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Diabetes and Cause-Specific Mortality in Mexico City

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Abstract

Background: Most large prospective studies of diabetes and mortality have focused on high-income countries where patients have reasonably good medical care and glycemic control and diabetes less than doubles all-cause mortality. Few have been done in middle-income countries where obesity and diabetes may be common and glycemic control, poor.

Methods: In 1998-2004, a prospective study in Mexico City recruited 50,000 men and 100,000 women aged ≥ 35 years, recorded previously diagnosed diabetes, stored blood, and tracked 12-year disease-specific mortality through January 1, 2014 (diabetes coded as the underlying cause only for deaths from acute diabetic crises). Mortality rate ratios (RRs, with versus without diabetes) were estimated after excluding people with other chronic diseases.

Results: At recruitment, obesity was common, and diabetes prevalence rose steeply with age ($>20\%$ by age 60). Participants with diabetes had poor glycemic control (mean HbA1c 9.0 [SD2.5]); few were taking other risk-reducing medication. Previously diagnosed diabetes was associated with all-cause mortality RRs of 5.4 (95% CI 5.0-6.0) at ages 35-59, 3.1 (2.9-3.3) at ages 60-74 and 1.9 (1.8-2.1) at ages 75-84, accounting for one-third of all deaths at ages 35-74 years; the largest absolute excesses involved renal (RR 20.1 [17.2-23.4]), cardiac (RR 3.7 [3.2-4.2]), and infectious (RR 4.7 [4.0-5.5]) disease, as well as acute diabetic crises (8% of all deaths with diabetes). Marked excesses of stroke and peripheral artery disease, but not cirrhosis, cancer, or COPD were present.

Conclusions: In this study, diabetes was common in overweight individuals from a middle-income country and carried a far worse prognosis than found in similar patients from high-income countries.

Diabetes is increasingly common in many countries^{1,2} and increases mortality from a wide range of diseases.³ However, most large studies of diabetes have been in high-income countries with reasonably good medical care and glycemic control. In a recent meta-analysis of 97 prospective studies, mainly from such countries, self-reported diabetes less than doubled all-cause mortality rates.^{3,4} In middle-income and low-income countries, however, where resources to manage diabetes may be more limited and vascular-protective treatments under-utilized,⁵ the effects of diabetes on mortality from other diseases could be substantially larger, and in many such countries diabetes prevalence has increased substantially in recent years.^{1,2}

Mexico is a middle-income country⁶ with among the highest prevalence of obesity and diabetes in the world,^{1,7} and, among persons with diabetes, glycemic control is often poor⁸ and not combined with treatment to control other risk factors (e.g., elevated blood pressure and hypercholesterolemia). Here we report the findings from a prospective study of the impact of diabetes on cause-specific mortality in 150,000 Mexican adults followed for 12 years.

METHODS

Recruitment

From 1998-2004, we visited households within two districts of Mexico City, inviting all residents aged ≥ 35 years to participate in a prospective study.⁹ We recorded age, sex, socioeconomic status, lifestyle factors (e.g., alcohol intake, smoking, physical activity), current medication, and medical history (including previously diagnosed diabetes). Height, weight, waist/hip circumference, and seated blood pressure were measured. 10mL of blood was taken, transported at 4-10°C in insulated boxes containing ice packs, refrigerated at 4°C overnight, and separated next morning. Plasma and buffy coat samples were stored locally at -80°C, then transported in 5 shipments on dry ice to Oxford (U.K.) for long-term storage

over liquid nitrogen. Research ethics approval was obtained from the Mexican Ministry of Health, Mexican National Council for Science and Technology, and University of Oxford, U.K.

Glycosylated Hemoglobin (HbA1c) Measurements

HbA1c can be assayed reliably¹⁰ from buffy coat samples. We did this in CTSU's ISO17025-accredited Wolfson laboratories, using validated high-performance liquid chromatography methods on HA-8180 analysers with calibrators traceable to International Federation of Clinical Chemistry standards. These IFCC mmol/mol values are then converted to DCCT HbA1c percentages (using $\text{HbA1c} = 0.0915 \times \text{mmol/mol} + 2.15$).¹¹

Mortality Follow-up

Death registration in Mexico City is reliable and complete, with almost all adult deaths certified medically and few attributed to unknown causes.¹² Deaths were tracked up to January 1, 2014, through electronic linkage to the death registry. Subsequent home visits confirmed correct mortality linkage. The registry codes all diseases on the death certificate according to ICD-10.¹³ Study clinicians reviewed death certificates, and labeled diabetes as the underlying cause only for deaths deemed due to acute diabetic crises. For all other deaths with any mention of diabetes as an immediate or antecedent cause of death (i.e., on Part I of the certificate), they selected an appropriate underlying cause other than diabetes.

