

# Impaired long-term outcomes of patients with schizophrenia spectrum disorder after coronary artery bypass surgery: nationwide case–control study

Mika Kallio, Jyrki Korkeila, Markus Malmberg, Jarmo Gunn, Päivi Rautava, Päivi Korhonen and Ville Kytö

## Background

Patients with schizophrenia spectrum disorder have increased risk of coronary artery disease.

## Aims

To investigate long-term outcomes of patients with schizophrenia spectrum disorder and coronary artery disease after coronary artery bypass grafting surgery (CABG).

## Method

Data from patients with schizophrenia spectrum disorder ( $n = 126$ ) were retrospectively compared with propensity-matched (1:20) control patients without schizophrenia spectrum disorder ( $n = 2520$ ) in a multicentre study in Finland. All patients were treated with CABG. The median follow-up was 7.1 years. The primary outcome was all-cause mortality.

## Results

Patients with diagnosed schizophrenia spectrum disorder had an elevated risk of 10-year mortality after CABG, compared with control patients (42.7 v. 30.3%; hazard ratio 1.56; 95% CI 1.13–2.17;  $P = 0.008$ ). Schizophrenia spectrum diagnosis was associated with a higher risk of major adverse cardiovascular events during follow-up (49.9 v. 32.6%, subdistribution hazard ratio 1.59; 95% CI 1.18–2.15;  $P = 0.003$ ). Myocardial infarction (subdistribution hazard ratio 1.86;  $P = 0.003$ ) and cardiovascular mortality (subdistribution hazard ratio 1.65;  $P = 0.017$ ) were more frequent in patients with versus those without schizophrenia spectrum disorder, but there was no difference for stroke. Psychiatric ward admission, antipsychotic

medication, antidepressant use and benzodiazepine use before CABG were not associated with outcome differences. After CABG, patients with schizophrenia spectrum disorder received statin therapy less often and had lower doses; the use of other cardiovascular medications was similar between schizophrenia spectrum and control groups.

## Conclusions

Patients with schizophrenia spectrum disorder have higher long-term risks of death and major adverse cardiovascular events after CABG. The results underline the vulnerability of these patients and highlight the importance of intensive secondary prevention and risk factor optimisation.

## Keywords

Cardiovascular; coronary artery disease; myocardial infarction; severe mental disorder; schizophrenia.

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Patients with schizophrenia have a substantially higher overall mortality rate compared with the general population,<sup>1–4</sup> and cardiovascular disease is the major cause of death.<sup>5</sup> Coronary artery disease (CAD) is the largest contributor to the life expectancy gap between patients with schizophrenia and the general population.<sup>6–9</sup> Previous studies have associated schizophrenia with adverse clinical outcomes and increased early mortality after myocardial infarction.<sup>10–12</sup> Inequalities in treatment might contribute to mortality disparities because patients with severe mental illness, especially schizophrenia spectrum disorder (SCZ), are less likely to be treated with invasive coronary interventions.<sup>13–16</sup> Recent findings suggest that patients with schizophrenia benefit from revascularisation as much as the general population does, despite a higher 1-year mortality rate after the procedure.<sup>17</sup> No long-term studies are available about patients with schizophrenia who are treated with coronary artery bypass grafting surgery (CABG); however, CABG is the standard invasive treatment of choice in severe multivessel or left-main CAD.<sup>18</sup> Our aim was to investigate the long-term outcomes of patients with chronic SCZ treated with CABG, using a large nationwide registry. We hypothesized that patients with schizophrenia or other chronic SCZ have poorer prognoses than patients who have CAD without SCZ.

## Method

### Study design

We studied the outcomes of patients with SCZ compared with patients without SCZ after CABG. Baseline differences between study groups were balanced by using propensity score matching. The primary outcome of interest was 10-year mortality. Secondary outcomes were 10-year major adverse cardiovascular event (MACE; including cardiovascular death, myocardial infarction and stroke) and use of postoperative medication. Patients with CAD treated with primary CABG between 1 January 2004 and 31 December 2014 ( $n = 35\,067$ ) were retrospectively identified from The Care Register for Healthcare in Finland (CRHF). This nationwide, mandated-by-law registry includes data on all hospital and emergency department admissions and major surgical procedures in Finland.<sup>19</sup> CABG was performed in eight hospitals (six public and two private) during the study period in Finland, and all were included in the study. Patients with prior cardiac surgery; concomitant surgery of heart valves; surgery of the aorta, ventricles or pulmonary vasculature defects; bypass surgery using gastroepiploic arterial or prosthetic grafts

