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## **Diabetes Incidence and Prevalence in Hong Kong, China during 2006-2014**

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## **Abstract**

### **AIMS**

To estimate recent secular changes of diabetes and pre-diabetes incidence and prevalence among Hong Kong Chinese adults, and thus show possible future trends for developing mainland China.

### **METHODS**

Based on a complete census of public sector health records of 6.4 million people from 2006 to 2014, diabetes cases were ascertained by different methods including the World Health Organization 2011 guidelines (HbA<sub>1c</sub>, fasting plasma glucose and glucose tolerance test); American Diabetes Association (ADA) 2015 guidelines (plus random plasma glucose); and additionally recorded diagnosis codes, and medication dispensation. Pre-diabetes was defined by ADA 2015 guidelines.

### **RESULTS**

We identified 697,201 people with diabetes (54.2% were incident cases); and 1,229,731 people with diabetes or pre-diabetes. In 2014, the overall incidence of diabetes was 9.46 per 1,000 person-years (95% CI 9.38-9.54), and overall prevalence was 10.29% (95% CI 10.27%-10.32%). Incidence of diabetes decreased significantly from 2007 to 2014 (quadratic trend,  $p < 0.001$ ). From 2006 to 2014, the prevalence of diabetes significantly increased in both sexes and across all age groups (quadratic trend,  $p < 0.001$ ). The overall incidence of pre-diabetes in 2014 was 18.88 per 1,000 person-years (95% CI 18.76-18.99), and the overall prevalence of pre-diabetes was 8.90% (95% CI 8.87%-8.92%).

### **CONCLUSIONS**

Similar to other developed western and Asian populations, diabetes (and pre-diabetes) incidence in Hong Kong Chinese appeared to have stabilized and made small declines during the period of observation. Ageing and survivorship will likely drive a continued increase in the prevalence of diabetes and pre-diabetes, albeit with a decelerating growth rate if past trends persist.

### **Novelty Statements**

- Similar to other developed western and Asian populations, the incidence of diabetes in Hong Kong Chinese appeared to have stabilized and made small declines.
- The prevalence of diabetes has increased in the overall population and among all age groups, albeit with a decelerating growth rate.
- The incidence of pre-diabetes has declined in recent years.
- These trends are consistent across different ascertainment criteria including those of the World Health Organization and American Diabetes Association.

# Diabetes Incidence and Prevalence in Hong Kong, China during 2006-2014

## Introduction

Global prevalence and incidence of diabetes has steadily risen. The number of adults with diabetes worldwide is estimated at 415 million in 2015, and is projected to reach 642 million by 2040 [1]. Annual worldwide healthcare spending on diabetes is estimated at US \$673 billion, representing 11.6% of total health expenditure [1].

China has the largest absolute burden of diabetes in the world at 114 million in 2010, and also one of the highest prevalence ratios [2]. The recorded prevalence of diabetes in China has risen by an order of magnitude from under 1% in 1980, to 9.7% in 2007, and to 11.6% in 2010 [2-4], and is expected to further increase as 50.1% of Chinese adults meet the American Diabetes Association 2010 criteria for pre-diabetes [2]. Whilst the prevalence of diabetes has continued to rise, studies from US, UK, Denmark and Korea have suggested the incidence rate of diabetes has stabilized in recent years [5-9].

The prevalence of diabetes in China increases with age and economic development [2]. Hong Kong, the most socioeconomically developed Chinese city, is at an advanced stage of population ageing, lifestyle and economic trends. The majority (94%) of the population is ethnically Chinese [10], mostly second or third generation immigrants from the southern Chinese province of Guangdong [11]. Therefore, Hong Kong is a reliable sentinel for future trends in Mainland China.

There is a lack of published data on current trends in diabetes incidence and prevalence, either in Hong Kong or other developed Chinese settings. To estimate the incidence and prevalence of diabetes, we took advantage of a complete population-based administrative dataset based on the electronic health records from all public sector health care services in Hong Kong from 2006 to 2014.

