Title: Disability-Free Survival after Major Cardiac Surgery in a Population-Based Cohort

Authors: Louise Y. Sun, MD, SM; Anan Bader Eddeen, MSc; Thierry G. Mesana, MD, PhD

Affiliations: From the Division of Cardiac Anesthesiology, Department of Anesthesiology and Pain Medicine, University of Ottawa Heart Institute, Ontario, Canada (LYS); the School of Epidemiology and Public Health, University of Ottawa, Ontario, Canada (LYS); the Institute for Clinical Evaluative Sciences, Ontario, Canada (LYS, ABE); the Division of Cardiac Surgery, Department of Surgery, University of Ottawa Heart Institute, Ontario, Canada (TGM).

Address for Correspondence and Reprints:

Louise Y. Sun, MD, SM, FRCPC, FAHA

Room H2410, 40 Ruskin Street

Ottawa, ON K1Y 4W7

Phone: 1 613 696 7381 Fax: 1 613 696 7099

Email: lsun@ottawaheart.ca

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ABSTRACT

Background: Cardiovascular research has been dedicated to "tombstone" outcomes such as death and complications, with little attention paid to outcomes that may also be important from a patient's perspective. We examined the rates of disability-free survival as a novel, patient-defined outcome after cardiac surgery.

Methods: This was a retrospective cohort study of patients ≥40 years of age who underwent coronary artery bypass grafting (CABG) and/or aortic, mitral, tricuspid valve surgery in Ontario between October 1 2008-December 31 2016. The primary outcome was disability (composite of stroke, ≥3 non-elective hospitalizations and long-term care admission) within one year after surgery. The procedure-specific risk of disability was assessed using a multivariable Fine and Gray subdistribution hazards model with death as a competing risk.

Results: Of 72,824 patients, 2,431 (4.6%) developed disability in the year after CABG, 677 (6.5%) after single valve, 118 (9.0%) after multiple valves, 718 (9.0%) after CABG/single valve, and 87 (13.1%) after CABG/multiple valve surgery. With isolated CABG as the reference group, the adjusted HRs for disability were 1.34 (95% CI: 1.21-1.48) after single valve, 1.43 (1.18-1.75) after multiple valves, 1.38 (1.26-1.51) after CABG/single valve, and 1.78 (1.43-2.23) after CABG/multiple valve surgery. Combined CABG/multiple valve surgery, heart failure, creatinine ≥180 μmol/L, alcoholism, dementia and depression were independent disability risk factors.

Interpretation: We found that the cumulative incidence of disability was lowest after isolated CABG and highest after combined CABG/multiple valve reconstruction. Our findings point to a need for personalized disability risk prediction models to better enable patient-centered care.

INTRODUCTION

Cardiac surgery is a growing field, with two million procedures currently being performed globally each year.[1] The last two decades have seen important advances in surgical and perioperative care, as well as improved patient survival.[2-4] On the other hand, as patients presenting for surgery become increasingly elderly and frail, they shift their goals and priorities towards how surgery might affect personal freedom and mobility, rather than to provide longevity alone.[5-9] New or residual impairments after surgery are of particular concern to patients and clinicians alike, but the quality and standard of cardiac care long has been assessed by traditional "tombstone" measures such as mortality and major adverse cardiovascular events (MACE).[5, 8, 10-12] Indeed, patient-centered care represents a priority area for modern medical practice and research, and the facilitation of shared surgical decision making could be improved by incorporating patient perspectives and patient-derived data.[13-15]

Our group has recently derived "disability-free survival" as a novel, patient-defined outcome through a large-scale survey of > 3000 patients with cardiovascular diseases.[16] According to patient preferences and values, disability was defined as the composite of stroke, recurrent non-elective hospitalizations and nursing home admission.[16] Before this outcome measure could be meaningfully utilized to inform patient-centered decision-making, its epidemiology and impact need to first be described at the population level. We therefore conducted the current study to examine the rates of disability-free survival after major cardiac surgery in a population-based cohort.

METHODS

Design and Study Population

We conducted a population-based, retrospective cohort study in Ontario, Canada. The use of data in this project was authorized under section 45 of Ontario's *Personal Health Information Protection Act*, which does not require review by a Research Ethics Board.[17]

Included were adult Ontario residents 40 years of age or older, who underwent CABG, and/or aortic, mitral or tricuspid valve surgery between October 1, 2008 and December 31, 2016. For those patients who underwent multiple cardiac procedures during the study period, the first procedure was considered the index procedure. Exclusion criteria were non-Ontario residency status, those with missing information regarding age and sex, and those who had concomitant arrhythmia, pulmonic valve or thoracic aorta surgery. A flow diagram detailing the process used to select the study cohort is shown in Supplemental Figure 1. During the study period, Ontario was Canada's most populous province with a publicly funded, universal health care system that reimbursed all covered services and providers.

Data Sources

We used the administrative healthcare databases from the Institute for Clinical Evaluative Sciences (ICES) with information on all Ontario residents, and the detailed clinical registry data from CorHealth Ontario. CorHealth Ontario maintains a prospective registry of all patients who undergo invasive cardiac procedures in Ontario. All 20 advanced cardiac hospitals in Ontario participate in the registry. It captures demographic, comorbidity and procedural-related information and has been validated through selected chart audits. In addition, CorHealth Ontario ejection fraction and angiographic data undergo core laboratory validation.[18]

Individuals who underwent the specified cardiac procedures were identified from the CorHealth Ontario registry, and linked deterministically to the ICES administrative databases by using encrypted unique confidential codes. Specifically, the date and type of cardiac procedures, physiologic and comorbidity data from CorHealth Ontario were linked with the Canadian Institute for Health Information's Discharge Abstract Database (DAD; comorbidities and hospital admissions) and Same Day Surgery (SDS) database (comorbidities), the Ontario Health Insurance Plan (OHIP) database (physician service claims), the Registered Persons Database (RPDB; ascertainment of vital statistics), the Continuing Care Reporting System (CCRS; admissions to long-term care facilities) and Canadian census. These administrative databases have been validated for many outcomes, exposures, and comorbidities, including heart failure (HF), chronic obstructive pulmonary disease (COPD), asthma, hypertension, myocardial infarction (MI) and diabetes.[19-22]

