ORIGINAL RESEARCH

Economic Impact of Subsequent Depression in Patients With a New Diagnosis of Stable Angina: A Population-Based Study

Natalie Szpakowski, MD; Feng Qiu, MSc; Shannon Masih, MSc, MPH; Paul Kurdyak, MD, PhD; Harindra C. Wijeysundera, MD, PhD

Background—Depression is strongly linked to increased morbidity and mortality in patients with chronic stable angina; however, its associated healthcare costs have been less well studied. Our objective was to identify the characteristics of chronic stable patients found to have depression and to determine the impact of an occurrence of depression on healthcare costs within 1 year of a diagnosis of stable angina.

Methods and Results—In this population-based study conducted in Ontario, Canada, we identified patients diagnosed with stable angina based on angiogram between October 1, 2008, and September 30, 2013. Depression was ascertained by physician billing codes and hospital admission diagnostic codes contained within administrative databases. The primary outcome was cumulative mean 1-year healthcare costs following index angiogram. Generalized linear models were developed with a logarithmic link and γ distribution to determine predictors of cost. Our cohort included 22 917 patients with chronic stable angina. Patients with depression had significantly higher mean 1-year healthcare costs (\$32 072$\pm$\$41 963) than patients without depression (\$23 021$\pm$\$25 741). After adjustment for baseline comorbidities, depression was found to be a significant independent predictor of cost, with a cost ratio of 1.33 (95% confidence interval, 1.29–1.37). Higher costs in depressed patients were seen in all healthcare sectors, including acute and ambulatory care.

Conclusions—Depression is an important driver of healthcare costs in patients following a diagnosis of chronic stable angina. Further research is needed to understand whether improvements in the approach to diagnosis and treatment of depression will translate to reduced expenditures in this population. **(*J Am Heart Assoc*. 2017;6:e006911. DOI: 10.1161/JAHA.117.006911.)**

Key Words: cost • depression • stable coronary artery disease

Coronary artery disease (CAD) poses a major public health and economic burden globally. In Canada, the yearly estimate for direct medical costs related to cardiovascular diseases was \$11.7 billion in 2008.[1] CAD also incurs an indirect economic impact due to disability, lost work productivity, and premature mortality.[2] Cumulatively, these figures are expected to grow with the rise in prevalence of CAD related to the aging population.[3]

To develop efficient strategies that will improve outcomes and reduce expenditures, it is important to understand drivers of cost among patients with CAD. Depression is a frequent comorbidity in patients with chronic diseases and is known to magnify healthcare costs.[4] Among patients with CAD, depression is the most common psychiatric disorder.[5] Depression is present in ≈20% of patients with CAD and is an independent risk factor for adverse outcomes, including cardiac events and mortality.[6] The exact nature of this relationship is unclear but is likely related to certain behavioral and physiological characteristics of depressed patients.[7] In the setting of myocardial infarction, depression has been shown to increase healthcare utilization related to higher hospital readmission rates, longer length of stay, and more frequent ambulatory care and emergency room visits.[8–12] Similarly, this relationship has been observed in depressed patients with coronary artery bypass grafting (CABG)[13] and congestive heart failure.[14]

From the Schulich Heart Centre, Division of Cardiology, Sunnybrook Health Sciences Centre (N.S., H.C.W.), Sunnybrook Research Institute (H.C.W.), Institute for Health Policy Management and Evaluation (P.K., H.C.W.), and Department of Psychiatry and Institute of Medical Science (P.K.), University of Toronto, Toronto, Ontario, Canada; Institute for Clinical Evaluative Sciences, Toronto, Ontario, Canada (F.Q., S.M., P.K., H.C.W.); Social and Epidemiological Research Department, Centre for Addiction and Mental Health, Toronto, Ontario, Canada (P.K.).

Accompanying Tables S1 through S3 are available at http://jaha.ahajournals.org/content/6/10/e006911/DC1/embed/inline-supplementary-material-1.pdf

Correspondence to: Harindra C. Wijeysundera, MD, PhD, 2075 Bayview Avenue, Suite A202, Toronto, Ontario M4N3M5. E-mail: harindra.wijeysundera@sunnybrook.ca

Received July 24, 2017; accepted August 29, 2017.

Clinical Perspective

What Is New?

- An occurrence of depression within 1 year of a diagnosis of chronic stable angina is a significant driver of mean 1-year healthcare costs.
- Among patients with chronic stable angina, depression is associated with increased costs in nearly all healthcare sectors, not only mental health services.