## Methods

### Setting

Hong Kong has a mixed public-private health care economy. The public system is based on the British National Health Service model, with 94.2% of the funding derived from government general revenue [12]. All residents are eligible to use public health care services at highly subsidized rates. Public sector services are provided by the Hospital Authority, which runs hospitals, specialist outpatient clinics and general outpatient clinics (primary care). The Hospital Authority provides the majority of inpatient care (90% total bed-days and 80% of admissions), and 50% of specialist outpatient care, while the private sector provides 70% of first-contact outpatient services [12, 13].

### Data sources

The Hospital Authority's electronic health records system (Clinical Management System) contains inpatient records from 1997; specialist outpatient and emergency room data from 2000; and general outpatient (primary care), clinical laboratory and medications data from 2006. Relevant variables included age, sex, residential district, and diagnostic codes of every health care episode. Diagnoses were coded according to the International Classification of Disease 9th revision (ICD-9) for emergency room visits, specialist outpatient attendances and inpatient admissions; and the International Classification of Primary Care 2nd Edition (ICPC-2) for general outpatient attendances. Deaths were ascertained through the government Immigration Department that were cross-referenced with Hospital Authority data. This study was approved by the Institutional Review Board of all seven Hospital Authority clusters.

### Study participants

The Hospital Authority Clinical Management System data comprised all 6.4 million unique individuals who used Hospital Authority services from January 1, 2006 to December 31, 2014 inclusive. Each individual is identified by the Hong Kong Identity Card number as well as a Hospital Authority patient number, both of which are unique identifiers that can be used to track individuals through the system. All population figures were based on estimates by the government Census and Statistics Department for 2006-2014 [14].

## Ascertainment of diabetes and pre-diabetes

Participants were diagnosed with diabetes mellitus by four different ascertainment methods (Supplemental Table S1): (a) WHO 2011 guidelines [15, 16]; (b) American Diabetes Association (ADA) 2015 guidelines [17]; (c) methods by Nichols and colleagues [5]; and (d) our own analysis criteria. The WHO 2011 guidelines define diabetes as any one of: (a) HbA<sub>1c</sub>  $\geq$ 48 mmol/mol ( $\geq$ 6.5%); (b) Fasting plasma glucose  $\geq$ 7.0 mmol/L ( $\geq$ 126 mg/dL); or (c) Oral glucose tolerance test (OGTT)  $\geq$ 11.1 mmol/L (200 mg/dL) [15, 16]. The ADA 2015 guidelines has an additional diagnostic criterion compared with the WHO 2011 guidelines: random plasma glucose  $\geq$ 11.1 mmol/L ( $\geq$ 200 mg/dL) in a patient with classic symptoms of hyperglycemia [17].

By the method of Nichols and colleagues [5], ascertainment of diabetes was: one inpatient diagnosis (ICD-9 codes as above), or any combination of two other qualifying events occurring within 24 months of each other. Other qualifying events exclude OGTT, but include: (a) HbA<sub>1c</sub>; (b) fasting plasma glucose; (c) random plasma glucose; (d) ICD-9 or ICPC-2 code for diabetes for outpatients; (e) dispensation of anti-glycemic medication (except for metformin and thiazolidinediones as they have other non-diabetes indications).

We defined diabetes in our main analysis by any one of: (a) WHO 2011 guidelines; (b) random plasma glucose  $\geq$ 11.1 mmol/L ( $\geq$ 200 mg/dL) on two occasions; (c) diagnosis code for diabetes (ICD-9 codes 250, 357.2, 366.41 and 362.01-362.07; or ICPC codes T89 and T90), (d) dispensation of anti-hyperglycemic medication (including insulins, metformin, thiazolidinediones, sulfonylureas, incretin mimetics/glucagon-like peptide-1 analogues, glucosidase inhibitors, and dipeptidyl peptidase inhibitors). Since the WHO and ADA guidelines are exclusively laboratory-based definitions, we included diagnosis codes from patient admissions and attendances as diagnostic based on administrative data. As we did not have data on clinical history to match classic symptoms of hyperglycemia with raised random plasma glucose values as per the ADA 2015 guidelines, we defined diabetes when the random plasma glucose was raised on two occasions. We excluded metformin and thiazolidinediones as a sensitivity analysis because these medications can be used for indications other than diabetes control.