Statistical Analyses

The main analyses defined diabetes as self-reported previous medical diagnosis of diabetes and/or use of anti-diabetic medication. Sensitivity analyses included in the diabetes definition persons without this evidence, but with baseline $\text{HbA1c} \geq 6.5$. We considered those with diagnosis of diabetes before age 35 years who were taking insulin at recruitment as likely to have had type 1 diabetes.

Cox regression analysis related diabetes at recruitment to mortality, excluding people with other chronic diseases (Fig. 1 footnotes) or any covariates missing. These mortality rate ratios (RRs) were adjusted for age-at-risk (5-year categories), location (2 districts), education (4 groups), smoking (never, former, light, moderate, heavy), and anthropometry (height, weight, waist, and hip measurements), but not blood pressure or lipids (which could themselves be affected by diabetes – and, adjustment for them would make little difference³). Most age-specific analyses averaged male and female RRs (which were generally similar).

Mortality rates among study participants may differ substantially from those among other Mexicans. In extrapolating to Mexico as a whole, therefore, we estimated absolute disease-specific mortality rates for those with and without diabetes by applying our disease-specific RRs to the 2012 Mexican national death rates.¹⁴ Defining premature mortality as death before age 75, we used these age- and sex-specific mortality rates to calculate the average mortality rate (for men and women combined) at ages 35-74, and then subdivided this in proportion to the underlying causes of death in our study to estimate 2012 national disease-specific death rates. For each disease, we used the RR at ages 35-74 to calculate the average mortality rate among the proportions p with and $(1-p)$ without diabetes as $RR \times A$ and A , such that $(p \times RR \times A) + (1-p) \times A$ equalled the estimated disease-specific national mortality rate. Analyses used SAS v9.3 and R v2.11.1.

RESULTS

Recruitment

Of 112,333 eligible households visited, 106,059 (94%) took part, yielding 159,755 participants. Of these potential participants, 8135 had a history of ischemic heart disease, stroke, cancer, cirrhosis, chronic obstructive pulmonary disease or chronic kidney disease (CKD), and were excluded, while a further 5574 participants were excluded because of

missing data or age ≥ 85 years at recruitment. Table 1 shows characteristics at recruitment of the remaining 146,046 participants.

Self-reported Diabetes and HbA1c at Recruitment

The prevalence of previously diagnosed diabetes increased steeply from 3% at ages 35-39 to $>20\%$ in both sexes by age 60 years (Fig. 1). At ages 35-59, 60-74, and 75-84, the mean (SD) time since diabetes diagnosis was, respectively, 7 (6), 10 (7) and 13 (8) years. Most of the diabetes was type 2, with only 1% of participants diagnosed before age 35 years and requiring insulin. Of those with diagnosed diabetes, two-thirds reportedly used sulfonylureas, one-fifth biguanide, and 80% at least some anti-diabetic medication.

Baseline HbA1c was available for 135,104 (93%) of participants. Among those with diagnosed diabetes, mean baseline HbA1c was 9.0, 36% had baseline HbA1c >10.0 (86 mmol/mol), and the HbA1c was higher among younger participants (Supplementary Appendix, Fig. S1). By contrast, mean baseline HbA1c among those without diagnosed diabetes was 5.7, with only 5.8% having HbA1c ≥ 6.5 (indicating undiagnosed diabetes) and 1.5% having HbA1c >10.0 .

There was little difference in body-mass index (BMI, weight in kilograms divided by the square of height in meters) between those with and without previously diagnosed diabetes (Table 1). However, among those without diabetes BMI at recruitment was strongly predictive of incident diabetes during follow-up, as indicated by its strong relationship with diabetes prevalence in a subset of survivors resurveyed in 2015 (Supplementary Appendix, Fig. S1).

Diabetes and All-cause Mortality

During about 12 years of follow-up, there were 9674 deaths from all causes at ages 35-84 years in participants with no known disease (other than diabetes) before recruitment. Figure 1 gives the age-specific, sex-specific all-cause mortality RRs comparing participants with

and without diagnosed diabetes. These RRs were similar for men and women, and averaged 5.4 (95% CI, 5.0-6.0) at ages 35-59, 3.1 (2.9-3.3) at ages 60-74 and 1.9 (1.8-2.1) at ages 75-84 years. The age-specific RRs were similar in the two study districts (data not shown).