and those with unavailable follow-up data (0.23%), were excluded from the study (Supplementary Fig. 1 available at <https://doi.org/10.1192/bjo.2022.10>). Patients with SCZ were identified by following diagnostic codes from the International Classification of Disease version 10 (ICD-10)<sup>20</sup>: F20 (schizophrenia), F21 (schizotypal disorder) and F25 (schizoaffective disorder). Other SCZ diagnoses were excluded to assure diagnostic stability.<sup>1</sup> SCZs were identified in the CRHF and the national registry for drug reimbursement permissions held by the Social Insurance Institute.

## Definitions

Comorbidities were identified in the CRHF, the national registry of drug reimbursement permissions and the nationwide Finnish Cancer Registry, using previously described ICD-10 codes and applicable drug purchase reimbursement codes.<sup>21</sup> Myocardial infarction (ICD-10 code I21\* or I22\*) and stroke (ICD-10 codes I60\*–I64\*) occurring during follow-up were detected from the CRHF and death certificates. Cardiovascular death was defined with an ICD-10 code of I\* as the underlying cause of death. Postoperative prescription medications (drugs purchased within 90 days after discharge) were identified with applicable anatomical therapeutic chemical (ATC) codes (Supplementary Tables 1 and 2). In Finland, all psychiatric and cardiovascular disease medications are available only via prescription and are captured in the nationwide registry. Purchase of antipsychotics and benzodiazepines, as well as ward treatment in psychiatric hospitals during the year preceding CABG, were identified in a subgroup of patients with SCZ who underwent CABG between 2005 and 2017, using ATC codes and the CRHF. Regular medication use was defined as four or more drug purchases within a year. Sequential admissions after CABG were combined when studying the duration of admission. Prescription drug purchase data (including ATC codes and

purchase dates) and drug purchase reimbursement permission data were obtained from a nationwide registry held by the Social Insurance Institution of Finland. Mortality data were obtained from a nationwide cause-of-death registry held by Statistics Finland. These registries are mandated by law and fully cover the Finnish population. Follow-up ended on 31 December 2018.

## Permissions and patient and public involvement statement

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. According to Finnish legislation, no ethical approval or informed consent is needed for register-based studies. The legal basis for processing of personal data was public interest and scientific research (EU General Data Protection Regulation 2016/679, Article 6(1)(e) and Article 9(2)(j); Data Protection Act, Sections 4 and 6). The study was approved by the National Institute for Health and Welfare of Finland (permission number THL/2245/5.05.00/2019), the National Social and Health Data Permit Authority (permission number THL/164/14.02.00/2021), and Statistics Finland (permission number TK-53-484-20).