With the exception of the method by Nichols and colleagues (which adopted the later of two dates) [5], onset of diabetes was determined by the earliest date an individual met the defining criteria. When objectively identified diabetes cases also had a self-reported diagnosis date, the earliest date was taken as date of onset.

Pre-diabetes was defined according to the ADA 2015 guidelines, namely HbA<sub>1c</sub>  $\geq$ 39 and  $<$ 48 mmol/mol ( $\geq$ 5.7% and  $<$ 6.5%); impaired fasting plasma glucose of  $\geq$ 5.6 and  $<$ 7 mmol/L ( $\geq$ 100 and  $<$ 126 mg/dL); or impaired glucose tolerance (2-hour OGTT)  $\geq$ 7.8 and  $<$ 11.1 mmol/L ( $\geq$ 140 and  $<$ 200 mg/dL) [17].

Since it is not possible to distinguish between type 1 and type 2 diabetes based on blood glucose alone, participants were excluded if they were aged below 20 years at the time of diagnosis.

## Adjustments

We estimated the proportion of people with diabetes who had never sought relevant care in the public sector (i.e. services that would have triggered the defining criteria) during the period of observation, using data from a territory-wide population survey (Thematic Household Survey 2010) [13]. We analyzed the effect of under-diagnosis on our diabetes prevalence estimate in 2014 by adjusting for the proportion of people previously unaware of their diabetes status from previous studies in mainland China [2], Hong Kong [18], Canada [19], and the US [9]. We conducted a two-way sensitivity analysis to account for people identified with diabetes in our dataset who may not report awareness of their diabetes status.

## Statistical analysis

Crude incidence was estimated for each calendar year from 2007 to 2014. Participants with diabetes were enumerated as an incident case in the year of onset, thus excluded from the numerator and denominator for subsequent years. All participants with a diagnosis date up to, and inclusive of, December 31, 2006 were classed as pre-existing diabetes and excluded from the incidence calculations. Similarly for pre-diabetes, the person-time at risk denominator excluded cases of pre-diabetes from previous years and prevalent cases of diabetes.

The prevalence of diabetes and pre-diabetes from 2007 to 2014, stratified by age group and sex, was computed as the number of participants with diabetes (or pre-diabetes) alive during mid-year divided by the corresponding Hong Kong population estimate of adults aged 20 years or over.

Annual incidence and prevalence were adjusted for age and sex by direct standardization, using sex-specific five-year age strata and the Hong Kong mid-year population in 2014 as the standard population. Exact 95% confidence intervals for incidence and prevalence were calculated based on a Poisson and binomial distribution respectively. Risk ratios were calculated using exact methods.

Trends in incidence and prevalence were tested in a logistic regression model using the midpoint of each year as a continuous variable. Trends in incidence were also tested using a Poisson offset model, with log number of person-years as offset. We added a quadratic term to test for nonlinear trends; inclusion of the quadratic term in the final model was based on assessment of model fit measured by the Akaike Information Criteria. Analyses using the Poisson offset model were consistent with the logistic regression model, so we only present the Poisson offset model in our results for incidence. To allow for multiple comparisons, type I error was set at 0.0015 (Bonferroni correction). All data were analyzed using R (version 3.2, The R Foundation for Statistical Computing).

