SUPPLEMENTARY MATERIAL - Prediabetes and risk of all-cause and cause-specific mortality: a prospective study of 114,062 adults in Mexico City

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SUPPLEMENTARY METHODS

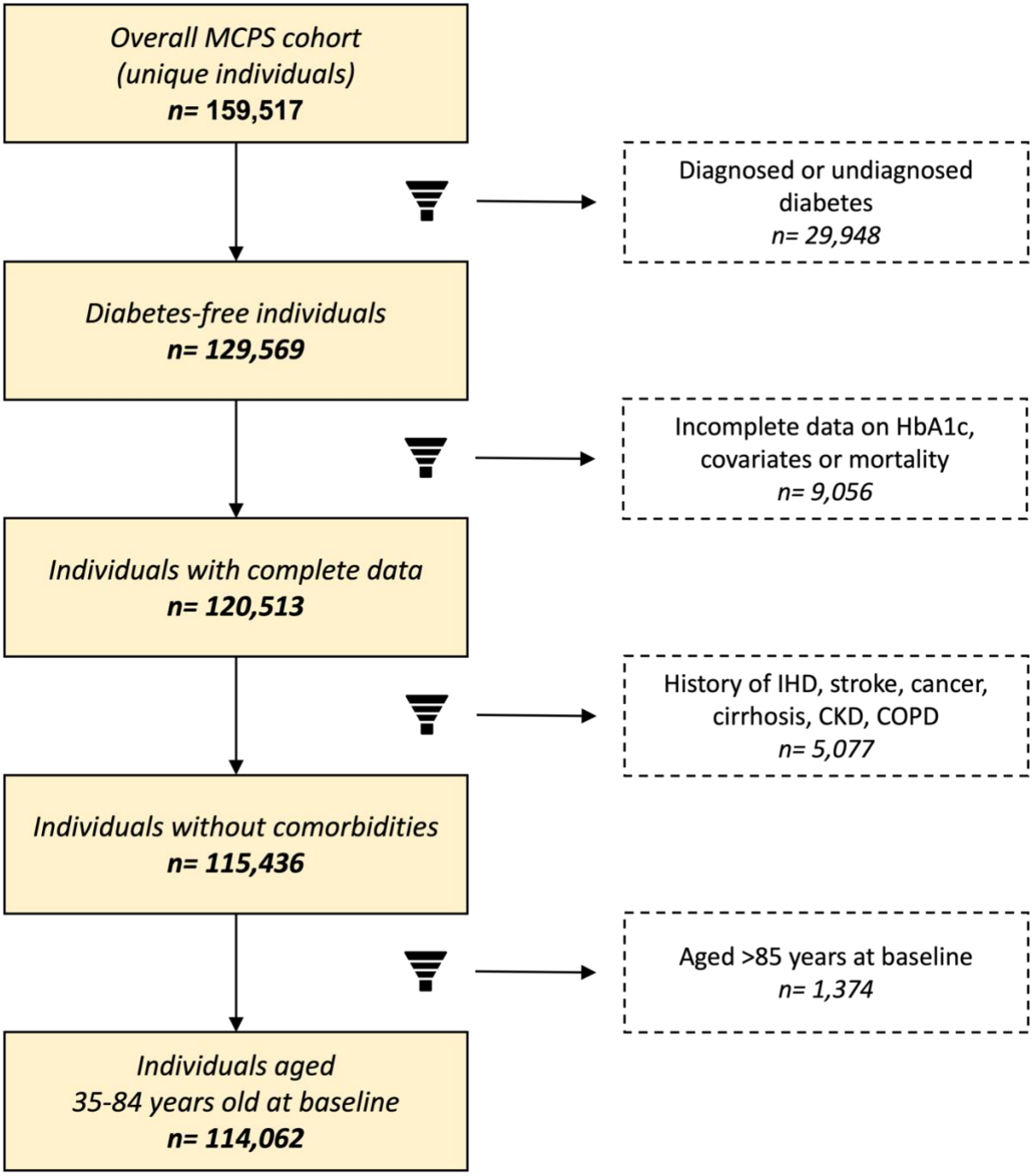
ICD-10 codes for cause-specific mortality, indicating number of deaths in brackets.

