**Supplemental data**

**Supplemental table I. Unadjusted and multiple-adjusted rates of myocardial infarction (per 10,000 person-years) by sex and diabetes status.**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Women** | **Men** | **Difference of rate Differences (women-men)** |
| **Unadjusted** |  |  |  |
| No diabetes | 7∙7 (7∙3;8∙1) | 24∙0 (23∙2;24∙8) | Reference |
| Prediabetes | 15∙1 (13∙7;16∙6) | 38∙2 (35∙6;40∙8) | -6∙8 (-9∙9;-3∙6) |
| Undiagnosed diabetes | 23∙2 (14∙3;32∙2) | 53∙0 (41∙7;64∙3) | -13∙5 (-27∙9;1∙0) |
| Previously diagnosed diabetes | 27∙0 (23∙4;30∙5) | 53∙6 (49∙2;57∙9) | -10∙3 (-16∙0;-4∙6) |
| **Multivariable-adjusted\*** |  |  |  |
| No diabetes | 8∙7 (8∙2;9∙2) | 25∙4 (24∙5;26∙3) | Reference |
| Prediabetes | 10∙9 (9∙8;12∙0) | 29∙7 (27∙5;31∙9) | -2∙1 (-4∙8;0∙5) |
| Undiagnosed diabetes | 14∙3 (8∙4;20∙1) | 38∙9 (30∙2;47∙6) | -7∙9 (-18∙5;2∙6) |
| Previously diagnosed diabetes | 20∙4 (17∙1;23∙6) | 46∙1 (41∙4;50∙8) | -9∙0 (-14∙8;-3∙2) |

\* The multivariable-adjusted model is adjusted for age, smoking (never, former, current), BMI, systolic blood pressure, lipid-lowering medication, cholesterol, antihypertensive medication, the Townsend social deprivation score, and interaction terms between each variable and sex.

**Supplemental table II. Unadjusted and multiple-adjusted rates of myocardial infarction (per 10,000 person-years) by sex and HbA1c levels.**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Women** | **Men** | **Difference of rate Difference (women-men)** |
| **Unadjusted** |  |  |  |
| No previously diagnosed diabetes± | 8∙7 (8∙3;9∙0) | 25∙9 (25∙2;26∙7) | Reference |
| ≤6∙5% | 18∙9 (14∙2;23∙5) | 42∙4 (36∙3;48∙6) | -6∙3 (-14∙0;1∙44) |
| 6∙5 - ≤7∙5% | 27∙1 (20∙1;34∙1) | 52∙5 (44∙3;60∙6) | -8∙1 (-18∙9;2∙6) |
| >7∙5% | 41∙6 (32∙5;50∙8) | 72∙3 (62∙2;82∙4) | -13∙4 (-27∙0;0∙2) |
| **Multivariable-adjusted\*** |  |  |  |
| No previously diagnosed diabetes± | 9∙3 (8∙8;9∙8) | 26∙5 (25∙6;27∙4) | Reference |
| ≤6∙5% | 12∙3 (8∙5;16∙2) | 31∙9 (25∙9;37∙9) | -2∙4 (-9∙7;4∙9) |
| 6∙5 - ≤7∙5% | 15∙2 (9∙4;21∙0) | 38∙7 (30∙0;47∙4) | -6∙3 (-17∙0;4∙4) |
| >7∙5% | 22∙3 (13∙8;30∙7) | 51∙5 (39∙6;63∙3) | -12∙0 (-26∙8;2∙8) |

**\*** The multivariable-adjusted model is adjusted for age, smoking (never, former, current), BMI, systolic blood pressure, lipid-lowering medication, cholesterol, antihypertensive medication, the Townsend social deprivation score, glucose-lowering medication, and interaction terms between each variable and sex. HbA1c 6.5% = 48mmol/mol; HbA1c 7.5% = 58mmol/mol.

**Supplemental table III. Age-adjusted and multiple-adjusted hazard ratios and ratios of hazard ratios of myocardial infarction according to diabetes status**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Women, n (%)** | **Men, n (%)** | **Women (HR 95% CI)** | **Men (HR 95% CI)** | **Women-to men RHR (95% CI)** |
| **Age-adjusted model** |  |  |  |  |  |
| No diabetes | 1,533 (0·7%) | 3,659 (2·1%) | 1·0 | 1·0 | NA |
| Prediabetes | 417 (1·4%) | 792 (3·4%) | 1·58 (1·42;1·77) | 1·36 (1·26;1·47) | 1·16 (1·02;1·33) |
| Undiagnosed diabetes | 26 (2·1%) | 84 (4·7%) | 2·55 (1·73;3·76) | 2·03 (1·63;2·52) | 1·26 (0·81;1·96) |
| Previously diagnosed diabetes | 221 (2·4%) | 584 (4·7%) | 3·02 (2·62;3·48) | 1·85 (1·69;2·02) | 1·63 (1·38;1·93) |
| **Multiple-adjusted – main effects model\*** |  |  |  |  |  |
| No diabetes | 1,404 (0·7%) | 3,392 (2·1%) | 1·0 | 1·0 | NA |
| Prediabetes | 390 (1·3%) | 739 (3·4%) | 1·32 (1·18;1·48) | 1·14 (1·05;1·24) | 1·15 (1·00;1·32) |
| Undiagnosed diabetes | 23 (2%) | 78 (4·7%) | 1·71 (1·13;2·58) | 1·51 (1·20;1·89) | 1·13 (0·71;1·81) |
| Previously diagnosed diabetes | 194 (2·3%) | 520 (4·6%) | 2·66 (2·27;3·11) | 1·72 (1·55;1·91) | 1·54 (1·29;1·84) |
| **Multiple-adjusted – full interaction model\*\*** |  |  |  |  |  |
| No diabetes | 1,404 (0·7%) | 3,392 (2·1%) | 1∙0 | 1∙0 | NA |
| Prediabetes | 390 (1·3%) | 739 (3·4%) | 1∙25 (1∙11;1∙40) | 1∙17 (1∙08;1∙27) | 1∙07 (0∙93;1∙23) |
| Undiagnosed diabetes | 23 (2%) | 78 (4·7%) | 1∙64 (1∙08;2∙49) | 1∙53 (1∙22;1∙92) | 1∙07 (0∙67;1∙72) |
| Previously diagnosed diabetes | 194 (2·3%) | 520 (4·6%) | 2∙33 (1∙96;2∙78) | 1∙81 (1∙63;2∙02) | 1∙29 (1∙05;1∙58) |