## Results

Among the Hong Kong population from 2006 to 2014, we identified 697,201 participants with diabetes, of which 377,565 (54.2%) were incident cases; and 1,229,731 people with diabetes or pre-diabetes (Table 1). In 2014, the overall incidence was 9.46 per 1,000 person-years (95% CI 9.38-9.54) (Table 2). Women had a significantly lower incidence of diabetes (RR: 0.75, 95% CI 0.74-0.75). Incidence of diabetes increased significantly with age (Supplemental Table S2). The overall prevalence of diabetes in 2014 was 10.29% (95% CI 10.27%-10.32%). Our overall prevalence estimate for diabetes including previously unaware cases is sensitive to the assumed proportion of under-diagnosis, ranging from 12.59% to 34.22% (Supplemental Table S3).

Age- and sex- adjusted incidence decreased significantly from 2007 to 2014 from 10.01 per 1,000 person-years (95% CI 9.93-10.10) to 9.46 per 1,000 person-years (95% CI 9.38-9.54) (quadratic trend,  $p < 0.001$ , Table 2). A declining incidence trend was observed across all ascertainment criteria groups (Supplemental Table S4). Declines were greater for case ascertainment based exclusively on laboratory measures: WHO criteria (from 10.88 to 8.15 per 1,000 person-years), and the ADA criteria group (from 13.56 to 9.85 per 1,000 person-years), than Nichols et al. (from 8.44 to 7.61 per 1,000 person-years) and our main analysis (from 10.01 to 9.46 per 1,000 person-years). Subgroup analysis showed divergent incidence trends, with significant increases among the 40-59 year olds but significant decreases among 60-79 and over 80 year olds (Supplemental Table S2).

From 2006 to 2014, overall prevalence of diabetes significantly increased from 7.21% (95% CI 7.18%-7.23%) to 10.29% (95% CI 10.27%-10.32%) (quadratic trend,  $p < 0.001$ , Table 2). Prevalence increased among all of the ascertainment criteria groups (Supplemental Table S4). The increase was greater among the WHO criteria group (5.42% to 9.28%), and ADA criteria group (5.64% to 10.02%), than Nichols et al. criteria group (6.72% to 9.03%) and our main analysis group (7.21% to 10.29%). Prevalence of diabetes significantly increased in both sexes and across all age groups in our main analysis (quadratic trend,  $p < 0.001$ , Table 2).

The overall incidence of pre-diabetes in 2014 was 18.88 per 1,000 person-years (95% CI 18.76-18.99), and the overall prevalence of pre-diabetes was 8.90% (95% CI 8.87%-8.92%) (Table 3). Women again had a lower incidence of pre-diabetes (OR: 0.94, 95% CI 0.93-0.94). Incidence of pre-diabetes increased significantly with age (Supplemental Table S5). Incidence of pre-diabetes among both sexes and for all age groups followed a significant quadratic trend ( $p < 0.001$ ); incidence rose from 2007 to peak at 2011 and subsequently declined through to 2014. Prevalence of pre-diabetes significantly increased from 2006 to 2014 among all subgroups (quadratic trend,  $p < 0.001$ ).

## Discussion

We have provided contemporary population-based estimates of diabetes and pre-diabetes incidence and prevalence among Hong Kong adults, who are reliable epidemiologic sentinels for the rest of China [20].

Prevalence estimates overall were consistent across ascertainment criteria groups (ranging from 9.03% to 10.29% in 2014). These are higher than previous local estimates according to Thematic Household Surveys by self-reported diagnosis [13, 21-23], as our ascertainment criteria included laboratory data, health service attendances and medication dispensations. Previous estimates in mainland China based on population screening by laboratory testing have found a

higher prevalence of 11.6%, where 69.9% were previously unaware of their diabetes status (14.3% and 63.6% respectively in economically developed cities) [2]. The Hong Kong Cardiovascular Risk Factor Prevalence Study conducted in 1994-1996 estimated a similar proportion (64.4%) being unaware of their own diabetes status [18]. Socioeconomic development leading to greater health awareness and improved health service delivery for non-communicable diseases during the intervening two decades were likely to have reduced the proportion of undiagnosed [9]. In high-income countries such as the US and Canada, 36.4% and 40.9% of cases were undiagnosed respectively [9, 19]. Applying the estimates from the US and Canada gives an adjusted overall prevalence range of 12.59%-17.43% in Hong Kong, comparable to levels in economically developed regions of mainland China. Our overall population estimate is, as would be expected, sensitive to the assumed proportion of under-diagnosis and the assumed proportion of participants identified with diabetes who may not report awareness of their diabetes status.