Comorbidities

Comorbidities were identified from the CorHealth Ontario registry and supplemented with data from DAD, SDS and OHIP using International Classification of Diseases 10th Revision (ICD-10-CA) codes[23] within five years prior to the index procedure, according to validated algorithms.[19,21,24,24,25, 26] We estimated socioeconomic status based on patients' neighborhood median income in the Canadian census, and determined their residence (rural versus urban) using the definitions from Statistics Canada.[27] Procedural urgency was ascertained from the CorHealth Ontario registry. Height, weight and body mass index (BMI) were identified from the CorHealth Ontario registry, and used to define morbid obesity (weight >159 kg or BMI ≥40 kg/m^2).[16, 26, 28, 29] Frailty status was identified using the Johns Hopkins Adjusted Clinical Groups frailty-defining

diagnoses indicator, which is an instrument designed and validated for research of frailty-related outcomes and resource utilization using administrative data.[29-34]

Outcomes

The primary outcome was disability, defined as patient-derived composite of stroke, nursing home admission, and recurrent non-elective hospital admissions of ≥ 3 episodes occurring within 1 year of surgery. Secondary outcomes consisted of all-cause death and each individual component of disability. Stroke requiring hospitalization was identified using a validated algorithm with 70% sensitivity and 99% specificity.[35] Non-elective hospital admissions were ascertained by using the DAD, and long-term care admissions were ascertained using the CCRS.

Statistical Analysis

Continuous variables are expressed as mean (standard deviation) and categorical variables as number (proportions). Outcomes were assessed through December 31, 2017. Patients were censored when they lost possession of a valid Ontario health insurance card. Disability-free survival was defined as survival time from the date of index surgery until the date of a disability-defining event, death or last follow-up, whichever occurred earlier. For patients experiencing recurrent non-elective hospitalizations, disability was considered to occur on the date of the first admission. To account for death as a competing risk, we estimated the cumulative incidence of disability over time using Cumulative Incidence Functions (CIFs), and the risk of disability and each of the disability-defining events with multivariable Fine and Gray subdistribution hazards models using the variables listed in Table 3. We explored whether sex

had a modifying effect on the relationship between disability and type of surgery, by using a multiplicative interaction term of sex*type of surgery within each of the multivariable time-to-event models.

Analyses were performed using SAS 9.4 (SAS Institute, Cary, NC), with statistical significance defined by a two-sided P-value of < 0.05. We used the adjusted hazard ratio (HR) and associated 95% confidence intervals (CI) to describe the measure of association, and defined a clinically meaningful effect as HR ≥ 1.50.

RESULTS

Baseline Characteristics

A total of 72,824 patients were included in the study. The baseline patient characteristics according to type of surgery are summarized in Table 1. Isolated CABG accounted for 72% of the provincial procedure volume. These were most likely to be performed in younger men with a history of previous MI and PCI; and least likely to be performed in those with HF. Compared to those who underwent combined CABG/valve procedures, those who underwent isolated valve surgery were younger and were more likely to have preserved LVEF and a lower burden of comorbidities as evidenced by a lower Charlson comorbidity index. Further, those who underwent combined CABG/multiple valve surgery were amongst the frailest and burdened with the highest number of comorbidities.

Effect Modification by Sex

As we did not observe a statistically significant interaction effect between sex and type of surgery (interaction p = 0.07), subsequent analyses were not stratified by sex.

Disability-Free Survival

Table 2 summarizes the rates of disability, death and individual disability-defining events according to surgery type. Figure 1 illustrates the cumulative incidence of disability, and Figure 2 the estimated survival at one-year. The incidence proportions of disability and death were as follows: 2,431 (4.6%) vs. 1,839 (3.5%) in the CABG-only group; 677 (6.5%) vs. 540 (5.2%) in the single valve group; 118 (9.0%) vs. (10.7%) in the multiple valves group; 718 (9.0%) vs. 734 (9.2%) in the CABG/single valve group; and 87 (13.1%) vs. 94 (14.1%) in the CABG/multiple

valves group. Overall, the one-year cumulative incidence of disability was lowest in patients who underwent isolated CABG and highest after CABG/multiple valve surgery. Disability occurred more frequently than death in the year after isolated CABG and single valve surgery.

Disability-Defining Events

The cumulative incidence of stroke, recurrent non-elective hospitalizations and long-term care admissions varied by type of surgery (Table 1 and Supplemental Figures 2-4). Specifically, the rates of all three events were lowest after isolated CABG, highest after combined CABG/multiple valve reconstruction, and were similar after multiple valve and CABG/single valve surgery.

Disability Risk Factors

The multivariable predictors of disability are summarized in Table 3. With isolated CABG as the reference group, the adjusted subdistribution HRs for disability were 1.34 (95% CI, 1.21-1.48) for single valve, 1.43 (1.18-1.75) for multiple valves, 1.38 (1.26-1.51) for CABG/single valve and 1.78 (1.43-2.23) for CABG/multiple valve reconstruction. Other statistically significant risk factors of disability were age, female sex, emergent operative status, low income, a history of hypertension, atrial fibrillation, MI, HF, cerebrovascular disease, peripheral arterial disease, current smoker, COPD, diabetes, anemia, renal insufficiency, liver disease, alcoholism, dementia, depression, and cancer. Of these, CABG/multiple valve surgery, HF, baseline creatinine $\geq$ 180 μmol/L, alcoholism, dementia and depression were the most clinically significant predictors of disability.

INTERPRETATION

To our knowledge, this is the first population-based study to systematically describe the incidence and risk factors of patient-defined disability after common cardiac procedures. We found that: 1) the cumulative incidence of disability was lowest after isolated CABG and highest after CABG/multiple valve surgery. 2) Disability occurred more frequently than death in the year after isolated CABG and single valve surgery. 3) Combined CABG/multiple valve surgery, HF, baseline creatinine ≥ 180 μmol/L, alcoholism, dementia and depression were important predictors of disability in the year after cardiac surgery.

