**Supplemental Online Content**

**Postprandial plasma glucose and associated cancer mortality**

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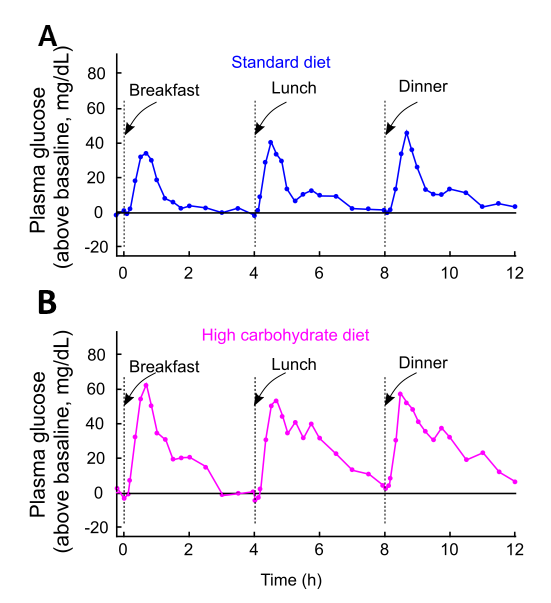
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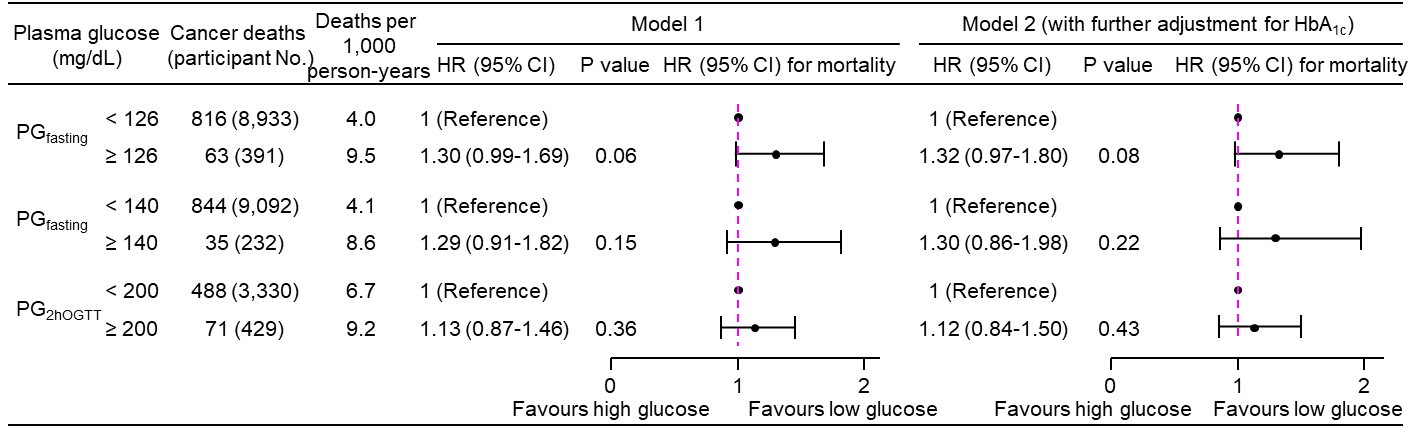
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**eReferences**



**eFigure 1. Effect of mealtime and meal type on postprandial plasma glucose.**

Mean plasma glucose after consumption of 3 consecutive identical meals over 12 h in 22 healthy participants. **A**, Participants (N=12 including 5 females) consumed a standard diet (% carbohydrate/fat/protein= 40/49/11). **B**, Participants (N=10 including 4 females) consumed a high carbohydrate diet (% carbohydrate/fat/protein= 63/27/10). The results were from a published study (Journal of Diabetes Science and Technology 2022:16:1532).1 eFigure 1 was modified from a figure from the cited study which was published under a Creative Commons Attribution **CC BY** license.



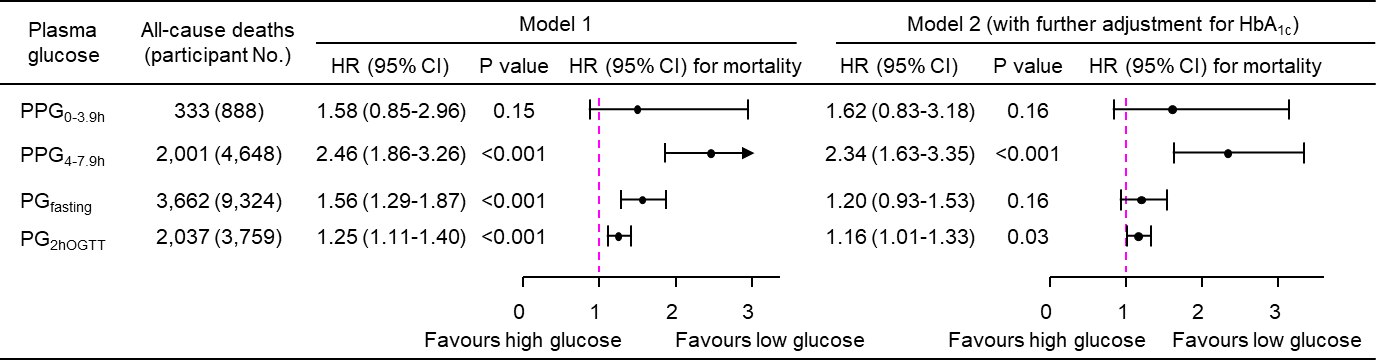
**eFigure 2. Cancer mortality risk associated with plasma glucose (categorical).**

The cutoff for high PGfasting was 126 (criterion after 1997)2,3 or 140 mg/dL (criterion before 1997).3 The cutoff for high PG2hOGTT was 200 mg/dL.2,3

Model 1: adjusted for age, sex, ethnicity, body mass index, education, poverty-income ratio, survey period, physical activity, alcohol consumption, smoking status, systolic blood pressure, total cholesterol, HDL cholesterol, family history of diabetes, and fasting time.

Model 2: adjusted for all the factors in Model 1 plus HbA1c.

CI, confidence interval; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; HR, hazard ratio; No., number; PG2hOGTT, plasma glucose measured from blood taken at 2 h after an oral glucose tolerance test; PGfasting, plasma glucose measured from blood taken in a fasting state (fasting time ≥8 h).

