26.6	59	1.0
Current (<20/day)	372	12.1	96	1.6
Current (≥20/day)	614	20.0	39	0.6
Alcohol intake*				
Non-drinker	1009	32.8	5447	88.6
1st tertile	515	16.7	232	3.8
2nd tertile	652	21.2	185	3.0
3rd tertile	900	29.3	283	4.6
Family history of diabetes (+)	291	9.5	768	12.5
Physical activity (leisure time; active)	795	25.8	1818	29.6
Walking				
<0.5 h/day	370	12.0	768	12.5
0.5–0.9 h/day	627	20.4	1342	21.8
1–1.9 h/day	602	19.6	1368	22.3
≥2 h/day	1477	48.0	2669	43.4
Physical activity (daily)				
Light	420	13.7	955	15.5
Moderate	1346	43.8	4466	72.7
Slightly heavy	1106	36.0	663	10.8
Heavy	204	6.6	63	1.0
Hypertension (+)	1421	46.2	2392	38.9
Coffee intake				
<1 cups/day	1795	58.4	3967	64.5
1–1.9 cups/day	629	20.4	1213	19.7
2–2.9 cups/day	369	12.0	779	12.7
≥3 cups/day	283	9.2	188	3.1
Hemoglobin A1c	5.5	5.2–5.7	5.5	5.3–5.7

Age and hemoglobin A1c values are median values (interquartile range). Body mass index values are mean (standard deviation). Other variables are numbers of subjects (proportion [%]).
*Alcohol intake was divided into tertiles based on weekly ethanol intake (1st tertile, <16 g/week for men and <35.2 g/week for women; 2nd tertile, 161–321.9 g/week for men and 35.3–80.4 g/week for women; 3rd tertile, ≥322 g/week for men and ≥80.5 g/week for women).

DISCUSSION

In the present study, we examined the effect of risk factors for diabetes, which were established in Western populations, in a Japanese population. Although we reported such an evaluation previously[7], there was a major difference between the definition of diabetes in the two studies, which was self-report and HbA_{1c} in the present study as opposed to self-report alone in the previous study, in addition a difference in the follow-up period and study population. One of the main problems in the previous study was the relatively low sensitivity of self-reported diabetes. In the previous study, the sensitivity of self-reported diabetes was estimated to be approximately 46%. In fact, just 208 of the 518 incident cases of diabetes were diagnosed by self-report in the present analysis. The previous study used the data obtained from a 1990 survey in cohort I as the baseline data, and followed-up 10 years later, therefore the area, the ages of the subjects at baseline and follow-up period of the present study were also different from those of the previous study. Despite these differences, however, the results were not very different; that is, the established risk factors of age, body mass index and family history of diabetes increased the risk of diabetes in both studies. The effect of smoking was stronger in the present study, and although the reason for the difference is unclear, there are several possible explanations. As the baseline survey in the present study was carried out 5 or 10 years after the baseline survey in the previous study, the cumulative exposure of the smokers might have been greater in the present study. The effect of smoking became stronger with the duration of the smoking period[8,9] and that might be why the effect of smoking was stronger in the current study. Another possible explanation is the difference between the accuracy of self-reports of diabetes by smokers and by non-smokers, that is, smokers are generally less health-conscious than non-smokers, and the proportion of unrecognized diabetes among men in the incident cases of diabetes was in fact larger among the current smokers (60%) than the non-smokers (49%) in the present study.

We also examined the effect of walking, daily physical activity and coffee intake in the present study, because these have been regarded as factors that protect against diabetes[10–13]. Although their effects were not statistically significant, walking and coffee intake tended to reduce the risk of diabetes in both men and women, and daily physical activity tended to reduce the risk of

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Table 2 | Odds ratios for 5-year incidence of diabetes mellitus