The Need for Patient-Defined Outcomes in Cardiovascular Research

Traditional revascularization trials have sometimes been referred to as "tombstone trials"[6] due to their focus on death and complications. However, a survey of cardiovascular patients indicated that important outcomes identified by patients were in fact very different compared to those from the clinician's view.[16] Indeed, the incorporation of patient perceptions and values into the design of outcome measures has been proposed as a priority area for cardiovascular research. Such a paradigm shift has been shown to increase the relevance of the research to the end user, speed up the uptake of research into practice, and empower patients to make better informed decisions.[36]

To date, few studies have directly engaged surgical patients to determine what outcomes were meaningful to them as important end users of the research. Such studies include surveys of noncardiac surgery patients to rank outcomes such as postoperative nausea, vomiting, pain and somnolence in order of unpleasantness,[37-39] but similar research has not been conducted in the realm of cardiac surgery. "Patient-centered" cardiac surgery research has instead employed

standard, clinician-derived instruments (e.g., Seattle Angina Questionnaire, Rose Dyspnea Score, and Patient Health Questionnaire) that were based on expert consensus alone without active input from patients.[40] These standard instruments may not be meaningful to all patients as they do not capture all relevant aspects of outcomes after treatment.[41] Outcomes are an important determinant of treatment satisfaction, and the use of patient-defined outcomes has the unique advantage of improving both patient satisfaction and adherence to treatment.

There is no universal agreement on the definition of disability in cardiovascular research.[11] Prospective studies using clinician-derived instruments are often limited by small sample size and short follow-up durations within a single center setting. In the present study, we used a novel and versatile definition of disability based on patient preferences, which is adaptable to both prospective trials and large retrospective cohorts. Knowledge generated from this broad epidemiologic study will inform areas of focus for practice-changing research in the future.

Disability After Cardiac Surgery

CABG is an advancing field where operative mortality has steadily declined over the years.[42] This, together with the younger age of presentation for CABG, could explain the lower observed rates of disability after this procedure as compared to complex CABG/multiple valve procedures, which are often performed on older and frailer patients. Complex surgery is associated with greater physiologic stresses such as fluid and electrolyte shifts, prolonged bypass durations, and a higher likelihood of exposure to low cardiac output, hypotension, end organ injury and death.[43]

To date, disability after cardiac surgery has been reported in the form of health-related quality of life (QoL), using instruments such as the SF-36, in several small observational studies.

In a single center study of 112 patients, patients reported higher than normative scores in subscales of social functioning, role physical and role emotional; and lower scores in physical function, bodily pain, general health, vitality social function and mental health; at one year after CABG.[44] In a study of 534 consecutive cardiac surgery patients over the age of 75 years, mean reported QoL improved at 6 months postoperatively as compared to baseline.[45] In a study of 154 nonagenarians who underwent CABG and/or valve procedures, 83% of the survivors reported an improvement in QoL and 4% a decline in QoL, one year after surgery.[46] Our findings demonstrate that the incidence of patient-defined disability may in fact be greater than previously described by traditional instruments. Moreover, we were able to describe the population-based incidence of disability by type of surgery and across a wider patient age range. We found that the burden of disability was higher than death after routine procedures such as isolated CABG and single valve surgery, and these findings were driven mostly by recurrent hospital admissions, followed by stroke, especially in those with HF, renal dysfunction, alcoholism, dementia and depression. As patients' ability to make informed decisions is often influenced by the emotional and logistical repercussions of their disease diagnosis as well as limitations in health literacy, patients with these high-risk features should be the focus of informed perioperative counseling and undergo formal heart team evaluation regarding the risks and benefits of alternative treatment strategies.

Limitations

This study has several limitations. *Firstly*, data pertaining to stroke severity is unavailable in the databases used. As some stroke patients experience full functional recovery, our findings may have over-estimated the burden of stroke-related disability. *Secondly*, our definition of

disability was based solely on patient perceptions and values. Further studies could aim to additionally elicit feedback from family members and caregivers to co-define outcomes, with input and guidance from clinicians. *Lastly*, cohort studies are by nature subjected to residual confounding.

CONCLUSIONS

We studied the procedure-specific incidence of a patient-defined disability outcome in a large cohort of cardiac surgical patients. We found disability to be a more frequent complication than death in the year after isolated CABG and single valve surgeries. In addition, patients who undergo combined CABG/multiple valve surgery, and those who have a history of HF, baseline creatinine ≥ 180 μmol/L, alcoholism, dementia and depression are at the greatest risk for developing disability. Future research should be dedicated to personalized disability risk prediction to better inform the joint therapeutic decision-making process and in doing so, to improve the efficiency and effectiveness of health care delivery as well as patient satisfaction.