\*The main effects model is adjusted for age, smoking (never, former, current), BMI, systolic blood pressure, lipid-lowering medication, cholesterol, antihypertensive medication, and the Townsend social deprivation score. \*\*The full interaction model is additionally adjusted for interaction terms between each variable and sex. NA = not applicable; HR = hazard ratio; RHR = ratio of hazard ratios; n (%) = number of events.

**Supplemental table IV.**  **Age-adjusted and multiple-adjusted hazard ratios and ratios of hazard ratios of MI according to levels of glycaemia.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Women, n (%)** | **Men, n (%)** | **Women (HR 95% CI)** | **Men (HR 95% CI)** | **Women-to men RHR (95% CI)** |
| **Age-adjusted model** |  |  |  |  |  |
| No previously diagnosed diabetes± | 1,976 (0·8%) | 4,535 (2·3%) | 1·0 | 1·0 | NA |
| HbA1c ≤6∙5% | 64 (1·7%) | 183 (3·7%) | 1·95 (1·52;2·50) | 1·33 (1·14;1·54) | 1·47 (1·10;1·97) |
| HbA1c >6∙5% - ≤7∙5% | 58 (2·4%) | 160 (4·6%) | 2·58 (1·99;3·35) | 1·65 (1·41;1·94) | 1·56 (1·15;2·12) |
| HbA1c >7∙5% | 80 (3·7%) | 198 (6·3%) | 4·41 (3·53;5·52) | 2·53 (2·20;2·92) | 1·74 (1·34;2·27) |
| **Multiple-adjusted – main effects model\*** |  |  |  |  |  |
| No previously diagnosed diabetes± | 1,817 (0·8%) | 4,209 (2·3%) | 1·0 | 1·0 | NA |
| HbA1c ≤6∙5% | 58 (1·6%) | 168 (3·6%) | 1·56 (1·18;2·06) | 1·12 (0·93;1·35) | 1·39 (1·03;1·88) |
| HbA1c >6∙5% - ≤7∙5% | 56 (2·5%) | 151 (4·7%) | 2·02 (1·49;2·74) | 1·35 (1·09;1·68) | 1·50 (1·10;2·05) |
| HbA1c >7∙5% | 73 (3·6%) | 179 (6·2%) | 3·03 (2·28;4·03) | 1·79 (1·44;2·24) | 1·69 (1·28;2·23) |
| **Multiple-adjusted – full interaction model\*\*** |  |  |  |  |  |
| No previously diagnosed diabetes± | 1,817 (0·8%) | 4,209 (2·3%) | 1∙0 | 1∙0 | NA |
| HbA1c ≤6∙5% | 58 (1·6%) | 168 (3·6%) | 1∙32 (0∙95;1∙83) | 1∙20 (0∙99;1∙46) | 1∙09 (0∙75;1∙60) |
| HbA1c >6∙5% - ≤7∙5% | 56 (2·5%) | 151 (4·7%) | 1∙63 (1∙09;2∙43) | 1∙46 (1∙16;1∙85) | 1∙11 (0∙70;1∙77) |
| HbA1c >7∙5% | 73 (3·6%) | 179 (6·2%) | 2∙40 (1∙61;3∙58) | 1∙94 (1∙53;2∙47) | 1∙24 (0∙78;1∙97) |

\*The main effects model is adjusted for age plus smoking (never, former, current), BMI, systolic blood pressure, lipid-lowering medication, cholesterol, antihypertensive medication, the Townsend social deprivation score, and glucose-lowering medication. \*\*The full interaction model is additionally adjusted for interaction terms between each variable and sex. **±** No previously diagnosed diabetes, including prediabetes and undiagnosed diabetes.NA = not applicable; HR = hazard ratio; RHR = ratio of hazard ratios. n (%) = number of events. HbA1c 6.5% = 48mmol/mol; HbA1c 7.5% = 58mmol/mol.