	n	Cases	Multivariate-adjusted*		HbA_{1c}-adjusted†	
			OR	95% CI	OR	95% CI
Men						
Age (years)						
46–55 (reference)	533	22	1		1	
56–65	1257	99	2.25	1.37–3.68	1.84	1.09–3.09
66–75	1286	111	2.64	1.60–4.37	2.23	1.32–3.78
Body mass Index‡						
1st quartile (reference)	769	44	1		1	
2nd quartile	766	55	1.30	0.86–1.98	1.35	0.87–2.10
3rd quartile	771	63	1.59	1.06–2.41	1.51	0.97–2.33
4th quartile	770	70	1.73	1.15–2.62	1.51	0.98–2.34
Smoking						
Never (reference)	1273	69	1		1	
Past	817	68	1.52	1.06–2.17	1.16	0.80–1.69
Current (<20/day)	372	35	2.00	1.29–3.10	1.76	1.11–2.80
Current (≥20/day)	614	60	2.29	1.56–3.35	1.72	1.14–2.59
Alcohol intake						
Non-drinker (reference)	1009	74	1		1	
1st tertile	515	29	0.85	0.54–1.34	0.76	0.47–1.23
2nd tertile	652	56	1.22	0.84–1.78	1.12	0.76–1.67
3rd tertile	900	73	1.07	0.75–1.52	1.01	0.69–1.47
Family history of diabetes (+)	291	46	2.73	1.91–3.91	2.41	1.64–3.55
Physical activity (leisure time; active)	795	61	0.98	0.72–1.35	1.04	0.74–1.45
Walking						
<0.5 h/day (reference)	370	36	1		1	
0.5–0.9 h/day	627	47	0.74	0.46–1.18	0.64	0.39–1.06
1–1.9 h/day	602	48	0.81	0.50–1.32	0.75	0.45–1.27
≥2 h/day	1477	101	0.76	0.49–1.19	0.60	0.36–0.97
Physical activity (daily)						
Light (reference)	420	37	1		1	
Moderate	1346	104	0.95	0.62–1.44	0.87	0.55–1.37
Slightly heavy	1106	80	0.99	0.62–1.58	0.98	0.59–1.61
Heavy	204	11	0.73	0.34–1.56	0.64	0.29–1.41
Hypertension (+)	1421	123	1.20	0.90–1.60	1.27	0.93–1.72
Coffee intake						
<1 cups/day (reference)	1795	139	1		1	
1–1.9 cups/day	629	47	1.01	0.71–1.43	0.98	0.67–1.42
2–2.9 cups/day	369	26	0.98	0.63–1.54	0.93	0.58–1.50
≥3 cups/day	283	20	1.09	0.65–1.84	0.91	0.52–1.59
HbA_{1c} (per 0.1% increase)					1.36	1.30–1.42
Women						
Age (years)						
46–55 (reference)	1310	47	1		1	
56–65	2907	139	1.18	0.83–1.67	0.76	0.52–1.11
66–75	1930	100	1.26	0.87–1.83	0.79	0.52–1.19
Body mass index‡						
1st quartile (reference)	1535	31	1		1	
2nd quartile	1538	59	1.92	1.23–2.99	1.86	1.18–2.96
3rd quartile	1531	77	2.41	1.57–3.70	2.02	1.29–3.16
4th quartile	1543	119	3.68	2.44–5.55	2.64	1.72–4.07
Smoking						
Never (reference)	5953	279	1		1	
Past	59	3	1.17	0.35–3.83	1.92	0.56–6.57
Current (<20/day)	96	3	0.92	0.28–2.96	0.76	0.21–2.70
Current (≥20/day)	39	1	0.63	0.08–4.72	0.79	0.09–6.75

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Table 2 | (*Continued*)

	n	Cases	Multivariate-adjusted*		HbA_{1c}-adjusted†	
			OR	95% CI	OR	95% CI
Alcohol intake						
Non-drinker (reference)	5447	262	1		1	
1st tertile	232	7	0.62	0.29–1.35	0.55	0.25–1.25
2nd tertile	185	10	1.18	0.61–2.29	0.94	0.47–1.90
3rd tertile	283	7	0.54	0.25–1.17	0.44	0.20–0.99
Family history of diabetes (+)	768	69	2.47	1.85–3.30	1.69	1.23–2.32
Physical activity (leisure time) (active)	1818	87	1.03	0.79–1.34	0.97	0.73–1.29
Walking						
<0.5 h/day (reference)	768	39	1		1	
0.5–0.9 h/day	1342	62	0.89	0.58–1.36	0.89	0.57–1.40
1–1.9 h/day	1368	66	0.94	0.61–1.44	0.84	0.53–1.33
≥2 h/day	2669	119	0.94	0.63–1.41	0.80	0.52–1.22
Physical activity (daily)						
Light (reference)	955	45	1		1	
Moderate	4466	209	1.02	0.72–1.46	0.99	0.68–1.44
Slightly heavy	663	28	0.99	0.59–1.66	0.81	0.47–1.41
Heavy	63	4	1.32	0.44–3.91	0.81	0.25–2.59
Hypertension (+)	2392	148	1.42	1.11–1.83	1.52	1.16–1.99
Coffee intake						
<1 cups/day (reference)	3967	196	1		1	
1–1.9 cups/day	1213	51	0.85	0.61–1.17	0.86	0.61–1.22
2–2.9 cups/day	779	35	0.97	0.66–1.43	1.04	0.69–1.57
≥3 cups/day	188	4	0.46	0.17–1.26	0.55	0.19–1.57
HbA_{1c} (per 0.1% increase)					1.52	1.45–1.59

