**Supplemental Material**

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**Supplemental Methods**

**Data linkage**

Approximately 75% of English CPRD practices have consented to participate in a linkage scheme, providing linked patient-level data from sources including the Office for National Statistics (ONS) for mortality information, Hospital Episode Statistics (HES) for hospitalisation data and deprivation data (Index of Multiple Deprivation (IMD 2010)).1 The IMD is a measure of deprivation at the small area level (Lower Layer Super Output Area (LSOA)), which is made up of 7 domain indices related to: income, employment, health, education, housing and crime.2 Patient-level IMD information is available for the subgroup of English practices that have consented to linkage, based on LSOA of residence.

Due to this restriction in participating practices, linkage reduces the sample size and may result in a loss of geographical generalisability; however, combining data sources can provide a more enriched and comprehensive dataset.3,4 Importantly, linking to hospital and death records allows for identification of further cases of MACE.3 Recording of secondary care information into patient primary care records is generally inputted manually from hospital discharge letters or referral notes. This can result in under-recording, inaccuracies, and delays in the recording of diagnoses made in secondary care. 3 A comparison between CPRD and secondary care data on the incidence of myocardial infarction identified a 25% lower rate when using CPRD data alone compared to using fully-linked data. 3 Using a combination of CPRD, HES, and ONS data was particularly important for this study to try and reduce the potential of underestimation of cardiovascular events and identification of cardiovascular deaths.

**Definition of baseline biological variables**

To increase data availability for defining obesity and chronic kidney disease, diagnostic Read codes and test values were sourced. Obesity was defined using Read codes indicative of obesity and body mass index measurements (BMI≥30 kg/m2). Chronic kidney disease was defined using Read codes for stage 3 and above or an estimated glomerular filtration rate < 60 ml/min.

Elevated HbA1c was defined as a value >7% (53mmol/mol) and >8% (64mmol/mol). These HbA1c levels were chosen as they correspond to the recommended HbA1c targets in the National Institute for Health and Care Excellence (NICE) guidelines for management of type 2 diabetes.5 High blood pressure was defined as measurements >140/80mmHg or >130/80mmHg in those with target organ damage. Hypercholesterolaemia was defined as total cholesterol>4mmol/L or LDL cholesterol>2mmol/L.

Microalbuminuria was defined as an albumin:creatinine ratio (ACR) value of 3.5-30 mg/mmol in women and 2.5-30 mg/mmol in men. Proteinuria was defined as an ACR value > 30 mg/mmol or a protein:creatinine ratio (PCR) value > 40 mg/mmol.

**Definition of baseline risk factor control**

Recorded HbA1c, blood pressure and cholesterol measurements were used to define risk factor control.

Baseline hyperglycaemia (HbA1c >7% [53mmol/mol]), hypertension (blood pressure >140/80mmHg or >130/80mmHg for those with target organ damage) and hypercholesterolaemia (total cholesterol>4mmol/L or LDL cholesterol>2mmol/L) were defined as 2 consecutive test values above the threshold cut-offs, up to 6 months before and 3 months after the index date (diabetes diagnosis date or corresponding index date for controls).

The proportion of T2DM patients with missing data on risk factors at baseline was 17.8% for hyperglycaemia, 29.5% for hypertension and 65.8% for elevated cholesterol.

**Charlson Comorbidity Index (CCI)**

Comparison of original CCI to the CCI used in this study. Diabetes and cardiovascular conditions were excluded from the score.

The CCI was defined at baseline using Read codes, up to the index date.

|  |  |
| --- | --- |
| **Original CCI** | **CCI used in this study** |
| **Comorbid condition** | **Weight** | **Comorbid condition** | **Weight** |
| Myocardial infarction | 1 | - | - |
| Congestive heart failure | 1 | - | - |
| Peripheral vascular disease | 1 | - | - |
| Cerebrovascular disease | 1 | - | - |
| Dementia | 1 | Dementia | 1 |
| Chronic pulmonary disease | 1 | Chronic pulmonary disease | 1 |
| Connective tissue disease | 1 | Connective tissue disease | 1 |
| Diabetes without complications | 1 | - | - |
| Peptic ulcer disease | 1 | Peptic ulcer disease | 1 |
| Mild liver disease | 1 | Mild liver disease | 1 |
|  |  |  |  |
| Hemiplegia | 2 | Hemiplegia | 2 |
| Moderate or severe renal disease | 2 | Moderate or severe renal disease | 2 |
| Diabetes with complications | 2 | - | - |
| Cancer | 2 | Cancer | 2 |
|  |  |  |  |
| Moderate or severe liver disease | 3 | Moderate or severe liver disease | 3 |
|  |  |  |  |
| Metastatic solid tumour | 6 | Metastatic solid tumour | 6 |
| AIDS | 6 | AIDS | 6 |

**Multiple Imputation**

Multiple imputation was implemented using the two-fold fully conditional specification algorithm to impute missing longitudinal data (annual measurements for obesity, hypertension, hypercholesterolaemia and raised HbA1c). This algorithm has been validated for use in electronic health care databases where the pattern of missing longitudinal data tends to be intermittent and potentially non-monotonic.6,7 Missing values at a specific time point are imputed from a model using information from that time point and immediately adjacent time points (default time window width is 1).6,7 This approach increases the plausibility of the missing at random assumption by using repeated measures over time.5

Imputation models were estimated separately for men and women with a 2-year time window around missing data time points used. We implemented a time window width of 2 to increase the availability of information being used to impute missing values. In a simulation study this increase in time window width to 2 showed slight improvements in bias and precision compared to a time window width of 1.8 Data measurements past 2 years were unlikely to provide substantial additional information. Factors included in the imputation model were: age, diabetes status, ethnicity, deprivation, calendar year, history of cardiovascular disease at index date, baseline measures of smoking status, obesity, HbA1c, hypertension and hypercholesterolaemia, longitudinal measures of smoking status, obesity, HbA1c, hypertension and hypercholesterolaemia and the cardiovascular outcome. Five imputed datasets were generated and combined.

**Sensitivity Analyses**

*Major cardiovascular event risk associated with diabetes*

Data was stratified into two time periods, diabetes diagnoses between 2007-2010 and 2011-2013 to allow for comparison between a time period close to the introduction and implementation of guidelines and QOF and a later period.

Sex-specific hazard ratios were estimated from Cox proportional hazard models in both time periods for the primary (MI, stroke and cardiovascular death) and secondary outcomes (fatal/non-fatal MI and non-fatal stroke) in people with type 2 diabetes compared to controls without diabetes. Four models were applied; 1) unadjusted, 2) adjusted for baseline calendar year, age, ethnicity, and deprivation, 3) additional adjustment for baseline smoking, obesity, hypertension, hypercholesterolaemia, and Charlson Comorbidity Index, and 4) further adjustment for time-varying smoking, obesity, hypertension, hypercholesterolaemia and raised HbA1c.

*Attainment of Standards of Care*

Prevalent CVD was expected to be greater in men and those with any history of CVD were likely to be treated more aggressively; therefore, we assessed for sex differences within type 2 diabetes groups with and without prevalent CVD for specific standards of care indicators to observe any treatment and management differences. This included the following indicators: “last measured total cholesterol levels below the recommended target of 5 mmol/L”, “last blood pressure ≤140/80mmHg” and “treated with statins”.

We also assessed for sex-related treatment bias in those aged <50 years and ≥50 years in part because some drugs with teratogenic effects are not recommended in women of child-bearing age. This related to the indicators: “treated with ACE inhibitors for microalbuminuria/proteinuria” and “treated with statins”.

Multiple logistic regression models were used to assess sex differences in attainment of standard of care indicators within follow-up time bands.

