Additional file

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|  **Table S1 ICD-10 codes** |  |  |
|   |   |   |
| Atrial fibrillation |   | I48 |
| Cancer |   | C00-C99 |
| Chronic obstructive pulmonary disease |   | J42, J44 |
| Heart failure |   | I11.0, I13.0, I42, I50 |
| Hypertension |   | I10-I15 |
| Ischemic heart disease  |  | I20, I25  |
| Microvascular complications |  | E11.2-11.8 |
| Myocardial infarction |   | I21, I22 |
| Peripheral atherosclerosis |  | I70.2-I70.5 |
| Renal disease |   | N03-N08, N11, N14, N18, N19, N25-N29, I12, I13, Q61 |
| Stroke |   | I61, I63, I64 |
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| **ATC codes** |  |  |
| Metformin |   | A10BA02 |
| Insulin |   | A10A |
| GLP-1 RA |   | A10BJ01, A10BJ02, A10BJ03-6, A10BX04 A10BX07, A10BX10, A10BX13 |
| SGLT-2 inhibitor | A10BD15, A10BD20-21, A10BK01-02, A10BX09, A10BX11-12 |
| DPP-4 inhibitor |   | A10BDO1-08, A10BD10-11, A10BD13 |
| Sulfonylurea |   | A10BB01, A10BB03, A10BB07, A10BB09, A10BB12, A10BX02 |
| Statin |   | C10A |
| ACE inhibitor / Angiontensin receptor blocker |   | C09 |
| Mineralocorticoid receptor antagonist |   | C03D |
| Thiazide |   | C03A |
| Calcium channel blockers |   | C08 |
| Beta blockers |   | C07 |
| Platelet inhibitors |   | B01AC04, B01AC06 |
| Digoxin |   | C01AA05 |
| Loop diuretics |   | C03CA01 |

 **Table S2:**

A sensitivity analysis, in which patients were followed until a prescription was filled for any anti-diabetic therapy different from the initial treatment.

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| **Follow-up until first change in treatment** |
| Treatment | Hospitalisation for HFHR (95% CI), p-value | MACE (MI, Stroke, CV death)HR (95% CI), p-value | All-cause mortalityHR (95% CI), p-value |
| DPP-4 inhibitors | 1.00 (Ref). | 1.00 (Ref). | 1.00 (Ref). |
| GLP-1 RA | 1.11 (0.89-1.39), p=0.34 | 0.82 (0.67-0.97), p=0.0210 | 0.71 (0.57-0.89), p=0.003 |
| SGLT-2 inhibitors | 0.84 (0.52-1.36), p=0.48 | 0.79 (0.56-1.12), p=0.19 | 0.52 (0.32-0.87), p=0.013 |
| Sulfonylurea | 0.98 (0.77-1.26), p=0.90 | 1.22 (1.03-1.44), p=0.0193 | 1.35 (1.13-1.60), p<0.001 |
| Insulin | 1.54 (1.25-1.90), p<0.001 | 1.26 (1.07-1.47), p=0.0045 | 3.47 (3.01-4.00), p<0.001 |

**Table S3:**

Follow-up was extended to three years instead of the initial two years in the primary analysis.

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| **Three-year follow-up** |
| Treatment | Hospitalisation for HFHR (95% CI), p-value | MACE (MI, Stroke, CV death)HR (95% CI), p-value | All-cause mortalityHR (95% CI), p-value |
| DPP-4 inhibitors | 1.00 (Ref). | 1.00 (Ref). | 1.00 (Ref). |
| GLP-1 RA | 1.10 (0.92-1.31), p=0.30 | 0.86 (0.74-0.99), p=0.018 | 0.90 (0.80-1.02), p=0.09 |
| SGLT-2 inhibitors | 0.91 (0.60-1.37), p=0.64 | 0.88 (0.65-1.20), p=0.42 | 0.77 (0.59-1.03), p=0.070 |
| Sulfonylurea | 1.06 (0.87-1.30), p=0.58 | 1.21 (1.04-1.39), p=0.0119 | 1.08 (0.96-1.21), p=0.21 |
| Insulin | 1.49 (1.25-1.78), p<0.001 | 1.21 (1.21-1.39), p<0.001 | 2.15 (1.95-2.37), p<0.001 |

**Table S4:**

Sensitivity analyses: (A) excluding patients a high or very high cardiovascular risk, (B) only including patients at high or very high cardiovascular risk (B).