*Adjusted for age, body mass index, smoking status, alcohol intake, family history of diabetes, leisure time physical activity, walking, daily physical activity, hypertension and coffee intake.
†Adjusted for variables listed above and baseline hemoglobin A1c (HbA_{1c}) value.
‡Body mass index was divided into quartiles (1st quartile, <21.6 kg/m² for men and <21.5 kg/m² for women; 2nd quartile, 21.6–23.5 kg/m² for men and 21.5–23.4 kg/m² for women; 3rd quartile, 23.6–25.4 kg/m² for men and 23.5–25.5 kg/m² for women; 4th quartile, ≥25.5 kg/m² for men and ≥25.6 kg/m² for women).

diabetes in men, but not in women. The difference between the men and women might be a result of the difference in recognition of housework among the women. The failure of the differences to reach the level of significance might be a result of the relatively small numbers of subjects or the limitation of our assessment of physical activity. A negative association between coffee intake and risk of type 2 diabetes has been reported in studies carried out on various populations and in various countries[12,13]. As Japanese people consume much less coffee than Western people[14], the categorization of coffee intake was shifted to a small amount compared with studies in Western countries. That might be the reason why the effect of coffee intake against diabetes did not become significant in the present study.

We also found that the baseline HbA_{1c} value was a significant risk factor for diabetes mellitus, and the other risk factors had independent associations of baseline HbA_{1c} value. The finding that most of the risk factors have independent associations of baseline HbA_{1c} value is important, because some risk factors were correlated with the HbA_{1c} values and the risk associated with such factors might be attributable to confounding with baseline HbA_{1c}. For example, HbA_{1c} and age were correlated, and HbA_{1c} increased as age increased[15]. However, because the risk associated with age did not change markedly and remained statistically significant after adjustment for baseline HbA_{1c} in the men, age increased the risk of diabetes for men independently of the baseline HbA_{1c} value. In contrast, the risk associated with age decreased after adjustment for baseline HbA_{1c} in women. Although the risk associated with age in women was not significant before adjustment for baseline HbA_{1c} and this might come from the relatively small numbers of incident cases, the decrease in risk associated with age in women after adjustment of baseline HbA_{1c} suggests that the risk was mainly mediated by HbA_{1c}. This also holds in the case of body mass index in men, that is, the risk associated with body mass index in men was mainly mediated by HbA_{1c}.

In the present study, we defined diabetes based on HbA_{1c} values. In 2010, the JDS released new diagnostic criteria and a single examination of HbA1c ≥ 6.5% alone can be defined as diabetes mellitus in epidemiological studies[5]. Diagnosing diabetes based on HbA_{1c} values is quite appealing, especially for

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epidemiological studies, because no glucose tolerance test or fasting blood sample is required. In addition, chronic hyperglycemia, which is the characteristic of diabetes mellitus, can be detected by a single measurement by using HbA_{1c}. Furthermore, because the variability of HbA_{1c} values is low compared with that of fasting plasma glucose or 2-h plasma glucose values[16–18], the risk of misclassification is considered to be low. However, there are several problems with diagnosing diabetes based on HbA_{1c} value alone. Aside from the standardization problem, HbA_{1c} values do not reflect the plasma glucose level of subjects with hemoglobinopathy or diseases that result in abnormal erythrocyte turnover, such as anemia or liver cirrhosis[18–20]. However, these problems do not seem to have caused serious problems in the present study because (i) we excluded subjects with severe diseases, such as liver cirrhosis; (ii) diabetes was diagnosed not only on the basis of the HbA_{1c} values, but self-report as well; and (iii) misclassification occurs only when a shift in HbA_{1c} as a result of hemoglobinopathy or disease crosses the threshold value, that is, the HbA_{1c} value shifts from ≥6.5% to <6.5% or *vice versa* and therefore it is possible to misclassify subjects with HbA_{1c} values around 6.5%, but the number of subjects with values around the HbA_{1c} value was not large and the number of misclassified subjects are expected to be small.

The main limitation of the current study was the relatively low proportion of subjects who participated in the follow-up survey (47%). This was a limitation that was attributable to the study design, because the subjects of the present study were voluntary participants in a health check-up and only a small proportion of subjects of the JPHC study received the check-up (26.8%)[21]. However, the differences between the baseline characteristics (including major risk factors for diabetes) of the subjects who participated in follow-up study and those who did not were not large (data not shown), and we do not think that the relatively low rate of participation in the follow-up survey introduced a large bias in the present study. Another limitation was that the subjects of the present study were the participants of health check-ups and, generally, health check-up participants were more health conscious compared with those who did not participate[21]. Therefore, it is not clear whether the results of the present study can be generalized to the whole population and further studies are needed to clarify this point.