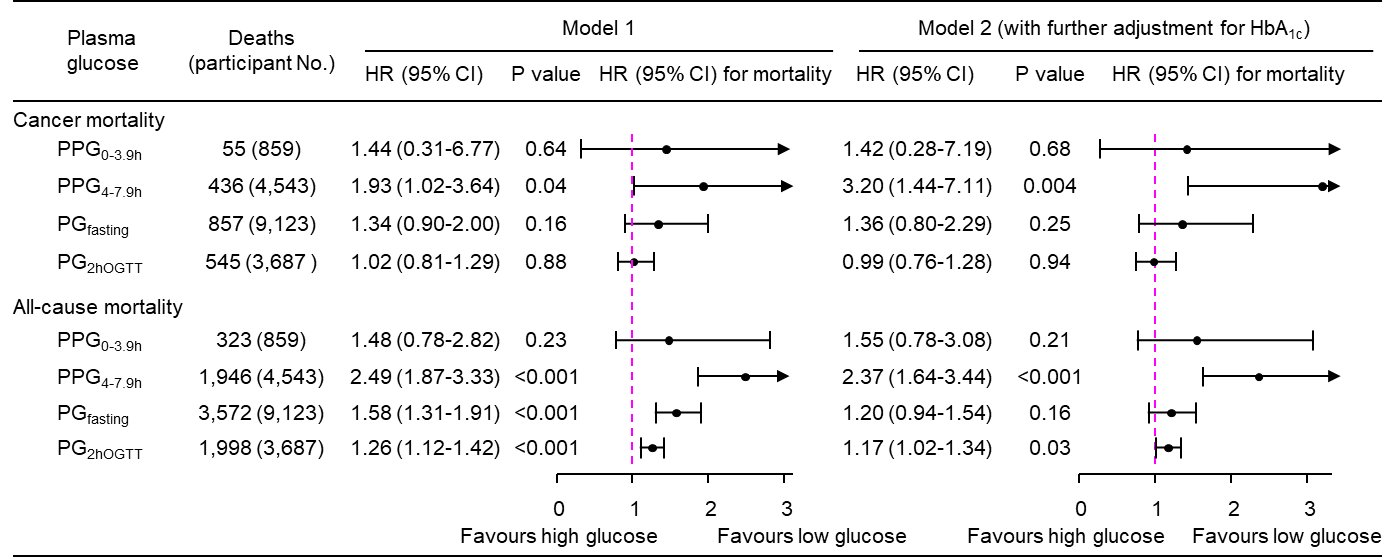


**eFigure 3. All-cause mortality risk associated with a 1-natural-log-unit increase in plasma glucose.**

Model 1: adjusted for age, sex, ethnicity, body mass index, education, poverty-income ratio, survey period, physical activity, alcohol consumption, smoking status, systolic blood pressure, total cholesterol, HDL cholesterol, family history of diabetes, and fasting time.

Model 2: adjusted for all the factors in Model 1 plus HbA1c.

CI, confidence interval; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; HR, hazard ratio; No., number; PG2hOGTT, plasma glucose measured from blood taken at 2 h after an oral glucose tolerance test; PGfasting, plasma glucose measured from blood taken in a fasting state (fasting time ≥8 h); PPG0-3.9h, postprandial plasma glucose measured from blood taken between 0 and 3.9 h; PPG4-7.9h, postprandial plasma glucose measured from blood taken between 4 and 7.9 h.



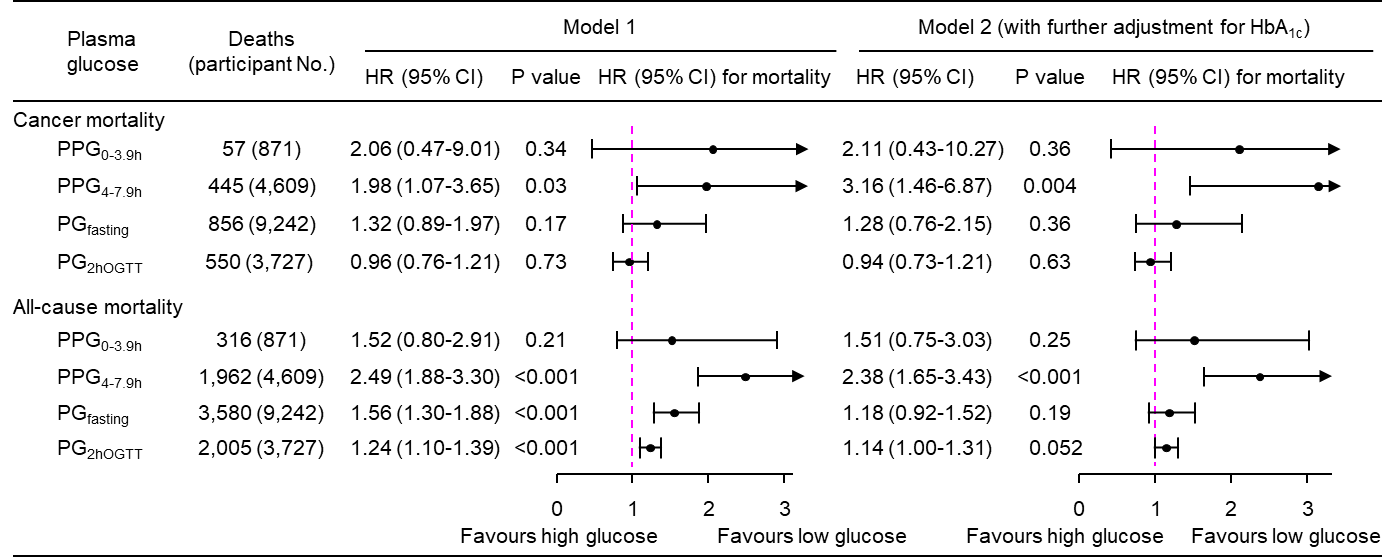
**eFigure 4. Sensitivity analysis of mortality risk associated with a 1-natural-log-unit increase in plasma glucose when the imputed data were not used.**

Out of 14,860 participants, 335 (2.3%) had missing data which were imputed in the main analysis. In this sensitivity analysis, those 335 participants were excluded.

Model 1: adjusted for age, sex, ethnicity, body mass index, education, poverty-income ratio, survey period, physical activity, alcohol consumption, smoking status, systolic blood pressure, total cholesterol, HDL cholesterol, family history of diabetes, and fasting time.

Model 2: adjusted for all the factors in Model 1 plus HbA1c.

CI, confidence interval; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; HR, hazard ratio; No., number; PG2hOGTT, plasma glucose measured from blood taken at 2 h after an oral glucose tolerance test; PGfasting, plasma glucose measured from blood taken in a fasting state (fasting time ≥8 h); PPG0-3.9h, postprandial plasma glucose measured from blood taken between 0 and 3.9 h; PPG4-7.9h, postprandial plasma glucose measured from blood taken between 4 and 7.9 h.



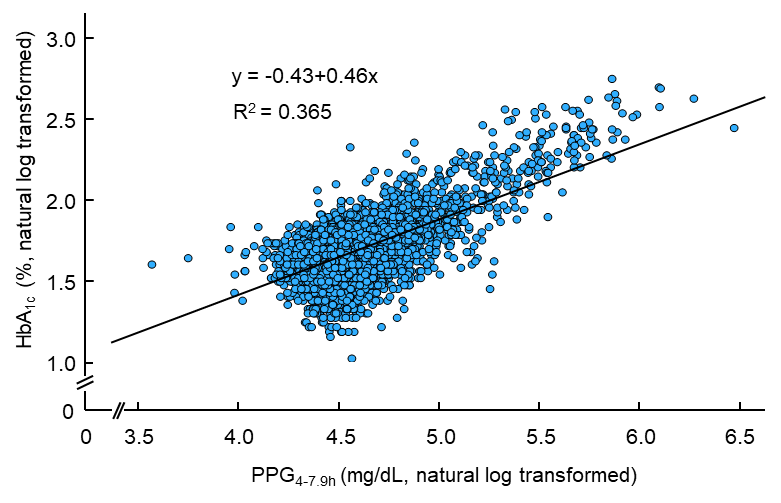
**eFigure 5. Sensitivity analysis of mortality risk associated with a 1-natural-log-unit increase in plasma glucose when those with a follow-up of <1 year were excluded.**

A total of 138 participants had a follow-up time of <1 year and they were excluded in this sensitivity analysis.

