**Supplementary Material**

**Real-world use of sodium–glucose co-transporter 2 inhibitors in patients with heart failure and reduced ejection fraction: data from the Swedish Heart Failure Registry.**

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**Supplementary Table 1. Comorbidities from National Patients Registry.**

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| --- | --- | --- |
| **Variables** | **Definition** | **Period** |
| Hypertension | ICD-10 codes:I10-I15 | 0-5 years |
| T2DM | ICD-10 codes: E10-E14 | 0-5 years |
| IHD | ICD-10 codes: 410-1, I20-5 | 0- years |
| PCI | OP:FNG | 0- years |
| CABG | ICD:Z951,Z955 OP:FNA,FNB,FNC,FND,FNE,FNF,FNH | 0- years |
| History of AF/flutter | ICD-10 code: I48 | 0-5 years |
| PAD | ICD:I70-3 | 0-5 years |
| Valve disease | Diagnosis in SwedeHF or in NPR (ICD-10 codes: A520, I05-I08, I091, I098, I34-I39, Q230-Q233, Z952, Z954) | 0- years |
| Dialysis | Diagnosis in the NPR (ICD:Z491,Z492 OP:DR014,DR015,DR016,DR020,DR012,DR013,DR023,DR024,TJA33,TJA35) | 0-5 years |
| Stroke or TIA | Diagnosis in the NPR (ICD-9 codes: 430-4, 438; ICD-10 codes: I60-4, I690-4, G45) | 0- years |
| Liver disease | Diagnosis in the NPR (ICD-10 codes: B18, I85, I864, I982, K70, K710, K711, K713-7, K72-4, K760, K762-9) | 0-5 years |
| COPD | Diagnosis in the NPR (ICD-10 codes: J40-4) | 0-5 years |
| History of cancer within 3 years | Diagnosis in the NPR (ICD-10 codes: C) | 0-5 years |

Abbreviations. AF: atrial fibrillation; CABG: coronary artery by-pass grafting; COPD: chronic obstructive pulmonary disease; HF: heart failure; ICD-10: International Classification of Diseases; IHD: ischemic heart disease, NPR: National Patient Registry; OP: operation codes; PAD: peripheral artery disease; PCI: percutaneous coronary intervention; T2DM: type 2 diabetes mellitus; TIA: transitory ischemic attack.

**Supplementary Table 2. Missing data.**

|  |  |
| --- | --- |
| **Variable** | **Missing rate (%)** |
| **Sex** | 0 |
| **Age** | 0 |
| **Outpatient** | 5 |
| **F-up referral HF nurse clinic** | 3.3 |
| **F-up referral speciality** | 2.1 |
| **Year of registration** | 0 |
| **HF duration > 6 months** | 1.3 |
| **NYHA class** | 14.6 |
| **SBP, mmHg** | 4.4 |
| **DBP, mmHg** | 4.4 |
| **MAP** | 4.4 |
| **HR** | 5.2 |
| **eGFR** | 3.0 |
| **NT-proBNP** | 13.7 |
| **Dyskalemia** | 3.5 |
| **BMI** | 20.5 |
| **Smoking** | 20.3 |
| **T2DM** | 4.2 |
| **AF** | 0 |
| **Ischemic heart disease** | 0 |
| **Anemia** | 12.3 |
| **Hypertension** | 0 |
| **Peripheral artery disease** | 0 |
| **Revascularization** | 0 |
| **Stroke/TIA** | 0 |
| **Valve disease** | 0 |
| **Malignant cancer <3 years** | 0 |
| **COPD** | 0 |
| **Liver disease** | 0 |
| **Charlson comorbidity index** | 0 |
| **MRA** | 0.1 |
| **Diuretics** | 0.1 |
| **Digoxin** | 0.1 |
| **Antiplatelet therapy** | 0.1 |
| **Anticoagulant therapy** | 0.1 |
| **Statins** | 0.1 |
| **Nitrates** | 0.1 |
| **ICD** | 0 |
| **CRT** | 0 |
| **Family type Living alone** | 0.1 |
| **Children** | 0 |
| **Education** | 1.1 |
| **Income** | 0.1 |

*For abbreviations see Table 1*

**Supplementary Table 3. Regional distribution of SGLT2i use in Sweden.**

|  |  |
| --- | --- |
| **Region** | **n SGLT2i users/n Total (%)** |
| **Blekinge** | 76 (38.4%) |
| **Dalarna** | 106 (35.9%) |
| **Gavleborg** | 101 (36.2%) |
| **Gotland** | 14 (40.0%) |
| **Halland** | 144 (29.4%) |
| **Jamtland Harjedalen** | 4 (16%) |
| **Lonkiping** | 64 (16%) |
| **Kalmar** | 32 (30.5%) |
| **Kronoberg** | - |
| **Norrbotten** | 88 (48.1%) |
| **Orebro** | 165 (42.6%) |
| **Ostergotland** | 237 (41.6%) |
| **Skane** | 263 (34.6%) |
| **Sormland** | 88 (31.5%) |
| **Stockholm** | 698 (48%) |
| **Uppsala** | 106 (34.3%) |
| **Varmland** | 78 (35.3%) |
| **Vasterbotten** | 78 (39.4%) |
| **Vasterrnorland** | 159 (43.9%) |
| **Vastmanland** | 73 (32.4%) |
| **Vastra Gotaland** | 437 (30.9%) |