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FIGURES

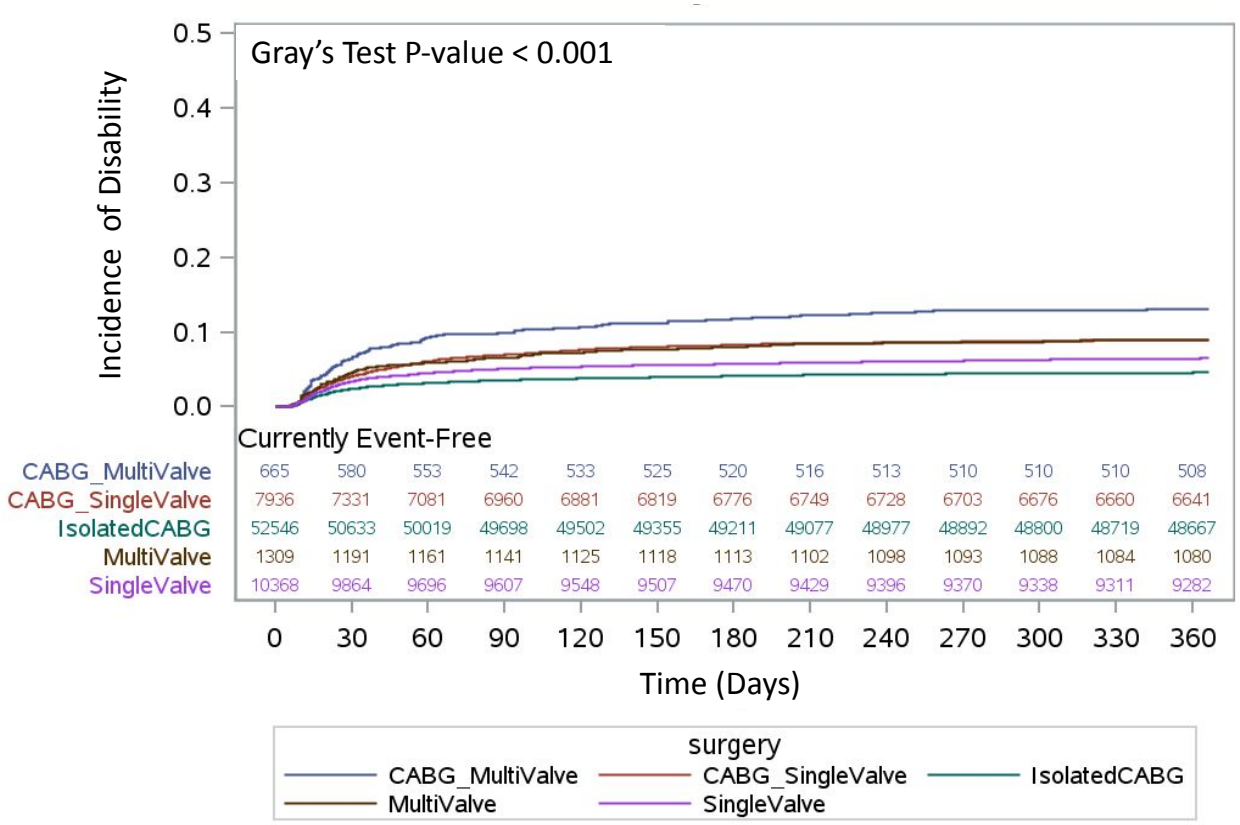


Figure 1. Cumulative incidence of disability within one year after cardiac surgery.

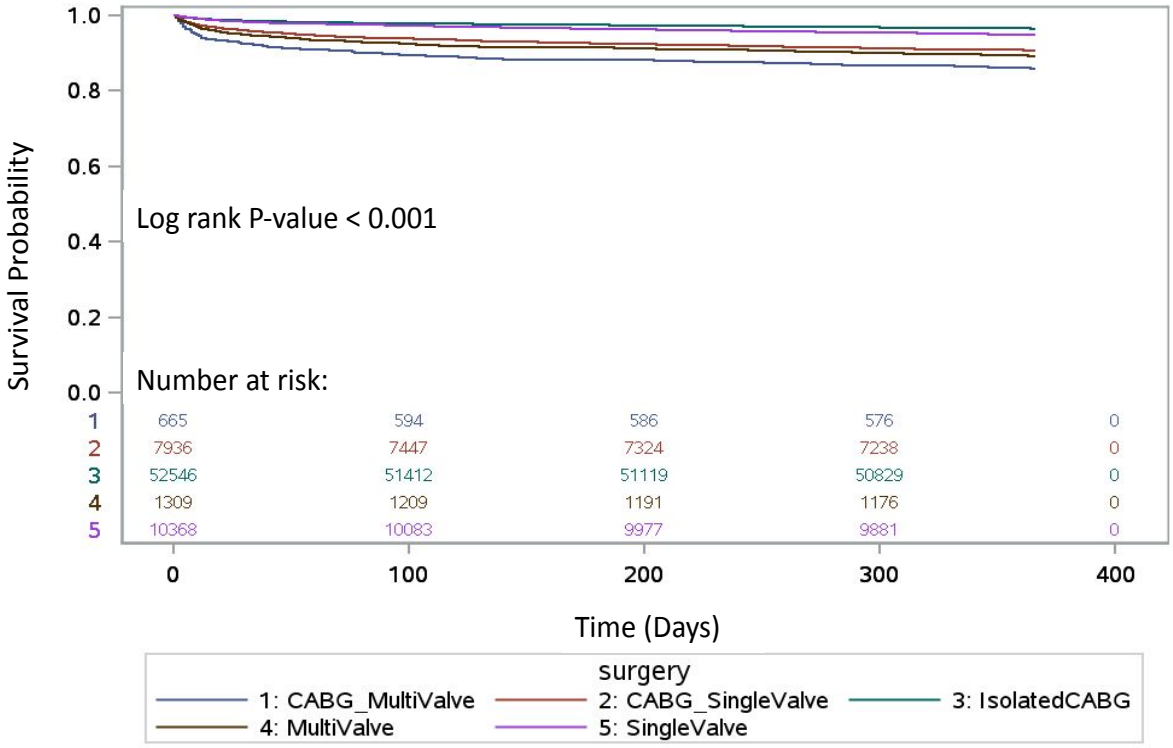


Figure 2. Estimated survival within one year after cardiac surgery.

Table 1. Baseline characteristics, stratified by type of surgery

Variable	No. (%) of patients*						P value
	Overall population (N=72 824)	Isolated CABG (N= 52 546)	Single valve† (N= 10 368)	Multiple valves‡ (N= 1 309)	CABG + single valve† (N= 7 936)	CABG + multiple valves‡ (N= 665)	
Age, mean ± SD, y	67.0 ± 10.2	65.9 ± 9.8	67.5 ± 11.2	68.3 ± 11.4	72.6 ± 9.0	72.5 ± 9.1	<0.001
40-64	28 941 (39.7)	22 925 (43.6)	3 969 (38.3)	458 (35.0)	1 460 (18.4)	129 (19.4)	<0.001
65-74	25 229 (34.6)	18 626 (35.4)	3 197 (30.8)	395 (30.2)	2 795 (35.2)	216 (32.5)	
75-84	16 806 (23.1)	10 220 (19.4)	2 801 (27.0)	388 (29.6)	3 128 (39.4)	269 (40.5)	
≥85	1 848 (2.5)	775 (1.5)	401 (3.9)	68 (5.2)	553 (7.0)	51 (7.7)	
Rural Residence	11 763 (16.2)	8 204 (15.6)	1 756 (16.9)	203 (15.5)	1 457 (18.4)	143 (21.5)	
Income quintile							
1 (lowest)	13 448 (18.5)	10 003 (19.0)	1 728 (16.7)	245 (18.7)	1 370 (17.3)	102 (15.3)	<0.001
2	14 696 (20.2)	10 724 (20.4)	1 959 (18.9)	257 (19.6)	1 608 (20.3)	148 (22.3)	
3	14 759 (20.3)	10 627 (20.2)	2 117 (20.4)	249 (19.0)	1 609 (20.3)	157 (23.6)	