Model 1: adjusted for age, sex, ethnicity, body mass index, education, poverty-income ratio, survey period, physical activity, alcohol consumption, smoking status, systolic blood pressure, total cholesterol, HDL cholesterol, family history of diabetes, and fasting time.

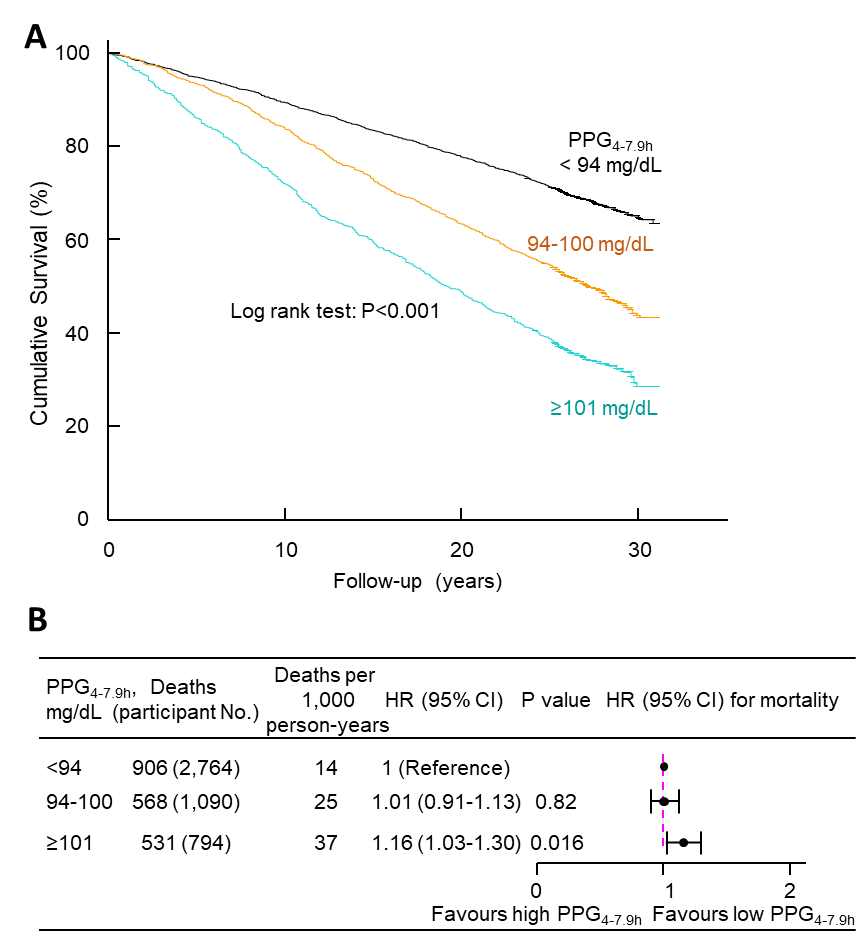
Model 2: adjusted for all the factors in Model 1 plus HbA1c.

CI, confidence interval; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; HR, hazard ratio; No., number; PG2hOGTT, plasma glucose measured from blood taken at 2 h after an oral glucose tolerance test; PGfasting, plasma glucose measured from blood taken in a fasting state (fasting time ≥8 h); PPG0-3.9h, postprandial plasma glucose measured from blood taken between 0 and 3.9 h; PPG4-7.9h, postprandial plasma glucose measured from blood taken between 4 and 7.9 h.



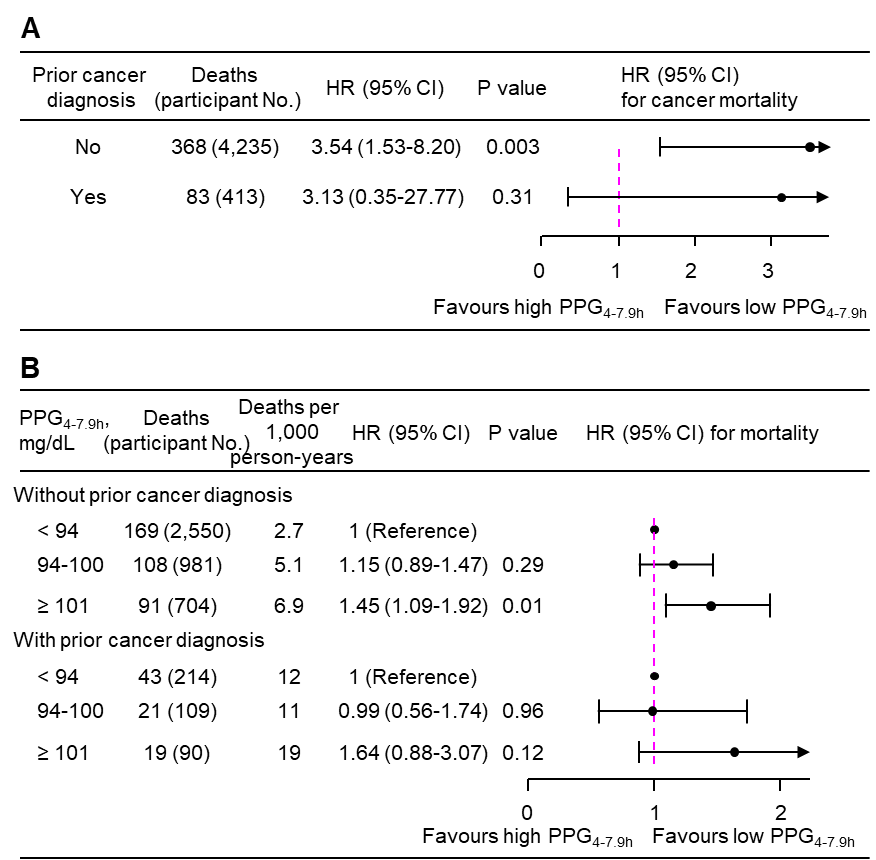
**eFigure 6. Scatter plot, PPG4-7.9h versus HbA1c.**

HbA1c, hemoglobin A1c; PPG4-7.9h, postprandial plasma glucose measured from blood taken between 4 and 7.9 h.