Cause-specific mortality, Number of deaths	***ICD-10 codes***
Cardiac deaths, N=3231	*I018 (1), I050 (4), I051 (1), I059 (16), I070 (1), I071 (3), I080 (5), I081 (1), I091 (1), I099 (14), I110 (161), I119 (29), I200 (2), I209 (6), I210 (4), I211 (9), I213 (1), I219 (2379), I220 (1), I221 (2), I229 (1), I248 (1), I249 (19), I251 (58), I255 (4), I258 (7), I259 (110), I270 (8), I272 (3), I279 (12), I289 (1), I301 (1), I318 (1), I330 (4), I340 (5), I348 (1), I350 (13), I351 (1), I358 (3), I38X (8), I420 (14), I429 (1), I441 (1), I442 (5), I443 (2), I459 (1), I469 (5), I471 (2), I472 (1), I480 (1), I489 (8), I48X (12), I490 (7), I499 (16), I500 (70), I501 (12), I509 (118), I518 (3), I519 (8), Q210 (1), Q231 (1), Q238 (1), Q248 (1), R570 (38)*
Cerebrovascular deaths, N=968	*F019 (10), I600 (2), I602 (1), I608 (1), I609 (79), I610 (1), I613 (1), I614 (1), I615 (1), I618 (1), I619 (229), I620 (10), I629 (4), I633 (3), I634 (26), I635 (13), I638 (1), I639 (96), I64X (131), I652 (1), I671 (11), I672 (1), I673 (1), I674 (4), I678 (128), I679 (145), I690 (2), I691 (1), I693 (10), I694 (16), I698 (37)*
Other vascular deaths, N=292	*E115 (4), E145 (4), I260 (4), I269 (86), I709 (2), I710 (3), I712 (1), I713 (8), I714 (9), I718 (1), I719 (2), I729 (1), I739 (5), I740 (1), I741 (1), I771 (12), I776 (1), I779 (1), I802 (6), I803 (2), I822 (1), I828 (2), I829 (4), I872 (8), I879 (1), I888 (1), I890 (1), I99X (1), K550 (97), K552 (1), K559 (20), K761 (1)*
Renal deaths, N=880	*E102 (2), E112 (107), E142 (37), I120 (162), I129 (3), I130 (2), I131 (1), I132 (17), N002 (1), N009 (6), N039 (11), N059 (9), N10X (1), N12X (3), N133 (1), N151 (9), N170 (1), N179 (105), N180 (9), N185 (7), N189 (155), N19X (28), N200 (5), N201 (1), N202 (1), N289 (1), N300 (1), N308 (1), N309 (3), N390 (186), Q612 (1), Q613 (2), Q619 (1)*
Acute diabetic deaths, N=186	*E110 (61), E111 (59), E140 (34), E141 (26), E162 (6)*
Neoplastic deaths, N=2387	*A047 (3), A090 (25), A099 (46), A09X (8), A183 (1), B169 (2), B171 (19), B181 (2), B182 (13), B189 (1), B190 (2), B199 (2), D134 (1), D136 (1), I850 (12), I859 (4), K052 (1), K088 (1), K102 (1), K137 (1), K20X (2), K219 (1), K223 (3), K228 (1), K251 (5), K254 (21), K255 (13), K256 (2), K259 (11), K264 (12), K265 (7), K266 (1), K269 (5), K272 (1), K274 (2), K275 (3), K290 (11), K291 (3), K292 (1), K295 (7), K296 (1), K297 (7), K311 (2), K318 (11), K319 (1), K352 (4), K353 (4), K358 (2), K37X (4), K389 (1), K403 (7), K404 (2), K409 (2), K413 (3), K419 (1), K420 (6), K421 (1), K429 (2), K430 (2), K431 (1), K439 (3), K460 (6), K461 (1), K469 (3), K509 (1), K513 (1), K519 (2), K529 (4), K560 (3), K562 (5), K566 (78), K567 (2), K572 (3), K573 (4), K578 (13), K579 (22), K593 (8), K610 (3), K611 (1), K631 (23), K632 (4), K638 (2), K639 (6), K650 (28), K658 (1), K659 (54), K701 (19), K702 (1), K703 (150), K704 (19), K709 (14), K711 (1), K716 (1), K720 (9), K721 (68), K729 (192), K740 (1), K742 (1), K743 (3), K745 (3), K746 (267), K750 (10), K754 (2), K759 (1), K760 (3), K764 (1), K766 (11), K767 (12), K768 (1), K769 (14), K800 (7), K801 (7), K802 (2), K803 (6), K805 (1), K810 (17), K811 (10), K819 (6), K820 (1), K821 (1), K829 (5), K830 (21), K831 (3), K851 (3), K852 (3), K858 (1), K859 (36), K85X (17), K861 (2), K863 (1), K914 (1), K918 (1), K920 (47), K921 (4), K922 (152), K931 (1), Q447 (1)*