What Are the Clinical Implications?

- Depression has important economic consequences in patients with chronic stable angina.
- Higher costs in both acute and ambulatory care are seen in depressed patients.
- Additional research is needed to determine whether interventions such as screening for depression will lessen healthcare utilization in this group of patients.

In comparison, there is a paucity of data on the pattern of healthcare use and cost in patients with chronic stable angina and depression; studies to date have been small[15,16] and conducted in primary care settings.[17] Chronic stable angina constitutes the most prevalent form of CAD,[2] and depression also negatively affects morbidity and mortality in this large group of patients.[18] A more comprehensive understanding of how healthcare costs in stable angina patients are affected by a diagnosis of depression is a necessary step toward improving care and cost containment in this population. Accordingly, to address this gap in knowledge, the aim of our study was to identify the characteristics of chronic stable patients found to have depression and evaluate the healthcare costs associated with the occurrence of depression within 1 year of a new diagnosis of chronic stable angina.

Methods

This study was approved by the institutional research ethics board at Sunnybrook Health Sciences Center, Toronto, Canada. The need for patient consent was exempted under Ontario's Personal Health Information Protection Act (the province's legislation regarding privacy of health information).

Data Sources

This retrospective cohort study was conducted using population-based databases in Ontario, Canada, where 13.6 million residents receive universal medical coverage funded by a single third-party payer, the Ministry of Health and Long Term Care. Data were obtained from a clinical registry that is maintained by the Cardiac Care Network of Ontario (CCN). CCN includes a network of 19 hospitals in Ontario that perform cardiac procedures, such as angiography, percutaneous coronary intervention, and CABG.[19,20] Demographics, comorbidities, cardiac stress testing, and coronary anatomy are among the details collected by the CCN Cardiac Registry on patients who have undergone cardiac procedures. The accuracy of this registry has been assessed through retrospective chart review.[21,22]

Linkage of CCN Cardiac Registry data to population-based administrative databases at the Institute for Clinical Evaluative Sciences (ICES) was performed using unique encoded identifiers to protect patient confidentiality. The administrative databases that were utilized in this study included the Ontario Health Insurance Plan (OHIP) Claims Database, the Registered Persons Database (RPDB), the Canadian Institute for Health Information Discharge Abstract Database (CIHI-DAD), the National Ambulatory Care Reporting System (NACRS), the ICES Physician Database (IPDB), the Ontario Mental Health Reporting System (OMHRS), and the Ontario Drug Benefit (ODB) Claims Database. All physician service claims, which include diagnostic codes and dates of service, are captured by OHIP. The RPDB contains vital statistics information for all Ontario residents and was used to determine mortality. Clinical information regarding discharges from acute and chronic inpatient hospitalizations was obtained from CIHI-DAD, and information from emergency department records was obtained from NACRS. The IPDB reports physician demographics and specialization. Data on hospitalizations for mental illness are contained within the OMHRS database. Persons aged >65 years receive full coverage for prescription medications from the ODB program, and drug claims information with reliable dispensing records is found within the ODB database.

Cohort Selection

Our cohort consisted of Ontario residents aged >20 years who underwent an index angiogram between October 1, 2008, and September 30, 2013, for the investigation of stable angina and were found to have obstructive CAD, defined as having any stenosis >70% in ≥1 epicardial vessel or any stenosis >50% in the left main coronary artery.[23,24] Patients who presented with acute coronary syndrome or who had a prior history of CAD (previous myocardial infarction, acute coronary syndrome, percutaneous coronary intervention, or CABG) were excluded. Patients were followed from the date of their index angiogram for up to 1 year. If a patient underwent >1 angiogram during the study period, only the first was considered for the purposes of eligibility and inclusion in the cohort. We excluded patients who experienced depression during the 3 years preceding the start date of accrual for the cohort.

Definition of Depression

Patients were identified as having an occurrence of depression if they were diagnosed by a medical professional or were hospitalized for depression within 1 year of their index angiogram (October 1, 2008, to September 30, 2013). The diagnostic codes from physician service claims (OHIP) that were used included reactive depression (300) and depressive or other nonpsychotic disorder not classified elsewhere (311). The occurrence of depression was also identified using the *International Classification of Diseases, 10th Revision* diagnostic codes obtained from in-hospital and emergency department visits from CIHI-DAD and NACRS, respectively (see Table S1). The validity of these codes has not been assessed by retrospective chart audits; however, they have been used in studies examining depression with administrative data.[25–27] The *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* codes for a single (296.20–0.26) or recurrent (296.30–0.36) episode of major depressive disorder from OMHRS were also used to identify depressed patients. Of note, any codes associated with bipolar disorder were excluded. If information regarding the same hospitalization for depression was obtained from both OMHRS and CIHI-DAD, this was considered a single hospitalization in the statistical analyses.