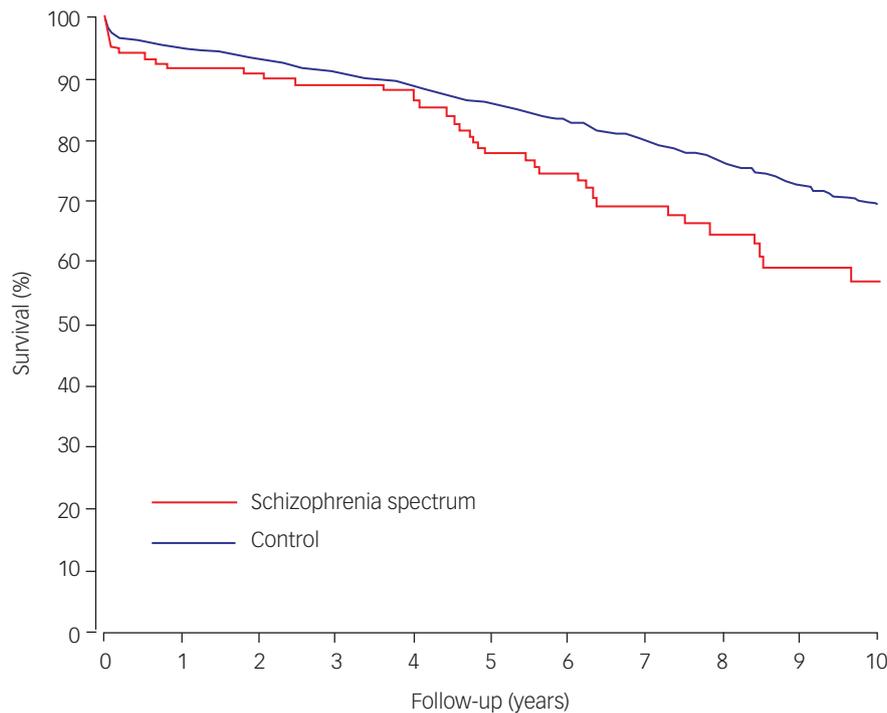
## Statistical analysis

A propensity score based on age, gender, atrial fibrillation, cerebrovascular disease, chronic pulmonary disease, diabetes, heart failure, hypertension, malignancy, myocardial infarction (new and prior), peripheral vascular disease, rheumatic disease, renal failure, type of bypass graft, off-pump CABG, number of grafted anastomoses, surgical centre and year of surgery (Table 1) was created with

**Table 1** Baseline features of patients who underwent coronary artery bypass with and without schizophrenia spectrum disorder

Variable	All patients				Matched patients			
	Schizophrenia spectrum <i>n</i> = 126	Control <i>n</i> = 29094	<i>P</i> -value	SMD	Schizophrenia spectrum <i>n</i> = 126	Control <i>n</i> = 2520	<i>P</i> -value	SMD
Age, years (s.d.)	64.0 (8.7)	66.8 (9.1)	0.001	0.318	64.0 (8.7)	64.0 (9.1)	0.758	0.001
Male gender	93 (73.8%)	22800 (78.4)	0.215	0.107	93 (73.8%)	1867 (74.1%)	0.821	0.006
Atrial fibrillation	13 (10.3%)	3259 (11.2%)	0.754	0.029	13 (10.3%)	242 (9.6%)	0.405	0.024
Cerebrovascular disease	13 (10.3%)	2419 (8.3%)	0.417	0.069	13 (10.3%)	263 (10.4%)	0.885	0.004
Chronic pulmonary disease	18 (14.3%)	3165 (10.9%)	0.221	0.103	18 (14.3%)	345 (13.7%)	0.532	0.017
Diabetes	41 (32.5%)	7785 (26.8%)	0.144	0.127	41 (32.5%)	822 (32.6%)	0.950	0.002
Heart failure	24 (19.1%)	4483 (15.4%)	0.259	0.097	24 (19.1%)	478 (19.0%)	0.942	0.002
Hypertension	67 (53.2%)	16033 (55.1%)	0.663	0.039	67 (53.2%)	1348 (53.5%)	0.821	0.006
Malignancy	8 (6.4%)	2627 (9.0%)	0.295	0.101	8 (6.4%)	171 (6.8%)	0.516	0.018
Peripheral vascular disease	9 (7.1%)	2209 (7.6%)	0.849	0.017	9 (7.1%)	153 (6.1%)	0.128	0.043
Prior myocardial infarction	34 (27.0%)	6097 (21.0%)	0.097	0.142	34 (27.0%)	693 (27.5%)	0.674	0.012
Rheumatic disease	8 (6.4%)	1326 (4.6%)	0.336	0.079	8 (6.4%)	167 (6.6%)	0.678	0.011
Renal failure	3 (2.4%)	626 (2.2%)	0.483	0.062	3 (2.4%)	70 (2.8%)	0.369	0.025
Myocardial infarction <sup>a</sup>	19 (15.1%)	2745 (9.4%)	0.031	0.173	19 (15.1%)	395 (15.7%)	0.535	0.017
Type of bypass graft			0.939	0.028			0.124	0.028
Only arterial	20 (15.9%)	4310 (14.8%)			20 (15.9%)	382 (15.2%)		
Only venous	8 (6.4%)	1796 (6.2%)			8 (6.4%)	159 (6.3%)		
Arterial and venous	98 (77.8%)	22988 (79.0%)			98 (77.8%)	1979 (78.5%)		
Off-pump surgery	6 (4.8%)	910 (3.1%)	0.294	0.084	6 (4.8%)	118 (4.7%)	0.678	0.004
Number of anastomoses			0.471	0.081			0.646	0.027
1	18 (14.3%)	2833 (9.7%)			18 (14.3%)	313 (12.4%)		
2	18 (14.3%)	3941 (13.6%)			18 (14.3%)	385 (15.3%)		
3	34 (27.0%)	9128 (31.4%)			34 (27.0%)	786 (31.2%)		
4	36 (28.6%)	8306 (28.6%)			36 (28.6%)	675 (26.8%)		
≥5	20 (15.9%)	4886 (16.8%)			20 (15.9%)	361 (14.3%)		
Surgical centre ( <i>n</i> = 8)			0.002	0.423			0.349	0.025
Year of surgery			0.007	0.250			0.348	0.035