The excess number of deaths before age 75 associated with diabetes diagnosed before recruitment is shown in Table 2. Even though previously diagnosed diabetes is a crude exposure measure, and misses any effects of diabetes onset during follow-up, it still accounted for 30% of all deaths. Extending the diabetes definition to include all participants with HbA1c \geq 6.5 at recruitment increased the proportion to 35% (Supplementary Appendix Table S1).

Diabetes and Disease-specific Mortality

Figure 2 lists the mortality RRs for several underlying causes of death. (For additional details, see Supplementary Appendix Figs. S2-S7.) Among those with diabetes diagnosed before recruitment, 300 of the 3786 deaths (8%) were from acute diabetic crises. In addition, there were 92 acute deaths due to diabetes among participants without previously diagnosed diabetes (their median baseline HbA1c was 6.1). Thus, only three-quarters of 12-year acute diabetes mortality was in participants with diabetes diagnosed before recruitment.

Likewise, for mortality from the aggregate of all renal disease, there were 1032 deaths among those with and 390 deaths among those without diabetes before recruitment, so almost three-quarters of 12-year renal mortality was in people diagnosed with diabetes before recruitment. The RRs were 31.1 (95% CI, 24.2-39.8) at ages 35-59, 13.9 (11.5-16.9) at 60-74, and 5.1 (4.1-6.3) at 75-84.

Apart from diabetic crises and renal disease, the conditions associated with the greatest relative risk were cardiac disease, cerebrovascular and other vascular diseases, and infections. All involved similar age-specific RRs, which were more extreme at younger ages (and virtually identical for men and women: data not shown).

Diabetes was also strongly associated with mortality from peptic ulcer disease, but not with mortality from cirrhosis (much of which was alcoholic). There was little association between diabetes and death from chronic obstructive pulmonary disease, from cancer as a whole (RR=1.01, 0.88-1.15), or from particular types of cancer (Supplementary Appendix Fig. S6), although there were too few cancer deaths for this to be a reliably null finding.

Overall, the excess mortality associated with diabetes accounted for about one-third of all vascular deaths and one-third of all other deaths. The mortality analyses were not materially affected when repeated without adjustment for smoking, education and anthropometry; with additional adjustment for alcohol, physical activity and blood pressure; with inclusion of those with prior disease or exclusion of the first 5 years of follow-up (data not shown); or by using for disease-specific outcome death with any mention of the disease of interest on Part I of the certificate (Supplementary Appendix Fig. S8).

Estimates of Absolute Excess Mortality

Figure 3 (absolute risks) combines the proportions dying at ages 35-74 from particular diseases in the current study, the disease-specific RRs at ages 35-74, and 2012 Mexican national mortality rates (see Methods). Between ages 35-74, the absolute excess mortality associated with diabetes was greatest for renal disease, followed by cardiac disease, infection, acute glycaemic crises, and the aggregate of all other vascular diseases.

DISCUSSION

In this middle-income country, diabetes was more common,¹⁵ and had a much larger impact on mortality, than in major high-income countries.^{3,4,16} By ages 60-74 years about one-quarter of the participants in the present study had received a medical diagnosis of diabetes (compared with about 7% in the UK¹⁷ and 15% in the US during a similar time period¹⁵), and, even after adjustment for other risk factors, the all-cause mortality rate at ages 35-74 years

was approximately quadrupled among participants with such a diagnosis. In contrast, recent meta-analyses of prospective studies from mostly high-income countries showed less than a doubling in the all-cause mortality rate for those with diabetes.³

A likely explanation for our more marked all-cause mortality RRs is inadequate medical care, including poor glycemic control.^{18,19} Over one-third of participants with diabetes diagnosed before recruitment had a baseline HbA1c > 10.0 (86 mmol/mol) as compared with only about 5% of people with diagnosed diabetes in high-income country cohorts.^{3,16,20} Further, 8% of all deaths of those with diabetes in the present study were due to acute diabetic crises, compared with <1% in the US.²¹ In contrast to previous studies,³ our all-cause mortality RRs were similar in both sexes, reflecting similar glycemic control and diabetes duration (Table 1).