Between 2006 and 2014, age- and sex- adjusted overall prevalence increased significantly by all ascertainment criteria and for all age groups. The increase in prevalence is consistent with local Thematic Household surveys [13, 21-23], and are in keeping with the declining age-standardized death rate of diabetes in Hong Kong over this period [24]. We found a significant quadratic trend indicating the rate of increase is slowing. This may be partly due to the initial under-ascertainment of prevalent cases in the earlier years, particularly for the WHO and ADA laboratory criteria that would not have identified well-controlled diabetes. The slowing rate of increase is consistent with prevalence estimates in other economically developed regions including the US and Korea [8, 9].

Similarly our incidence estimates are consistent with those reported elsewhere, such as in the US and Korea [5, 8]. Standardized incidence in our main analysis stabilized with small declines from 2007 to 2014, again in keeping with patterns seen in the UK, US, Korea and Denmark [5-8]. This correlates with our finding of a decline in the incidence of pre-diabetes in the latter years, and also with a small reduction in obesity in Hong Kong over the same period, although it is unlikely causal given lead time bias [25]. Small declines in incidence in the older age groups (60 years or over), when interpreted together with corresponding increases observed in the younger age groups suggests that diabetes might have been diagnosed earlier, either due to earlier onset of disease or improved health assessment or both.

Study strengths include the territory-wide public health service records of 6.4 million unique people across 8 years, from 2006 to 2014. The Hospital Authority Clinical Management System platform records all available electronic clinical information and care documentation for all clinical specialties, allied health disciplines and public sector care settings [26]. This dataset had wide population coverage as the vast majority (87.4%) of people with diabetes sought care in the public sector based on data from a territory-wide population survey [13]. The incidence and prevalence estimates were based on a dynamic population, allowing replacement of at-risk individuals; in contrast to a fixed cohort where the observed incidence may flatten or decline over time as individuals at high risk are diagnosed earlier, and where the observed prevalence may rise as individuals who go on to develop diabetes are not replenished. Case ascertainment was based on a comprehensive definition including laboratory tests, diagnostic coding and anti-glycemic medications. Sensitivity analyses excluding metformin and thiazolidinediones gave very similar results (data not shown). Applying different ascertainment criteria yielded similar prevalence and incidence trends in the later years of the observation period, indicating internal consistency. Trends in incidence of diabetes and pre-diabetes were also internally consistent.

Our study has a number of limitations. Given that clinical records were available only from 2006, there was likely under-ascertainment at baseline thus initial overestimation of incidence from “harvesting”, with an accompanying subsequent apparent incidence decline as well as an artefactually inflated rise in prevalence [27]. Case ascertainment based on laboratory glucose measurement was particularly affected as participants previously diagnosed with diabetes might have been receiving adequate therapy to control blood sugar levels within normal limits, yielding the observed sharp incidence decline and corresponding prevalence increase from 2006 to 2010 by the WHO and ADA criteria. This effect could also explain the observed trends for pre-diabetes.

Precise and accurate date of onset can only be determined by serial blood glucose measurements prospectively, from birth ideally. Ascertainment by routine data capture as in our study necessary relied on testing people who attended public health care services, and might have been influenced by secular changes in testing practice, case mix, patient demographics and health-seeking behavior. Although there had not been notable changes in screening or clinical practice guidelines during the observation period, changes in doctor behavior and/or patient awareness

could have potentially biased the secular trends although likely not the most recent prevalence estimate (given its cumulative nature). The lack of serial blood glucose measurements means we could not account for the possibility that some participants with pre-diabetes may have taken measures such as diet and exercise to regress below the pre-diabetes glucose threshold. However, this proportion is expected to be small [28].”