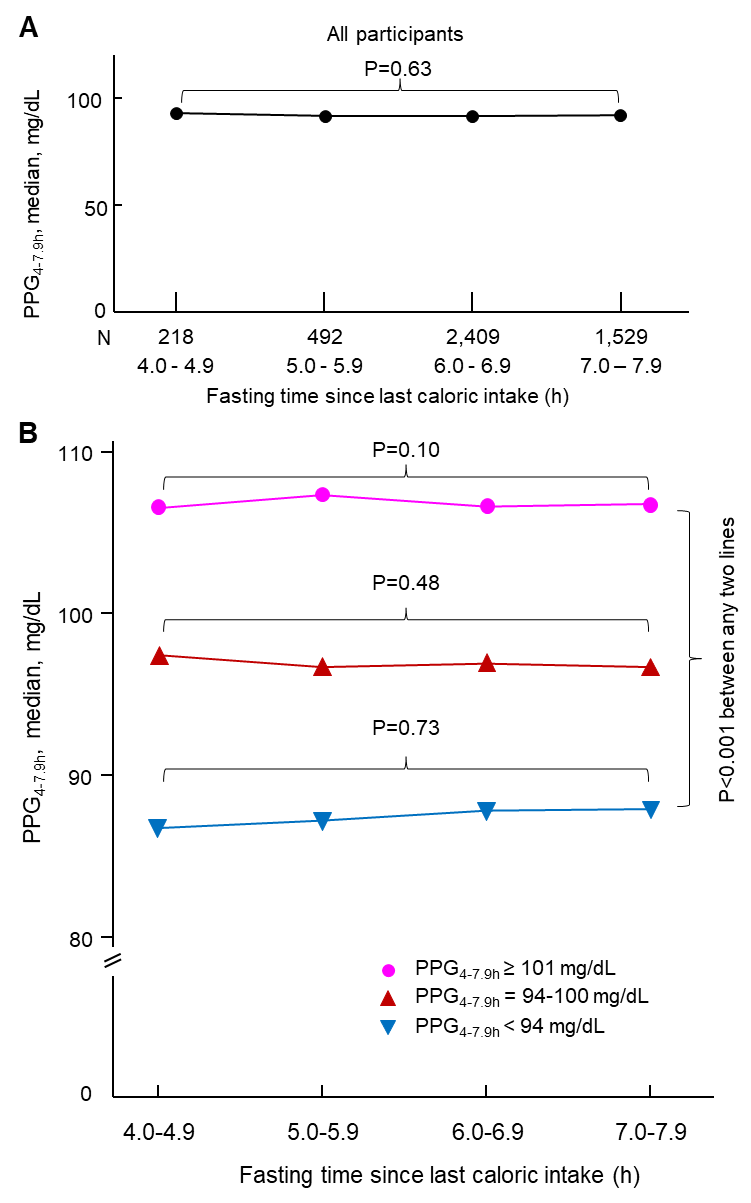
**eFigure 7. All-cause mortality risk associated with normal, borderline high, and high PPG4-7.9h.**

**A**, Kaplan-Meier survival curves. **B**, All-cause mortality risk associated with normal, borderline high, and high PPG4-7.9h. The analysis was adjusted for age, sex, ethnicity, body mass index, education, poverty-income ratio, survey period, physical activity, alcohol consumption, smoking status, systolic blood pressure, total cholesterol, high-density lipoprotein (HDL) cholesterol, family history of diabetes, fasting time, and HbA1c. CI, confidence interval; HbA1c, hemoglobin A1c; HR, hazard ratio; No., number; PPG4-7.9h, postprandial glucose measured from blood taken between 4 and 7.9 h.



**eFigure 8. Cancer mortality risk associated with PPG4-7.9h, stratified by prior diagnosis of cancer.**

Cancer mortality risk associated with continuous (**A**) or categorical PPG4-7.9h (**B**). The analysis was adjusted for age, sex, ethnicity, body mass index, education, poverty-income ratio, survey period, physical activity, alcohol consumption, smoking status, systolic blood pressure, total cholesterol, high-density lipoprotein (HDL) cholesterol, family history of diabetes, fasting time, and HbA1c. CI, confidence interval; HbA1c, hemoglobin A1c; HR, hazard ratio; No., number; PPG4-7.9h, postprandial plasma glucose measured from blood taken between 4 and 7.9 h.



**eFigure 9.** **Hourly PPG4-7.9h.**

Hourly PPG4-7.9h in all participants who had PPG4-7.9h (**A**) or in sub-groups of participants with normal, borderline high, or high PPG4-7.9h (**B**). PPG4-7.9h, postprandial plasma glucose measured from blood taken between 4 and 7.9 h.

**eTable 1. Baseline characteristics of 14,860 participants.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | All participants | Sub-cohort 1a | Sub-cohort 2b | Sub-cohort 3c |
| Sample size | 14,860 | 888 | 4,648 | 9,324 |
| PG, mg/dL, median (IQR) | 93 (87-101) | 95 (86-105) | 92 (87-98) | 94 (88-102) |
| HbA1c, %, median (IQR) | 5.3 (5.0-5.7) | 5.4 (5.0-5.7) | 5.3 (5.0-5.7) | 5.3 (5.0-5.7) |
| HbA1c, N (%) |  |  |  |  |
| <5.7% | 11,017 (74.1) | 632 (71.2) | 3,427 (73.7) | 6,958 (74.6) |
| 5.7%-6.4% | 3,217 (21.6) | 220 (24.8) | 1,010 (21.7) | 1,987 (21.3) |
| ≥6.5% | 626 (4.2) | 36 (4.1) | 211 (4.5) | 379 (4.1) |
| BMI, kg/m2, median (IQR) | 26 (23-30) | 26 (23-29) | 26 (23-30) | 26 (23-30) |
| SBP, mm Hg, median (IQR) | 121 (111-136) | 121 (110-135) | 123 (112-138) | 121 (111-134) |
| Total cholesterol, mg/dL, median (IQR) | 201 (174-232) | 196 (168-229) | 204 (177-235) | 200 (174-230) |
| HDL cholesterol, mg/dL, median (IQR) | 49 (41-60) | 49 (40-60) | 50 (41-60) | 49 (40-60) |
| Age, y, mean (SD) | 47 (19) | 45 (20) | 49 (19) | 46 (19) |
| Fasting time, h, mean (SD) | 10.9 (4.6) | 2.2 (1.0) | 6.6 (0.8) | 13.9 (2.9) |
| Sex (male), N (%) | 6,996 (47.1) | 445 (50.1) | 2,136 (46.0) | 4,415 (47.4) |
| Ethnicity, N (%) |  |  |  |  |
| Non-Hispanic white | 6,213 (41.8) | 249 (28.0) | 2,211 (47.6) | 3,753 (40.3) |
| Non-Hispanic black | 4,029 (27.1) | 353 (39.8) | 1,082 (23.3) | 2,594 (27.8) |
| Mexican-American | 4,014 (27.0) | 230 (25.9) | 1,177 (25.3) | 2,607 (28.0) |
| Other | 604 (4.1) | 56 (6.3) | 178 (3.8) | 370 (4.0) |
| Education, N (%) |  |  |  |  |
| < High School | 5,824 (39.2) | 394 (44.4) | 1,782 (38.3) | 3,648 (39.1) |
| High School | 4,599 (30.9) | 267 (30.1) | 1,432 (30.8) | 2,900 (31.1) |
| > High School | 4,343 (29.2) | 216 (24.3) | 1,404 (30.2) | 2,723 (29.2) |
| Unknown | 94 (0.6) | 11 (1.2) | 30 (0.6) | 53 (0.6) |
| Poverty-income ratio, N (%) |  |  |  |  |
| < 130% | 4,355 (29.3) | 341 (38.4) | 1,242 (26.7) | 2,772 (29.7) |
| 130%-349% | 6,006 (40.4) | 306 (34.5) | 1,920 (41.3) | 3,780 (40.5) |
| ≥ 350% | 3,156 (21.2) | 149 (16.8) | 1,121 (24.1) | 1,886 (20.2) |
| Unknown | 1,343 (9.0) | 92 (10.4) | 365 (7.9) | 886 (9.5) |
| Physical activity, N (%) |  |  |  |  |
| Active | 5,493 (37.0) | 318 (35.8) | 1,705 (36.7) | 3,470 (37.2) |
| Insufficiently active | 6,155 (41.4) | 323 (36.4) | 1,964 (42.3) | 3,868 (41.5) |
| Inactive | 3,212 (21.6) | 247 (27.8) | 979 (21.1) | 1,986 (21.3) |
| Alcohol consumption, N (%) |  |  |  |  |
| 0 drink/week | 2,538 (17.1) | 160 (18.0) | 806 (17.3) | 1,572 (16.9) |
| < 1 drink/week | 1,736 (11.7) | 90 (10.1) | 527 (11.3) | 1,119 (12.0) |
| 1-6 drinks/week | 2,914 (19.6) | 175 (19.7) | 900 (19.4) | 1,839 (19.7) |
| ≥ 7 drinks/week | 1,952 (13.1) | 116 (13.1) | 590 (12.7) | 1,246 (13.4) |
| Unknown | 5,720 (38.5) | 347 (39.1) | 1,825 (39.3) | 3,548 (38.1) |
| Smoking status, N (%) |  |  |  |  |
| Past smoker | 3,941 (26.5) | 312 (35.1) | 1,132 (24.4) | 2,497 (26.8) |
| Current smoker | 3,569 (24.0) | 169 (19.0) | 1,193 (25.7) | 2,207 (23.7) |
| Other | 7,350 (49.5) | 407 (45.8) | 2,323 (50.0) | 4,620 (49.5) |
| Survey period, N (%) |  |  |  |  |
| 1988-1991 | 7,247 (48.8) | 362 (40.8) | 2,290 (49.3) | 4,595 (49.3) |
| 1991-1994 | 7,613 (51.2) | 526 (59.2) | 2,358 (50.7) | 4,729 (50.7) |
| Family history of diabetes, N (%) |  |  |  |  |
| Yes | 6,404 (43.1) | 314 (35.4) | 2,006 (43.2) | 4,084 (43.8) |
| No | 8,211 (55.3) | 559 (63.0) | 2,558 (55.0) | 5,094 (54.6) |
| Unknown | 245 (1.6) | 15 (1.7) | 84 (1.8) | 146 (1.6) |