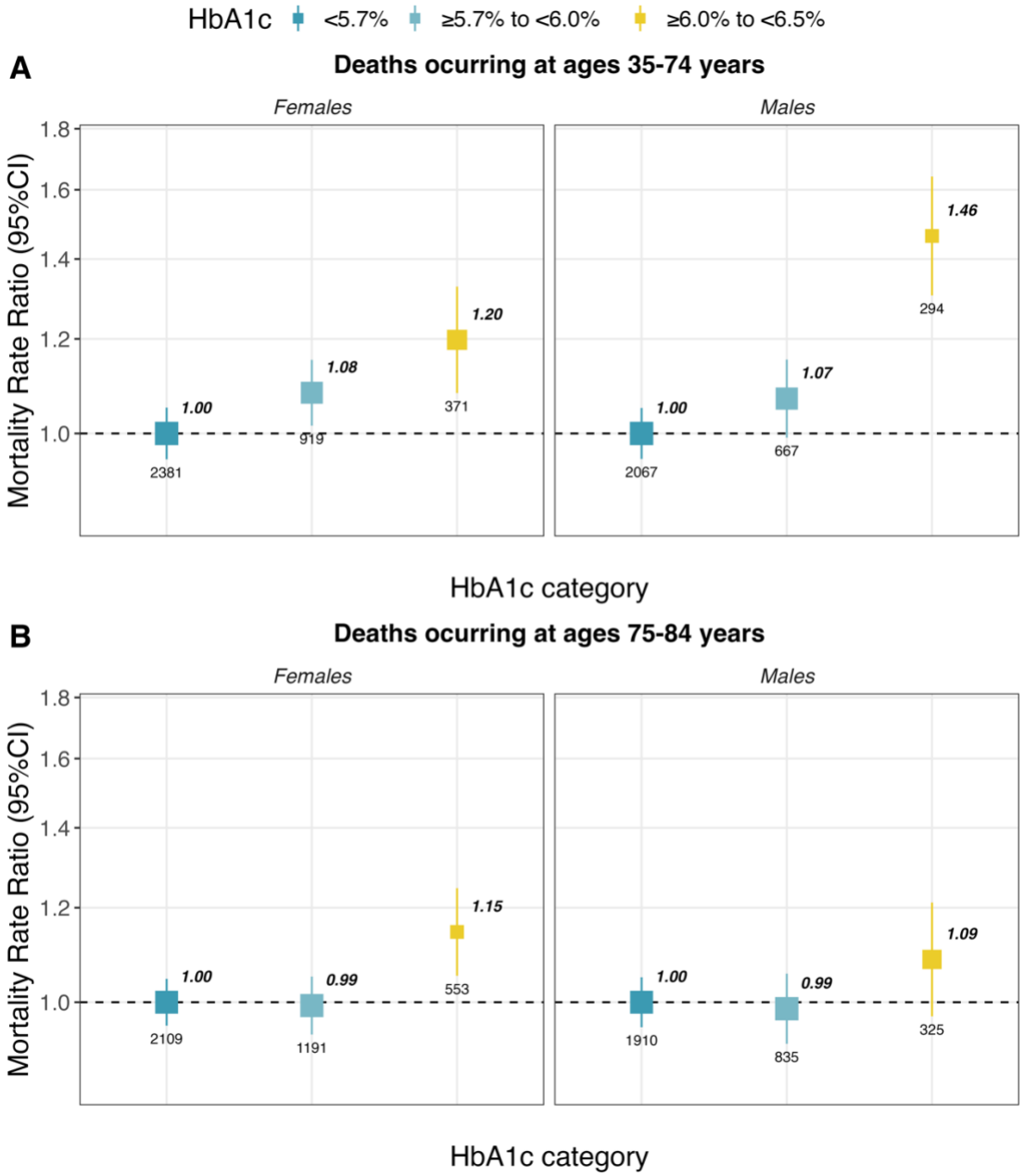
Respiratory deaths, N=2401	*C009 (1), C01X (1), C029 (12), C049 (1), C059 (1), C069 (4), C07X (5), C089 (1), C099 (1), C109 (4), C119 (2), C139 (1), C140 (7), C159 (21), C160 (3), C169 (212), C170 (14), C179 (2), C181 (1), C182 (1), C183 (1), C187 (3), C189 (128), C19X (8), C20X (19), C210 (1), C220 (52), C221 (23), C227 (1), C229 (111), C23X (33), C240 (8), C241 (7), C248 (3), C249 (18), C250 (25), C258 (1), C259 (117), C260 (1), C269 (2), C310 (1), C311 (1), C319 (1), C329 (14), C33X (2), C340 (1), C349 (183), C37X (1), C382 (1), C383 (2), C384 (1), C402 (1), C410 (1), C412 (2), C414 (1), C419 (7), C435 (1), C437 (2), C439 (21), C442 (1), C443 (1), C444 (3), C445 (1), C447 (1), C449 (9), C450 (2), C451 (2), C457 (1), C459 (4), C469 (1), C479 (1), C480 (11), C482 (6), C490 (1), C492 (2), C493 (1), C495 (1), C499 (14), C509 (180), C519 (5), C52X (1), C530 (1), C539 (108), C541 (24), C549 (2), C55X (12), C56X (102), C609 (2), C61X (152), C629 (3), C64X (87), C65X (1), C679 (27), C680 (2), C689 (1), C709 (1), C710 (17), C711 (1), C718 (3), C719 (40), C720 (1), C729 (1), C73X (30), C749 (1), C751 (1), C753 (1), C759 (2), C760 (13), C762 (7), C763 (3), C764 (1), C767 (1), C780 (6), C786 (2), C787 (14), C788 (3), C790 (1), C793 (3), C794 (2), C795 (1), C796 (1), C798 (4), C800 (36), C809 (21), C80X (5), C811 (1), C817 (1), C819 (11), C833 (14), C839 (2), C844 (1), C845 (3), C851 (1), C857 (1), C859 (57), C880 (1), C900 (52), C902 (1), C910 (25), C911 (2), C919 (2), C920 (32), C921 (5), C924 (1), C927 (4), C929 (5), C930 (1), C950 (1), C959 (5), C97X (2), D371 (3), D372 (1), D374 (2), D376 (8), D377 (7), D380 (1), D381 (6), D383 (2), D391 (3), D397 (1), D410 (1), D414 (1), D430 (11), D431 (2), D432 (1), D449 (1), D483 (1), D486 (1), D487 (5), D489 (1)*
Gastrointestinal (including hepatobiliary) deaths, N=1764	*A150 (1), A162 (10), B206 (2), B909 (1), E840 (1), E848 (1), J069 (1), J09 (2), J100 (3), J129 (6), J150 (1), J151 (2), J152 (2), J157 (1), J159 (38), J180 (83), J181 (49), J182 (2), J189 (689), J209 (12), J22X (23), J348 (1), J399 (1), J40X (2), J42X (29), J439 (65), J440 (238), J441 (8), J448 (13), J449 (360), J459 (20), J46X (2), J47X (3), J64X (10), J65X (1), J679 (2), J680 (1), J684 (1), J690 (2), J80X (5), J81X (8), J841 (101), J849 (10), J852 (1), J869 (2), J90X (5), J920 (1), J939 (1), J960 (7), J961 (3), J969 (3), J980 (1), J981 (1), J984 (25), J985 (2), J988 (14), J989 (2), Q311 (1), U071 (264), U072 (255)*
External, ill-defined, or other deaths, N=1513	*A181 (1), A182 (1), A199 (3), A415 (1), A418 (1), A419 (146), A810 (2), A86X (1), B200 (1), B201 (1), B207 (3), B208 (6), B210 (1), B212 (1), B218 (1), B227 (2), B238 (4), B24X (4), B465 (2), B690 (2), B699 (1), B948 (1), B99X (1), D033 (1), D181 (1), D27X (1), D329 (9), D464 (1), D469 (11), D479 (1), D529 (1), D530 (1), D594 (1), D619 (4), D62X (1), D649 (9), D65X (3), D682 (1), D691 (1), D693 (2), D694 (1), D696 (2), D699 (3), D762 (1), E031 (1), E035 (1), E039 (10), E049 (1), E055 (1), E059 (3), E116 (1), E119 (4), E149 (3), E230 (1), E249 (2), E279 (1), E43X (5), E440 (1), E46X (7), E500 (1), E509 (1), E660 (1), E835 (1), E86X (7), E870 (1), E871 (1), E872 (12), E875 (2), E878 (8), E889 (2), F03X (26), F09X (1), F102 (6), F182 (1), F209 (1), F329 (3), G009 (2), G039 (2), G049 (6), G060 (2), G10X (6), G121 (1), G122 (14), G20X (29), G219 (1), G301 (7), G309 (16), G310 (1), G312 (1), G319 (1), G35X (3), G379 (1), G403 (2), G406 (1), G409 (11), G419 (2), G473 (1), G589 (2), G603 (1), G610 (4), G700 (1), G709 (1), G710 (1), G809 (1), G822 (1), G919 (5), G931 (8), G934 (7), G935 (1), G936 (1), G937 (1), G939 (1), G958 (2), G959 (1), I10X (4), L020 (1), L021 (2), L022 (1), L023 (2), L031 (3), L032 (1), L039 (4), L088 (1), L089 (30), L100 (2), L108 (1), L109 (1), L512 (5), L899 (20), L89X (1), L905 (6), L921 (1), L984 (14), L988 (1), L989 (1), M009 (2), M050 (2), M068 (1), M069 (23), M109 (1), M139 (1), M165 (1), M199 (1), M300 (1), M311 (1), M313 (1), M319 (1), M321 (4), M329 (3), M331 (2), M349 (1), M350 (1), M471 (1), M623 (20), M726 (3), M798 (25), M809 (1), M819 (3), M869 (1), M993 (1), N40X (15), N410 (1), N498 (4), N499 (1), N719 (1), N739 (3), N823 (1), N939 (1), N948 (1), O720 (1), R048 (1), R092 (2), R100 (2), R13X (1), R190 (1), R54X (1), R571 (11), R578 (2), R579 (2), R58X (6), R64X (2), R688 (20), R69X (1), R91X (1), R99X (301), S729 (2), T07X (1), V011 (1), V031 (1), V049 (1), V051 (1), V093 (3), V099 (87), V149 (1), V209 (1), V439 (1), V494 (1), V499 (8), V580 (1), V581 (1), V719 (1), V785 (1), V878 (5), V892 (6), V899 (5), W018 (1), W050 (1), W100 (15), W104 (2), W108 (2), W126 (1), W130 (13), W134 (3), W135 (1), W138 (1), W139 (2), W170 (4), W172 (1), W174 (2), W176 (1), W178 (1), W179 (1), W180 (6), W181 (1), W184 (3), W188 (1), W189 (1), W190 (15), W194 (2), W199 (4), W200 (1), W206 (1), W228 (1), W250 (1), W314 (1), W340 (1), W370 (1), W557 (1), W704 (1), W744 (1), W748 (2), W769 (1), W780 (3), W789 (1), W808 (1), W849 (2), W87 (1), W871 (1), W878 (1), X09 (1), X090 (3), X094 (1), X219 (1), X440 (1), X449 (1), X459 (1), X470 (1), X530 (1), X590 (6), X594 (1), X598 (1), X599 (37), X650 (1), X680 (1), X700 (5), X702 (1), X708 (1), X740 (4), X780 (2), X910 (2), X912 (1), X914 (2), X950 (4), X954 (15), X955 (1), X959 (1), X990 (6), X994 (5), X999 (2), Y018 (1), Y044 (2), Y084 (1), Y090 (2), Y094 (1), Y099 (1), Y159 (1), Y200 (1), Y239 (1), Y240 (1), Y244 (3), Y245 (1), Y248 (1), Y249 (1), Y260 (2), Y280 (1), Y330 (1), Y334 (2), Y338 (1), Y340 (3), Y344 (9), Y345 (1), Y346 (1), Y348 (3), Y349 (18), Y579 (2), Y609 (1), Y839 (3), Y86X (3), Y899 (1)*