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**Supplemental Tables**

**Supplemental Table 1. Baseline clinical characteristics of people with type 2 diabetes at diagnosis by CVD status**

|  |  |
| --- | --- |
|  | **T2DM (N=79,985)** |
| **Without CVD (N=63,718)** | **With CVD (N=16,267)** |
| Women | Men | Women | Men |
| **n, %** | 29,348 (46.1) | 34,370 (54.0) | 6,048 (37.2) | 10,219 (62.8) |
| **Age, years** | 62.1±14.2 | 59.0±12.7 | 72.8±11.4 | 68.9±10.7 |
| **Ethnicity** |   |   |   |   |
| White | 22,700 (77.4) | 25,452 (74.1) | 5,390 (89.1) | 9,069 (88.8) |
| South Asian | 1,402 (4.8) | 1,534 (4.5) | 142 (2.4) | 258 (2.5) |
| Black | 714 (2.4) | 668 (1.9) | 70 (1.2) | 80 (0.8) |
| Other | 368 (1.3) | 442 (1.3) | 32 (0.5) | 65 (0.6) |
| Unknown | 4,164 (14.2) | 6,274 (18.3) | 414 (6.9) | 747 (7.3) |
| **Deprivation** |   |   |   |   |
| IMD 1 (least deprived) | 5,390 (18.4) | 6,925 (20.2) | 940 (15.5) | 1,885 (18.5) |
| IMD 2 | 6,288 (21.4) | 7,884 (22.9) | 1,336 (22.1) | 2,341 (22.9) |
| IMD 3 | 5,915 (20.2) | 6,970 (20.3) | 1,148 (19.0) | 2,069 (20.3) |
| IMD 4 | 6,284 (21.4) | 6,894 (20.1) | 1,330 (22.0) | 2,067 (20.2) |
| IMD 5 (most deprived) | 5,426 (18.5) | 5,666 (16.5) | 1,282 (21.2) | 1,844 (18.0) |
| Unknown | 45 (0.2) | 31 (1.0) | 12 (0.2) | 13 (0.1) |
| **Obese** | 15,879 (54.1) | 17,395 (50.6) | 2,638 (43.6) | 4,616 (45.2) |
| **Smoking** |   |   |   |   |
| Current | 8,698 (29.5) | 14,617 (42.5) | 2,505 (41.4) | 6,266 (61.3) |
| Ex-smoker | 8,285 (28.3) | 9,182 (26.7) | 1,638 (27.1) | 2,382 (23.3) |
| Never  | 1,692 (5.8) | 1,218 (3.5) | 300 (5.0) | 250 (2.5) |
| Unknown | 10,673 (36.4) | 9,353 (27.2) | 1,605 (26.5) | 1,321 (12.9) |
| **HbA1c >7% (53mmol/mol)** | 13,413 (45.7) | 17,604 (51.2) | 2,406 (39.8) | 4,263 (41.7) |
| **HbA1c >8% (64mmol/mol)** | 7,733 (26.4) | 11,490 (33.4) | 1,111 (18.4) | 2,109 (20.6) |
| **BP>140/80 mmHg** | 9,281 (31.6) | 12,025 (35.0) | 1,401 (23.2) | 2,174 (21.3) |
| **BP>130/80 mmHg** | 13,208 (45.0) | 15,978 (46.5) | 2,369 (39.2) | 3,660 (35.8) |
| with target organ damage | 3,009 (10.3) | 1,889 (5.5) | 1,528 (25.3) | 1,771 (17.3) |
| **Hypercholesterolaemia\***  | 7,709 (26.3) | 8,406 (24.5) | 1,264 (20.9) | 1,838 (18.0) |
| **Risk factors in control †** |   |   |   |   |
| 1 RF in control | 12,024 (41.0) | 13,223 (38.5) | 2,585 (42.7) | 4,305 (42.1) |
| 2 RF in control | 3,711 (12.6) | 3,689 (10.7) | 1,105 (18.3) | 2,126 (20.8) |
| 3 RF in control | 326 (1.1) | 419 (1.2) | 178 (2.9) | 399 (3.9) |
| **Cardiovascular disease** | - | - | 6,048 (100.0) | 10,219 (100.0) |
| Coronary heart disease | - | - | 3,910 (64.7) | 7,506 (73.5) |
| Cerebrovascular disease | - | - | 2,175 (36.0) | 2,737 (26.8) |
| Peripheral vascular disease | - | - | 946 (15.6) | 1,808 (17.7) |
| **Chronic kidney disease** | 5,474 (18.7) | 3,302 (9.6) | 2,447 (40.5) | 2,672 (26.2) |
| **Microalbuminuria or proteinuria** | 2,653 (9.0) | 4,318 (12.6) | 763 (12.6) | 1,605 (15.7) |
| **Peripheral neuropathy** | 241 (0.8) | 331 (1.0) | 102 (1.7) | 196 (1.9) |
| **Retinopathy** | 1,023 (3.5) | 1,334 (3.9) | 255 (4.2) | 491 (4.8) |
| **History of pregnancy** | 9,055 (30.9) | - | 1,257 (20.8) | - |
| **Hormone-replacement therapy** (current use) ‡ | 396 (1.4) | - | 55 (0.9) | - |
| **Oral contraceptives** (current use )‡ | 391 (1.3) | - | 6 (0.1) | - |

Data presented as N(%) or mean±SD \* total cholesterol>4mmol/L or LDL cholesterol>2mmol/L

† HbA1c <7% (53mmol/mol); BP < 130/80mmHg; lipids: total cholesterol<4mmol/L or LDL cholesterol<2mmol/L

‡ Current use defined as prescriptions up to 90 days prior to index date

**Supplemental Table 2. Overall and sex-specific cardiovascular incidence rates in patients with type 2 diabetes and controls**

**a. Including individuals with prevalent CVD**

|  |  |  |
| --- | --- | --- |
|  | **T2DM (N=79,985)** | **Controls (N=386,547)** |
| **All** | **Women (N=35,396)** | **Men (N=44,589)** | **All** | **Women (N=172,994)** | **Men (N=213,553)** |
| **n** | **IR (95% CI)**  | **n** | **IR (95% CI)** | **n** | **IR (95% CI)** | **n** | **IR (95% CI)** | **n** | **IR (95% CI)** | **n** | **IR (95% CI)** |
| **MACE** | 9,806 | 32.6(31.9-33.2) | 4,091 | 30.5(29.6-31.5) | 5,715 | 34.2(33.3-35.1) | 30,226 | 22.0(21.7-22.2) | 12,850 | 20.4(20.0-20.7) | 17,376 | 23.4(23.0-23.7) |
|  ***MI\****  | 6,697 | 22.2(21.7-22.8) | 2,640 | 19.7(19.0-20.5) | 4,057 | 25.3(23.5-25.0) | 17,883 | 13.0(12.8-13.2) | 7,063 | 11.2(10.9-11.5) | 10,820 | 14.5(14.3-14.8) |
|  ***Stroke\**** | 2,016 | 6.7(6.4-7.0) | 963 | 7.2(6.7-7.7) | 1,053 | 6.3(5.9-6.7) | 7,756 | 5.6(5.5-5.8) | 3,750 | 5.9(5.8-6.1) | 4,006 | 5.4(5.2-5.6) |
|  ***Non-fatal MI*** | 6,453 | 21.4(20.9-22.0) | 2,558 | 19.1(18.4-19.9) | 3,895 | 23.3(22.6-24.1) | 16,999 | 12.4(12.2-12.5) | 6,735 | 10.7(10.4-10.9) | 10,264 | 13.8(13.5-14.1) |

IR (incidence rate per 1,000 person-years)

\* fatal and non-fatal events

**b. Excluding individuals with prevalent CVD**

|  |  |  |
| --- | --- | --- |
|  | **T2DM (N=63,718)** | **Controls (N=277,176)** |
| **All** | **Women (N=29,348)** | **Men (N=34,370)** | **All** | **Women (N=130,524)** | **Men (N=146,652)** |
| **n** | **IR (95% CI)**  | **n** | **IR (95% CI)** | **n** | **IR (95% CI)** | **n** | **IR (95% CI)** | **n** | **IR (95% CI)** | **n** | **IR (95% CI)** |
| **MACE** | 4,564 | 18.2 (17.6-18.7) | 2,042 | 17.6(16.8-18.3) | 2,522 | 18.7(18.0-19.4) | 11,665 | 11.4 (11.2-11.6) | 5,364 | 10.9 (10.6-11.2) | 6,301 | 11.9(11.6-12.2) |
|  ***MI\****  | 2,697 | 10.7 (10.3-11.1) | 1,118 | 9.6(9.1-10.2) | 1,579 | 11.7(11.1-12.3) | 6,111 | 6.0(5.8-6.1) | 2,524 | 5.1(4.9-5.3) | 3,587 | 6.8(6.6-7.0) |
|  ***Stroke\**** | 1,230 | 4.9(4.6-5.2) | 621 | 5.3(4.9-5.8) | 609 | 4.5(4.2-4.9) | 3,641 | 3.6(3.5-3.7) | 1,912 | 3.9 (3.7-4.1) | 1,729 | 3.3(3.1-3.4) |
|  ***Non-fatal MI*** | 2,560 | 10.2 (9.8-10.6) | 1,061 | 9.1(8.6-9.7) | 1,499 | 11.1(10.5-11.7) | 5,693 | 5.6 (5.4-5.7) | 2,365 | 4.8(4.6-5.0) | 3,328 | 6.3(6.1-6.5) |

IR (incidence rate per 1,000 person-years)