Abbreviations: BMI, body mass index; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; IQR, interquartile range; N, number; PG, plasma glucose; SBP, systolic blood pressure; SD, standard deviation; y, year.

a Sub-cohort 1, 888 participants whose blood was taken with a fasting time of 0-3.9 h.

b Sub-cohort 2, 4,648 participants whose blood was taken with a fasting time of 4-7.9h.

c Sub-cohort 3, 9,324 participants whose blood was taken with a fasting time of ≥8 h.

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**eTable 2. Baseline characteristics of Sub-cohort 1: participants with PPG0-3.9h.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Bottom 9 deciles | Top decile | Overall | P value |
| Sample size | 799 | 89 | 888 | N/A |
| PPG0-3.9h,  mg/dL, median (IQR) | 93 (86-101) | 136 (125-158) | 95 (86-105) | <0.001 |
| HbA1c, %, median (IQR) | 5.3 (5.0-5.7) | 5.7 (5.3-6.4) | 5.4 (5.0-5.7) | <0.001 |
| BMI, kg/m2, median (IQR) | 26 (22-29) | 27 (24-31) | 26 (23-29) | 0.01 |
| SBP, mm Hg, median (IQR) | 120 (110-134) | 133 (119-145) | 121 (110-135) | <0.001 |
| Total cholesterol, mg/dL, median (IQR) | 195 (168-229) | 205 (173-229) | 196 (168-229) | <0.001 |
| HDL cholesterol, mg/dL, median (IQR) | 50 (41-61) | 44 (36-55) | 49 (40-60) | 0.25 |
| Age, y, mean (SD) | 43 (20) | 56 (21) | 45 (20) | <0.001 |
| Fasting time, h, mean (SD) | 2.3 (1.0) | 1.9 (1.0) | 2.2 (1.0) | <0.001 |
| Sex (male), N (%) | 391 (48.9) | 54 (60.7) | 445 (50.1) | 0.04 |
| Ethnicity, N (%) |  |  |  | 0.45 |
| Non-Hispanic white | 226 (28.3) | 23 (25.8) | 249 (28.0) |  |
| Non-Hispanic black | 317 (39.7) | 36 (40.4) | 353 (39.8) |  |
| Mexican-American | 209 (26.2) | 21 (23.6) | 230 (25.9) |  |
| Other | 47 (5.9) | 9 (10.1) | 56 (6.3) |  |
| Education, N (%) |  |  |  | <0.001 |
| < High School | 333 (41.7) | 61 (68.5) | 394 (44.4) |  |
| High School | 256 (32.0) | 11 (12.4) | 267 (30.1) |  |
| > High School | 199 (24.9) | 17 (19.1) | 216 (24.3) |  |
| Unknown | 11 (1.4) | 0 (0) | 11 (1.2) |  |
| Poverty-income ratio, N (%) |  |  |  | 0.28 |
| < 130% | 303 (37.9) | 38 (42.7) | 341 (38.4) |  |
| 130%-349% | 279 (34.9) | 27 (30.3) | 306 (34.5) |  |
| ≥ 350% | 138 (17.3) | 11 (12.4) | 149 (16.8) |  |
| Unknown | 79 (9.9) | 13 (14.6) | 92 (10.4) |  |
| Physical activity, N (%) |  |  |  | 0.03 |
| Active | 289 (36.2) | 29 (32.6) | 318 (35.8) |  |
| Insufficiently active | 298 (37.3) | 25 (28.1) | 323 (36.4) |  |
| Inactive | 212 (26.5) | 35 (39.3) | 247 (27.8) |  |
| Alcohol consumption, N (%) |  |  |  | 0.76 |
| 0 drink/week | 144 (18.0) | 16 (18.0) | 160 (18.0) |  |
| < 1 drink/week | 84 (10.5) | 6 (6.7) | 90 (10.1) |  |
| 1-6 drinks/week | 156 (19.5) | 19 (21.3) | 175 (19.7) |  |
| ≥ 7 drinks/week | 106 (13.3) | 10 (11.2) | 116 (13.1) |  |
| Unknown | 309 (38.7) | 38 (42.7) | 347 (39.1) |  |
| Smoking status, N (%) |  |  |  | 0.13 |
| Past smoker | 284 (35.5) | 28 (31.5) | 312 (35.1) |  |
| Current smoker | 145 (18.1) | 24 (27.0) | 169 (19.0) |  |
| Other | 370 (46.3) | 37 (41.6) | 407 (45.8) |  |
| Survey period, N (%) |  |  |  | 0.19 |
| 1988-1991 | 320 (40.1) | 42 (47.2) | 362 (40.8) |  |
| 1991-1994 | 479 (59.9) | 47 (52.8) | 526 (59.2) |  |
| Family history of diabetes, N (%) |  |  |  | 0.90 |
| Yes | 283 (35.4) | 31 (34.8) | 314 (35.4) |  |
| No | 502 (62.8) | 57 (64.0) | 559 (63.0) |  |
| Unknown | 14 (1.8) | 1 (1.1) | 15 (1.7) |  |

Abbreviations: BMI, body mass index; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; IQR, interquartile range; N, number; NA, not applicable; PPG0-3.9h, postprandial plasma glucose measured from blood taken between 0 and 3.9 h; SBP, systolic blood pressure; SD, standard deviation; y, year.