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| **A: Excluding patients at high and very high cardiovascular risk** |
| Treatment | Hospitalisation for HFHR (95% CI), p-value | MACE (MI, Stroke, CV death)HR (95% CI), p-value | All-cause mortalityHR (95% CI), p-value |
| DPP-4 inhibitors | 1.00 (Ref). | 1.00 (Ref). | 1.00 (Ref). |
| GLP-1 RA | 1.41 (0.95-2.11), p=0.09 | 0.70 (0.54-0.96), p=0.0233 | 0.76 (0.79-1.17), p=0.67 |
| SGLT-2 inhibitors | 1.12 (0.53-2.382), p=0.76 | 0.66 (0.35-1.23), p=0.19 | 0.88 (0.59-1.33), p=0.56 |
| Sulfonylurea | 1.02 (0.67-1.54), p=0.93 | 1.05 (0.81-1.62), p=0.73 | 1.25 (1.06-1.47), p=0.0095 |
| Insulin | 1.53 (1.04-2.23), p=0.0296 | 1.27 (1.00-1.63), p=0.053 | 2.7 (2.34-3.12), p<0.001 |
| **B: Only including patients at high and very high cardiovascular risk** |
| DPP-4 inhibitors | 1.00 (Ref). | 1.00 (Ref). | 1.00 (Ref). |
| GLP-1 RA | 0.98 (0.75-1.28), p=0.90 | 0.85 (0.69-1.05), p=0.12 | 0.83 (0.66-1.05), p=0.12 |
| SGLT-2 inhibitors | 0.67 (0.34-1.26), p=0.21 | 0.82 (0.54-1.27), p=0.38 | 0.65 (0.41-1.05), p=0.076 |
| Sulfonylurea | 0.96 (070-1.31), p=0.79 | 1.36 (1.90-1.70), p=0.0064 | 0.88 (0.66-1.16), p=0.36 |
| Insulin | 1.49 (1.15-1.92), p=0.0022 | 1.21 (0.98-1.49), p=0.0749 | 1.73 (1.43-2.10), p<0.001 |

**Table S5:**

Sensitivity analyses splitting the cohort in two according to the year of inclusion (A) Patients with a date of inclusion set between 2010 January - 2013 September, (B) Patients with a date of inclusion set between 2013 October - 2017August.

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| **A: First half of follow-up (2010 January - 2013 September)** |
| Treatment | Hospitalisation for HFHR (95% CI), p-value | MACE (MI, Stroke, CV death)HR (95% CI), p-value | All-cause mortalityHR (95% CI), p-value |
| DPP-4 inhibitors | 1.00 (Ref). | 1.00 (Ref). | 1.00 (Ref). |
| GLP-1 RA | 1.11 (0.89-1.39), p=0.34 | 0.65 (0.55-0.88), p=0.002 | 1.05 (0.86-1.27), p=0.66 |
| SGLT-2 inhibitors | - | - | - |
| Sulfonylurea | 0.84 (0.52-1.36), p=0.48 | 1.11 (0.88-1.39), p=0.39 | 1.15 (0.94-1.40), p=0.18 |
| Insulin | 0.98 (0.76-1.26), p=0.90 | 1.21 (0.98-1.50), p=0.08 | 2.39 (2.01-2.84), p<0.001 |
| **B: Second half of follow-up (2013 October - 2017 August)**  |
| DPP-4 inhibitors | 1.00 (Ref). | 1.00 (Ref). | 1.00 (Ref). |
| GLP-1 RA | 1.03 (0.74-1.45), p=0.85 | 0.83 (0.63-1.09), p=0.1762 | 0.91 (0.80-1.03), p=0.12 |
| SGLT-2 inhibitors | 0.85 (0.52-1.39, p=052 | 0.81 (0.56-1.16), p=0.25 | 0.77 (0.58-1.03), p=0.073 |
| Sulfonylurea | 1.02 (0.73-1.43), p=0.91 | 1.36 (1.07-1.73), p=0.012 | 1.13 (1.04-1.28), p=0.043 |
| Insulin | 1.51 (1.14-2.01), p=0.043 | 1.30 (1.03-1.66), p=0.030 | 2.32 (2.10-2.56), p<0.001 |

**Table S6:**

A sensitivity analysis in which sulfonylurea was used as reference as opposed to DPP-4 inhibitors which was used in the primary analysis.

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| **Sulfonylurea as reference** |
| Treatment | Hospitalisation for HFHR (95% CI), p-value | MACE (MI, Stroke, CV death)HR (95% CI), p-value | All-cause mortalityHR (95% CI), p-value |
| Sulfonylurea  | 1.00 (Ref). | 1.00 (Ref). | 1.00 (Ref). |
| DPP-4 inhibitors  | 1.01 (0.79-1.30), p=0.90 | 0.82 (0.70-0.97), p=0.019 | 0.88 (0.77-1.01), p=0.12 |
| GLP-1 RA  | 1.13 (0.86-1.49), p=0.37 | 0.68 (0.56-0.82), p<0.001 | 0.80 (0.68-0.94), p=0.0082 |
| SGLT-2 inhibitors | 0.86 (0.51-1.43), p=0.55 | 0.65 (0.45-0.93), p=0.0205 | 0.69 (0.50-0.96), p=0.043 |
| Insulin | 1.56 (1.21-2.03), p=0.0007 | 1.03 (0.86-1.24), p=0.73 | 2.05 (1.79-2.35), p<0.001 |