\* fatal and non-fatal events

**Supplemental Table 3. Unadjusted and multivariable-adjusted hazard ratios for incident CVD comparing people with and without T2DM by sex, including the ratio of risks (RRR) between women and men showing the excess risk for incident CVD in women**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Model | Adjustments |  | **Primary Outcome: MACE** | **Secondary Outcome: MI** **(fatal/non-fatal)** | **Secondary Outcome: non-fatal MI**  | **Secondary Outcome: Stroke (fatal/non-fatal)** |
| Risk of CV associated with the presence of diabetes; **HR (95% CI)** | Ratio of risks between women and men;**RRR (95% CI)** | Risk of CV associated with the presence of diabetes; **HR (95% CI)** | Ratio of risks between women and men;**RRR (95% CI)** | Risk of CV associated with the presence of diabetes; **HR (95% CI)** | Ratio of risks between women and men;**RRR (95% CI)** | Risk of CV associated with the presence of diabetes; **HR (95% CI)** | Ratio of risks between women andmen;**RRR (95% CI)** |
| 1 | Unadjusted | Women | 1.44 (1.36-1.52) | **1.05 (0.98-1.13)** | 1.68 (1.56-1.81) | **1.09 (0.99-1.20)** | 1.82 (1.70-1.96) | **1.08 (0.98-1.18)** | 1.24 (1.13-1.37) | **1.06 (0.92-1.22)** |
| Men | 1.37 (1.31-1.44) | 1.54 (1.45-1.64) | 1.69 (1.59-1.79) | 1.17 (1.06-1.30) |
| 2 | Calendar year, age, ethnicity, deprivation, general practice | Women | 1.36 (1.29-1.44) | **1.08 (1.00-1.16)** | 1.55 (1.44-1.67) | **1.12 (1.01-1.23)** | 1.66 (1.55-1.79) | **1.09 (0.99-1.20)** | 1.18 (1.07-1.30) | **1.04 (0.93-1.18)** |
| Men | 1.26 (1.20-1.33) | 1.39 (1.30-1.48) | 1.52 (1.43-1.61) | 1.13 (1.05-1.21) |
| 3 | Model 2 plus baseline smoking, obesity, hypertension, hypercholesterolaemia, and CCI | Women | 1.23 (1.16-1.32)  | **1.05 (0.97-1.14)**  | 1.35 (1.24-1.48)  | **1.07 (0.95-1.20)**  | 1.45 (1.34-1.58)  | **1.05 (0.94-1.17)**  | 1.15 (1.03-1.28) | **1.06 (0.93-1.22)** |
| Men | 1.17 (1.11-1.23)  | 1.26 (1.17-1.36)  | 1.38 (1.29-1.48)  | 1.08 (1.00-1.17) |
| 4 | Model 3 plus time-varying smoking, obesity, hypertension, hypercholesterolaemia and raised HbA1c | Women | 1.20 (1.12-1.28)  | **1.07 (0.98-1.17)**  | 1.31 (1.20-1.43)  | **1.09 (0.98-1.22)**  | 1.40 (1.29-1.53)  | **1.06 (0.95-1.18)**  | 1.13 (1.01-1.26)  | **1.09 (0.93-1.28)**  |
| Men | 1.12 (1.06-1.19)  | 1.20 (1.12-1.28)  | 1.32 (1.23-1.41)  | 1.04 (0.92-1.16)  |

 *Ratio of relative risks (RRR) greater than 1 indicates an excess risk for incident cardiovascular disease in women who developed diabetes compared to men who developed diabetes*

**Supplemental Table 4. Unadjusted and multivariable-adjusted hazard ratios for incident CVD comparing people with and without T2DM by sex, including the ratio of risks (RRR) between women and men showing the excess risk for incident CVD in women stratified by year of diagnosis**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Model | Adjustments |  | **Primary Outcome: MACE** | **Secondary Outcome: MI** **(fatal/non-fatal)** | **Secondary Outcome: Stroke (fatal/non-fatal)** |
| Risk of CV associated with the presence of diabetes; **HR (95% CI)** | Ratio of risks between women and men;**RRR (95% CI)** | Risk of CV associated with the presence of diabetes; **HR (95% CI)** | Ratio of risks between women and men;**RRR (95% CI)** | Risk of CV associated with the presence of diabetes; **HR (95% CI)** | Ratio of risks between women and men;**RRR (95% CI)** |
| 1 | Unadjusted | Women | 1.46 (1.36-1.58) | **1.07 (0.96-1.18)** | 1.77 (1.60-1.96) | **1.17 (1.03-1.34)** | 1.20 (1.05-1.37) | **0.96 (0.80-1.16)** |
| Men | 1.37 (1.28-1.47) | 1.51 (1.39-1.65) | 1.25 (1.10-1.43) |
| 2 | Calendar year, age, ethnicity, deprivation, general practice | Women | 1.38 (1.28-1.48) | **1.10 (0.99-1.21)** | 1.64 (1.48-1.82) | **1.22 (1.07-1.40)** | 1.12 (0.98-1.28) | **0.97 (0.80-1.17)** |
| Men | 1.26 (1.18-1.35) | 1.34 (1.23-1.47) | 1.16 (1.02-1.33) |
| 3 | Model 2 plus baseline smoking, obesity, hypertension, hypercholesterolaemia, and CCI | Women | 1.26 (1.16-1.38) | **1.08 (0.96-1.21)** | 1.44 (1.28-1.62) | **1.16 (0.99-1.36)** | 1.12 (0.96-1.30) | **1.01 (0.82-1.25)** |
| Men | 1.17 (1.08-1.27) | 1.24 (1.12-1.38) | 1.11 (0.96-1.29) |
| 4 | Model 3 plus time-varying smoking, obesity, hypertension, hypercholesterolaemia and raised HbA1c | Women | 1.22 (1.12-1.33) | **1.09 (0.97-1.22)** | 1.39 (1.24-1.57) | **1.19 (1.01-1.39)** | 1.09 (0.94-1.27) | **1.00 (0.82-1.23)** |
| Men | 1.12 (1.04-1.20) | 1.17 (1.05-1.30) | 1.09 (0.95-1.25) |

**a. 2007-2010**

*Ratio of relative risks (RRR) greater than 1 indicates an excess risk for incident cardiovascular disease in women who developed diabetes compared to men who developed diabetes*

**b. 2011-2013**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Model | Adjustments |  | **Primary Outcome: MACE** | **Secondary Outcome: MI** **(fatal/non-fatal)** | **Secondary Outcome: Stroke (fatal/non-fatal)** |
| Risk of CV associated with the presence of diabetes; **HR (95% CI)** | Ratio of risks between women and men;**RRR (95% CI)** | Risk of CV associated with the presence of diabetes; **HR (95% CI)** | Ratio of risks between women and men;**RRR (95% CI)** | Risk of CV associated with the presence of diabetes; **HR (95% CI)** | Ratio of risks between women and men;**RRR (95% CI)** |
| 1 | Unadjusted | Women | 1.52 (1.32-1.75) | **0.95 (0.79-1.14)** | 1.67 (1.37-2.03) | **0.94 (0.73-1.20)** | 1.61 (1.28-2.02) | **1.29 (0.93-1.79)** |
| Men | 1.60 (1.42-1.80) | 1.78 (1.53-2.07) | 1.25 (0.99-1.58) |
| 2 | Calendar year, age, ethnicity, deprivation, general practice | Women | 1.45 (1.25-1.67) | **1.00 (0.83-1.21)** | 1.52 (1.24-1.86) | **0.97 (0.75-1.26)** | 1.60 (1.27-2.03) | **1.36 (0.97-1.90)** |
| Men | 1.45 (1.28-1.64) | 1.56 (1.33-1.82) | 1.18 (0.93-1.50) |
| 3 | Model 2 plus baseline smoking, obesity, hypertension, hypercholesterolaemia, and CCI | Women | 1.31 (1.11-1.53) | **0.94 (0.76-1.17)** | 1.38 (1.10-1.72) | **0.97 (0.72-1.31)** | 1.43 (1.11-1.85) | **1.15 (0.79-1.69)** |
| Men | 1.39 (1.20-1.60) | 1.42 (1.17-1.72) | 1.24 (0.93-1.64) |
| 4 | Model 3 plus time-varying smoking, obesity, hypertension, hypercholesterolaemia and raised HbA1c | Women | 1.27 (1.07-1.49) | **0.94 (0.75-1.18)** | 1.33 (1.04-1.68) | **0.98 (0.72-1.33)** | 1.41 (1.07-1.84) | **1.13 (0.74-1.72)** |
| Men | 1.35 (1.16-1.58) | 1.36 (1.12-1.66) | 1.25 (0.90-1.73) |

*Ratio of relative risks (RRR) greater than 1 indicates an excess risk for incident cardiovascular disease in women who developed diabetes compared to men who developed diabetes*