A key feature of our study is clinician review of death certificates, which had detailed, previously validated,²² information recorded on them. WHO coding rules attribute to diabetes all vascular and renal deaths in persons with diabetes recorded in Part I of the certificate.¹³ This results in undercounting of vascular and renal deaths among people with diabetes, which biases downwards the RRs that associate diabetes with these diseases. In the present work we labeled diabetes the underlying cause only for deaths that occurred during acute diabetic crises, yielding large RRs for vascular and, particularly, renal mortality. Our coding conventions do not, however, affect the RRs for overall mortality, which are also large.

Our study has certain limitations. It is not representative of Mexico as a whole. Response rates were high, however, so the study should be reasonably representative of the adults contacted at home (two-thirds female) in the two study districts. Moreover, our baseline estimates of diabetes prevalence are similar to those obtained by a large national survey in Mexico carried out around the same time.²³ Subsequent nationally representative 2006 and

2012 surveys of HbA1c in Mexican adults obtained similar prevalence estimates, and, importantly, glycemic control among those with diagnosed diabetes in those surveys was, if anything, worse than in our study,⁸ so our estimates of the importance of diabetes to mortality in Mexico as a whole may if anything be slightly low. As in many prospective studies,³ we did not check self-reports of medically-diagnosed diabetes against medical records, but the HbA1c findings (and high RRs for overall mortality) suggest that such reports were reasonably reliable, with generally normal HbA1c levels in those reporting no diabetes. Sensitivity analyses that redefined diabetes to include any and all participants with HbA1c \geq 6.5 at baseline increased the mortality attributed to diabetes from 30% to 35%, while further inclusion of deaths due to the effects of diabetes with onset after recruitment would increase this still further (perhaps to about 40%; for example 14% of the deaths from acute diabetic crises were of people without previously diagnosed diabetes and baseline HbA1c <6.5). We cannot, however, rule out some residual confounding.

The greatest absolute excess mortality associated with diabetes was from renal disease (mainly CKD), cardiovascular disease, infection, acute diabetic crises, and stroke. Assuming causality, about three-quarters of the mortality at ages 35-74 years among Mexicans with diabetes is due (directly or indirectly) to their diabetes. Age-specific mortality rates correlated with diabetes duration (data not shown), so the lifetime hazard would be even greater for people who develop diabetes in early rather than later adult life. Overall, we estimated diabetes to be a direct or indirect cause of at least one-third of all mortality at ages 35-74 years in our study, double recent indirect estimates for Mexico that relied on RRs from other countries.^{1,24} In addition to their relevance to Mexico, our results are relevant to many other populations worldwide, including many millions of US Mexican-Americans, who have twice the US non-Hispanic white prevalence of diabetes¹⁵ and worse glycemic control.²⁰

In Mexico, the aggregate of vascular, diabetic and renal mortality rates at ages 35-74 years increased slowly from 1998 to 2008, a time during which rates declined steeply in the US

(Figs. S9-10, Supplementary Appendix). When recruitment into this study ended in 2004, half of all Mexican adults had no health insurance, but over the next 8 years healthcare provision improved substantially with the introduction of *Seguro Popular*,²⁵ which extended health insurance nationwide during 2004-2012.²⁶ In 2008, Mexican mortality rates from vascular, diabetic and renal disease began to decrease, perhaps reflecting better healthcare provision.⁸ Nevertheless, mortality rates remain high, as does the prevalence of diabetes.^{1,8}

The high mortality from diabetes in this overweight middle-income country reflected both the high prevalence of diabetes, partly due to widespread obesity affecting diabetes incidence, and its poor prognosis, partly due to inadequate treatment of diabetes, associated risk factors,⁸ and diabetic complications. Poor glycemic control increases the risk of microvascular disease,²⁷ but during the period of our study, regular testing for albuminuria was rare⁸ and renal replacement therapy was limited. Thus, persons with CKD often had poor outcomes.²⁸ Mexico recently introduced its *National Strategy for Overweight, Obesity and Diabetes*, including health education, improved exercise opportunities, taxation of sugary drinks and high-calorie foods, and earlier identification and monitoring of risk factors, including diabetes.²⁹ Within a year of the introduction of this new National Strategy, preliminary data suggested that the consumption of sugary drinks had diminished.³⁰ However, despite whatever is achieved in the next few decades by lifestyle interventions (e.g., on adiposity, exercise, and smoking),^{29,30} many people in Mexico will still develop diabetes and require treatment to reduce their risk of premature death.