**Supplemental table V. Multiple-adjusted hazard ratios and ratios of hazard ratios of myocardial infarction per 1% HbA1c change, stratified by age, BMI, socioeconomic status, and use of glucose-lowering medication.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Women, n (%)** | **Men, n (%)** | **Women (HR 95% CI)** | **Men (HR 95% CI)** | **Women-to-men RHR (95% CI)** | **P for interaction** |
| **Multiple-adjusted main effects model\*** |  |  |  |  |  |  |
| Overall | 1,936 (0·8%) | 4,518 (2·5%) | 1·24 (1·20;1·28) | 1·14 (1·10;1·19) | 1·09 (1·03;1·14) | NA |
| **Age** |  |  |  |  |  |  |
| <60 | 669 (0·5%) | 1,830 (1·7%) | 1·33 (1·23;1·43) | 1·17 (1·11;1·22) | 1·13 (1·04;1·24) |  |
| ≥60 | 1,267 (1·3%) | 2,688 (3·5%) | 1·21 (1·16;1·27) | 1·12 (1·07;1·18) | 1·08 (1·01;1·15) | 0∙355 |
| **BMI** |  |  |  |  |  |  |
| <25 | 606 (0·7%) | 891 (1·9%) | 1·36 (1·20;1·54) | 1·21 (1·12;1·31) | 1·12 (0·97;1·30) |  |
| ≥25 | 1,330 (1·0%) | 3,627 (2·7%) | 1·23 (1·19;1·28) | 1·13 (1·08;1·18) | 1·09 (1·04;1·15) | 0∙744 |
| **Socioeconomic status** |  |  |  |  |  |  |
| High | 1,173 (0·8%) | 2,986 (2·4%) | 1·22 (1·17;1·28) | 1·16 (1·11;1·22) | 1·05 (0·99;1·12) |  |
| Low | 763 (1·0%) | 1,532 (2·6%) | 1·27 (1·29;1·37) | 1·13 (1·07;1·20) | 1·13 (1·04;1·22) | 0∙197 |
| **Use of glucose-lowering medication** |  |  |  |  |  |  |
| No | 1,795 (0·8%) | 4,156 (2·4%) | 1∙21 (1∙16;1∙27) | 1∙17 (1∙12;1∙23) | 1∙03 (0∙97;1∙11) |  |
| Yes | 141 (3·0%) | 362 (5·2%) | 1∙20 (1∙08;1∙34) | 1∙19 (1∙11;1∙28) | 1∙01 (0∙89;1∙15) | 0∙735 |
| **Multiple-adjusted full interaction model\*\*** |  |  |  |  |  |  |
| Overall | 1,936 (0·8%) | 4,518 (2·5%) | 1∙18 (1∙13;1∙24) | 1∙18 (1∙13;1∙23) | 1∙00 (0∙94;1∙07) | NA |
| Age |  |  |  |  |  |  |
| <60 | 669 (0·5%) | 1,830 (1·7%) | 1∙25 (1∙14;1∙36) | 1∙19 (1∙14;1∙25) | 1∙05 (0∙95;1∙15) |  |
| ≥60 | 1,267 (1·3%) | 2,688 (3·5%) | 1∙16 (1∙09;1∙24) | 1∙16 (1∙10;1∙22) | 1∙00 (0∙93;1∙09) | 0∙484 |
| **BMI** |  |  |  |  |  |  |
| <25 | 606 (0·7%) | 891 (1·9%) | 1∙24 (1∙08;1∙42) | 1∙24 (1∙15;1∙34) | 1∙00 (0∙86;1∙16) |  |
| ≥25 | 1,330 (1·0%) | 3,627 (2·7%) | 1∙18 (1∙12;1∙24) | 1∙17 (1∙12;1∙22) | 1∙01 (0∙94;1∙08) | 0∙891 |
| **Socioeconomic status** |  |  |  |  |  |  |
| High | 1,173 (0·8%) | 2,986 (2·4%) | 1∙18 (1∙11;1∙25) | 1∙19 (1∙14;1∙25) | 0∙99 (0∙92;1∙07) |  |
| Low | 763 (1·0%) | 1,532 (2·6%) | 1∙20 (1∙10;1∙30) | 1∙16 (1∙10;1∙22) | 1∙03 (0∙94;1∙14) | 0∙440 |
| **Use of glucose-lowering medication** |  |  |  |  |  |  |
| No | 1,795 (0·8%) | 4,156 (2·4%) | 1∙19 (1∙12;1∙25) | 1∙19 (1∙14;1∙24) | 1∙00 (0∙93;1∙07) |  |
| Yes | 141 (3·0%) | 362 (5·2%) | 1∙20 (1∙08;1∙34) | 1∙19 (1∙11;1∙28) | 1∙01 (0∙89;1∙15) | 0∙880 |

\*The main effects model is adjusted for age plus smoking (never, former, current), BMI, systolic blood pressure, lipid-lowering medication, cholesterol, antihypertensive medication, the Townsend social deprivation score, history of diabetes (no previously diagnosed diabetes including prediabetes and undiagnosed, diabetes), and glucose-lowering medication. \*\*The full interaction model is additionally adjusted for interaction terms between each variable and sex. NA = not applicable; BMI = body mass index; HR = hazard ratio; RHR = ratio of hazard ratios; n (%) = number of events.