**Supplemental Table 5. Comparisons between women and men of the proportion and rate of risk factor checks, risk factor levels, interventions, and prescriptions from the diagnosis of T2DM up to 7 years after diagnosis**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Risk factor checks, levels, interventions and prescriptions** | **Year 1** | **Years 2-3** | **Years 4-5** | **Years 6-7** |
| **Women** | **Men** | **Women** | **Men** | **Women** | **Men** | **Women** | **Men** |
| **n (%)** | 35,396 (44.3) | 44,589(55.8) | 24,957 (44.3) | 31,352 (55.7) | 14,996 (44.6) | 18,667 (55.5) | 7,614 (45.1) | 9,257(54.9) |
| **No. of consultations/person/year** |  |  |  |  |  |  |  |  |  |
| Face-to-face interactions | 15 | 13 | 10 | 7 | 10 | 8 | 10 | 8 |
| Telephone interactions | 1.1 | 0.8 | 0.7 | 0.5 | 0.8 | 0.6 | 0.8 | 0.6 |
| **No. of risk factor checks/person/year** |  |  |  |  |  |  |  |  |  |
| HbA1c tests | 2.09 | 2.04 | 1.32 | 1.26 | 1.28 | 1.24 | 1.28 | 1.24 |
| Blood pressure checks | 3.49 | 3.32 | 2.04 | 1.82 | 1.92 | 1.77 | 1.82 | 1.70 |
| Lipids checks | 1.75 | 1.80 | 1.01 | 0.99 | 0.96 | 0.96 | 0.92 | 0.94 |
| BMI measured | 2.67 | 2.37 | 1.44 | 1.21 | 1.33 | 1.18 | 1.25 | 1.14 |
| Smoking cessation discussed | 0.50 | 0.52 | 0.32 | 0.31 | 0.31 | 0.32 | 0.29 | 0.32 |
| **Risk factors levels** |  |  |  |  |  |  |  |  |  |
| HbA1c >7% (53mmol/mol), % | 54.1 | 57.9 | 46.5 | 50.3 | 49.3 | 52.8 | 48.6 | 51.6 |
| HbA1c >8% (64mmol/mol), % | 30.0 | 35.8 | 22.5 | 26.0 | 25.6 | 28.7 | 26.6 | 29.0 |
|  |  |  |  |  |  |  |  |  |
| Blood pressure >140/80, % | 53.8 | 53.5 | 44.0 | 43.2 | 37.9 | 37.2 | 30.0 | 29.3 |
|  *On BP medication* | 79.8 | 76.7 | 84.5 | 83.4 | 86.5 | 85.7 | 88.9 | 87.6 |
|  |  |  |  |  |  |  |  |  |
| Blood pressure >130/80, % | 67.7 | 66.7 | 59.5 | 58.6 | 54.6 | 53.9 | 47.0 | 46.0 |
|  *On BP medication* | 78.2 | 75.1 | 82.7 | 81.4 | 84.7 | 83.3 | 87.3 | 85.6 |
|  |  |  |  |  |  |  |  |  |
| Blood pressure >130/80 and end organ damage, % | 25.0 | 15.8 | 26.9 | 19.4 | 27.2 | 20.6 | 26.1 | 19.4 |
|  *On BP medication* | 90.7 | 90.4 | 90.9 | 89.6 | 90.8 | 89.4 | 92.1 | 90.4 |
|  |  |  |  |  |  |  |  |  |
| Cholesterol >target (LDL>2 or TC>4), % | 55.6 | 48.5 | 45.7 | 36.0 | 38.1 | 28.8 | 29.8 | 21.5 |
|  *On lipid-lowering medication* | 70.0 | 69.8 | 76.0 | 74.8 | 75.6 | 76.9 | 76.3 | 77.6 |
|  |  |  |  |  |  |  |  |  |
| Obese, % | 57.0 | 54.1 | 50.5 | 46.8 | 48.0 | 44.3 | 42.4 | 40.0 |
|  |  |  |  |  |  |  |  |  |
| Current smoking, % | 13.9 | 15.5 | 11.8 | 12.9 | 10.8 | 11.6 | 9.1 | 10.3 |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Risk factor checks, levels, interventions and prescriptions** | **Year 1** | **Years 2-3** | **Years 4-5** | **Years 6-7** |
| **Women** |  | **Men** | **Women** | **Men** | **Women** | **Men** | **Women** | **Men** |
| **n (%)** | 35,396 (44.3) |  | 44,589(55.8) | 24,957 (44.3) | 31,352 (55.7) | 14,996 (44.6) | 18,667 (55.5) | 7,614 (45.1) | 9,257 (54.9) |
| **Interventions** |  |  |  |  |  |  |  |  |  |
| Diet intervention offered, % | 59.7 | 60.0 | 51.0 | 50.6 | 53.8 | 54.9 | 64.5 | 63.2 |
| Exercise intervention offered, % | 43.1 | 44. | 39.0 | 39.1 | 37.5 | 38.0 | 33.4 | 33.2 |
| Structured education offered, % | 16.6 | 17.0 | 3.1 | 3.3 | 4.0 | 4.5 | 5.7 | 6.8 |
| Bariatric surgery, % | 0.14 | 0.03 | 0.21 | 0.09 | 0.12 | 0.06 | 0.17 | 0.04 |
| **Drug Prescriptions** |  |  |  |  |  |  |  |  |  |
| **Diabetes** |  |  |  |  |  |  |  |  |
| Any oral hypoglycaemic agent, % | 57.7 | 59.0 | 67.9 | 70.4 | 72.8 | 75.9 | 76.0 | 79.1 |
|  Metformin, % | 52.2 | 53.5 | 60.7 | 64.2 | 64.0 | 68.7 | 66.1 | 71.2 |
|  Sulphonylurea, % | 13.7 | 14.3 | 20.6 | 23.0 | 26.0 | 29.2 | 28.9 | 33.2 |
|  Glitazone, % | 2.1 | 2.0 | 3.9 | 4.3 | 4.8 | 5.5 | 5.0 | 6.1 |
|  DPP4i, % | 1.6 | 1.5 | 6.9 | 6.9 | 10.8 | 11.6 | 13.6 | 15.3 |
|  SGLT2i, % | 0.1 | 0.1 | 0.4 | 0.4 | 0.9 | 0.9 | 1.9 | 1.9 |
|  GLP-1 agonist, % | 0.3 | 0.2 | 2.0 | 1.5 | 3.5 | 2.7 | 4.2 | 3.5 |
|  Meglitinide, % | 0.2 | 0.2 | 0.3 | 0.3 | 0.3 | 0.3 | 0.4 | 0.3 |
|  Insulin, % | 4.4 | 4.2 | 5.5 | 4.8 | 7.5 | 6.4 | 9.9 | 9.1 |
|  Combination, % | 0.6 | 0.8 | 1.1 | 1.5 | 1.2 | 1.8 | 1.2 | 1.7 |
|  |  |  |  |  |  |  |  |  |
| **Antihypertensive agent** |  |  |  |  |  |  |  |  |
|  Any, % | 69.4 | 66.7 | 72.3 | 71.0 | 74.5 | 73.8 | 76.4 | 75.7 |
|  Alpha-blocker, % | 5.3 | 6.4 | 6.4 | 7.9 | 6.9 | 8.5 | 7.4 | 8.9 |
|  Angiotensin II receptor blocker, % | 15.0 | 11.7 | 17.8 | 14.4 | 19.5 | 15.5 | 20.4 | 16.4 |
|  ACE inhibitor, % | 37.1 | 42.9 | 39.7 | 47.1 | 40.6 | 49.2 | 41.8 | 50.1 |
|  Beta-blocker, % | 21.8 | 23.1 | 20.6 | 22.0 | 20.5 | 21.8 | 20.7 | 21.5 |
|  Calcium channel blocker, % | 28.4 | 28.8 | 30.5 | 31.9 | 31.7 | 33.3 | 33.0 | 34.8 |
|  Diuretic: thiazide, potassium  sparing or loop, % | 36.9 | 24.8 | 34.3 | 23.9 | 34.7 | 24.6 | 34.0 | 24.4 |
|  |  |  |  |  |  |  |  |  |
| **Lipid lowering therapy** |  |  |  |  |  |  |  |  |
|  Any, % | 66.5 | 70.4 | 73.8 | 75.9 | 75.2 | 78.2 | 76.3 | 79.5 |
|  Statin, % | 65.2 | 69.1 | 71.8 | 74.5 | 73.0 | 76.4 | 73.7 | 77.5 |
|  Fibrate, % | 1.2 | 1.6 | 1.7 | 2.0 | 1.7 | 2.2 | 1.9 | 2.3 |
|  Ezetimibe, % | 4.1 | 3.6 | 4.8 | 4.0 | 5.2 | 4.3 | 5.7 | 4.4 |
|  Other, % | 2.7 | 2.9 | 3.9 | 3.5 | 3.7 | 3.4 | 3.6 | 3.0 |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Risk factor checks, levels, interventions and prescriptions** | **Year 1** | **Years 2-3** | **Years 4-5** | **Years 6-7** |
| **Women** | **Men** | **Women** | **Men** | **Women** | **Men** | **Women** | **Men** |
| **n (%)** | 35,396 (44.3) | 44,589 (55.8) | 24,957 (44.3) | 31,352 (55.7) | 14,996 (44.6) | 18,667 (55.5) | 7,614 (45.1) | 9,257(54.9) |
| **Antiplatelets** |  |  |  |  |  |  |  |  |
|  Any, % | 30.5 | 36.2 | 30.3 | 36.3 | 29.0 | 35.6 | 28.8 | 35.9 |
|  Aspirin, % | 28.8 | 34.4 | 28.6 | 34.4 | 27.2 | 33.6 | 26.6 | 33.7 |
|  Clopidogrel, % | 3.6 | 4.9 | 3.0 | 4.2 | 3.1 | 4.0 | 3.6 | 3.9 |

Data presented as %,or age-adjusted rate, as indicated

% missing data for risk factor levels;

HbA1c: Baseline 4.2% (women 4.3%, men 4.1%), Years 2-3 11.5% (women 11.3%, men 11.6%); Years 4-5 13.9% (women 14.1%, men 13.7%); Years 6-7 18.8% (women 18.7%, men 18.9%)