Since it is not possible to distinguish between type 1 and type 2 diabetes based on blood glucose alone, limiting the case definition to adults aged 20 years and older meant the vast majority of incident cases were type 2 diabetes. Sensitivity analyses excluding pregnancy-related diagnosis codes to allow for gestational diabetes yielded almost identical results (data not shown).

Similar to other highly developed western and Asian populations, diabetes incidence in Hong Kong Chinese appeared to have stabilized and showed small declines from 2007 to 2014. Similar declines in incidence from 2011 to 2014 were observed for pre-diabetes. Given ageing and longevity, we observed a continued increase in the prevalence of diabetes and pre-diabetes, albeit with a decelerating rate of growth.

### **Author contributions**

C.H.C., S.C.S., S.Y.T., N.M.W., J.W., and J.M.J. collected the data. J.Q. researched data and wrote the first draft. J.Q., T.K.L. and H.P. performed statistical analysis. G.M.L. conceived and together with J.Q. designed the study. All authors reviewed and revised the manuscript and approved the final version. J.Q. is the guarantor of this work, and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

### **Competing interests**

We report no conflicts of interest.

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## Tables

Table 1 - Baseline characteristics of participants with diabetes and pre-diabetes, 2006-2014

	<b>Diabetes (n=697,201)</b>	<b>Diabetes or Pre-diabetes (n= 1,229,731)</b>
Incident cases <sup>a</sup>	377,565	849,486
Age at diagnosis, mean (SD), years	61.3 (14.3)	60.8 (14.6)
Age group, years (%)		
20-39	6.5	8.1
40-59	39.4	39.1
60-79	43.2	42.0
≥80	10.9	10.8
Female (%)	49.6	51.3

<sup>a</sup> Incident cases from 2007 to 2014. SD, Standard Deviation.

Table 2 - Diabetes Incidence and Prevalence among Adults aged 20 Years or Older, 2006-2014

	2006	2007	2008	2009	2010	2011	2012	2013	2014	<i>p</i> value <sup>a</sup>	Risk Ratio
<b>Incidence (per 1,000 person-years)</b>											
Overall	-	10.01	10.05	10.24	9.96	10.16	10.07	9.97	9.46	<0.001	
		9.93, 10.10	9.96, 10.14	10.15, 10.32	9.87, 10.04	10.07, 10.24	9.99, 10.15	9.89, 10.05	9.38, 9.54		
Men	-	11.40	11.53	11.64	11.48	11.81	11.70	11.72	11.33	<0.001	1
		11.26, 11.54	11.39, 11.67	11.51, 11.78	11.35, 11.62	11.67, 11.94	11.57, 11.83	11.59, 11.86	11.20, 11.45		
Women	-	8.87	8.83	9.07	8.70	8.80	8.73	8.52	7.92	<0.001	0.75
		8.76, 8.98	8.72, 8.94	8.96, 9.18	8.59, 8.81	8.69, 8.90	8.62, 8.83	8.42, 8.62	7.82, 8.02		0.74, 0.75
<b>Prevalence (%)</b>											
Overall	7.21	7.74	8.23	8.70	9.06	9.42	9.77	10.10	10.29	<0.001	
	7.18, 7.23	7.72, 7.77	8.20, 8.25	8.67, 8.72	9.04, 9.09	9.39, 9.45	9.75, 9.80	10.08, 10.13	10.27, 10.32		
Men	7.45	8.10	8.71	9.29	9.77	10.25	10.71	11.15	11.44	<0.001	1
	7.41, 7.49	8.06, 8.14	8.67, 8.75	9.25, 9.33	9.73, 9.80	10.21, 10.29	10.67, 10.75	11.11, 11.19	11.40, 11.48		
Women	7.00	7.45	7.83	8.21	8.48	8.74	9.00	9.24	9.35	<0.001	0.87
	6.97, 7.04	7.41, 7.48	7.80, 7.87	8.18, 8.24	8.45, 8.52	8.71, 8.78	8.97, 9.03	9.21, 9.28	9.32, 9.39		0.87, 0.87