**Supplemental table VI. Multiple-adjusted hazard ratios and ratios of hazard ratios of myocardial infarction per 1% HbA1c change.**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Women**  **(HR 95% CI)** | **Men**  **(HR 95% CI)** | **Women-to-men RHR (95% CI)** |
| Multiple-adjusted full interaction model\* | 1∙18 (1∙13;1∙24) | 1∙18 (1∙13;1∙23) | 1∙00 (0∙94;1∙07) |
| Multiple-adjusted full interaction model excl. history of diabetes | 1.19 (1.13;1.25) | 1.19 (1.14;1.23) | 1.00 (0.94;1.07) |

**\***The full interaction model is adjusted for age, smoking (never, former, current), BMI, systolic blood pressure, lipid-lowering medication, cholesterol, antihypertensive medication, the Townsend social deprivation score, history of diabetes (no previously diagnosed diabetes including prediabetes and undiagnosed, diabetes), glucose-lowering medication, and interaction terms between each variable and sex. HR = hazard ratio; RHR = ratio of hazard ratios.

**Supplemental table VII. Number (%) of women and men with depression and certain sleep characteristics.**

|  |  |  |
| --- | --- | --- |
|  | **Number (%) of women** | **Number (%) of men** |
| **Use of antidepressants** |  |  |
| Yes | 11,548 (4.4%) | 4,800 (2.3%) |
| No | 251,747 (95.6%) | 203,876 (97.7%) |
| **Told to have depression during the verbal interview1** |  |  |
| Yes | 17,561 (6.7%) | 8,466 (4.1%) |
| No | 245,724 (93.3%) | 200,210 (95.9%) |
| **Told to have depression during the verbal interview OR using antidepressants** |  |  |
| Yes | 22,035 (8.4%) | 10,229 (4.9%) |
| No | 241,260 (91.6%) | 198,447 (95.1%) |
| **Told to have depression during the verbal interview AND using antidepressants** |  |  |
| Yes | 7,074 (2.7%) | 3,037 (1.5%) |
| No | 256,221 (97.3%) | 205,639 (98.5%) |
| **Told to have sleep apnoea during the verbal interview1** |  |  |
| Yes | 354 (0.1%) | 1,025 (0.5%) |
| No | 262,941 (99.9%) | 207,651 (99.5%) |
| **Use of medication to treat insomnia - extensive2** |  |  |
| Yes | 2,533 (1.0%) | 1,277 (0.6%) |
| No | 260,762 (99.0%) | 207,399 (99.4%) |
| **Use of medication to treat insomnia – restricted3** |  |  |
| Yes | 1,992 (0.8%) | 953 (0.5%) |
| No | 261,303 (99.2%) | 207,723 (99.5%) |

**1**“In the touch screen you selected that you have been told by a doctor that you have other (non-cancer) serious illnesses or disabilities, could you now tell me what they are?” asked by a trained nurse during the verbal interview stage of data collection. The nurse used a tree structure organized by system and loosely based on International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10), codes to record a diagnosis of depression or sleep apnoea (UK Biobank field: 20002) using given codes 1286 and 1123 respectively. **2**Participants using the following medication were considered to have trouble sleeping (insomnia): Diazepam, Flunitrazepam, Flurazepam, Loprazolam, Lorazepam, Lormetazepam, Nitrazepam, Oxazepam, Temazepam, Zolpidem, Zoplicon and Zaleplon. **3**Several drugs used to treat insomnia have multiple treatment indications including panic disorders. The variable “use of medication to treat insomnia – restricted” included medication with a more strict indication for insomnia, including: Flunitrazepam, Flurazepam, Loprazolam, Lormetazepam, Nitrazepam, Temazepam, Zolpidem, Zopiclon, and Zaleplon.