Cohorts of all and propensity score–matched patients (1:20). SMD, standardised mean difference.  
a. As indication for surgery.



**Fig. 1** Survival of patients with schizophrenia spectrum disorder and of matched controls patients after coronary artery bypass surgery.

logistic regression. Patients with nonoverlapping propensity scores were excluded ( $n = 321$  patients without SCZ). A trimmed propensity score was used for local, optimal 1:20 calibre matching without replacement, using a 0.05-caliper width of the logit of the s.d.<sup>22</sup> Differences between nonmatched groups were studied with the  $t$ -test and the  $\chi^2$ -test, and differences between matched groups were studied with the paired  $t$ -test, Wilcoxon signed-rank test and McNemar's test. Effect sizes in baseline characteristics between the study groups were evaluated by standardised difference scores. Use of prescription medications after CABG was studied with logistic regression. Time-dependent outcomes were studied with the Kaplan–Meier method and Cox regression (primary outcome), and with the Fine-Gray method to account for the competitive risk of death (secondary outcomes). Matched regression models were used in the analysis of the matched cohort. Multivariable regressions were used in the analysis of the subgroup of patients with SCZ who underwent operations between 2005 and 2017 ( $n = 118$ ). Schoenfeld residuals were examined for confirmation of proportional hazard assumptions. The median follow-up time of matched patients was 7.1 years (interquartile range (IQR) 4.0–10.0 years), and there was no difference between the study groups ( $P = 0.567$ ). Results are given as the mean, median, percentage, standardised mean difference, hazard ratio or odds ratio with 95% confidence intervals. Statistical significance was inferred by a  $P$ -value  $< 0.05$ . Analyses were performed with SAS version 9.4 for Windows (SAS Institute Inc., Cary, North Carolina, USA).

## Results

Of all included patients with CAD and treated with CABG ( $n = 29220$ ; median age 68 years; 78.4% men), 0.4% ( $n = 126$ ) had SCZ. Patients with SCZ were younger and underwent operation because of myocardial infarction more often compared with patients in the control group (Table 1). Neither the type of bypass

graft nor the number of grafted coronary anastomoses differed significantly between study groups. Propensity matching (1:20) identified 126 patients with SCZ and 2520 patients in the control group with balanced features (Table 1). The median duration of hospital admission after CABG was 14 days (IQR 10–25 days) in those with SCZ and 10 days (IQR 8–14 days) in matched controls ( $P < 0.001$ ).