**eTable 3. Baseline characteristics of Sub-cohort 2: participants with PPG4-7.9h.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Bottom 9 deciles | Top decile | Overall | P value |
| Sample size | 4,182 | 466 | 4,648 | N/A |
| PPG4-7.9h, mg/dL, median (IQR) | 91 (86-96) | 113 (108-124) | 92 (87-98) | <0.001 |
| HbA1c, %, median (IQR) | 5.3 (5.0-5.6) | 5.8 (5.4-6.7) | 5.3 (5.0-5.7) | <0.001 |
| BMI, kg/m2, median (IQR) | 26 (23-30) | 28 (24-31) | 26 (23-30) | <0.001 |
| SBP, mm Hg, median (IQR) | 122 (111-136) | 136 (123-150) | 123 (112-138) | <0.001 |
| Total cholesterol, mg/dL, median (IQR) | 203 (175-234) | 214 (189-247) | 204 (177-235) | 0.0497 |
| HDL cholesterol, mg/dL, median (IQR) | 50 (41-60) | 48 (40-58) | 50 (41-60) | <0.001 |
| Age, y, mean (SD) | 48 (18) | 61 (18) | 49 (19) | <0.001 |
| Fasting time, h, mean (SD) | 6.6 (0.8) | 6.6 (0.8) | 6.6 (0.8) | 0.47 |
| Sex (male), N (%) | 1,908 (45.6) | 228 (48.9) | 2,136 (46.0) | 0.18 |
| Ethnicity, N (%) |  |  |  | 0.002 |
| Non-Hispanic white | 1,986 (47.5) | 225 (48.3) | 2,211 (47.6) |  |
| Non-Hispanic black | 1,003 (24.0) | 79 (17.0) | 1,082 (23.3) |  |
| Mexican-American | 1,033 (24.7) | 144 (30.9) | 1,177 (25.3) |  |
| Other | 160 (3.8) | 18 (3.9) | 178 (3.8) |  |
| Education, N (%) |  |  |  | <0.001 |
| < High School | 1,541 (36.8) | 241 (51.7) | 1,782 (38.3) |  |
| High School | 1,310 (31.3) | 122 (26.2) | 1,432 (30.8) |  |
| > High School | 1,303 (31.2) | 101 (21.7) | 1,404 (30.2) |  |
| Unknown | 28 (0.7) | 2 (0.4) | 30 (0.6) |  |
| Poverty-income ratio, N (%) |  |  |  | <0.001 |
| < 130% | 1,100 (26.3) | 142 (30.5) | 1,242 (26.7) |  |
| 130%-349% | 1,744 (41.7) | 176 (37.8) | 1,920 (41.3) |  |
| ≥ 350% | 1,030 (24.6) | 91 (19.5) | 1,121 (24.1) |  |
| Unknown | 308 (7.4) | 57 (12.2) | 365 (7.9) |  |
| Physical activity, N (%) |  |  |  | <0.001 |
| Active | 1,550 (37.1) | 155 (33.3) | 1,705 (36.7) |  |
| Insufficiently active | 1,784 (42.7) | 180 (38.6) | 1,964 (42.3) |  |
| Inactive | 848 (20.3) | 131 (28.1) | 979 (21.1) |  |
| Alcohol consumption, N (%) |  |  |  | <0.001 |
| 0 drink/week | 702 (16.8) | 104 (22.3) | 806 (17.3) |  |
| < 1 drink/week | 490 (11.7) | 37 (7.9) | 527 (11.3) |  |
| 1-6 drinks/week | 834 (19.9) | 66 (14.2) | 900 (19.4) |  |
| ≥ 7 drinks/week | 532 (12.7) | 58 (12.4) | 590 (12.7) |  |
| Unknown | 1,624 (38.8) | 201 (43.1) | 1,825 (39.3) |  |
| Smoking status, N (%) |  |  |  | <0.001 |
| Past smoker | 1,043 (24.9) | 89 (19.1) | 1,132 (24.4) |  |
| Current smoker | 1,035 (24.7) | 158 (33.9) | 1,193 (25.7) |  |
| Other | 2,104 (50.3) | 219 (47.0) | 2,323 (50.0) |  |
| Survey period, N (%) |  |  |  | 0.11 |
| 1988-1991 | 2,044 (48.9) | 246 (52.8) | 2,290 (49.3) |  |
| 1991-1994 | 2,138 (51.1) | 220 (47.2) | 2,358 (50.7) |  |
| Family history of diabetes, N (%) |  |  |  | 0.49 |
| Yes | 1,795 (42.9) | 211 (45.3) | 2,006 (43.2) |  |
| No | 2,313 (55.3) | 245 (52.6) | 2,558 (55.0) |  |
| Unknown | 74 (1.8) | 10 (2.1) | 84 (1.8) |  |

Abbreviations: BMI, body mass index; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; IQR, interquartile range; N, number; NA, not applicable; PPG4-7.9h, postprandial plasma glucose measured from blood taken between 4 and 7.9 h; SBP, systolic blood pressure; SD, standard deviation; y, year.