**Supplemental table VIII. Multiple-adjusted hazard ratios and ratios of hazard ratios of myocardial infarction according to diabetes status.**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Women**  **(HR 95% CI)** | **Men**  **(HR 95% CI)** | **Women-to men RHR**  **(95% CI)** |
| **Multiple-adjusted – full interaction model\*** |  |  |  |
| No diabetes | 1∙0 | 1∙0 | NA |
| Prediabetes | 1∙248 (1∙112;1∙401) | 1∙170 (1∙080;1∙269) | 1∙067 (0∙927;1∙230) |
| Undiagnosed diabetes | 1∙642 (1∙084;2∙488) | 1∙533 (1∙222;1∙922) | 1∙072 (0∙668;1∙720) |
| Previously diagnosed diabetes | 2∙334 (1∙960;2∙780) | 1∙815 (1∙630;2∙020) | 1∙286 (1∙048;1∙579) |
| **+ use of antidepressants** |  |  |  |
| No diabetes | 1∙0 | 1∙0 | NA |
| Prediabetes | 1∙245 (1∙109;1∙397) | 1∙168 (1∙077;1∙268) | 1∙065 (0∙925;1∙227) |
| Undiagnosed diabetes | 1∙634 (1∙078;2∙475) | 1∙535 (1∙224;1∙926) | 1∙064 (0∙663;1∙708) |
| Previously diagnosed diabetes | 2∙318 (1∙946;2∙760) | 1∙808 (1∙624;2∙012) | 1∙282 (1∙045;1∙574) |
| **+ told to have depression during the verbal interview1** |  |  |  |
| No diabetes | 1∙0 | 1∙0 | NA |
| Prediabetes | 1∙247 (1∙111;1∙400) | 1∙170 (1∙078;1∙269) | 1∙067 (0∙926;1∙229) |
| Undiagnosed diabetes | 1∙637 (1∙081;2∙480) | 1∙533 (1∙222;1∙923) | 1∙068 (0∙665;1∙714) |
| Previously diagnosed diabetes | 2∙333 (1∙959;2∙779) | 1∙814 (1∙630;2∙020) | 1∙286 (1∙048;1∙579) |
| **+ told to have depression during the verbal interview OR using antidepressants** |  |  |  |
| No diabetes | 1∙0 | 1∙0 | NA |
| Prediabetes | 1∙246 (1∙110;1∙398) | 1∙169 (1∙078;1∙268) | 1∙066 (0∙925;1∙228) |
| Undiagnosed diabetes | 1∙643 (1∙085;2∙489) | 1∙533 (1∙222;1∙923) | 1∙072 (0∙668;1∙720) |
| Previously diagnosed diabetes | 2∙327 (1∙954;2∙771) | 1∙811 (1∙627;2∙016) | 1∙285 (1∙047;1∙577) |
| **+ told to have depression during the verbal interview AND using antidepressants** |  |  |  |
| No diabetes | 1∙0 | 1∙0 | NA |
| Prediabetes | 1∙247 (1∙111;1∙400) | 1∙169 (1∙077;1∙268) | 1∙067 (0∙926;1∙229) |
| Undiagnosed diabetes | 1∙631 (1∙077;2∙472) | 1∙535 (1∙224;1∙926) | 1∙063 (0∙662;1∙706) |
| Previously diagnosed diabetes | 2∙329 (1∙956;2∙773) | 1∙811 (1∙627;2∙016) | 1∙286 (1∙048;1∙579) |
| **+ told to have sleep apnoea during the verbal interview1** |  |  |  |
| No diabetes | 1∙0 | 1∙0 | NA |
| Prediabetes | 1∙248 (1∙112;1∙401) | 1∙169 (1∙078;1∙269) | 1∙068 (0∙927;1∙230) |
| Undiagnosed diabetes | 1∙642 (1∙084;2∙488) | 1∙533 (1∙222;1∙923) | 1∙071 (0∙667;1∙719) |
| Previously diagnosed diabetes | 2∙334 (1∙960;2∙780) | 1∙813 (1∙629;2∙019) | 1∙287 (1∙049;1∙581) |
| **+use of medication to treat insomnia - extensive2** |  |  |  |
| No diabetes | 1∙0 | 1∙0 | NA |
| Prediabetes | 1∙252 (1∙115;1∙405) | 1∙170 (1∙078;1∙269) | 1∙070 (0∙929;1∙233) |
| Undiagnosed diabetes | 1∙648 (1∙088;2∙497) | 1∙532 (1∙221;1∙922) | 1∙076 (0∙670;1∙726) |
| Previously diagnosed diabetes | 2∙333 (1∙959;2∙779) | 1∙815 (1∙630;2∙020) | 1∙286 (1∙047;1∙578) |
| **+use of medication to treat insomnia – restricted3** |  |  |  |
| No diabetes | 1∙0 | 1∙0 | NA |
| Prediabetes | 1∙252 (1∙116;1∙406) | 1∙170 (1∙078;1∙269) | 1∙071 (0∙929;1∙233) |
| Undiagnosed diabetes | 1∙647 (1∙087;2∙494) | 1∙532 (1∙222;1∙922) | 1∙074 (0∙669;1∙725) |
| Previously diagnosed diabetes | 2∙338 (1∙963;2∙784) | 1∙815 (1∙630;2∙020) | 1∙288 (1∙050;1∙582) |

**\***The full interaction model is adjusted for age, smoking (never, former, current), BMI, systolic blood pressure, lipid-lowering medication, cholesterol, antihypertensive medication, the Townsend social deprivation score, and interaction terms between each variable and sex. NA = not applicable; HR = hazard ratio; RHR = ratio of hazard ratios.**1**“In the touch screen you selected that you have been told by a doctor that you have other (non-cancer) serious illnesses or disabilities, could you now tell me what they are?” asked by a trained nurse during the verbal interview stage of data collection. The nurse used a tree structure organized by system and loosely based on International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10), codes to record a diagnosis of depression or sleep apnoea (UK Biobank field: 20002) using given codes 1286 and 1123 respectively. **2**Participants using the following medication were considered to have trouble sleeping (insomnia): Diazepam, Flunitrazepam, Flurazepam, Loprazolam, Lorazepam, Lormetazepam, Nitrazepam, Oxazepam, Temazepam, Zolpidem, Zoplicon and Zaleplon. **3**Several drugs used to treat insomnia have multiple treatment indications including panic disorders. The variable “use of medication to treat insomnia – restricted” included medication with a more strict indication for insomnia, including: Flunitrazepam, Flurazepam, Loprazolam, Lormetazepam, Nitrazepam, Temazepam, Zolpidem, Zopiclon, and Zaleplon.