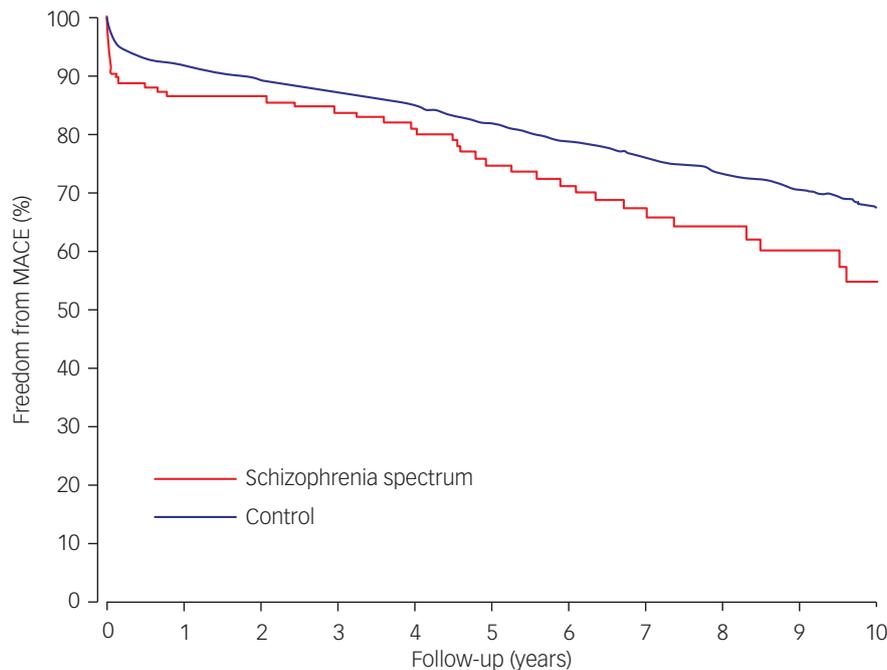
## Mortality

During the 10-year follow-up of the matched cohort, 572 deaths occurred (37 in the SCZ group and 535 in matched controls). In-hospital mortality was 4.8% in the SCZ group and 2.9% in the control group ( $P = 0.364$ ), and 30-day mortality rates were 4.8% and 2.4%, respectively ( $P = 0.095$ ). Patients with and without SCZ had comparable all-cause mortality up to 4 years after CABG, but mortality was significantly higher in the SCZ group in the long-term follow-up (Fig. 1). Ten-year all-cause mortality was 42.7% in patients with SCZ and 30.3% in the control group after CABG (hazard ratio 1.56; 95% CI 1.13–2.17;  $P = 0.008$ ).

## MACE

MACE occurred in 670 patients ( $n = 46$  in the SCZ group) during the follow-up. The 30-day non-perioperative MACE incidence was 12.9% in patients with SCZ and 5.0% in the control group ( $P = 0.0001$ ). The difference between the study groups persisted during follow-up (Fig. 2). The cumulative incidence of MACE was 49.9% in the SCZ group and 32.6% in the control group at the 10-year follow-up (subdistribution hazard ratio 1.59; 95% CI 1.18–2.15;  $P = 0.003$ ).

The cumulative incidence of myocardial infarction during the 10-year follow-up was 28.8% in patients with SCZ compared with 15.3% in patients in the control group (subdistribution hazard ratio 1.86; 95% CI 1.25–2.78;  $P = 0.003$ ; Supplementary Fig. 2). The 10-year cumulative stroke incidence was 15.5% in the SCZ



**Fig. 2** Freedom from major adverse cardiovascular events (MACE) in patients with schizophrenia spectrum disorder and in matched control patients after coronary artery bypass grafting.

group and 14.1% in the control group (subdistribution hazard ratio 0.91; 95% CI 0.50–1.66;  $P = 0.765$ ; Supplementary Fig. 2). Cardiovascular mortality during follow-up was 26.7% in the SCZ group compared with 17.4% in the control group (subdistribution hazard ratio 1.65; 95% CI 1.10–2.48;  $P = 0.017$ ; Supplementary Fig. 2).

### Postoperative medication

Prescription medications after CABG are presented in Table 2. Statins were used less frequently by patients with SCZ than by controls (80.8 v. 87.8%;  $P = 0.022$ ). When statin therapy was used, high-intensity doses were less common in the SCZ compared with

the non-SCZ group (12.4 v. 22.0%;  $P = 0.023$ ). No significant differences were observed between patients with SCZ and matched controls in the use of antithrombotics, antidiabetics, antiarrhythmics, angiotensin pathway-targeting drugs, beta-blockers, calcium channel blockers, digitalis, diuretics or nitrates. Benzodiazepines, antidepressants and antipsychotics were used more frequently by patients with SCZ than those without SCZ after CABG (Table 2).