SUPPLEMENTARY FIGURES

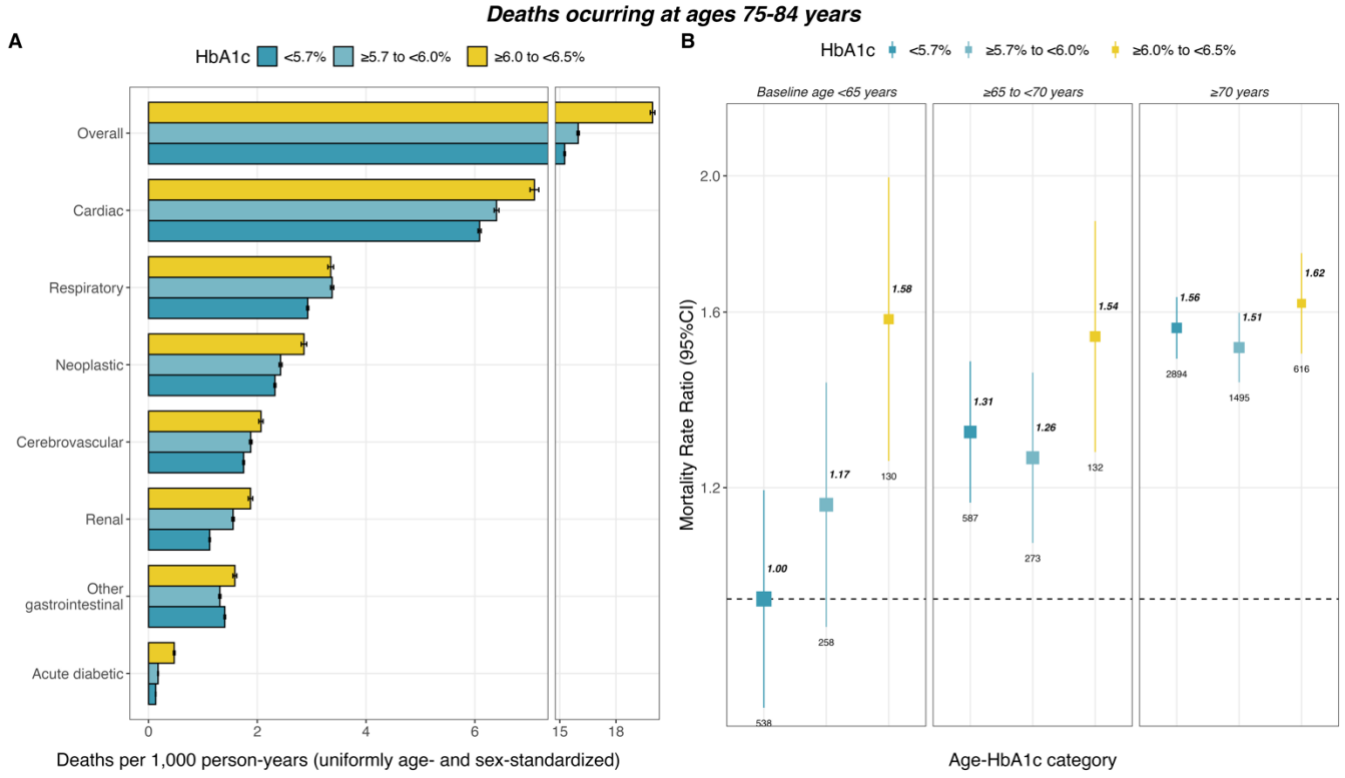
Supplementary Figure 1. Flowchart of study participant selection in individuals included in the baseline 1998-2004 evaluation of the Mexico City Prospective Study. MCPS: Mexico City Prospective Study. IHD: Ischemic heart disease. CKD: Chronic kidney disease. COPD: Chronic obstructive pulmonary disease.