All estimates standardized by age and sex to the 2014 population. Diabetes was defined as any one of: WHO 2011 guidelines on HbA<sub>1c</sub>, fasting glucose and oral glucose tolerance test; random plasma glucose  $\geq 11.1$  mmol/L ( $\geq 200$  mg/dL) on two occasions; diagnosis code for diabetes (ICD-9 codes 250, 357.2, 366.41 and 362.01-362.0, or ICPC codes T89 and T90); dispensation of anti-hyperglycemic medication. <sup>a</sup> Quadratic trend.

Table 3 - Pre-diabetes Incidence and Prevalence among Adults aged 20 Years or Older based on American Diabetes Association 2015 guidelines, 2006-2014

	2006	2007	2008	2009	2010	2011	2012	2013	2014	<i>p</i> value <sup>a</sup>	Risk Ratio
<b>Incidence (per 1,000 person-years)</b>											
Overall	-	12.50	12.85	13.38	15.86	20.76	20.12	19.31	18.88	<0.001	
		12.40, 12.60	12.75, 12.95	13.27, 13.48	15.75, 15.97	20.63, 20.88	20.00, 20.24	19.20, 19.43	18.76, 18.99		
Men	-	13.47	13.63	14.02	16.49	21.36	20.50	19.92	19.38	<0.001	1
		13.31, 13.62	13.48, 13.79	13.87, 14.18	16.32, 16.66	21.18, 21.55	20.32, 20.68	19.74, 20.09	19.20, 19.55		
Women	-	11.72	12.22	12.85	15.36	20.27	19.81	18.83	18.47	<0.001	0.94
		11.59, 11.85	12.09, 12.36	12.72, 12.99	15.21, 15.50	20.10, 20.43	19.65, 19.97	18.67, 18.99	18.32, 18.63		0.93, 0.94
<b>Prevalence (%)</b>											
Overall	0.78	1.91	2.80	3.65	4.56	5.67	6.93	7.92	8.90	<0.001	
	0.77, 0.79	1.90, 1.92	2.79, 2.81	3.63, 3.66	4.54, 4.57	5.65, 5.69	6.91, 6.96	7.90, 7.94	8.87, 8.92		
Men	0.86	2.08	3.02	3.88	4.81	5.91	7.15	8.10	9.04	<0.001	1
	0.85, 0.88	2.06, 2.10	3.00, 3.04	3.85, 3.90	4.78, 4.84	5.88, 5.94	7.12, 7.19	8.06, 8.13	9.00, 9.07		
Women	0.72	1.76	2.62	3.45	4.35	5.47	6.75	7.77	8.78	<0.001	0.94
	0.71, 0.73	1.75, 1.78	2.60, 2.64	3.43, 3.48	4.33, 4.37	5.45, 5.50	6.73, 6.78	7.74, 7.80	8.75, 8.81		0.94, 0.94

All estimates standardized by age and sex to the 2014 population. Pre-diabetes was defined according to the ADA 2015 guidelines: HbA<sub>1c</sub>  $\geq 39$  and  $< 48$  mmol/mol ( $\geq 5.7\%$  and  $< 6.5\%$ ); impaired fasting plasma glucose of  $\geq 5.6$  and  $< 7$  mmol/L ( $\geq 100$  and  $< 126$  mg/dL); or impaired glucose tolerance (2-hour OGTT)  $\geq 7.8$  and  $< 11.1$  mmol/L ( $\geq 140$  and  $< 200$  mg/dL).<sup>a</sup> Quadratic trend.