Blood Pressure: Baseline 2.3% (women 2.3%, men 2.2%), Years 2-3 9.7% (women 9.2%, men 10.1%); Years 4-5 12.1% (women 11.9%, men 12.3%); Years 6-7 16.9% (women 16.2%, men 17.4%)

Cholesterol: Baseline 4.6% (women 5.1%, men 4.1%), Years 2-3 13.2% (women 13.0%, men 13.4%); Years 4-5 16.0% (women 16.2%, men 15.9%); Years 6-7 22.0% (women 22.0%, men 22.1%)

Obesity: Baseline 6.9% (women 7.7%, men 6.3%), Years 2-3 15.1% (women 15.3%, men 14.9%); Years 4-5 17.9% (women 18.2%, men 17.5%); Years 6-7 24.4% (women 24.8%, men 24.1%)

**Supplemental Table 6.** **Comparisons between women and men of risk factor checks, risk factor levels, interventions, and prescriptions from the diagnosis of T2DM to 7 years after diagnosis – analysis stratified by CVD status**

**a. with CVD (from baseline and through follow-up)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Risk factor checks, levels, interventions and prescriptions** | **Year 1** | **Years 2-3** | **Years 4-5** | **Years 6-7** |
| **Women****N=35,396** | **Men****N=44,589** | **Women****N=24,957** | **Men****N=31,352** | **Women****N=14,996** | **Men****N=18,667** | **Women****N=7,614** | **Men****N=9,257** |
| **n (%)** | 6,587 (18.6) | 10,897 (24.4) | 3,939 (15.8) | 6,871 (21.9) | 2,115 (14.1) | 3,723 (19.9) | 945 (12.4) | 1,657 (17.9) |
| **No. of consultations/person/year** |  |  |  |  |
| Face-to-face interactions | 21 | 15 | 14 | 8 | 12 | 9 | 13 | 9 |
| Telephone interactions | 2.1 | 0.8 | 1.7 | 0.5 | 0.7 | 0.6 | 0.6 | 0.6 |
| **No. of risk factor checks/person/year** |  |  |  |  |
| HbA1c tests  | 2.06 | 1.96 | 1.47 | 1.13 | 1.23 | 1.16 | 1.40 | 1.22 |
| Blood pressure checks | 4.15 | 3.67 | 2.51 | 2.14 | 2.20 | 2.46 | 2.55 | 1.91 |
| Lipids checks | 2.05 | 1.79 | 1.26 | 1.01 | 0.99 | 0.94 | 0.98 | 0.97 |
| BMI measured | 2.83 | 2.37 | 1.46 | 1.28 | 1.35 | 1.17 | 0.28 | 1.01 |
| Smoking cessation discussed | 0.83 | 0.77 | 0.86 | 0.31 | 0.35 | 0.29 | 0.58 | 0.28 |
| **Risk factors levels** |  |  |  |  |
| HbA1c >7% (53mmol/mol), % | 49.4 | 52.0 | 41.7 | 46.8 | 44.4 | 47.4 | 45.1 | 47.0 |
| HbA1c >8% (64mmol/mol), % | 23.9 | 26.5 | 18.7 | 21.3 | 21.4 | 23.4 | 23.5 | 23.4 |
|  |  |  |  |  |  |  |  |  |
| Blood pressure >140/80, % | 47.8 | 45.3 | 42.9 | 40.0 | 37.5 | 34.0 | 32.6 | 28.3 |
|  *On BP medication* | 94.7 | 93.3 | 95.2 | 95.3 | 93.8 | 95.7 | 96.4 | 95.5 |
| Blood pressure >130/80, % | 64.1 | 62.3 | 58.6 | 57.5 | 54.7 | 52.2 | 50.3 | 47.1 |
|  *On BP medication* | 94.3 | 92.8 | 94.9 | 94.2 | 93.3 | 94.5 | 95.8 | 94.2 |
|  |  |  |  |  |  |  |  |  |
| Cholesterol >target (LDL>2 or TC>4), % | 43.3 | 35.8 | 39.8 | 30.9 | 32.4 | 24.5 | 26.4 | 19.5 |
|  *On lipid-lowering medication* | 84.6 | 88.3 | 86.7 | 89.0 | 84.4 | 87.9 | 79.1 | 87.9 |
|  |  |  |  |  |  |  |  |  |
| Obese, % | 47.3 | 49.4 | 41.1 | 43.6 | 39.5 | 39.5 | 35.8 | 36.8 |
|  |  |  |  |  |  |  |  |  |
| Current smoking, % | 13.1 | 13.7 | 12.1 | 12.1 | 10.5 | 11.8 | 9.6 | 10.7 |
| **Risk factor checks, levels, interventions and prescriptions** | **Year 1** | **Years 2-3** | **Years 4-5** | **Years 6-7** |
| **Women****N=35,396** | **Men****N=44,589** | **Women****N=24,957** | **Men****N=31,352** | **Women****N=14,996** | **Men****N=18,667** | **Women****N=7,614** | **Men****N=9,257** |
| **n (%)** | 6,587 (18.6) | 10,897 (24.4) | 3,939 (15.8) | 6,871 (21.9) | 2,115 (14.1) | 3,723 (19.9) | 945 (12.4) | 1,657 (17.9) |
| **Interventions** |  |  |  |  |
| Diet intervention offered, % | 55.8 | 59.4 | 47.9 | 50.7 | 49.7 | 54.0 | 61.7 | 62.7 |
| Exercise intervention offered, % | 41.5 | 46.7 | 37.7 | 41.0 | 37.3 | 39.6 | 33.4 | 35.1 |
| Structured education offered, % | 13.9 | 16.0 | 2.6 | 2.6 | 2.7 | 3.8 | 4.4 | 6.0 |
| Bariatric surgery, % | 0.05 | 0.00 | 0.03 | 0.07 | 0.00 | 0.00 | 0.11 | 0.06 |
| **Drug Prescriptions** |  |  |  |  |
| **Diabetes** |  |  |  |  |  |  |  |  |
|  Any oral hyoglycaemic agent, % | 53.4 | 55.8 | 61.1 | 66.5 | 65.9 | 72.0 | 70.6 | 75.9 |
|  Metformin, % | 44.6 | 47.9 | 50.8 | 58.1 | 53.7 | 61.8 | 57.9 | 65.0 |
|  Sulphonylurea, % | 15.4 | 14.9 | 20.8 | 21.7 | 25.8 | 27.8 | 26.9 | 31.7 |
|  Glitazone, % | 2.0 | 1.5 | 3.1 | 3.1 | 3.6 | 3.7 | 3.8 | 4.2 |
|  DPP4i, % | 1.3 | 1.1 | 4.7 | 5.4 | 7.6 | 9.7 | 9.8 | 13.8 |
|  SGLT2i, % | 0.1 | 0.1 | 0.2 | 0.2 | 0.4 | 0.6 | 0.4 | 0.8 |
|  GLP-1 agonist, % | 0.2 | 0.2 | 1.0 | 1.2 | 1.6 | 2.0 | 1.9 | 3.0 |
|  Meglitinide, % | 0.2 | 0.2 | 0.3 | 0.4 | 0.2 | 0.3 | 0.3 | 0.3 |
|  Insulin, % | 5.4 | 5.4 | 6.0 | 5.4 | 8.0 | 7.0 | 11.2 | 9.0 |
|  Combination, % | 0.5 | 0.6 | 0.8 | 1.1 | 0.6 | 1.2 | 0.2 | 1.2 |
|  |  |  |  |  |  |  |  |  |
| **Antihypertensive agent** |  |  |  |  |  |  |  |  |
|  Any, % | 90.9 | 91.0 | 90.2 | 90.1 | 89.5 | 90.4 | 91.4 | 90.0 |
|  Alpha-blocker, % | 7.4 | 8.3 | 8.7 | 9.9 | 9.0 | 10.0 | 8.0 | 10.3 |
|  Angiotensin II receptor blocker, % | 20.9 | 16.4 | 22.8 | 17.7 | 22.9 | 18.1 | 25.2 | 19.0 |
|  ACE inhibitor, % | 47.1 | 57.6 | 49.0 | 58.3 | 47.2 | 59.5 | 47.6 | 58.4 |
|  Beta-blocker, % | 43.1 | 52.3 | 42.3 | 50.5 | 41.8 | 48.7 | 43.5 | 48.6 |
|  Calcium channel blocker, % | 40.1 | 37.8 | 41.8 | 39.8 | 40.9 | 39.8 | 43.8 | 41.3 |
|  Diuretic: thiazide, potassium  sparing or loop, % | 54.7 | 39.0 | 50.8 | 37.1 | 51.2 | 37.3 | 49.0 | 36.6 |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Risk factor checks, levels, interventions and prescriptions** | **Year 1** | **Years 2-3** | **Years 4-5** | **Years 6-7** |
| **Women****N=35,396** | **Men****N=44,589** | **Women****N=24,957** | **Men****N=31,352** | **Women****N=14,996** | **Men****N=18,667** | **Women****N=7,614** | **Men****N=9,257** |
| **n (%)** | 6,587 (18.6) | 10,897 (24.4) | 3,939 (15.8) | 6,871 (21.9) | 2,115 (14.1) | 3,723 (19.9) | 945 (12.4) | 1,657 (17.9) |
| **Lipid lowering therapy** |  |  |  |  |  |  |  |  |
|  Any, % | 83.5 | 89.6 | 83.7 | 88.6 | 82.4 | 87.9 | 82.8 | 88.1 |
|  Statin, % | 81.5 | 88.0 | 81.0 | 86.9 | 79.8 | 85.9 | 79.3 | 86.1 |
|  Fibrate, % | 1.8 | 2.2 | 2.4 | 2.6 | 2.4 | 2.8 | 3.2 | 2.8 |
|  Ezetimibe, % | 7.0 | 6.4 | 8.0 | 6.8 | 8.2 | 6.5 | 9.2 | 6.6 |
|  Other, % | 5.3 | 6.5 | 6.6 | 6.1 | 5.7 | 5.5 | 5.8 | 5.0 |
|  |  |  |  |  |  |  |  |  |
| **Antiplatelets** |  |  |  |  |  |  |  |  |
|  Any, % | 69.6 | 75.4 | 66.7 | 74.1 | 65.8 | 73.1 | 65.6 | 72.4 |
|  Aspirin, % | 62.8 | 69.6 | 60.3 | 68.3 | 58.6 | 66.8 | 57.4 | 65.7 |
|  Clopidogrel, % | 15.4 | 17.5 | 12.8 | 14.7 | 14.0 | 14.3 | 14.6 | 13.3 |