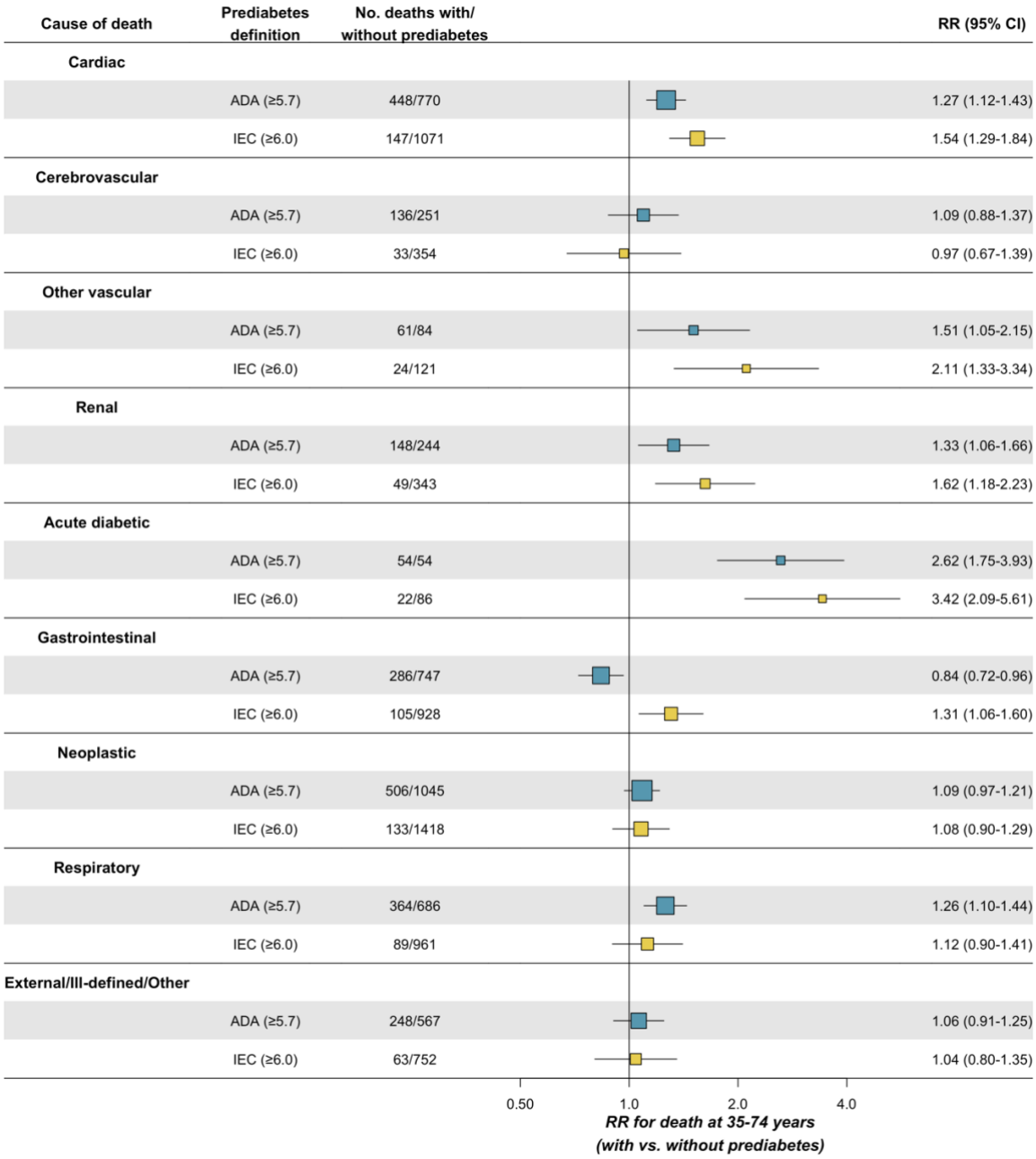
Supplementary Figure 2. Overall mortality rate ratios at ages 35-74 years and 75-84 years at different levels of HbA1c stratified by sex. Rate ratios with 95% confidence intervals for all-cause mortality associated with HbA1c categories, stratified by sex. Numbers represent the mortality RR (top, bold) and deaths (bottom) for each category, sample sizes are specified in ***Supplementary Table 5***. The size of the squares is proportional to the amount of statistical information. Models are stratified by age-at-risk and adjusted for municipality, education level, physical activity, smoking, and alcohol intake. Each 95% confidence interval reflects the variance of the log risk in that one group.



Supplementary Figure 3. Overall and cause-specific mortality rates and mortality rate ratios at ages 75-84 years and at different levels of HbA1c. Analyses limited to participants aged 75-84 years old at the end of follow-up and who did not have diabetes or other chronic disease at recruitment. (A) Uniformly age- and sex-standardized mortality rates per 1,000 person-years according to HbA1c categories, error bars represent 95% confidence intervals. (B) Rate ratios with 95% confidence intervals for all-cause mortality associated with HbA1c categories, stratified by age at recruitment (<50 years, 50-64 years, or ≥65 years). Numbers represent the mortality RR (top, bold) and deaths (bottom) for each category, sample sizes are specified in ***Supplementary Table 5***. The size of the squares is proportional to the amount of statistical information. Models are stratified by sex and age-at-risk and adjusted for municipality, education level, physical activity, smoking, and alcohol intake. Each 95% confidence interval reflects the variance of the log risk in that one group.