**Abbreviations.** SGLT2i: sodium–glucose co-transporter 2 inhibitors

**Supplementary Figure 1. Flow chart reporting cohort selection.**



Abbreviations: PINs: personal identification numbers, SCB: statistics Sweden, EF: ejection fraction, eGFR: estimated glomerular filtration rate

**Supplementary Figure 2. Unadjusted and adjusted associations between patients´ characteristics and use of SGLT2-i according to type 2 diabetes status.**



**Abbreviations.** ACEi/ARB/ARNI:angiotensin converting enzyme inhibitors/angiotensin receptor blockers/ angiotensin receptor neprilyisin inhibitor; BMI: body mass index; COPD: chronic obstructive pulmonary disease; CRT: cardiac resynchronization therapy; eGFR: estimated glomerular filtration rate; EF: ejection fraction; HF: heart failure; HR: heart rate; ICD: implantable cardioverter defibrillator; MAP: mean arterial pressure; MRA: mineralocorticoid receptor antagonist; NYHA: New York Heart Association; NT-proBNP: N-terminal pro-brain natriuretic peptide; OR: odds ratio; p int: p for interaction

**Supplementary Figure 3. Unadjusted and adjusted associations between patients´ characteristics and use of SGLT2-i according to renal function.**



**Abbreviations.** ACEi/ARB/ARNI:angiotensin converting enzyme inhibitors/angiotensin receptor blockers/ angiotensin receptor neprilyisin inhibitor; BMI: body mass index; COPD: chronic obstructive pulmonary disease; CRT: cardiac resynchronization therapy; eGFR: estimated glomerular filtration rate; EF: ejection fraction; HF: heart failure; HR: heart rate; ICD: implantable cardioverter defibrillator; MAP: mean arterial pressure; MRA: mineralocorticoid receptor antagonist; NYHA: New York Heart Association; NT-proBNP: N-terminal pro-brain natriuretic peptide; OR: odds ratio; p int: p for interaction

**Supplementary Figure 4. Unadjusted and adjusted associations between patients’ characteristics and use of SGLT2-i according to sex.**



**Abbreviations.** ACEi/ARB/ARNI:angiotensin converting enzyme inhibitors/angiotensin receptor blockers/ angiotensin receptor neprilyisin inhibitor; BMI: body mass index; COPD: chronic obstructive pulmonary disease; CRT: cardiac resynchronization therapy; eGFR: estimated glomerular filtration rate; EF: ejection fraction; HF: heart failure; HR: heart rate; ICD: implantable cardioverter defibrillator; MAP: mean arterial pressure; MRA: mineralocorticoid receptor antagonist; NYHA: New York Heart Association; NT-proBNP: N-terminal pro-brain natriuretic peptide; OR: odds ratio; p int: p for interaction

**Supplementary Figure 5. Unadjusted and adjusted associations between patients’ characteristics and use of SGLT2-i according to recent HF hospitalization.**



**Abbreviations.** ACEi/ARB/ARNI:angiotensin converting enzyme inhibitors/angiotensin receptor blockers/ angiotensin receptor neprilyisin inhibitor; BMI: body mass index; COPD: chronic obstructive pulmonary disease; CRT: cardiac resynchronization therapy; eGFR: estimated glomerular filtration rate; EF: ejection fraction; HF: heart failure; HR: heart rate; ICD: implantable cardioverter defibrillator; MAP: mean arterial pressure; MRA: mineralocorticoid receptor antagonist; NYHA: New York Heart Association; NT-proBNP: N-terminal pro-brain natriuretic peptide; OR: odds ratio; p int: p for interaction

**Supplementary Figure 6. Unadjusted and adjusted associations between patients’ characteristics and use of SGLT2-i according to location (i.e. inpatients vs outpatients).**



**Abbreviations.** ACEi/ARB/ARNI:angiotensin converting enzyme inhibitors/angiotensin receptor blockers/ angiotensin receptor neprilyisin inhibitor; BMI: body mass index; COPD: chronic obstructive pulmonary disease; CRT: cardiac resynchronization therapy; eGFR: estimated glomerular filtration rate; EF: ejection fraction; HF: heart failure; HR: heart rate; ICD: implantable cardioverter defibrillator; MAP: mean arterial pressure; MRA: mineralocorticoid receptor antagonist; NYHA: New York Heart Association; NT-proBNP: N-terminal pro-brain natriuretic peptide; OR: odds ratio; p int: p for interaction

**Supplementary Figure 6. Unadjusted and adjusted associations between patients’ characteristics and use of SGLT2-i according to duration of HF.**



**Abbreviations.** ACEi/ARB/ARNI:angiotensin converting enzyme inhibitors/angiotensin receptor blockers/ angiotensin receptor neprilyisin inhibitor; BMI: body mass index; COPD: chronic obstructive pulmonary disease; CRT: cardiac resynchronization therapy; eGFR: estimated glomerular filtration rate; EF: ejection fraction; HF: heart failure; HR: heart rate; ICD: implantable cardioverter defibrillator; MAP: mean arterial pressure; MRA: mineralocorticoid receptor antagonist; NYHA: New York Heart Association; NT-proBNP: N-terminal pro-brain natriuretic peptide; OR: odds ratio; > 6mo = ≥ 6 months; <6mo = < 6 months; p int: p for interaction