Data presented as %,or age-adjusted rate, as indicated

**b. without CVD (from baseline and through follow-up)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Risk factor checks, levels, interventions and prescriptions** | **Year 1** | **Years 2-3** | **Years 4-5** | **Years 6-7** |
| **Women****N=35,396** | **Men****N=44,589** | **Women****N=24,957** | **Men****N=31,352** | **Women****N=14,996** | **Men****N=18,667** | **Women****N=7,614** | **Men****N=9,257** |
| **n (%)** | 28,809 (81.4) | 33,692 (75.6) | 21,018 (84.2) | 24,481 (78.1) | 12,881 (85.9) | 14,944 (80.1) | 6,669 (87.6) | 7,600 (82.1) |
| **No. of consultations/person/year** |  |  |  |  |  |  |  |  |
| Face-to-face interactions | 15 | 13 | 10 | 8 | 10 | 8 | 10 | 8 |
| Telephone interactions | 1.0 | 0.7 | 0.7 | 0.5 | 0.7 | 0.6 | 0.8 | 0.5 |
| **No. of risk factor checks/person/year** |  |  |  |  |  |  |  |  |
| HbA1c tests  | 2.07 | 2.01 | 1.30 | 1.24 | 1.27 | 1.23 | 1.26 | 1.22 |
| Blood pressure checks | 3.42 | 3.24 | 2.00 | 1.76 | 1.88 | 1.71 | 1.78 | 1.65 |
| Lipids checks | 1.73 | 1.77 | 0.99 | 0.97 | 0.95 | 0.94 | 0.91 | 0.93 |
| BMI measured | 2.65 | 2.34 | 1.43 | 1.19 | 1.32 | 1.15 | 1.25 | 1.12 |
| Smoking cessation discussed | 0.48 | 0.49 | 0.31 | 0.29 | 0.30 | 0.31 | 0.28 | 0.31 |
| **Risk factors levels** |  |  |  |  |  |  |  |  |
| HbA1c >7% (53mmol/mol), % | 55.1 | 59.8 | 47.4 | 51.2 | 50.1 | 54.1 | 49.1 | 52.6 |
| HbA1c >8% (64mmol/mol), % | 31.4 | 38.8 | 23.2 | 27.4 | 26.3 | 30.1 | 27.0 | 30.2 |
|  |  |  |  |  |  |  |  |  |
| Blood pressure >140/80, % | 55.1 | 56.1 | 44.2 | 44.2 | 38.0 | 38.0 | 29.7 | 29.5 |
|  *On BP medication* | 76.9 | 72.4 | 82.6 | 80.3 | 85.3 | 83.5 | 87.7 | 86.0 |
| Blood pressure >130/80, % | 68.5 | 68.1 | 59.7 | 59.0 | 54.6 | 54.4 | 46.6 | 45.8 |
|  *On BP medication* | 74.7 | 69.8 | 80.5 | 77.9 | 83.3 | 80.7 | 86.0 | 83.7 |
|  |  |  |  |  |  |  |  |  |
| Cholesterol >target (LDL>2 or TC>4), % | 58.4 | 52.5 | 46.8 | 37.4 | 39.1 | 29.9 | 30.3 | 22.0 |
|  *On lipid-lowering medication* | 67.5 | 65.8 | 74.2 | 71.6 | 74.4 | 74.6 | 76.0 | 75.5 |
|  |  |  |  |  |  |  |  |  |
| Obese, % | 59.2 | 55.6 | 52.2 | 47.8 | 49.4 | 45.5 | 43.4 | 40.7 |
|  |  |  |  |  |  |  |  |  |
| Current smoking, % | 14.1 | 16.1 | 11.8 | 13.2 | 10.9 | 11.6 | 9.0 | 10.3 |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Risk factor checks, levels, interventions and prescriptions** | **Year 1** | **Years 2-3** | **Years 4-5** | **Years 6-7** |
| **Women****N=35,396** | **Men****N=44,589** | **Women****N=24,957** | **Men****N=31,352** | **Women****N=14,996** | **Men****N=18,667** | **Women****N=7,614** | **Men****N=9,257** |
| **n (%)** | 28,809 (81.4) | 33,692 (75.6) | 21,018 (84.2) | 24,481 (78.1) | 12,881 (85.9) | 14,944 (80.1) | 6,669 (87.6) | 7,600 (82.1) |
| **Interventions** |  |  |  |  |  |  |  |  |
| Diet intervention offered, % | 60.5 | 60.1 | 51.6 | 50.6 | 54.5 | 55.1 | 64.9 | 63.3 |
| Exercise intervention offered, % | 43.4 | 43.2 | 39.2 | 38.6 | 37.5 | 37.6 | 33.3 | 32.8 |
| Structured education offered, % | 17.2 | 17.3 | 3.2 | 3.5 | 4.2 | 4.7 | 5.9 | 7.0 |
| Bariatric surgery, % | 0.16 | 0.04 | 0.24 | 0.09 | 0.14 | 0.07 | 0.18 | 0.04 |
| **Drug Prescriptions** |  |  |  |  |  |  |  |  |
| **Diabetes** |  |  |  |  |  |  |  |  |
|  Any oral hyoglycaemic agent, % | 58.7 | 60.1 | 69.2 | 71.5 | 74.0 | 76.9 | 76.7 | 79.8 |
|  Metformin, % | 54.0 | 55.3 | 62.6 | 65.9 | 65.7 | 70.4 | 67.3 | 72.5 |
|  Sulphonylurea, % | 13.3 | 14.1 | 20.5 | 23.4 | 26.0 | 29.6 | 29.2 | 33.5 |
|  Glitazone, % | 2.1 | 2.2 | 4.0 | 4.6 | 5.0 | 5.9 | 5.1 | 6.6 |
|  DPP4i, % | 1.6 | 1.7 | 7.3 | 7.3 | 11.3 | 12.0 | 14.1 | 15.7 |
|  SGLT2i, % | 0.1 | 0.1 | 0.5 | 0.5 | 1.0 | 1.0 | 2.1 | 2.1 |
|  GLP-1 agonist, % | 0.4 | 0.2 | 2.2 | 1.6 | 3.8 | 2.9 | 4.5 | 3.6 |
|  Meglitinide, % | 0.2 | 0.2 | 0.3 | 0.3 | 0.3 | 0.3 | 0.4 | 0.3 |
|  Insulin, % | 4.1 | 3.8 | 5.4 | 4.6 | 7.4 | 6.3 | 9.7 | 9.1 |
|  Combination, % | 0.7 | 0.9 | 1.2 | 1.6 | 1.3 | 1.9 | 1.4 | 1.8 |
|  |  |  |  |  |  |  |  |  |
| **Antihypertensive agent** |  |  |  |  |  |  |  |  |
|  Any, % | 64.5 | 58.8 | 68.9 | 65.7 | 72.0 | 69.7 | 74.2 | 72.5 |
|  Alpha-blocker, % | 4.8 | 5.8 | 6.0 | 7.3 | 6.6 | 8.1 | 7.3 | 8.6 |
|  Angiotensin II receptor blocker, % | 13.7 | 10.2 | 16.9 | 13.5 | 18.9 | 14.9 | 19.7 | 15.9 |
|  ACE inhibitor, % | 34.8 | 38.2 | 37.9 | 44.0 | 39.5 | 46.7 | 41.0 | 48.3 |
|  Beta-blocker, % | 16.9 | 13.6 | 16.5 | 14.0 | 17.0 | 15.0 | 17.5 | 15.6 |
|  Calcium channel blocker, % | 25.7 | 25.9 | 28.4 | 29.7 | 30.3 | 31.6 | 31.4 | 33.4 |
|  Diuretic: thiazide, potassium  sparing or loop, % | 32.8 | 20.2 | 31.2 | 20.2 | 32.0 | 21.4 | 31.9 | 21.7 |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Risk factor checks, levels, interventions and prescriptions** | **Year 1** | **Years 2-3** | **Years 4-5** | **Years 6-7** |
| **Women****N=35,396** | **Men****N=44,589** | **Women****N=24,957** | **Men****N=31,352** | **Women****N=14,996** | **Men****N=18,667** | **Women****N=7,614** | **Men****N=9,257** |
| **n (%)** | 28,809 (81.4) | 33,692 (75.6) | 21,018 (84.2) | 24,481 (78.1) | 12,881 (85.9) | 14,944 (80.1) | 6,669 (87.6) | 7,600 (82.1) |
| **Lipid lowering therapy** |  |  |  |  |  |  |  |  |
|  Any, % | 62.6 | 64.1 | 72.0 | 72.4 | 74.0 | 75.8 | 75.3 | 77.6 |
|  Statin, % | 61.5 | 63.0 | 70.1 | 71.0 | 71.9 | 74.1 | 72.9 | 75.6 |
|  Fibrate, % | 1.0 | 1.4 | 1.5 | 1.8 | 1.6 | 2.0 | 1.7 | 2.1 |
|  Ezetimibe, % | 3.4 | 2.7 | 4.2 | 3.2 | 4.7 | 3.7 | 5.2 | 4.0 |
|  Other, % | 2.0 | 1.8 | 3.4 | 2.8 | 3.4 | 2.9 | 3.3 | 2.5 |
|  |  |  |  |  |  |  |  |  |
| **Antiplatelets** |  |  |  |  |  |  |  |  |
|  Any, % | 21.6 | 23.6 | 23.5 | 25.6 | 22.9 | 26.2 | 23.6 | 28.0 |
|  Aspirin, % | 21.0 | 23.1 | 22.7 | 24.9 | 22.0 | 25.3 | 22.2 | 26.8 |
|  Clopidogrel, % | 0.9 | 0.8 | 1.2 | 1.2 | 1.3 | 1.4 | 2.0 | 1.8 |