**Supplemental table IX.**  **Multiple-adjusted hazard ratios and ratios of hazard ratios of MI according to levels of glycaemia.**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Women**  **(HR 95% CI)** | **Men**  **(HR 95% CI)** | **Women-to men RHR**  **(95% CI)** |
| **Multiple-adjusted – full interaction model\*** |  |  |  |
| No previously diagnosed diabetes± | 1∙0 | 1∙0 | NA |
| HbA1c ≤6∙5% | 1∙319 (0∙949;1∙833) | 1∙207 (0∙994;1∙465) | 1∙093 (0∙746;1∙602) |
| HbA1c >6∙5% - ≤7∙5% | 1∙631 (1∙095;2∙430) | 1∙465 (1∙161;1∙849) | 1∙113 (0∙702;1∙767) |
| HbA1c >7∙5% | 2∙404 (1∙614;3∙583) | 1∙943 (1∙532;2∙465) | 1∙237 (0∙778;1∙968) |
| **+ use of antidepressants** |  |  |  |
| No previously diagnosed diabetes± | 1∙0 | 1∙0 | NA |
| HbA1c ≤6∙5% | 1∙310 (0∙943;1∙821) | 1∙203 (0∙991;1∙461) | 1∙089 (0∙743;1∙596) |
| HbA1c >6∙5% - ≤7∙5% | 1∙646 (1∙105;2∙42) | 1∙469 (1∙164;1∙853) | 1∙121 (0∙706;1∙778) |
| HbA1c >7∙5% | 2∙414 (1∙619;3∙601) | 1∙942 (1∙531;2∙464) | 1∙243 (0∙781;1∙980) |
| **+ told to have depression during the verbal interview1** |  |  |  |
| No previously diagnosed diabetes± | 1∙0 | 1∙0 | NA |
| HbA1c ≤6∙5% | 1∙313 (0∙945;1∙825) | 1∙206 (0∙994;1∙465) | 1∙088 (0∙743;1∙595) |
| HbA1c >6∙5% - ≤7∙5% | 1∙636 (1∙098;2∙438) | 1∙469 (1∙164;1∙854) | 1∙114 (0∙702;1∙768) |
| HbA1c >7∙5% | 2∙406 (1∙614;3∙587) | 1∙947 (1∙535;2∙470) | 1∙236 (0∙776;1∙967) |
| **+ told to have depression during the verbal interview OR using antidepressants** |  |  |  |
| No previously diagnosed diabetes± | 1∙0 | 1∙0 | NA |
| HbA1c ≤6∙5% | 1∙308 (0∙941;1∙818) | 1∙204 (0∙992;1∙462) | 1∙086 (0∙741;1∙591) |
| HbA1c >6∙5% - ≤7∙5% | 1∙647 (1∙105;2∙455) | 1∙469 (1∙164;1∙853) | 1∙121 (0∙707;1∙780) |
| HbA1c >7∙5% | 2∙415 (1∙619;3∙603) | 1∙944 (1∙532;2∙466) | 1∙243 (0∙780;1∙979) |
| **+ told to have depression during the verbal interview AND using antidepressants** |  |  |  |
| No previously diagnosed diabetes± | 1∙0 | 1∙0 | NA |
| HbA1c ≤6∙5% | 1∙315 (0∙946;1∙828) | 1∙205 (0∙993;1∙464) | 1∙091 (0∙745;1∙599) |
| HbA1c >6∙5% - ≤7∙5% | 1∙634 (1∙096;2∙435) | 1∙470 (1∙165;1∙855) | 1∙112 (0∙700;1∙764) |
| HbA1c >7∙5% | 2∙404 (1∙613;3∙584) | 1∙946 (1∙534;2∙469) | 1∙235 (0∙776;1∙966) |
| **+ told to have sleep apnoea during the verbal interview1** |  |  |  |
| No previously diagnosed diabetes± | 1∙0 | 1∙0 | NA |
| HbA1c ≤6∙5% | 1∙319 (0∙949;1∙833) | 1∙206 (0∙993;1∙464) | 1∙094 (0∙746;1∙603) |
| HbA1c >6∙5% - ≤7∙5% | 1∙631 (1∙095;2∙430) | 1∙465 (1∙161;1∙849) | 1∙113 (0∙702;1∙767) |
| HbA1c >7∙5% | 2∙404 (1∙614;3∙583) | 1∙940 (1∙530;2∙461) | 1∙239 (0∙779;1∙971) |
| **+use of medication to treat insomnia - extensive2** |  |  |  |
| No previously diagnosed diabetes± | 1∙0 | 1∙0 | NA |
| HbA1c ≤6∙5% | 1∙315 (0∙946;1∙828) | 1∙206 (0∙994;1∙465) | 1∙090 (0∙744;1∙598) |
| HbA1c >6∙5% - ≤7∙5% | 1∙632 (1∙095;2∙431) | 1∙465 (1∙161;1∙848) | 1∙114 (0∙702;1∙768) |
| HbA1c >7∙5% | 2∙416 (1∙621;3∙601) | 1∙943 (1∙532;2∙465) | 1∙243 (0∙781;1∙978) |
| **+use of medication to treat insomnia – restricted3** |  |  |  |
| No previously diagnosed diabetes± | 1∙0 | 1∙0 | NA |
| HbA1c ≤6∙5% | 1∙315 (0∙946;1∙827) | 1∙207 (0∙994;1∙465) | 1∙089 (0∙743;1∙597) |
| HbA1c >6∙5% - ≤7∙5% | 1∙632 (1∙095;2∙431) | 1∙465 (1∙161;1∙849) | 1∙114 (0∙702;1∙767) |
| HbA1c >7∙5% | 2∙412 (1∙619;3∙595) | 1∙944 (1∙532;2∙465) | 1∙241 (0∙780;1∙975) |