In conclusion, we evaluated risk factors for diabetes mellitus established in Western populations in a Japanese population defining diabetes based on the subjects' HbA_{1c} values, and the results showed that the established risk factors for diabetes were also risk factors in a Japanese population.

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REFERENCES

1. Zimmet P, Alberti KG, Shaw J. Global and societal implications of the diabetes epidemic. *Nature* 2001; 414: 782–787.
2. Knowler WC, Barrett-Connor E, Fowler SE, *et al.* Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 2002; 346: 393–403.
3. Yamaoka K, Tango T. Efficacy of lifestyle education to prevent type 2 diabetes: a meta-analysis of randomized controlled trials. *Diabetes Care* 2005; 28: 2780–2786.
4. Chan JC, Malik V, Jia W, *et al.* Diabetes in Asia: epidemiology, risk factors, and pathophysiology. *JAMA* 2009; 301: 2129–2140.
5. The Committee of the Japan Diabetes Society on the Diagnostic Criteria of Diabetes Mellitus. Report of the Committee on the Classification and Diagnostic Criteria of Diabetes Mellitus. *J Diabetes Invest* 2010; 1: 212–228.
6. Tsugane S, Sobue T. Baseline survey of JPHC study – design and participation rate. Japan Public Health Center-based Prospective Study on Cancer and Cardiovascular Diseases. *J Epidemiol* 2001; 11: S24–S29.
7. Waki K, Noda M, Sasaki S, *et al.* Alcohol consumption and other risk factors for self-reported diabetes among middle-aged Japanese: a population-based prospective study in the JPHC study cohort I. *Diabet Med* 2005; 22: 323–331.
8. Manson JE, Ajani UA, Liu S, *et al.* A prospective study of cigarette smoking and the incidence of diabetes mellitus among US male physicians. *Am J Med* 2000; 109: 538–542.
9. Willi C, Bodenmann P, Ghali WA, *et al.* Active smoking and the risk of type 2 diabetes: a systematic review and meta-analysis. *JAMA* 2007; 298: 2654–2664.
10. Jeon CY, Lokken RP, Hu FB, *et al.* Physical activity of moderate intensity and risk of type 2 diabetes: a systematic review. *Diabetes Care* 2007; 30: 744–752.
11. Caspersen CJ, Fulton JE. Epidemiology of walking and type 2 diabetes. *Med Sci Sports Exerc* 2008; 40: S519–S528.
12. van Dam RM, Hu FB. Coffee consumption and risk of type 2 diabetes: a systematic review. *JAMA* 2005; 294: 97–104.

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13. Huxley R, Lee CM, Barzi F, *et al*. Coffee, decaffeinated coffee, and tea consumption in relation to incident type 2 diabetes mellitus: a systematic review with meta-analysis. *Arch Intern Med* 2009; 169: 2053–2063.
14. Grigg D. The worlds of tea and coffee: patterns of consumption. *GeoJournal* 2002; 57: 283–294.
15. Pani LN, Korenda L, Meigs JB, *et al*. Effect of aging on A1C levels in individuals without diabetes: evidence from the Framingham Offspring Study and the National Health and Nutrition Examination Survey 2001–2004. *Diabetes Care* 2008; 31: 1991–1996.
16. Mooy JM, Grootenhuis PA, de Vries H, *et al*. Intra-individual variation of glucose, specific insulin and proinsulin concentrations measured by two oral glucose tolerance tests in a general Caucasian population: the Hoorn Study. *Diabetologia* 1996; 39: 298–305.
17. Rohlfing C, Wiedmeyer HM, Little R, *et al*. Biological variation of glycohemoglobin. *Clin Chem* 2002; 48: 1116–1118.
18. Sacks DB, Bruns DE, Goldstein DE, *et al*. Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. *Clin Chem* 2002; 48: 436–472.
19. Schnedl WJ, Liebminger A, Roller RE, *et al*. Hemoglobin variants and determination of glycated hemoglobin (HbA1c). *Diabetes Metab Res Rev* 2001; 17: 94–98.
20. Lahousen T, Hegenbarth K, Ille R, *et al*. Determination of glycated hemoglobin in patients with advanced liver disease. *World J Gastroenterol* 2004; 10: 2284–2286.
21. Iwasaki M, Yamamoto S, Otani T, *et al*. Generalizability of relative risk estimates from a well-defined population to a general population. *Eur J Epidemiol* 2006; 21: 253–262.

SUPPORTING INFORMATION

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

Appendix S1 | Assessment of diabetes.

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