Data presented as %,or age-adjusted rate, as indicated

**Supplemental Table 7. Comparison of the proportions of women and men meeting minimum standards of care over 7 years of follow-up years from diagnosis of diabetes**

|  |  |  |  |
| --- | --- | --- | --- |
| **Minimum Standard of Care Indicator Assessed in the Previous 15 Months** | **Years 2-3** | **Years 4-5** | **Years 6-7** |
| **Women****N=13,917** | **Men****N=17,304** | **OR (95% CI)** | **Women****N=6,839** | **Men****N=8,257** | **OR† (95% CI)** | **Women****N=1,959** | **Men****N=2,252** | **OR (95% CI)** |
|  |  |  |  |  |  |  |  |  |  |  |
| **1** | **BMI recorded** | 91.6 | 91.8 | 0.98 (0.90-1.06) | 91.6 | 91.7 | 0.98 (0.87-1.10) | 89.8 | 91.7 | 0.80 (0.65-0.99) |
| **2** | **HbA1c recorded**  | 94.8 | 94.7 | 1.02 (0.92-1.13) | 94.8 | 94.9 | 0.98 (0.85-1.14) | 95.0 | 95.7 | 0.84 (0.63-1.12) |
| **3** | **Blood pressure recorded**  | 96.5 | 95.9 | 1.15 (1.03-1.30) | 96.3 | 95.8 | 1.15 (0.97-1.35) | 95.1 | 96.0 | 0.81 (0.60-1.08) |
| **4** | **Microalbuminuria tested** | 45.5 | 48.8 | 0.88 (0.84-0.92) | 53.3 | 56.5 | 0.88 (0.82-0.94) | 64.7 | 69.1 | 0.82 (0.72-0.93) |
| **5** | **Treated with ACE inhibitors if proteinuria or microalbuminuria**  | 51.4 | 59.0 | 0.74 (0.64-0.84) | 51.3 | 62.0 | 0.65 (0.54-0.77) | 54.8 | 62.7 | 0.72 (0.54-0.96) |
| **6** | **Last measured TC ≤5 mmol/l**  | 66.3 | 76.3 | 0.61 (0.58-0.64) | 67.9 | 78.4 | 0.58 (0.54-0.63) | 71.8 | 81.4 | 0.58 (0.50-0.67) |
|  **6a** |  **in those with prevalent CVD** | 72.7 | 84.4 | 0.49 (0.42-0.57) | 76.5 | 84.3 | 0.61 (0.48-0.77) | 78.8 | 86.6 | 0.57 (0.35-0.93) |
|  **6b** |  **in those without prevalent CVD** | 65.5 | 74.6 | 0.65 (0.61-0.68) | 67.0 | 77.3 | 0.60 (0.55-0.64) | 71.2 | 80.6 | 0.60 (0.61-0.69) |
| **7** | **eGFR or serum creatinine testing**  | 95.6 | 94.8 | 1.20 (1.08-1.33) | 95.2 | 95.0 | 1.04 (0.89-1.20) | 95.0 | 95.7 | 0.85 (0.64-1.14) |
| **8** | **Last IFCC-HbA1c ≤59 mmol/mol (≤7.5%)**  | 74.1 | 71.1 | 1.16 (1.11-1.22) | 69.0 | 67.0 | 1.10 (1.02-1.17) | 66.3 | 62.9 | 1.16 (1.02-1.32) |
| **9** | **Last blood pressure ≤140/80mmHg**  | 58.2 | 56.1 | 1.09 (1.04-1.14) | 61.2 | 59.2 | 1.09 (1.02-1.16) | 67.3 | 65.5 | 1.09 (0.96-1.24) |
|  **9a** |  **in those with prevalent CVD** | 62.0 | 66.6 | 0.82 (0.72-0.93) | 65.4 | 65.4 | 1.00 (0.82-1.22) | 67.7 | 66.3 | 1.06 (0.72-1.58) |
|  **9b** |  **in those without prevalent CVD** | 57.7 | 54.0 | 1.16 (1.11-1.22) | 60.7 | 58.1 | 1.12 (1.04-1.20) | 67.3 | 65.3 | 1.09 (0.95-1.25) |

Data presented as %; OR, odds ratio (values significantly <1 indicate lower standards of care in women compared to men). Indicators assessed during first 15 months of time block

**Supplemental Table 8. Comparison of the proportion of women and men receiving treatments over 7 years of follow-up years from diagnosis of diabetes, stratified by age and cardiovascular disease**

|  |  |  |  |
| --- | --- | --- | --- |
| **Drug treatment in the Previous 15 Months** | **Years 2-3** | **Years 4-5** | **Years 6-7** |
| **Women****N=13,917** | **Men****N=17,304** | **OR (95% CI)** | **Women****N=6,839** | **Men****N=8,257** | **OR (95% CI)** | **Women****N=1,959** | **Men****N=2,252** | **OR (95% CI)** |
| **Treated with ACE inhibitors if proteinuria or microalbuminuria** |  |  |  |  |  |  |  |  |  |
|  **a** | **<50**  | 46.9 | 55.7 | 0.70 (0.48-1.03) | 50.7 | 52.3 | 0.94 (0.53-1.66) | 33.3 | 59.4 | 0.34 (0.11-1.08) |
|  **b** | **≥50** | 52.1 | 59.5 | 0.74 (0.64-0.86) | 51.4 | 63.0 | 0.62 (0.52-0.74) | 56.4 | 62.9 | 0.76 (0.57-1.02) |
| **Treated with statins** | 74.3 | 76.6 | 0.88 (0.84-0.93) | 76.0 | 79.4 | 0.82 (0.76-0.89) | 78.7 | 81.7 | 0.83 (0.71-0.96) |
| **a** | **<50 *with prevalent CVD*** | 75.9 | 88.8 | 0.40 (0.14-1.14) | 71.4 | 87.1 | 0.37 (0.05-2.60) | - | 100.0 | - |
|  | **<50 *without prevalent CVD*** | 55.5 | 64.8 | 0.68 (0.60-0.76) | 58.5 | 68.6 | 0.64 (0.53-0.78) | 62.1 | 69.7 | 0.71 (0.46-1.10) |
| **b** | **≥50 *with prevalent CVD*** | 84.3 | 89.7 | 0.61 (0.51-0.74) | 83.6 | 90.1 | 0.56 (0.43-0.74) | 85.3 | 90.7 | 0.59 (0.34-1.04) |
|  | **≥50 *without prevalent CVD*** | 76.3 | 75.9 | 1.02 (0.96-1.09) | 77.7 | 79.0 | 0.93 (0.85-1.02) | 79.7 | 81.3 | 0.90 (0.76-1.07) |

Data presented as %; OR, odds ratio (values significantly <1 indicate lower standards of care in women compared to men). Indicators assessed during first 15 months of time block