**\***The full interaction model is adjusted for age, smoking (never, former, current), BMI, systolic blood pressure, lipid-lowering medication, cholesterol, antihypertensive medication, the Townsend social deprivation score, glucose-lowering medication, and interaction terms between each variable and sex. ±No previously diagnosed diabetes, including prediabetes and undiagnosed diabetes.NA = not applicable; HR = hazard ratio; RHR = ratio of hazard ratios. HbA1c 6.5% = 48mmol/mol; HbA1c 7.5% = 58mmol/mol. **1**“In the touch screen you selected that you have been told by a doctor that you have other (non-cancer) serious illnesses or disabilities, could you now tell me what they are?” asked by a trained nurse during the verbal interview stage of data collection. The nurse used a tree structure organized by system and loosely based on International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10), codes to record a diagnosis of depression or sleep apnoea (UK Biobank field: 20002) using given codes 1286 and 1123 respectively. **2**Participants using the following medication were considered to have trouble sleeping (insomnia): Diazepam, Flunitrazepam, Flurazepam, Loprazolam, Lorazepam, Lormetazepam, Nitrazepam, Oxazepam, Temazepam, Zolpidem, Zoplicon and Zaleplon. **3**Several drugs used to treat insomnia have multiple treatment indications including panic disorders. The variable “use of medication to treat insomnia – restricted” included medication with more strict indication for insomnia, including: Flunitrazepam, Flurazepam, Loprazolam, Lormetazepam, Nitrazepam, Temazepam, Zolpidem, Zopiclon, and Zaleplon.

**Supplemental table X. Multiple-adjusted hazard ratios and ratios of hazard ratios of myocardial infarction per 1% HbA1c change.**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Women**  **(HR 95% CI)** | **Men**  **(HR 95% CI)** | **Women-to-men RHR (95% CI)** |
| **Multiple-adjusted full interaction model\*** | 1∙184 (1∙126;1∙245) | 1∙179 (1∙134;1∙226) | 1∙004 (0∙942;1∙070) |
| + use of antidepressants | 1∙184 (1∙126;1∙246) | 1∙179 (1∙134;1∙226) | 1∙004 (0∙942;1∙070) |
| + told to have depression during the verbal interview1 | 1.185 (1.127;1.246) | 1∙180 (1∙134;1∙227) | 1∙004 (0∙942;1∙070) |
| + told to have depression during the verbal interview OR using antidepressants | 1.185 (1.127;1.246) | 1∙180 (1∙134;1∙227) | 1∙005 (0∙942;1∙071) |
| + told to have depression during the verbal interview AND using antidepressants | 1.184 (1.126;1.245) | 1∙180 (1∙134;1∙227) | 1∙004 (0∙942;1∙070) |
| + told to have sleep apnoea during the verbal interview1 | 1.184 (1.126;1.245) | 1∙179 (1∙134;1∙226) | 1∙004 (0∙942;1∙070) |
| +use of medication to treat insomnia - extensive2 | 1.185 (1.127;1.246) | 1∙179 (1∙134;1∙226) | 1∙005 (0∙943;1∙071) |
| +use of medication to treat insomnia – restricted3 | 1.185 (1.127;1.246) | 1∙179 (1∙134;1∙226) | 1∙005 (0∙943;1∙071) |

**\*** The full interaction model is adjusted for age, smoking (never, former, current), BMI, systolic blood pressure, lipid-lowering medication, cholesterol, antihypertensive medication, the Townsend social deprivation score, history of diabetes (no previously diagnosed diabetes including prediabetes and undiagnosed, diabetes), glucose-lowering medication, and interaction terms between each variable and sex. HR = hazard ratio; RHR = ratio of hazard ratios. **1**“In the touch screen you selected that you have been told by a doctor that you have other (non-cancer) serious illnesses or disabilities, could you now tell me what they are?” asked by a trained nurse during the verbal interview stage of data collection. The nurse used a tree structure organized by system and loosely based on International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10), codes to record a diagnosis of depression or sleep apnoea (UK Biobank field: 20002) using given codes 1286 and 1123 respectively. **2**Participants using the following medication were considered to have trouble sleeping (insomnia): Diazepam, Flunitrazepam, Flurazepam, Loprazolam, Lorazepam, Lormetazepam, Nitrazepam, Oxazepam, Temazepam, Zolpidem, Zoplicon and Zaleplon. **3**Several drugs used to treat insomnia have multiple treatment indications including panic disorders. The variable “use of medication to treat insomnia – restricted” included medication with more strict indication for insomnia, including: Flunitrazepam, Flurazepam, Loprazolam, Lormetazepam, Nitrazepam, Temazepam, Zolpidem, Zopiclon, and Zaleplon.