**eTable 4. Baseline characteristics of Sub-cohort 3: participants with PGfasting.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Bottom 9 deciles | Top decile | Overall | P value |
| Sample size | 8,383 | 941 | 9,342 | N/A |
| PGfasting, mg/dL, median (IQR) | 93 (87-99) | 123 (116-140) | 94 (88-102) | <0.001 |
| HbA1c, %, median (IQR) | 5.3 (5.0-5.6) | 6.1 (5.6-6.8) | 5.3 (5.0-5.7) | <0.001 |
| BMI, kg/m2, median (IQR) | 26 (23-30) | 29 (26-33) | 26 (23-30) | <0.001 |
| SBP, mm Hg, median (IQR) | 119 (110-132) | 134 (123-149) | 121 (111-134) | <0.001 |
| Total cholesterol, mg/dL, median (IQR) | 199 (173-228) | 215 (186-249) | 200 (174-230) | <0.001 |
| HDL cholesterol, mg/dL, median (IQR) | 50 (41-60) | 43 (37-52) | 49 (40-60) | <0.001 |
| Age, y, mean (SD) | 45 (19) | 60 (16) | 46 (19) | <0.001 |
| Fasting time, h, mean (SD) | 13.9 (3.0) | 13.8 (2.5) | 13.9 (2.9) | 0.53 |
| Sex (male), N (%) | 3,901 (46.5) | 514 (54.6) | 4,415 (47.4) | <0.001 |
| Ethnicity, N (%) |  |  |  | 0.18 |
| Non-Hispanic white | 3,353 (40.0) | 400 (42.5) | 3,753 (40.3) |  |
| Non-Hispanic black | 2,360 (28.2) | 234 (24.9) | 2,594 (27.8) |  |
| Mexican-American | 2,336 (27.9) | 271 (28.8) | 2,607 (28.0) |  |
| Other | 334 (4.0) | 36 (3.8) | 370 (4.0) |  |
| Education, N (%) |  |  |  | <0.001 |
| < High School | 3,150 (37.6) | 498 (52.9) | 3,648 (39.1) |  |
| High School | 2,648 (31.6) | 252 (26.8) | 2,900 (31.1) |  |
| > High School | 2,536 (30.3) | 187 (19.9) | 2,723 (29.2) |  |
| Unknown | 49 (0.6) | 4 (0.4) | 53 (0.6) |  |
| Poverty-income ratio, N (%) |  |  |  | 0.13 |
| < 130% | 2,471 (29.5) | 301 (32.0) | 2,772 (29.7) |  |
| 130%-349% | 3,409 (40.7) | 371 (39.4) | 3,780 (40.5) |  |
| ≥ 350% | 1,716 (20.5) | 170 (18.1) | 1,886 (20.2) |  |
| Unknown | 787 (9.4) | 99 (10.5) | 886 (9.5) |  |
| Physical activity, N (%) |  |  |  | <0.001 |
| Active | 3,147 (37.5) | 323 (34.3) | 3,470 (37.2) |  |
| Insufficiently active | 3,495 (41.7) | 373 (39.6) | 3,868 (41.5) |  |
| Inactive | 1,741 (20.8) | 245 (26.0) | 1,986 (21.3) |  |
| Alcohol consumption, N (%) |  |  |  | <0.001 |
| 0 drink/week | 1,399 (16.7) | 173 (18.4) | 1,572 (16.9) |  |
| < 1 drink/week | 1,040 (12.4) | 79 (8.4) | 1,119 (12.0) |  |
| 1-6 drinks/week | 1,696 (20.2) | 143 (15.2) | 1,839 (19.7) |  |
| ≥ 7 drinks/week | 1,126 (13.4) | 120 (12.8) | 1,246 (13.4) |  |
| Unknown | 3,122 (37.2) | 426 (45.3) | 3,548 (38.1) |  |
| Smoking status, N (%) |  |  |  | <0.001 |
| Past smoker | 2,301 (27.4) | 196 (20.8) | 2,497 (26.8) |  |
| Current smoker | 1,867 (22.3) | 340 (36.1) | 2,207 (23.7) |  |
| Other | 4,215 (50.3) | 405 (43.0) | 4,620 (49.5) |  |
| Survey period, N (%) |  |  |  | 0.19 |
| 1988-1991 | 4,112 (49.1) | 483 (51.3) | 4,595 (49.3) |  |
| 1991-1994 | 4,271 (50.9) | 458 (48.7) | 4,729 (50.7) |  |
| Family history of diabetes, N (%) |  |  |  | <0.001 |
| Yes | 3,619 (43.2) | 465 (49.4) | 4,084 (43.8) |  |
| No | 4,636 (55.3) | 458 (48.7) | 5,094 (54.6) |  |
| Unknown | 128 (1.5) | 18 (1.9) | 146 (1.6) |  |

Abbreviations: BMI, body mass index; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; IQR, interquartile range; N, number; NA, not applicable; PGfasting, plasma glucose measured from blood taken in a fasting state (fasting time ≥8 h); SBP, systolic blood pressure; SD, standard deviation; y, year.

**eTable 5. Baseline characteristics of Sub-cohort 4: participants with PG2hOGTT.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Bottom 9 deciles | Top decile | Overall | P value |
| Sample size | 3,383 | 376 | 3,759 | N/A |
| PGfasting, mg/dL, median (IQR) | 97 (91-104) | 127 (108-170) | 98 (91-106) | <0.001 |
| PG2hOGTT, mg/dL, median (IQR) | 114 (93-141) | 262 (225-322) | 119 (96-154) | <0.001 |
| HbA1c, %, median (IQR) | 5.4 (5.1-5.7) | 6.4 (5.8-7.7) | 5.5 (5.1-5.8) | <0.001 |
| BMI, kg/m2, median (IQR) | 27 (24-31) | 30 (26-33) | 27 (24-31) | <0.001 |
| SBP, mm Hg, median (IQR) | 126 (115-139) | 137 (126-150) | 127 (116-141) | <0.001 |
| Total cholesterol, mg/dL, median (IQR) | 213 (188-240) | 221 (195-255) | 214 (189-242) | <0.001 |
| HDL cholesterol, mg/dL, median (IQR) | 49 (40-60) | 44 (37-54) | 48 (40-59) | <0.001 |
| Age, y, mean (SD) | 55 (10) | 60 (9) | 56 (10) | <0.001 |
| Fasting time, h, mean (SD) | 13.7 (2.4) | 14.1 (3.3) | 13.7 (2.5) | 0.03 |
| Sex (male), N (%) | 1,650 (48.8) | 196 (52.1) | 1,846 (49.1) | 0.22 |
| Ethnicity, N (%) |  |  |  | <0.001 |
| Non-Hispanic white | 1,570 (46.4) | 146 (38.8) | 1,716 (45.7) |  |
| Non-Hispanic black | 890 (26.3) | 80 (21.3) | 970 (25.8) |  |
| Mexican-American | 778 (23.0) | 133 (35.4) | 911 (24.2) |  |
| Other | 145 (4.3) | 17 (4.5) | 162 (4.3) |  |
| Education, N (%) |  |  |  | <0.001 |
| < High School | 1,387 (41.0) | 216 (57.4) | 1,603 (42.6) |  |
| High School | 1,018 (30.1) | 96 (25.5) | 1,114 (29.6) |  |
| > High School | 957 (28.3) | 64 (17) | 1,021 (27.2) |  |
| Unknown | 21 (0.6) | 0 (0) | 21 (0.6) |  |
| Poverty-income ratio, N (%) |  |  |  | <0.001 |
| < 130% | 789 (23.3) | 125 (33.2) | 914 (24.3) |  |
| 130%-349% | 1,350 (39.9) | 147 (39.1) | 1,497 (39.8) |  |
| ≥ 350% | 925 (27.3) | 66 (17.6) | 991 (26.4) |  |
| Unknown | 319 (9.4) | 38 (10.1) | 357 (9.5) |  |
| Physical activity, N (%) |  |  |  | 0.42 |
| Active | 1,228 (36.3) | 131 (34.8) | 1,359 (36.2) |  |
| Insufficiently active | 1,444 (42.7) | 155 (41.2) | 1,599 (42.5) |  |
| Inactive | 711 (21.0) | 90 (23.9) | 801 (21.3) |  |
| Alcohol consumption, N (%) |  |  |  | <0.001 |
| 0 drink/week | 479 (14.2) | 80 (21.3) | 559 (14.9) |  |
| < 1 drink/week | 401 (11.9) | 33 (8.8) | 434 (11.5) |  |
| 1-6 drinks/week | 631 (18.7) | 51 (13.6) | 682 (18.1) |  |
| ≥ 7 drinks/week | 424 (12.5) | 46 (12.2) | 470 (12.5) |  |
| Unknown | 1,448 (42.8) | 166 (44.1) | 1,614 (42.9) |  |
| Smoking status, N (%) |  |  |  | 0.02 |
| Past smoker | 942 (27.8) | 87 (23.1) | 1,029 (27.4) |  |
| Current smoker | 1,044 (30.9) | 142 (37.8) | 1,186 (31.6) |  |
| Other | 1,397 (41.3) | 147 (39.1) | 1,544 (41.1) |  |
| Survey period, N (%) |  |  |  | 0.96 |
| 1988-1991 | 1,642 (48.5) | 182 (48.4) | 1,824 (48.5) |  |
| 1991-1994 | 1,741 (51.5) | 194 (51.6) | 1,935 (51.5) |  |
| Family history of diabetes, N (%) |  |  |  | 0.03 |
| Yes | 1,474 (43.6) | 191 (50.8) | 1,665 (44.3) |  |
| No | 1,868 (55.2) | 182 (48.4) | 2,050 (54.5) |  |
| Unknown | 41 (1.2) | 3 (0.8) | 44 (1.2) |  |