### Psychiatric hospital admissions and medications

Nine (7.6%) out of 118 patients with SCZ were treated in a psychiatric hospital ward in the year preceding CABG. The median length of hospital stay was 15 days (IQR 13–47 days). In the year preceding

**Table 2** Post-discharge cardiovascular prescription medication after coronary artery bypass grafting in hospital surviving patients who had schizophrenia spectrum disorder and in matched controls

	Schizophrenia spectrum <i>n</i> = 120	Control <i>n</i> = 2448	Odds ratio (95% CI)	<i>P</i> -value
ADP inhibitor	1 52 (10.0%)	329 (13.4%)	0.72 (0.39–1.32)	0.281
Anticoagulant	25 (20.8%)	503 (20.6%)	1.01 (0.64–1.59)	0.965
Antidiabetic	38 (31.7%)	705 (28.8%)	1.16 (0.78–1.73)	0.468
Insulin	13 (10.8%)	332 (13.6%)	0.78 (0.43–1.41)	0.405
Non-insulin	32 (26.7%)	534 (21.8%)	1.30 (0.86–1.98)	0.215
ACEi or ARB	75 (62.5%)	1704 (69.6%)	0.73 (0.50–1.07)	0.111
Antiarrhythmic	3 (2.5%)	97 (4.0%)	0.59 (0.19–1.90)	0.377
Beta-blocker	107 (89.2%)	2191 (89.5%)	0.97 (0.58–1.75)	0.920
Calcium channel blocker	17 (14.2%)	392 (16.0%)	0.86 (0.551–1.45)	0.570
Digitalis	5 (4.2%)	88 (3.6%)	1.12 (0.45–2.82)	0.805
Diuretic	61 (50.8%)	1054 (43.1%)	1.37 (0.95–1.98)	0.090
Nitrate	31 (25.8%)	597 (24.4%)	1.09 (0.71–1.68)	0.680
Statin	97 (80.8%)	2150 (87.8%)	0.58 (0.36–0.93)	0.022
High-intensity statin <sup>a</sup>	12 (12.4%)	473 (22.0%)	0.49 (0.26–0.91)	0.023
Antipsychotic	74 (61.7%)	43 (1.8%)	92.31 (51.01–167.07)	<0.0001
Antidepressant	24 (20.0%)	173 (7.1%)	3.27 (2.03–5.28)	<0.0001
Benzodiazepine	28 (23.3%)	141 (5.8%)	5.05 (3.20–7.98)	<0.0001

ADP, adenosine diphosphate; ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker.  
a. Reported as a portion of statin users.

CABG, 75.8% of patients with SCZ used antipsychotic prescription medication, 28.0% used antidepressants and 22.0% used benzodiazepines. These medications were used regularly by 58.6%, 13.6% and 19.5% of patients with SCZ, respectively. Psychiatric ward admission or use of antipsychotics, antidepressants or benzodiazepines before CABG was not associated with long-term mortality or MACE (Supplementary Table 3).

## Discussion

This multicentre, nationwide, retrospective case-control study showed that patients with SCZ had increased long-term all-cause mortality after CABG. MACE also occurred significantly more often in the SCZ group throughout the follow-up period, and appeared driven by increased cardiovascular mortality and myocardial infarction, but not by increased strokes. These results call attention to the need for aggressive secondary prevention in patients with SCZ and severe CAD.

Schizophrenia is a global health burden, resulting in up to 3.5-fold the standardised mortality<sup>23</sup> and a reduction in life expectancy by 15–25 years compared with the general population.<sup>6,24</sup> Cardiovascular mortality in schizophrenia is estimated to range from 40 to 50%, and therefore is a major contributor to shortened life expectancy.<sup>25</sup> In a previous register-based study, Attar et al<sup>26</sup> examined patients with schizophrenia after acute coronary syndrome and found that they had a higher overall mortality (hazard ratio 2.54), greater risk of MACE (hazard ratio 1.62) and greater risk of stroke (hazard ratio 1.51) after acute coronary syndrome compared with patients without schizophrenia. Patients with SCZ seem less likely than the general population to receive revascularisation therapy after myocardial infarction,<sup>16</sup> although revascularisation seems to benefit those with SCZ as much as it benefits the general population after myocardial infarction, at least during a 1-year follow-up period.<sup>17</sup> Studies investigating the long-term survival of patients with SCZ after revascularisation therapy are scarce; to our knowledge, this is the first study to explore outcomes after CABG.