Healthcare delivery can target both diabetes itself and other determinants of the risk of death or disability from the many different diseases that diabetes can cause.^{27,33,34,35} In this middle-income country with a high prevalence of overweight individuals with insufficient control of blood glucose, blood pressure and cholesterol, diabetes was a cause of at least one-third of all deaths at ages 35-74 years (twice current indirect estimates for Mexico),^{1,24} due chiefly to mortality from renal disease, vascular disease, infection, and acute diabetic crises.

Disclosure:

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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Figure Legends

Figure 1: Prevalence of Previously-diagnosed Diabetes, and its Relevance to All-cause Mortality during 12-year Follow-up

Prevalence includes all participants; RRs exclude any with prior chronic disease (chronic kidney disease, ischemic heart disease, stroke, cirrhosis, cancer, or emphysema). RR = mortality rate ratio for those with versus without prior diabetes at recruitment, adjusted for standard features (age, smoking, district, education, height, weight, waist and hip circumference)

Figure 2: Relevance of Previously-diagnosed Diabetes to Cause-specific Mortality during 12-year Follow-up

CI=Confidence interval; GI=Gastrointestinal; RR=Rate ratio (adjustments and exclusions as for RRs in Figure 1). * Number of deaths among those with/without clinically diagnosed diabetes before recruitment. † RRs not shown for acute diabetic deaths, since all such deaths were due to diabetes, irrespective of whether diagnosed before recruitment. Of the 393 people who died from an acute diabetic crisis, baseline HbA1c was available for 364 (93%), of which 313 (86%) either had diabetes diagnosed before recruitment or had baseline HbA1c \geq 6.5, and 51 (14%) had baseline HbA1c<6.5.

Figure 3: Mortality Rates for Each Cause of Death without and with Diagnosed Diabetes

Rates for 16% diabetic + 84% not diabetic match uniformly age-standardized 2012 Mexican national rates at ages 35-74 for 50% male + 50% female. All acute diabetic deaths are ascribed to diabetes, irrespective of whether diagnosed before recruitment. Infective diseases include peptic ulcer disease and exclude any infection in another plotted category. For stroke alone, annual rates are 0.05% without and 0.19% with diabetes. Rates for all bars sum to all-cause mortality rate. White, mortality rate without diabetes; white plus dark, mortality rate with diabetes.

Table 1: Baseline Characteristics, among Men and Women Aged 35-84, by Previously-diagnosed Diabetes

	Men (n=47 887): Previously diagnosed diabetes		Women (n=98 159): Previously diagnosed diabetes	
	Yes (n=6229)	No (n=41 658)	Yes (n=12 839)	No (n=85 320)
Age, diabetes duration and severity				
Age, years	59 (11)	52 (12)	59 (11)	50 (12)
Duration of diabetes, years*	9 (7)	-	9 (7)	-
Onset age < 35 and insulin use at baseline †	73 (1%)	-	142 (1%)	-
Number with HbA1c measured ‡	5821	38 034	12 078	79 171
Mean (SD) HbA1c, %	8.9 (2.5)	5.7 (1.0)	9.0 (2.4)	5.6 (0.9)
Median (IQR) HbA1c, %	8.7 (6.8-10.8)	5.4 (5.3-5.7)	8.8 (7.0-10.9)	5.4 (5.3-5.8)
HbA1c ≥ 6.5% **	4618 (79%)	2309 (6.1%)	9939 (82%)	4507 (5.7%)
HbA1c > 9.0% **	2737 (47%)	843 (2.0%)	5887 (49%)	1494 (1.9%)
HbA1c > 10.0% §	2001 (34%)	609 (1.6%)	4376 (36%)	1180 (1.5%)
Socio-economic status and smoking				
Resident of Coyoacán district	2316 (37%)	18 323 (44%)	4158 (32%)	33 273 (39%)
Resident of Iztapalapa (poorer district)	3913 (63%)	23 335 (56%)	8681 (68%)	52 047 (61%)
University/college educated	932 (15%)	10 598 (25%)	498 (4%)	11 032 (13%)
Current smoker	2430 (39%)	18 788 (45%)	1804 (14%)	17 935 (21%)
Anthropometry and blood pressure ¶				
Height, cm	163 (7)	163 (8)	150 (7)	150 (9)
Weight, kg	73 (13)	74 (15)	66 (13)	66 (17)
BMI, kg/m²	27.2 (5.1)	27.6 (5.8)	29.3 (5.2)	29.2 (6.7)
Waist circumference, cm	96 (12)	97 (13)	96 (12)	94 (16)
Hip circumference, cm	99 (11)	101 (12)	106 (11)	106 (14)
Waist-to-hip ratio	0.7 (0.07)	0.96 (0.08)	0.91 (0.07)	0.89 (0.09)
SBP, mmHg	132 (16)	131 (18)	134 (16)	129 (21)
DBP, mmHg	85 (10)	85 (12)	84 (10)	83 (13)
Anti-diabetic medication				
Insulin	358 (6%)	-	993 (8%)	-
Biguanide (eg, metformin)	1043 (17%)	-	2394 (19%)	-
Sulfonylurea	4235 (68%)	-	8847 (69%)	-
Other antidiabetic	86 (1%)	-	188 (1%)	-
Other long-term medication				
Renin-angiotensin system inhibitor	1012 (16%)	2626 (6%)	3425 (27%)	8756 (10%)
Other antihypertensive	353 (6%)	1332 (3%)	1190 (9%)	4251 (5%)
Subtotal: Any antihypertensive	1281 (21%)	3567 (9%)	4359 (34%)	12 006 (14%)
Any antithrombotic	138 (2%)	911 (2%)	298 (2%)	2277 (3%)
Any lipid lowering	92 (1%)	167 (<0.5%)	131 (1%)	352 (<0.5%)