4	15 017 (20.6)	10 714 (20.4)	2 214 (21.4)	257 (19.6)	1 705 (21.5)	127 (19.1)	
5 (highest)	14 532 (20.0)	10 184 (19.4)	2 310 (22.3)	292 (22.3)	1 617 (20.4)	129 (19.4)	
Missing	372 (0.5)	294 (0.6)	40 (0.4)	9 (0.7)	27 (0.3)	≤5	
Hypertension	62 852 (86.3)	46 111 (87.8)	7 954 (76.7)	1 007 (76.9)	7 185 (90.5)	595 (89.5)	<0.001
Atrial fibrillation	5 165 (7.1)	2 373 (4.5)	1 343 (13.0)	304 (23.2)	990 (12.5)	155 (23.3)	<0.001
Recent MI	22 952 (31.5)	20 684 (39.4)	422 (4.1)	55 (4.2)	1 659 (20.9)	132 (19.8)	<0.001
Remote MI	11 605 (15.9)	9 432 (17.9)	679 (6.5)	91 (7.0)	1 295 (16.3)	108 (16.2)	<0.001
Previous PCI	10 532 (14.5)	8 773 (16.7)	617 (6.0)	70 (5.3)	1 004 (12.7)	68 (10.2)	<0.001
Heart failure	19 847 (27.3)	10 126 (19.3)	4 729 (45.6)	848 (64.8)	3 714 (46.8)	430 (64.7)	<0.001
LVEF							
≥50%	48 185 (66.2)	32 237 (61.4)	8 843 (85.3)	1 040 (79.4)	5 630 (70.9)	435 (65.4)	
35-50%	15 448 (21.2)	12 762 (24.3)	967 (9.3)	176 (13.4)	1 398 (17.6)	145 (21.8)	
20-35%	6 044 (8.3)	4 911 (9.3)	346 (3.3)	67 (5.1)	654 (8.2)	66 (9.9)	
<20%	1 113 (1.5)	905 (1.7)	43 (0.4)	13 (1.0)	139 (1.8)	13 (2.0)	
Missing	2 034 (2.8)	1 731 (3.3)	169 (1.6)	13 (1.0)	115 (1.4)	6 (0.9)	<0.001
Cerebrovascular	7 420 (10.2)	5 132 (9.8)	970 (9.4)	163 (12.5)	1 073 (13.5)	82 (12.3)	<0.001

disease							
Peripheral arterial disease	9 139 (12.5)	6 424 (12.2)	1 079 (10.4)	139 (10.6)	1 389 (17.5)	108 (16.2)	<0.001
COPD or asthma	21 419 (29.4)	14 702 (28.0)	3 301 (31.8)	439 (33.5)	2 726 (34.3)	251 (37.7)	<0.001
Diabetes mellitus	32 812 (45.1)	25 267 (48.1)	3 218 (31.0)	422 (32.2)	3 639 (45.9)	266 (40.0)	<0.001
Morbid obesity	28 391 (39.0)	20 490 (39.0)	3 951 (38.1)	563 (43.0)	3 106 (39.1)	281 (42.3)	0.004
Hypothyroidism	1 419 (1.9)	969 (1.8)	206 (2.0)	40 (3.1)	186 (2.3)	18 (2.7)	<0.001
Liver disease	633 (0.9)	351 (0.7)	153 (1.5)	37 (2.8)	81 (1.0)	11 (1.7)	<0.001
Anemia	7 347 (10.1)	4 918 (9.4)	977 (9.4)	203 (15.5)	1 113 (14.0)	136 (20.5)	<0.001
Venous thromboembolism	288 (0.4)	173 (0.3)	57 (0.5)	10 (0.8)	46 (0.6)	≤5	<0.001
Dialysis	1 531 (2.1)	1 047 (2.0)	195 (1.9)	34 (2.6)	233 (2.9)	22 (3.3)	<0.001
Baseline Creatinine (μmol/L)							
120-179	6 635 (9.1)	4 487 (8.5)	855 (8.2)	163 (12.5)	1 037 (13.1)	93 (14.0)	<0.001
<120	60 190 (82.7)	43 934 83.6)	8 538 (82.3)	1 038 (79.3)	6 158 (77.6)	522 (78.5)	

≥ 180	2 435 (3.3)	1 698 (3.2)	261 (2.5)	63 (4.8)	381 (4.8)	32 (4.8)	
Missing	3 564 (4.9)	2 427 (4.6)	714 (6.9)	45 (3.4)	360 (4.5)	18 (2.7)	
Chronic renal disease	3 133 (4.3)	2 109 (4.0)	399 (3.8)	66 (5.0)	516 (6.5)	43 (6.5)	<0.001
Dementia	176 (0.2)	98 (0.2)	27 (0.3)	≤5	41 (0.5)	6 (0.9)	<0.001
Depression	1 089 (1.5)	733 (1.4)	157 (1.5)	37 (2.8)	149 (1.9)	13 (2.0)	<0.001
Psychosis	161 (0.2)	102 (0.2)	33 (0.3)	6 (0.5)	17 (0.2)	≤5	0.025
Primary tumor	3 770 (5.2)	2 486 (4.7)	601 (5.8)	96 (7.3)	539 (6.8)	48 (7.2)	<0.001
Metastatic cancer	375 (0.5)	248 (0.5)	72 (0.7)	10 (0.8)	40 (0.5)	≤5	0.03
Charlson score, median (IQR)	1 (0-3)	2 (0-3)	1 (0-2)	1 (0-2)	2 (0-3)	2 (1-3)	<0.001
Frailty[§]	11 685 (16.0)	8 623 (16.4)	1 204 (11.6)	213 (16.3)	1 491 (18.8)	154 (23.2)	<0.001

* Unless otherwise stated [†]Mitral, aortic or tricuspid valve surgery [‡]Mitral, aortic or tricuspid valve surgery

[§]According to the Johns Hopkins Adjusted Clinical Groups frailty-defining diagnoses indicator [29-34]

Abbreviations: CABG = coronary artery bypass grafting; COPD = chronic obstructive pulmonary disease; LVEF = left ventricular ejection fraction; MI = myocardial infarction; PCI = percutaneous coronary intervention; IQR = interquartile range

Table 2. Event rates within 1 year following cardiac surgery.