We found an increased all-cause mortality in patients with SCZ during the 10-year follow-up after CABG, but, notably, this difference was present only beyond 4 years after CABG. In addition, our results show that patients with SCZ were approximately 1.5 times more likely to suffer from MACE during the long-term follow-up after CABG. The cumulative incidence of myocardial infarction during the 10-year follow-up was almost double in the SCZ group compared with the control group. Patients with SCZ also had a 40% longer duration of hospital admission than those in the control group. No previous studies about the long-term outcomes of patients with SCZ after CABG are available for a direct comparison with our results. In a recent large register-based study, Paredes et al<sup>27</sup> evaluated the effects of pre-existing mental illness on postoperative outcomes. In that study, patients with severe mental disorders, including schizophrenia, were more likely than controls to have perioperative complications (odds ratio 1.71) and extended durations of hospital admission (odds ratio 2.34), and these differences in morbidity were particularly notable among patients with severe mental illnesses after CABG.<sup>27</sup> Hauck et al<sup>17</sup> investigated the impact of revascularisation after myocardial infarction on mortality among patients with schizophrenia. They used a retrospective cohort of patients with acute myocardial infarction in Ontario between 2008 and 2015, and identified schizophrenia in 1145 patients (1.1% of the total cohort).<sup>17</sup> The study focused on different outcomes but mainly explored the efficacy of revascularisation therapy for patients with schizophrenia; however, they reported a slightly higher all-cause mortality for

patients with schizophrenia after coronary revascularization treatment (CABG and percutaneous coronary intervention combined) compared with the control group (hazard ratio 1.38) in the 1-year follow-up period after acute myocardial infarction.<sup>17</sup> Our results on mortality among patients with SCZ after CABG were even more favourable: we did not find significant differences in mortality between the groups before 4 years of follow-up. Importantly, our results of poorer outcome in patients with SCZ in longer follow-up should not be interpreted in the way that would exclude these vulnerable patients from CABG.

Causes for poorer cardiovascular outcomes in SCZ are likely multiple. Patients with schizophrenia smoke considerably more often than the general population,<sup>28,29</sup> and those who smoke have a 12-fold increased risk of cardiac-related death relative to nonsmokers.<sup>30</sup> Patients with schizophrenia are also more likely to be obese and have a greater risk of metabolic syndrome.<sup>31</sup> Visceral obesity in particular is linked to an increased risk of adverse metabolic effects, and individuals with schizophrenia are prone to greater visceral adiposity compared with the general population.<sup>32</sup> Other unhealthy nutritional and exercise habits might also contribute to the difference between the groups.

Use of evidence-based cardiovascular medication is firmly shown to improve outcomes in CAD.<sup>18</sup> Patients with schizophrenia are at least as adherent to cardiovascular medication as the general population,<sup>33</sup> yet they are generally less likely to obtain treatment for their somatic conditions.<sup>34</sup> We found the statins were used significantly less frequently after CABG by patients with SCZ. Furthermore, when statins were used, lower, less effective dosages were more common in patients with SCZ. Of note, the proportion of high-dose statin users was relatively poor (22%) in the non-SCZ group as well. However, somewhat surprisingly, the use of renin-angiotensin system inhibitors, beta-blockers, anticoagulants and adenosine diphosphate inhibitors did not differ between study groups. Because effective statin therapy significantly reduces all-cause and cardiovascular mortality after CABG,<sup>35,36</sup> our results call for more intensive statin therapy after CABG, especially in patients with SCZ.

Antipsychotic medications are the first-line treatment for SCZ.<sup>37,38</sup> There is strong evidence that the long-term use of antipsychotic medication lowers mortality in patients with SCZ. A recent meta-analysis of studies evaluating antipsychotic medication and mortality of patients with SCZ showed a pooled risk ratio of 0.57 for all-cause mortality with patients using any antipsychotic medication.<sup>39</sup> We hypothesized that antipsychotic medication consumption would lead to lower mortality after CABG, but found no association of pre-CABG antipsychotic use with outcomes after CABG. However, antipsychotic medications are known for their adverse cardiometabolic effects.<sup>40–43</sup> It is possible that these metabolic adverse effects, at least in part, balanced the overall adverse effects of weak adherence to antipsychotic medication in this study.