Abbreviations: BMI, body mass index; HbA1c, hemoglobin A1c; HDL, high-density lipoprotein; IQR, interquartile range; N, number; NA, not applicable; PG2hOGTT, plasma glucose measured from blood taken at 2 h after an oral glucose tolerance test; PGfasting, plasma glucose measured from blood taken in a fasting state (fasting time ≥8 h); SBP, systolic blood pressure; SD, standard deviation; y, year.

**eTable 6. Mortality and follow-up.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Cohort | Sample size | All-cause deaths | Cancer deaths | Mean follow-up, y | Total follow-up, person-years |
| Whole cohort | 14,860 | 5,996 | 1,388 | 22.4 | 332,313 |
| Sub-cohort 1:  Fasting time 0-3.9 h | 888 | 333 | 58 | 22.1 | 19,597 |
| Sub-cohort 2:  Fasting time 4-7.9 h | 4,648 | 2,001 | 451 | 22.1 | 102,810 |
| Sub-cohort 3:  Fasting time ≥8 h | 9,324 | 3,662 | 879 | 22.5 | 209,906 |
| Sub-cohort 4:  Fasting time ≥8 h and with plasma glucose at 2 h after OGTT | 3,759 | 2,037 | 559 | 21.5 | 80,831 |

Abbreviations: OGTT, oral glucose tolerance test; y, year.

**eTable 7. Cancer mortality risk associated with a 1-natural-log-unit increase in HbA1c.**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | All participants | | | Sub-cohort 1 a | | | Sub-cohort 2 b | | | Sub-cohort 3 c | | | Sub-cohort 4 d | | |
|  | HR | 95% CI | P value | HR | 95% CI | P value | HR | 95% CI | P value | HR | 95% CI | P value | HR | 95% CI | P value |
| Model 1 | 1.40 | 0.90-2.16 | 0.13 | 1.95 | 0.21-18.40 | 0.56 | 1.07 | 0.47-2.44 | 0.87 | 1.53 | 0.91-2.59 | 0.11 | 1.40 | 0.76-2.60 | 0.28 |
| Model 2 | 1.23 | 0.79-1.93 | 0.36 | 1.60 | 0.16-16.36 | 0.69 | 0.78 | 0.34-1.81 | 0.56 | 1.47 | 0.86-2.52 | 0.16 | 1.30 | 0.69-2.45 | 0.42 |
| Model 3 | 1.08 | 0.67-1.72 | 0.76 | 1.10 | 0.08-14.57 | 0.94 | 0.73 | 0.30-1.78 | 0.48 | 1.31 | 0.74-2.30 | 0.35 | 1.27 | 0.65-2.50 | 0.49 |
| Model 4 | 1.05 | 0.66-1.68 | 0.84 | 1.09 | 0.07-15.93 | 0.95 | 0.72 | 0.29-1.76 | 0.47 | 1.27 | 0.72-2.25 | 0.40 | 1.26 | 0.64-2.50 | 0.50 |
| Model 5 | 1.03 | 0.64-1.65 | 0.91 | 1.11 | 0.08-16.47 | 0.94 | 0.72 | 0.29-1.77 | 0.47 | 1.24 | 0.70-2.18 | 0.47 | 1.18 | 0.59-2.35 | 0.64 |
| Model 6 | 1.03 | 0.64-1.65 | 0.91 | 1.15 | 0.08-16.36 | 0.92 | 0.72 | 0.29-1.77 | 0.47 | 1.23 | 0.70-2.18 | 0.47 | 1.18 | 0.59-2.34 | 0.65 |

Abbreviations: CI, confidence interval; HbA1c, hemoglobin A1c; HR, hazard ratio.

a Sub-cohort 1, 888 participants whose plasma glucose was measured from blood taken with a fasting time of 0-3.9 h.

b Sub-cohort 2, 4,648 participants whose plasma glucose was measured from blood taken with a fasting time of 4-7.9h.

c Sub-cohort 3, 9,324 participants whose plasma glucose was measured from blood taken with a fasting time of ≥8 h.

d Sub-cohort 4, 3,759 participants whose plasma glucose was measured from blood taken at 2 h after an oral glucose tolerance test (OGTT) with 75 g glucose.

Model 1: adjusted for age.

Model 2: adjusted for age, sex, and ethnicity.

Model 3: adjusted for all the factors in Model 2 plus body mass index, education, poverty-income ratio, survey period, physical activity, alcohol consumption, and smoking status.

Model 4: adjusted for all the factors in Model 3 plus systolic blood pressure, total cholesterol, and high-density lipoprotein (HDL) cholesterol.

Model 5: adjusted for all the factors in Model 4 plus family history of diabetes.

Model 6: adjusted for all the factors in Model 5 plus fasting time.

**eTable 8. PGfasting and PPG4-7.9h in patients with type 2 diabetes with relatively good diabetic control.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Study | Patients | N | PGfasting, mg/dL | PPG4-7.9h, mg/dL | Difference  (PGfasting - PPG4-7.9h), mg/dL |
| Avignon et al 4 | T2D with HbAlc<7.0% | 20 | 133 | 104 a | 29 |
| Peter et al 5 | T2D with HbA1c<7.3% | 18 | 127 | 102 b | 25 |
| Weighted Mean | N/A | N/A | 130.2 | 103.1 | 27.1 |

Abbreviations: HbA1c, hemoglobin A1c; PGfasting, plasma glucose measured from blood taken in a fasting state (fasting time ≥8 h); PPG4-7.9h, postprandial plasma glucose measured from blood taken between 4 and 7.9 h; Ref, reference; T2D, type 2 diabetes.

a PPG4-7.9h was defined as 5 h after lunch.

b PPG4-7.9h was defined as 4 h after breakfast, lunch and dinner.

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