Event, n (%)	CABG (n=52,546)	Single Valve (n=10,368)	Multiple Valves (n=1,309)	CABG + Single Valve (n=7,936)	CABG + Multiple Valves (n=665)	P-Value
Disability	2,431 (4.6)	677 (6.5)	118 (9.0)	718 (9.1)	87 (13.1)	<0.001
Death	1,839 (3.5)	540 (5.2)	140 (10.7)	734 (9.2)	94 (14.1)	<0.001
Stroke	808 (1.5)	258 (2.5)	48 (3.7)	280 (3.5)	38 (5.7)	<0.001
≥ 3 non-elective hospitalizations	1,454 (2.8)	367 (3.5)	57 (4.4)	373 (4.7)	41 (6.2)	<0.001
Long-term care admission	342 (0.7)	102 (1.0)	20 (1.5)	122 (1.5)	12 (1.8)	<0.001

Abbreviations: CABG = coronary artery bypass grafting

Table 3. Multivariable predictors of disability at one-year after major cardiac surgery.

Variable	HR (95% CI)	P-Value
Age	1.03 (1.02-1.03)	<0.001
Female	1.38 (1.28-1.48)	<0.001
Surgery Type		
Isolated CABG	Reference	Reference
Single Valve	1.34 (1.21-1.48)	<0.001
Multiple Valves	1.43 (1.18-1.75)	<0.001
CABG + Single Valve	1.38 (1.26-1.51)	<0.001
CABG + Multiple Valves	1.78 (1.43-2.23)	<0.001
Emergent Procedure	1.40 (1.26-1.57)	<0.001
Rural Residence	1.03 (0.94-1.12)	0.55
Income Quintile		
1 (Lowest)	1.33 (1.20-1.47)	<0.001
2	1.16 (1.05-1.29)	0.004
3	1.11 (1.00-1.23)	0.05
4	0.99 (0.89-1.10)	0.83
5 (Highest)	Reference	Reference
Hypertension	1.16 (1.03-1.31)	0.02
Atrial Fibrillation	1.25 (1.14-1.37)	<0.001
Heart Failure	1.66 (1.53-1.79)	<0.001
MI within 30 Days	1.26 (1.17-1.36)	<0.001
Remote MI	1.13 (1.04-1.23)	<0.001
Previous PCI	0.94 (0.85-1.03)	0.17
LVEF		
< 20%	1.10 (0.89-1.36)	0.37
20-34%	1.07 (0.99-1.16)	0.10
35-49%	1.00 (0.89-1.11)	0.94
≥ 50%	Reference	Reference
Cerebrovascular Disease	1.40 (1.29-1.53)	<0.001
Peripheral Arterial Disease	1.23 (1.14-1.34)	<0.001
Smoker		
Never	Reference	Reference
Current	1.19 (1.09-1.30)	<0.001
Former	1.07 (0.99-1.15)	0.08
COPD/Asthma	1.32 (1.24-1.41)	<0.001
Pulmonary Circlatory Disorder	1.07 (0.91-1.24)	0.42
Morbid Obesity	0.97 (0.91-1.03)	0.31

Diabetes	1.38 (1.29-1.47)	<0.001
Hypothyroidism	1.10 (0.93-1.31)	0.25
Anemia	1.39 (1.28-1.51)	<0.001
Baseline Creatinine (µmol/L)		
< 120	Reference	Reference
120-179	1.32 (1.21-1.45)	<0.001
≥ 180	1.81 (1.57-2.08)	<0.001
Dialysis	1.40 (1.19-1.64)	<0.001
Liver Disease	1.33 (1.06-1.68)	0.02
Alcoholism	1.68 (1.39-2.03)	<0.001
Dementia	1.59 (1.13-2.24)	0.01
Depression	1.66 (1.41-1.97)	<0.001
Psychosis	1.05 (0.62-1.76)	0.87
Primary Cancer	1.19 (1.06-1.34)	0.004
Metastatic Cancer	1.47 (1.08-1.99)	0.01

Abbreviations: CABG = coronary artery bypass grafting; MI = myocardial infarction; PCI = percutanoues coronary intervention; COPD = chronic obstructive pulmonary disease; HR = hazard ratio, CI = confidence interval

Supplemental Material

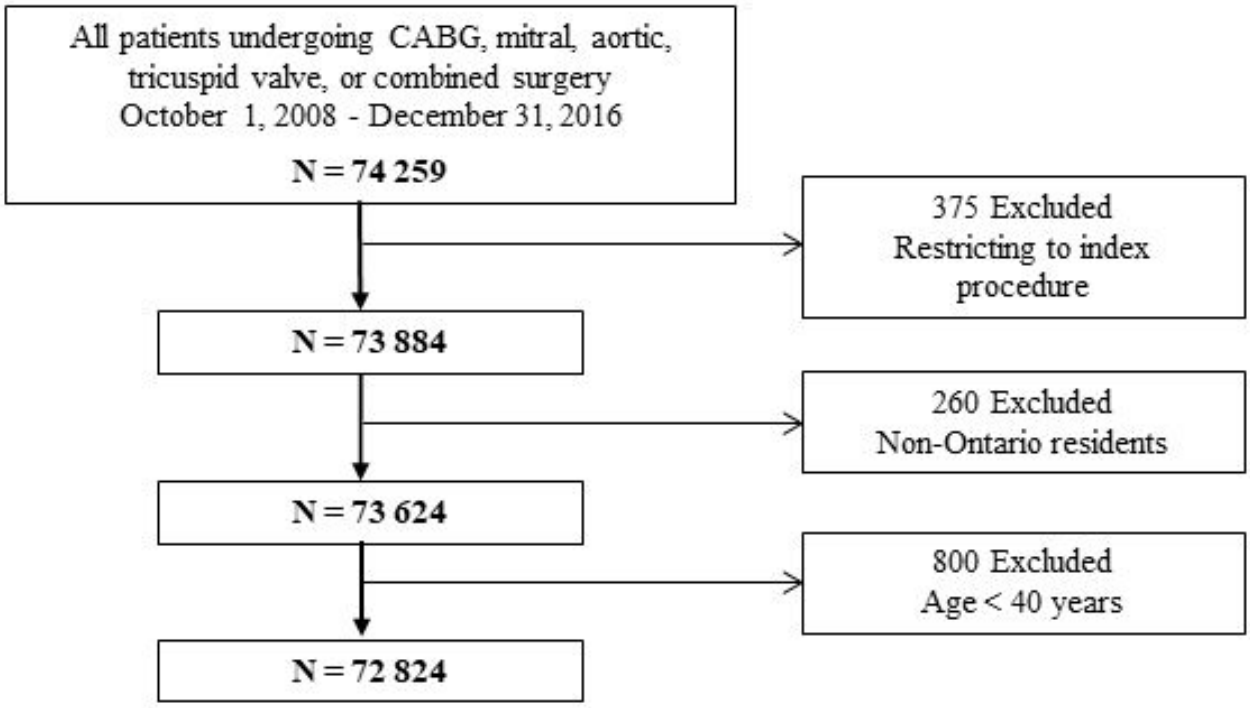
Supplemental Figure 1. Cohort selection flow chart