Evidence for polypharmacy in maintenance treatment of SCZ is sparse, but sometimes antipsychotic medications alone are inadequate to address all of the symptoms that occur in individuals with SCZ.<sup>44</sup> Benzodiazepine medication has been associated with an elevated risk of cardiovascular disease admissions and higher overall mortality in patients with schizophrenia.<sup>38</sup> However, we did not find significant differences in mortality or MACE for patients that used benzodiazepines before CABG. Psychiatric hospital admission implies severe symptoms in SCZ, and therefore is widely used as marker of unstable mental state in schizophrenia research.<sup>1,45</sup> Psychiatric hospital admission among patients with SCZ is associated with younger age; prior hospital admission; and comorbidities such as substance misuse, depression, anxiety and personality disorders.<sup>46</sup> Annual hospital admission rates range from approximately 23 to 27% in recent literature.<sup>46,47</sup> In our

study, the annual psychiatric hospital admission rate was only 7%. Older patient age might have contributed to the low hospital admission rate, but it is also likely that patient selection for CABG favours those with fewer psychiatric symptoms and better overall psychosocial functioning. It is also probable that individuals with more severe psychotic symptoms and comorbidities might avoid invasive treatments or might simply have higher early-age, all-cause mortality. In our data, pre-CABG psychiatric hospital treatment was not associated with mortality or MACE, although the small sample size is likely to yield insufficient statistical power to profoundly evaluate this association. Nevertheless, our results indicate that the need for psychiatric hospital admission or poorer adherence to antipsychotic medications should not be used as categorical grounds for denial of CABG. Further studies are needed on potential influence of CABG to psychiatric symptoms and well-being of patients with SCZ.

This register-based study has limitations. Our study design is retrospective and thus limits the potential to draw definitive conclusions. We used previously validated nationwide registries mandated by law in Finland.<sup>48</sup> Validity of SCZ diagnosis from these registers has been shown to be reliable.<sup>49</sup> However, it is still possible that the register data contain sources of bias. All diagnoses in the register were determined by treating clinicians, and there is a possibility of diagnostic or coding errors. Residual confounding by undetermined variables is possible. The prevalence of patients with SCZ diagnoses (ICD-10 groups F20, F21 and F25) in our cohort was only 0.4%, which is somewhat in line with a recent estimate of overall global prevalence of schizophrenia (0.3%),<sup>50</sup> but is considerably lower than a previously reported prevalence of 1.3% in Finland (for ICD-10 groups F20, F21 and F25 combined).<sup>51</sup> To improve the accuracy of a SCZ diagnosis, we did exclude diagnoses that might represent nonchronic and potentially aetiologically mixed groups of illnesses, such as ICD-10 code F29 (unspecified psychosis not due to a substance or known physiological condition). We did not have access to laboratory, smoking or income data, which limited the conclusions about the effectors of poorer outcomes. Medication purchases were used as a proxy for medication use, but we did not have direct information of actual use of purchased medications. Our results of CABG-treated patients may not be directly applicable to patients with CAD treated with percutaneous coronary intervention. Also, our sample of patients with SCZ was of limited size, which contributed to the limited statistical power for evaluation of weaker associations.

In conclusion, this study demonstrated that patients with CAD and SCZ are at a higher risk of death and adverse cardiovascular events during long-term follow-up after CABG. Neither psychiatric medication use nor psychiatric hospital admission before CABG were associated with long-term outcomes. Efforts should be targeted to optimise effective secondary prevention of CAD in patients with SCZ after CABG. Patients with chronic psychotic disorders constitute a unique and especially vulnerable subgroup among patients with CAD, and they could benefit from regular cardiovascular out-patient appointments with specialised protocols that encourage them toward healthy lifestyle choices and improved adherence to cardiovascular medication.

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## Supplementary material

Supplementary material is available online at <https://doi.org/10.1192/bjo.2022.10>.

## Data availability

The data that support the findings of this study are available on request from the national data authority Findata ([www.findata.fi](http://www.findata.fi)), for those fulfilling the requirements. The data are not publicly available because of legal restrictions.

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None.

## Author contributions

M.K. and V.K. drafted the article. M.K., J.K., M.M., P.K. and V.K. formulated the research question and designed the study. V.K. and P.R. were responsible for data acquisition and study funding. V.K. conducted data analysis and supervised the study. All authors revised the manuscript for intellectual content.

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## Declaration of interest

None.

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