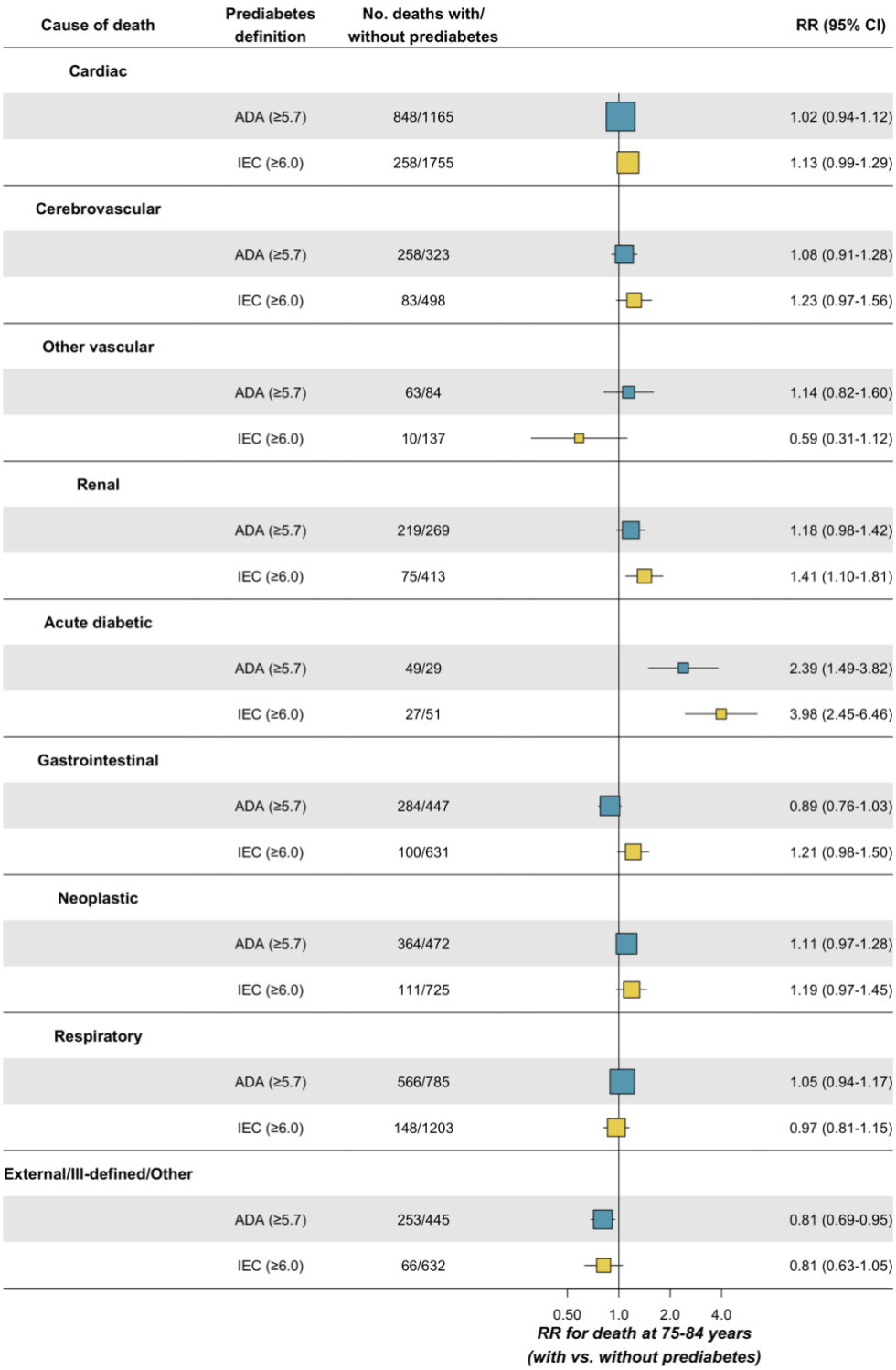


Supplementary Figure 4. Cause-specific mortality rate ratios at ages 35-74 years associated with ADA- and IEC-defined prediabetes.



ADA: American Diabetes Association. IEC: International Expert Committee. RR: Mortality rate ratio. CI: Confidence Interval. Analyses limited to 108,657 participants aged 35-74 and without previously diagnosed or undiagnosed diabetes (or other chronic disease) at recruitment. RRs are stratified by sex and age-at-risk and adjusted for municipality, education, physical activity, smoking, and alcohol intake.

Supplementary Figure 5. Cause-specific mortality rate ratios at ages 75-84 years associated with ADA- and IEC-defined prediabetes. ADA: American Diabetes Association. IEC: International Expert Committee. RR: Mortality rate ratio. CI: Confidence Interval. RRs are stratified by sex and age-at-risk and adjusted for municipality, education level, physical activity, smoking, and alcohol intake.



SUPPLEMENTARY TABLES

Supplementary Table 1. Baseline characteristics of 114,062 men and women aged 35-84 without previously diagnosed or undiagnosed diabetes or other chronic disease at recruitment, stratified by groups of baseline age.