**Supplemental Table 9. Comparison between men and women with type 2 diabetes for the time to intensification of drug regimens after risk factor levels exceed specified thresholds along with the probability of treatment intensification stratified by the number of medications prescribed for each risk factor and the presence of end organ damage**

|  |  |  |  |
| --- | --- | --- | --- |
| **Therapy and Cut-off value** | **Number of drugs at baseline** | **Months to treatment intensification in those with treatment modifications** | **Probability of treatment intensification over 7 years from diagnosis** |
| **Women** | **Men** | **P-value** | **Women** | **Men** | **P-value** |
| **Diabetes therapies** |
| ***HbA1c >7% (53mmol/mol)*** |  |  |  |  |  |  |
| n=33,050 | 0 | 4.3 | 4.4 | 0.371 | 98.2 | 99.0 | 0.206 |
| n=19,965 | 1 | 12.1 | 11.9 | 0.679 | 83.7 | 84.4 | 0.982 |
| n=3,271 |  2+ | 12.7 | 14.5 | 0.163 | 59.4 | 58.8 | 0.118 |
|  |  |  |  |  |  |  |  |
| ***HbA1c >8% (64mmol/mol)*** |  |  |  |  |  |  |
| n=18,927 | 0 | 2.4 | 2.6 | 0.002 | 99.3 | 99.4 | 0.061 |
| n=14,366 | 1 | 10.2 | 10.3 | 0.726 | 88.0 | 87.1 | 0.075 |
| n=3,095 |  2+ | 10.9 | 12.9 | 0.055 | 60.0 | 63.6 | 0.085 |
|  |  |  |  |  |  |  |  |
| **Antihypertensive therapies** |
| ***BP >130/80*** |  |  |  |  |  |  |  |
| n=22,373 | 0 | 5.5 | 6.4 | 0.003 | 82.8 | 77.6 | 0.989 |
| n=10,631 | 1 | 7.4 | 9.2 | 0.008 | 75.4 | 69.3 | 0.882 |
| n=11,561 |  2+ | 8.6 | 9.9 | 0.186 | 23.8 | 30.5 | 0.139 |
|  |  |  |  |  |  |  |  |
| ***BP >130/80 and target organ damage*** |  |  |  |  |  |  |
| n=4,376 | 0 | 3.1 | 4.0 | 0.019 | 65.4 | 76.7 | 0.544 |
| n=4,846 | 1 | 5.4 | 5.6 | 0.769 | 49.6 | 51.1 | 0.816 |
| n=9,199 |  2+ | 5.4 | 7.9 | 0.011 | 21.6 | 40.9 | 0.017 |
|  |  |  |  |  |  |  |  |
| ***BP >140/80*** |  |  |  |  |  |  |  |
| n=20,652 | 0 | 4.4 | 5.8 | <0.001 | 83.4 | 81.9 | 0.021 |
| n=13,367 | 1 | 6.7 | 8.5 | <0.001 | 75.8 | 71.4 | 0.801 |
| n=17,883 |  2+ | 7.3 | 9.6 | 0.001 | 25.2 | 33.9 | 0.068 |
|  |  |  |  |  |  |  |  |
| **Lipid-lowering therapies** |
| ***LDL >2 or TC>4 and CVD*** |  |  |  |  |  |  |
| n=3,797 | 0 | 5.0 | 4.6 | 0.238 | 71.5 | 81.7 | <0.001 |
| n=7,918 | 1 | 12.1 | 10.6 | 0.415 | 6.0 | 6.9 | 0.819 |
| n=502 |  2+ | 8.3 | 8.8 | 0.908 | 5.3 | 6.4 | 0.689 |
|  |  |  |  |  |  |  |  |
| ***LDL >2 or TC>4, no CVD*** |  |  |  |  |  |  |
| n=39,086 | 0 | 8.5 | 8.4 | 0.509 | 80.3 | 82.9 | 0.976 |
| n=18,464 | 1 | 20.4 | 17.2 | 0.066 | 5.9 | 5.9 | 0.419 |
| n=507 |  2+ | 12.1 | 11.5 | 0.908 | 7.2 | 4.7 | 0.394 |

**Supplemental Table 10. Unadjusted and multivariable-adjusted hazard ratios for incident MACE events comparing people with and without T2DM by sex and age of onset of T2DM**

|  |  |  |  |
| --- | --- | --- | --- |
| Model | Adjustments |  | **Primary Outcome: MACE** |
| **<50 years****T2DM: N=14,049****Controls: N=69,416** | **50-60 years****T2DM: N=15,587****Controls: N=73,962** | **60-70 years****T2DM: N=17,190****Controls: N=74,652** | **≥70 years****T2DM: N=16,892****Controls: N=59,146** |
| Risk of CV associated with the presence of diabetes; **HR (95% CI)** | Ratio of risks between women and men;**RRR (95% CI)** | Risk of CV associated with the presence of diabetes; **HR (95% CI)** | Ratio of risks between women and men;**RRR (95% CI)** | Risk of CV associated with the presence of diabetes; **HR (95% CI)** | Ratio of risks between women and men;**RRR (95% CI)** | Risk of CV associated with the presence of diabetes; **HR (95% CI)** | Ratio of risks between women and men;**RRR (95% CI)** |
| 1 | Unadjusted | Women | 3.73 (2.92-4.78) | 1.39 (1.03-1.87) | 2.10 (1.78-2.48) | 1.21 (1.00-1.48) | 1.74 (1.55-1.94) | 1.39 (1.21-1.60) | 1.19 (1.11-1.28) | 1.04 (0.94-1.16) |
| Men | 2.69 (2.28-3.18) | 1.73 (1.56-1.93) | 1.25 (1.15-1.37) | 1.14 (1.05-1.23) |
| 2 | Calendar year, ethnicity, deprivation, general practice | Women | 3.33 (2.56-4.31) | 1.41 (1.03-1.93) | 2.03 (1.70-2.42) | 1.33 (1.08-1.63) | 1.57 (1.40-1.76) | 1.38 (1.19-1.59) | 1.14 (1.06-1.23) | 1.05 (0.94-1.17) |
| Men | 2.36 (1.98-2.80) | 1.53 (1.37-1.71) | 1.14 (1.04-1.25) | 1.09 (1.01-1.19) |
| 3 | Model 2 plus baseline smoking, obesity, hypertension, hypercholesterolaemia and CCI | Women | 3.02 (2.11-4.34) | 1.31 (0.87-1.99) | 1.69 (1.36-2.10) | 1.22 (0.95-1.57) | 1.41 (1.24-1.60) | 1.34 (1.14-1.58) | 1.06 (0.98-1.15) | 1.05 (0.93-1.19) |
| Men | 2.30 (1.87-2.82) | 1.38 (1.22-1.57) | 1.05 (0.95-1.16) | 1.01 (0.92-1.11) |
| 4 | Model 3 plus time-varying smoking, obesity, hypertension, hypercholesterolaemia and raised HbA1c | Women | 2.83 (1.86-4.30) | 1.30 (0.80-2.09) | 1.67 (1.35-2.08) | 1.26 (0.98-1.61) | 1.38 (1.22-1.56) | 1.35 (1.15-1.60) | 1.04 (0.95-1.12) | 1.04 (0.92-1.18) |
| Men | 2.18 (1.73-2.74) | 1.33 (1.17-1.51) | 1.02 (0.89-1.11) | 1.00 (0.90-1.08) |

*Ratio of relative risks (RRR) greater than 1 indicates an excess risk for incident cardiovascular disease in women who developed diabetes compared to men who developed diabetes*

**Supplemental Table 11. Comparison of unadjusted hazard ratios for MACE events in incident T2DM and prevalent T2DM patients**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Model | Diabetes cohort |  | **Primary Outcome: MACE** | **Secondary Outcome: MI** **(fatal/non-fatal)** | **Secondary Outcome: Stroke (fatal/non-fatal)** |
| Risk of CV associated with the presence of diabetes; **HR (95% CI)** | Ratio of risks between women and men;**RRR (95% CI)** | Risk of CV associated with the presence of diabetes; **HR (95% CI)** | Ratio of risks between women and men;**RRR (95% CI)** | Risk of CV associated with the presence of diabetes; **HR (95% CI)** | Ratio of risks between women and men;**RRR (95% CI)** |
| 1 | **Incident T2DM \*** | Women | 1.44 (1.36-1.52) | **1.05 (0.98-1.13)** | 1.68 (1.56-1.81) | **1.09 (0.99-1.20)** | 1.24 (1.13-1.37) | **1.06 (0.92-1.22)** |
| Men | 1.37 (1.31-1.44) | 1.54 (1.45-1.64) | 1.17 (1.06-1.30) |
| 1 | **Prevalent T2DM †** | Women | 1.53 (1.24-1.82) | **1.06 (0.82-1.37)** | 1.75 (1.27-2.04) | **1.09 (0.80-1.47)** | 1.43 (1.06-2.10) | **1.12 (0.71-1.77)** |
| Men | 1.45 (1.22-1.72) | 1.61 (1.34-2.07) | 1.28 (0.95-1.75) |

\* Incident T2DM N=79,985; Controls N=386,547

† Prevalent T2DM N=77,494; Controls N=294,213