Mean (SD) or n (%) shown. Analyses exclude those with prior chronic disease (chronic kidney disease, ischaemic heart disease, stroke, cirrhosis, cancer, or emphysema). BMI=Body mass index, SBP=Systolic blood pressure, DBP=Diastolic blood pressure. * Estimated from age at recruitment and decade of diagnosis. † Suggestive of type 1 diabetes. ‡ HbA1c assays are 93% complete, and ongoing (in unselected order of sample storage). ** Non-diabetic HbA1c values are non-normally distributed, many being several standard deviations above the median. Values ≥6.5 indicate undiagnosed diabetes; diabetic values above 9 reflect poor glycaemic control. (Mean HbA1c was 8.4, 9.1 and 9.5 among those who reported taking 0, 1 or 2+ anti-diabetic treatments, but compliance with medication is unknown.) § Of those with diabetes, the proportion with HbA1c >10.0% was 44% at ages 35-44, 44% at ages 45-54, 37% at ages 55-64, 27% at ages 65-74 and 20% at ages 75-84. ¶ Standardised to the age distribution of all men and women without chronic disease (other than diabetes) at recruitment. For men, differences between those with and without diabetes were statistically significant (2p <0.05) for all characteristics except waist circumference, DBP, and use of anti-thrombotic medication. For women, all differences were statistically significant except for BMI and hip circumference.

Table 2: Excess Mortality Associated with Previously-diagnosed Diabetes at Recruitment

Age (years) at Recruitment	No. participants		Mean Years of Follow-up Per Survivor	No. Deaths during Follow-up (and before Age 75 Years)		All-cause Mortality Rate Ratio (95% CI)*	Excess Deaths Before Age 75 Years Associated with Previously-diagnosed Diabetes	
	With Diabetes	Without Diabetes		With Diabetes	Without Diabetes		No. Deaths	% (SE) of Total
35-44	2184	50 568	11.9	232	672	7.5 (6.5 - 8.7)	201	22% (0.3%)
45-54	5043	35 838	11.9	671	966	4.8 (4.4 - 5.3)	532	32% (0.4%)
55-64	5753	21 230	11.7	1128	1348	3.3 (3.0 - 3.5)	781	32% (0.6%)
65-74	4431	13 179	5.3	577	662	2.7 (2.4 - 3.1)	366	30% (1.0%)
Total	17 411	120 815		2608	3648		1880	30%†

*Age-specific mortality rate ratio estimates for those with vs without diabetes at recruitment are adjusted for age, sex, district, education, and smoking, height, weight, and waist & hip circumference. Analyses exclude those with any prior diagnosis of chronic kidney disease or ischaemic heart disease, stroke, cirrhosis, cancer or emphysema.

† Inclusion in definition of those with diabetes of undiagnosed diabetes (HbA1c ≥ 6.5) at recruitment would increase this figure of 30% to 35% (see Table S1 of Supplementary Appendix). The attributable fraction is about one-third for both vascular mortality and the aggregate of all other mortality. (This still excludes any mortality due to diabetes with onset after recruitment and with HbA1c < 6.5 at recruitment.)