Supplemental Figure 2. Cumulative incidence of stroke within one year after cardiac surgery.

Supplemental Figure 3. Cumulative incidence of long-term care (LTC) admissions within one year after cardiac surgery.

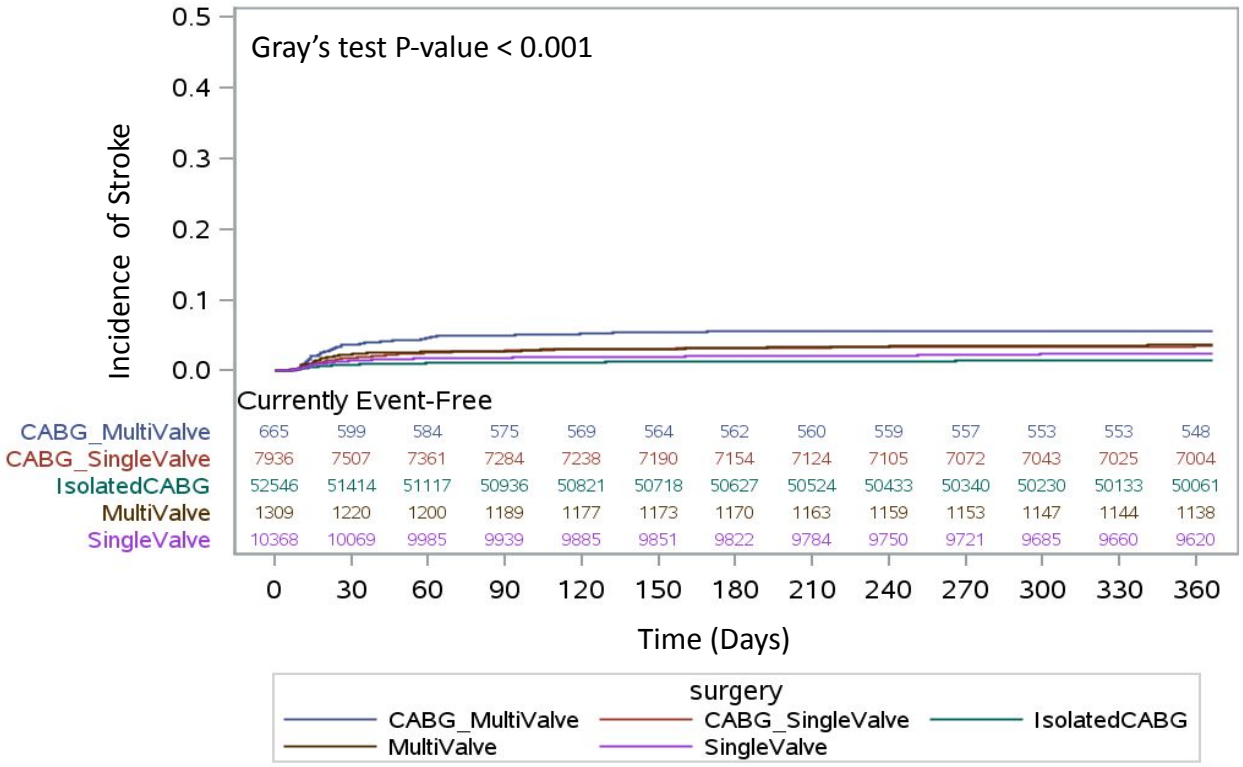
Supplemental Figure 4. Cumulative incidence of recurrent non-elective hospitalizations (≥3 episodes per year) within one year after cardiac surgery.