**Supplemental table XI. Multiple-adjusted hazard ratios and ratios of hazard ratios of myocardial infarction per 1% HbA1c change, stratified by depression and sleep characteristics.**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Women**  **(HR 95% CI)\*\*** | **Men**  **(HR 95% CI)\*\*** | **Women-to-men RHR (95% CI)\*\*\*** |
| **Multiple-adjusted full interaction model\*** | 1∙184 (1∙126;1∙245) | 1∙179 (1∙134;1∙226) | 1∙004 (0∙942;1∙070) |
| **Use of antidepressants** |  |  |  |
| Yes | 1.196 (1.139;1.255) | 1.187 (1.142;1.234) | 1.007 (0.946;1.072) |
| No | 1.001 (0.837;1.199) | 0.947 (0.789;1.136) | 1.058 (0.819;1.366) |
| P for interaction | 0.054 | 0.015 | 0.708 |
| **Told to have depression during the verbal interview1** |  |  |  |
| Yes | 1.190 (1.133;1.250) | 1.185 (1.139;1.232) | 1.00 (0.943;1.070) |
| No | 1.061 (0.869;1.294) | 1.054 (0.898;1.238) | 1.006 (0.779;1.298) |
| P for interaction | 0.257 | 0.155 | 0.992 |
| **Told to have depression during the verbal interview OR using antidepressants** |  |  |  |
| Yes | 1.196 (1.129;1.255) | 1.187 (1.142;1.235) | 1.007 (0.946;1.072) |
| No | 1.048 (0.897;1.225) | 1.043 (0.909;1.197) | 1.005 (0.816;1.237) |
| P for interaction | 0.099 | 0.066 | 0.985 |
| **Told to have depression during the verbal interview AND using antidepressants** |  |  |  |
| Yes | 1,189 (1.132;1.249) | 1.185 (1.139;1.231) | 1.004 (0.943;1.069) |
| No | 1.005 (0.779;1.297) | 0.900 (0.706;1.148) | 1,117 (0.785;1.588) |
| P for interaction | 0.197 | 0.026 | 0.551 |
| **Told to have sleep apnoea during the verbal interview1** |  |  |  |
| Yes | 1.185 (1.127;1.245) | 1.180 (1.134;1.227) | 1.004 (0.943;1.070) |
| No | 0.750 (0.218;2.585) | 1.124 (0.854;1.479) | 0.667 (0.188;2.370) |
| P for interaction | 0.469 | 0.730 | 0.527 |
| **Use of medication to treat insomnia - extensive2** |  |  |  |
| Yes | 1.186 (1.128;1.247) | 1.181 (1.1,135;1.228) | 1.005 (0.943;1.070) |
| No | 1.134 (0.817;1.573) | 1.063 (0.782;1.445) | 1.066 (0.681;1.670) |
| P for interaction | 0.787 | 0.504 | 0.794 |
| **Use of medication to treat insomnia – restricted3** |  |  |  |
| Yes | 1.184 (1.126;1.246) | 1.179 (1.134;1.226) | 1.004 (0.942;1.071) |
| No | 1.260 (0.925;1.716) | 1.179 (0.869;1.599) | 1.069 (0.692;1,650) |
| P for interaction | 0.696 | 0.999 | 0.780 |

\*The full interaction model is adjusted for age plus smoking (never, former, current), BMI, systolic blood pressure, lipid-lowering medication, cholesterol, antihypertensive medication, the Townsend social deprivation score, history of diabetes (no previously diagnosed diabetes including prediabetes and undiagnosed, diabetes), glucose-lowering medication, and interaction terms between each variable and sex. HR = hazard ratio; RHR = ratio of hazard ratios. **1**“In the touch screen you selected that you have been told by a doctor that you have other (non-cancer) serious illnesses or disabilities, could you now tell me what they are?” asked by a trained nurse during the verbal interview stage of data collection. The nurse used a tree structure organized by system and loosely based on International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10), codes to record a diagnosis of depression or sleep apnoea (UK Biobank field: 20002) using given codes 1286 and 1123 respectively. **2**Participants using the following medication were considered to have trouble sleeping (insomnia): Diazepam, Flunitrazepam, Flurazepam, Loprazolam, Lorazepam, Lormetazepam, Nitrazepam, Oxazepam, Temazepam, Zolpidem, Zoplicon and Zaleplon. **3**Several drugs used to treat insomnia have multiple treatment indications including panic disorders. The variable “use of medication to treat insomnia – restricted” included medication with more strict indication for insomnia, including: Flunitrazepam, Flurazepam, Loprazolam, Lormetazepam, Nitrazepam, Temazepam, Zolpidem, Zopiclon, and Zaleplon \*\*P-values for the sex-specific hazard ratios represent the two-way interaction terms including HbA1c and the variable that was stratified for. \*\*\*P-values for the women-to-men hazard ratios represent the three-way interaction terms including sex, HbA1c and the variable that was stratified for.