	All participants N = 114,062	Baseline age, years				
		35-44 N = 46,831	45-54 N = 31,972	55-64 N = 18,449	65-74 N = 11,405	75-84 N = 5,405
Age (Years)	50 (12)	39 (3)	49 (3)	59 (3)	69 (3)	79 (3)
HbA1c (%)	5.46 (0.37)	5.34 (0.34)	5.49 (0.36)	5.58 (0.36)	5.61 (0.37)	5.60 (0.37)
HbA1c category						
<5.7%	83,498 (73%)	39,794 (85%)	22,667 (71%)	11,303 (61%)	6,537 (57%)	3,197 (59%)
≥5.7% to <6.0%	22,860 (20%)	5,620 (12%)	7,055 (22%)	5,135 (28%)	3,462 (30%)	1,588 (29%)
≥6.0% to <6.5%	7,704 (7%)	1,417 (3%)	2,250 (7%)	2,011 (11%)	1,406 (12%)	620 (11%)
Female sex (%)	76,904 (67%)	32,526 (69%)	21,841 (68%)	11,956 (65%)	7,263 (64%)	3,318 (61%)
Residence in Coyoacán (%)	46,566 (41%)	18,346 (39%)	13,936 (44%)	7,859 (43%)	4,491 (39%)	1,934 (36%)
University/college educated (%)	19,498 (17%)	11,774 (25%)	5,193 (16%)	1,713 (9%)	624 (5%)	194 (4%)
Smoking (%)						
Never	55,308 (48%)	21,258 (45%)	15,275 (48%)	9,581 (52%)	6,161 (54%)	3,033 (56%)
Former	21,244 (19%)	6,930 (15%)	5,702 (18%)	4,081 (22%)	2,942 (26%)	1,589 (29%)
Current	37,510 (33%)	18,643 (40%)	10,995 (34%)	4,787 (26%)	2,302 (20%)	783 (14%)
Alcohol intake (%)						
Never	21,692 (19%)	8,648 (18%)	5,454 (17%)	3,424 (19%)	2,686 (24%)	1,480 (27%)
Former	7,024 (6%)	3,114 (7%)	2,108 (7%)	1,088 (6%)	509 (4%)	205 (4%)
Current	85,346 (75%)	35,069 (75%)	24,410 (76%)	13,937 (76%)	8,210 (72%)	3,720 (69%)
Regular leisure-time physical activity* (%)	25,994 (23%)	10,509 (22%)	7,253 (23%)	4,391 (24%)	2,747 (24%)	1,094 (20%)
Body Mass Index (kg/m^2)	28.9 (4.9)	28.6 (4.9)	29.4 (5.0)	29.5 (5.0)	28.8 (4.9)	27.4 (4.7)
Waist-to-Height Ratio	0.60 (0.08)	0.58 (0.07)	0.60 (0.08)	0.62 (0.08)	0.63 (0.08)	0.63 (0.08)
Waist-Hip Ratio	0.90 (0.08)	0.88 (0.07)	0.89 (0.07)	0.91 (0.08)	0.93 (0.08)	0.94 (0.08)
Systolic Blood Pressure (mmHg)	127 (17)	121 (14)	126 (16)	132 (17)	136 (18)	139 (20)
Diastolic Blood Pressure (mmHg)	83 (11)	80 (10)	84 (11)	85 (11)	86 (11)	85 (12)
Lipid measurements†	2.42 (0.90)	2.34 (0.86)	2.49 (0.91)	2.50 (0.96)	2.42 (0.95)	2.32 (0.92)
LDL cholesterol (mmol/L)						

	All participants N = 114,062	**Baseline age, years**				
		35-44 N = 46,831	**45-54 N = 31,972**	**55-64 N = 18,449**	**65-74 N = 11,405**	**75-84 N = 5,405**
HDL cholesterol (mmol/L)	0.97 (0.41)	0.97 (0.40)	0.98 (0.39)	0.97 (0.43)	0.97 (0.44)	0.97 (0.43)
Triglycerides (mmol/L)	1.48 (0.72)	1.43 (0.72)	1.54 (0.72)	1.55 (0.73)	1.47 (0.70)	1.35 (0.65)
Apolipoprotein A1 (g/L)	1.18 (0.41)	1.17 (0.40)	1.20 (0.40)	1.19 (0.44)	1.18 (0.44)	1.17 (0.43)
Apolipoprotein B (g/L)	0.86 (0.40)	0.83 (0.38)	0.88 (0.38)	0.88 (0.42)	0.86 (0.42)	0.84 (0.41)

Results are presented as either mean (SD) or n (%). All baseline characteristics differed among age groups (p <0.001, Kruskal-Wallis' test or Pearson's Chi-squared test), however, this reflects the large sample size rather than epidemiologically relevant differences. *Regular physical activity defined as at least 1 day per week. †Blood lipids were measured using the Nightingale Health nuclear magnetic resonance platform.

Supplementary Table 2. Association of HbA1c and ADA- and IEC-defined prediabetes with all-cause mortality at 35-74 years including individuals with comorbidities. Analyses limited to 112,941 adults aged 35-74 without diabetes at recruitment, including those with other chronic diseases. All models are stratified by sex and age-at-risk in 5-year increments using the Lexis expansion. RR: Mortality rate ratio. SBP: Systolic blood pressure. DBP: Diastolic blood pressure. LDL-c: Low density lipoprotein cholesterol. HDL-c: High density lipoprotein cholesterol. BMI: Body mass index. WHtR: Waist-to-height ratio. ADA: American Diabetes Association. IEC: International Expert Committee.

Predictor		RR (95% confidence interval)			
		Age-at-risk, sex, and district of residence	**+ Education, physical activity, smoking, and alcohol intake**	**+ Adiposity measures (BMI and WHtR)**	**+ SBP, DBP, LDL-c, HDL-c, triglycerides**
Continuous (per 0.5% unit)	HbA1c (%)	1.04 (1.00, 1.08)	1.02 (0.98, 1.06)	0.95 (0.91, 0.98)	0.97 (0.93, 1.00)
HbA1c category	<5.7%	1.00	1.00	1.00	1.00
	≥*5.7% to <6.0%*	1.07 (1.01, 1.14)	1.05 (0.99, 1.11)	0.98 (0.92, 1.03)	0.99 (0.94, 1.05)
	≥*6.0% to <6.5%*	1.31 (1.21, 1.42)	1.28 (1.18, 1.38)	1.12 (1.03, 1.22)	1.13 (1.04, 1.23)
Prediabetes definition	ADA ≥*5.7% to <6.5%*	1.13 (1.08, 1.19)	1.11 (1.05, 1.17)	1.01 (0.96, 1.07)	1.03 (0.98, 1.08)
	IEC ≥*6.0% to <6.5%*	1.28 (1.19, 1.38)	1.26 (1.16, 1.36)	1.13 (1.04, 1.22)	1.14 (1.05, 1.23)

Supplementary Table 3. Association of HbA1c and ADA- and IEC-defined prediabetes with all-cause mortality at ages 75-84 years. Analyses limited to 29,585 participants aged 75-84 years at the end of follow-up and without diabetes or other chronic disease at recruitment. All models are stratified by sex and age-at-risk in 5-year increments using the Lexis expansion. RR: Mortality rate ratio. SBP: Systolic blood pressure. DBP: Diastolic blood pressure. LDL-c: Low density lipoprotein cholesterol. HDL-c: High density lipoprotein cholesterol. BMI: Body mass index. WHtR: Waist-to-height ratio. ADA: American Diabetes Association. IEC: International Expert Committee.