Supplemental Figure 1. Cohort selection flow chart

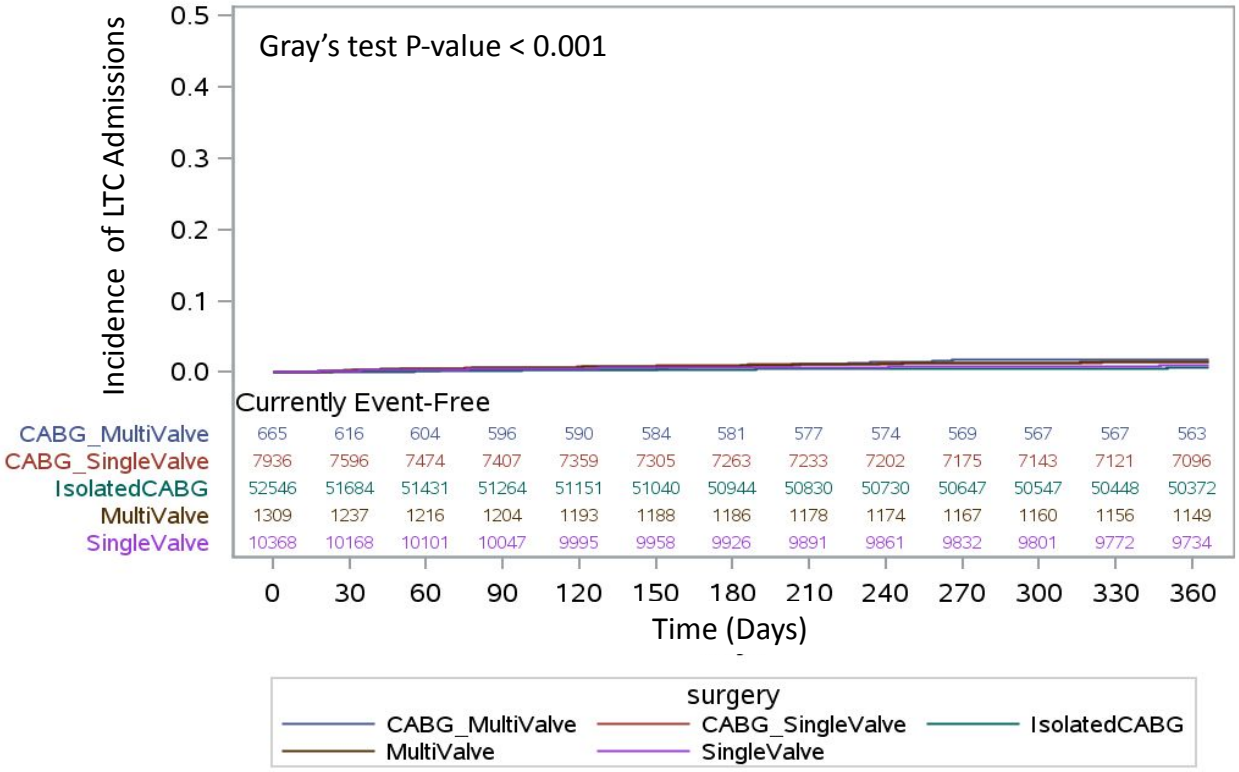


Abbreviation: CABG = coronary artery bypass surgery

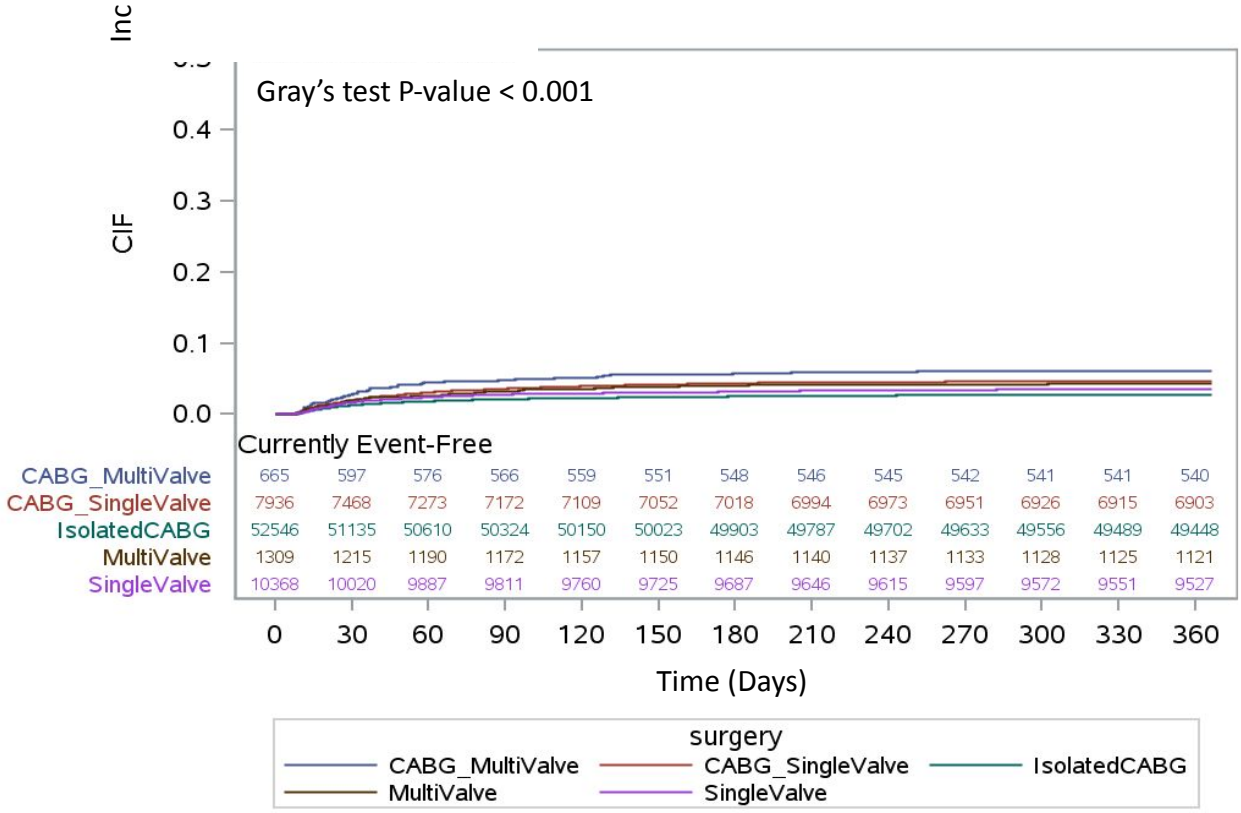
Supplemental Figure 2. Cumulative incidence of stroke within one year after cardiac surgery.



Supplemental Figure 3. Cumulative incidence of long-term care (LTC) admissions within one year after cardiac surgery.



Supplemental Figure 4. Cumulative incidence of recurrent non-elective hospitalizations (≥3 episodes per year) within one year after cardiac surgery.



STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Title page
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	2
Objectives	3	State specific objectives, including any prespecified hypotheses	2
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	3
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	3-4
Bias	9	Describe any efforts to address potential sources of bias	5-6
Study size	10	Explain how the study size was arrived at	3
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5-6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5-6
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, explain how loss to follow-up was addressed	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Suppl Fig 1
		(b) Give reasons for non-participation at each stage	Suppl Fig 1
		(c) Consider use of a flow diagram	Suppl Fig 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7
		(b) Indicate number of participants with missing data for each variable of interest	Table 1
		(c) Summarise follow-up time (eg, average and total amount)	5
Outcome data	15*	Report numbers of outcome events or summary measures over time	Table 2; p.7

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	p. 8; Table 3 Table 1 N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6-7
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11-12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12
Generalisability	21	Discuss the generalisability (external validity) of the study results	12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Title page

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.