Predictor		RR (95% confidence interval)			
		Age-at-risk, sex, and district of residence	**+ Education, physical activity, smoking, and alcohol intake**	**+ Adiposity measures (BMI and WHtR)**	**+ SBP, DBP, LDL-c, HDL-c, triglycerides**
Continuous (per 0.5 % unit)	HbA1c (%)	1.00 (0.97, 1.04)	1.00 (0.96, 1.03)	0.97 (0.94-1.01)	0.99 (0.5, 1.02)
HbA1c category	<5.7%	1.00	1.00	1.00	1.00
	≥*5.7% to <6.0%*	1.00 (0.94, 1.05)	0.99 (0.94, 1.05)	0.97 (0.91-1.02)	0.98 (0.93, 1.04)
	≥*6.0% to <6.5%*	1.13 (1.05, 1.21)	1.12 (1.04, 1.21)	1.07 (0.99-1.15)	1.08 (1.00, 1.17)
Prediabetes definition	ADA ≥*5.7% to <6.5%*	1.03 (0.98, 1.08)	1.03 (0.98, 1.08)	0.99 (0.94-1.04)	1.01 (0.96, 1.06)
	IEC ≥*6.0% to <6.5%*	1.13 (1.05, 1.21)	1.12 (1.04, 1.21)	1.08 (1.01, 1.16)	1.09 (1.02, 1.17)

Supplementary Table 4. Association of continuous HbA1c with all-cause and cause-specific mortality at ages 35-74 and 75-84 years. Analyses limited to 114,062 participants aged 35-84 years at the end of follow-up and without diabetes or other chronic disease at recruitment. All models are stratified by sex and age-at-risk in 5-year increments using the Lexis expansion. RR: Mortality rate ratio. SBP: Systolic blood pressure. DBP: Diastolic blood pressure. LDL-c: Low density lipoprotein cholesterol. HDL-c: High density lipoprotein cholesterol. BMI: Body mass index. WHtR: Waist-to-height ratio.

Outcome	Deaths at 35-74 years **RR (95% confidence interval)**			Deaths at 75-84 years **RR (95% confidence interval)**		
	Age-at-risk, sex, and district of residence	+ Education, physical activity, smoking, and alcohol intake	+ SBP, DBP, LDL-c, HDL-c, triglycerides, BMI and WHtR	Age-at-risk, sex, and district of residence	+ Education, physical activity, smoking, and alcohol intake	+ SBP, DBP, LDL-c, HDL-c, triglycerides, BMI and WHtR
All-cause deaths	1.07 (1.03, 1.12)	1.05 (1.01, 1.10)	0.99 (0.95, 1.03)	1.00 (0.97, 1.04)	1.00 (0.96, 1.03)	0.99 (0.95, 1.02)
Cardiac deaths	1.16 (1.06, 1.27)	1.14 (1.04, 1.25)	1.03 (0.94, 1.13)	0.99 (0.93, 1.06)	0.99 (0.93, 1.06)	0.97 (0.91, 1.04)
Cerebrovascular deaths	1.13 (0.98, 1.30)	1.12 (0.97, 1.29)	1.06 (0.91, 1.23)	1.10 (0.97, 1.25)	1.09 (0.96, 1.24)	1.08 (0.95, 1.23)
Other vascular	1.44 (1.10, 1.90)	1.42 (1.08, 1.87)	1.18 (0.90, 1.55)	0.92 (0.74, 1.15)	0.91 (0.73, 1.14)	0.90 (0.72, 1.13)
Cardiovascular deaths	1.18 (1.09, 1.27)	1.16 (1.08, 1.25)	1.05 (0.97, 1.13)	1.01 (0.95, 1.07)	1.01 (0.95, 1.07)	0.99 (0.94, 1.05)
Renal deaths	1.25 (1.06, 1.48)	1.22 (1.03, 1.44)	1.07 (0.91, 1.26)	1.19 (1.04, 1.36)	1.18 (1.03, 1.34)	1.09 (0.96, 1.25)
Acute diabetic deaths	2.09 (1.55, 2.82)	2.01 (1.48, 2.73)	1.63 (1.17, 2.27)	2.45 (1.68, 3.57)	2.41 (1.65, 3.51)	2.21 (1.52, 3.20)
Neoplastic deahts	1.04 (0.96, 1.12)	1.03 (0.95, 1.11)	1.01 (0.93, 1.09)	1.06 (0.96, 1.17)	1.05 (0.95, 1.16)	1.03 (0.93, 1.14)
Respiratory deaths	1.23 (1.12, 1.34)	1.20 (1.10, 1.31)	1.11 (1.01, 1.22)	1.00 (0.92, 1.08)	0.99 (0.92, 1.07)	1.02 (0.94, 1.10)

Supplementary Table 5. Sample size and number of deaths for each subgroup in HbA1c-age (above) and HbA1c-sex (below) stratifications. For the main analysis, we observed a total of 6,699 deaths at ages 35-74 years old. For the secondary analysis, we observed 6,923 deaths at ages 75-84 years old. Stratifications were done for age at baseline (and not age at risk).

HbA1c	***Deaths at ages 35-74 years old***		***Deaths at ages 75-84 years old***	
	Baseline age	***N (deaths)***	***Baseline age***	***N (deaths)***
<5.7%	<50	52,754 (2069)	<65	8,510 (538)
	50-64	20,157 (1886)	65-69	2,778 (587)
	≥65	7,390 (493)	≥70	6,549 (2894)
≥5.7% to <6.0%	<50	9,034 (501)	<65	3,607 (258)
	50-64	8,367 (849)	65-69	1,377 (273)
	≥65	3,871 (236)	≥70	3,473 (1495)
≥6.0% to <6.5%	<50	2,484 (188)	<65	1,354 (130)
	50-64	3,026 (371)	65-69	573 (132)
	≥65	1,574 (106)	≥70	1,364 (616)
	Sex	***N (deaths)***	***Sex***	***N (deaths)***
<5.7%	Female	53,995 (2381)	Female	10,922 (2109)
	Male	26,306 (2067)	Male	6,915 (1910)
≥5.7% to <6.0%	Female	14,611 (919)	Female	5,763 (1191)
	Male	6,661 (667)	Male	2,694 (835)
≥6.0 to <6.5%	Female	4,980 (371)	Female	2,338 (553)
	Male	2,104 (294)	Male	953 (325)