Healthcare Costs

The primary outcome was the total aggregate 1-year healthcare costs per patient following the index angiogram. Cost estimations to account for censored data were not required because the full cohort had complete cost data available from the 1-year time period or until death. Healthcare expenditures were divided broadly into 5 sectors: acute inpatient care, chronic care, outpatient care, physician costs, and prescription medication use. The acute inpatient care sector included costs related to inpatient hospitalizations and inpatient mental health care. The chronic care sector included costs related to long-term care, rehabilitation, home care services, and complex continuing care. In Ontario, complex continuing care programs manage medically complex inpatients who have medical and nursing care needs that cannot be met in the community or in long-term care. *Outpatient care* referred to the costs of outpatient clinic visits, emergency department visits, same-day surgery, laboratory testing, and dialysis. Last, physician costs consisted of expenditures associated with fee-for-service visits and physician capitation and were discrete from costs associated with the categories of inpatient, outpatient, and chronic care. Cost related to prescription medication use was available only for patients aged ≥65 years, given that only this age group has full drug coverage in Ontario.

We determined costs associated with physician visits and laboratory tests using data from the claims history of the OHIP database.[28] This database also includes shadow billings from providers of organizations covered by alternative payment arrangements. We estimated the cost of hospital admission using the resource intensity weights method.[29] In brief, resource intensity weights is a measure of how much resources were utilized during a patient's encounter with the healthcare system. We multiplied the resource intensity weights associated with the case-mix group for each hospital admission in the CIHI-DAD by the average provincial cost per weighted case for all Ontario acute and chronic care hospitals for that year.[29] This method yields a mean cost per hospital admission for cases assigned to a particular case-mix group category. We used a similar resource intensity weights method to determine the costs for emergency department visits and same day surgeries, both obtained from the NACRS database. We adjusted costs to 2013 Canadian dollars using the consumer price index.

Statistical Analyses

Differences in baseline characteristics between patients with and without depression during the first year following index angiogram were compared using the t test for continuous variables and the χ^2 test for categorical variables. Mean (SD) and median (interquartile range) costs with respect to each healthcare sector were compared between these 2 groups using the t test and the Kruskal-Wallis test, respectively. For these analyses, $P<0.05$ was considered the threshold for significance.

Healthcare cost data have several distinct features that are important to consider in modeling, including their highly skewed distribution due to a very small proportion of patients with large costs.[30] Consequently, we used generalized linear models with a logarithmic link consistent with the previous literature.[31,32] A logarithmic link was used to ensure nonnegative values for predicted costs. The final coefficient was exponentiated to obtain a rate ratio, referred to as a *cost ratio* (CR), which represents the percentage change in mean cost relative to the referent group. To determine the most appropriate distribution family, we conducted a modified Park test, which recommended a γ distribution to account for the skewed distribution of our cost data. Models included a random effect for hospitals to account for clustering of patients at each of the hospitals reported within the CCN Cardiac Registry. Models were adjusted for patient-, physician-, and hospital-level variables; because these models were explanatory, all clinically relevant variables were included. As a sensitivity analysis, we excluded costs associated with prescription drug use, which were available only for patients aged ≥65 years. SAS version 9.3 (SAS Institute Inc) was used for all data analyses.

Results

Cohort

During the period of interest, 272 250 coronary angiograms were performed for the investigation of stable angina. Roughly 12.7% of individuals (n=8067) were excluded from the cohort because of a diagnosis of depression within the past 3 years. Our final cohort consisted of 22 917 patients diagnosed with stable angina based on angiographic findings consistent with obstructive CAD (Figure 1). Of these patients, 1961 (8.6%) patients were diagnosed with depression within 1 year of angiogram. The mean and median time to occurrence of depression following angiogram was 145 days (SD: 108 days) and 126 days, respectively. There was no significant difference in the overall mortality rate among depressed and nondepressed patients within 1 year of diagnosis of stable angina (2.35% versus 2.02%, respectively).

Table 1 shows the association between baseline characteristics of the cohort and depression status within 1 year of catheterization. There were several notable differences between patients with and without depression during the first year following angiogram. A greater proportion of patients with

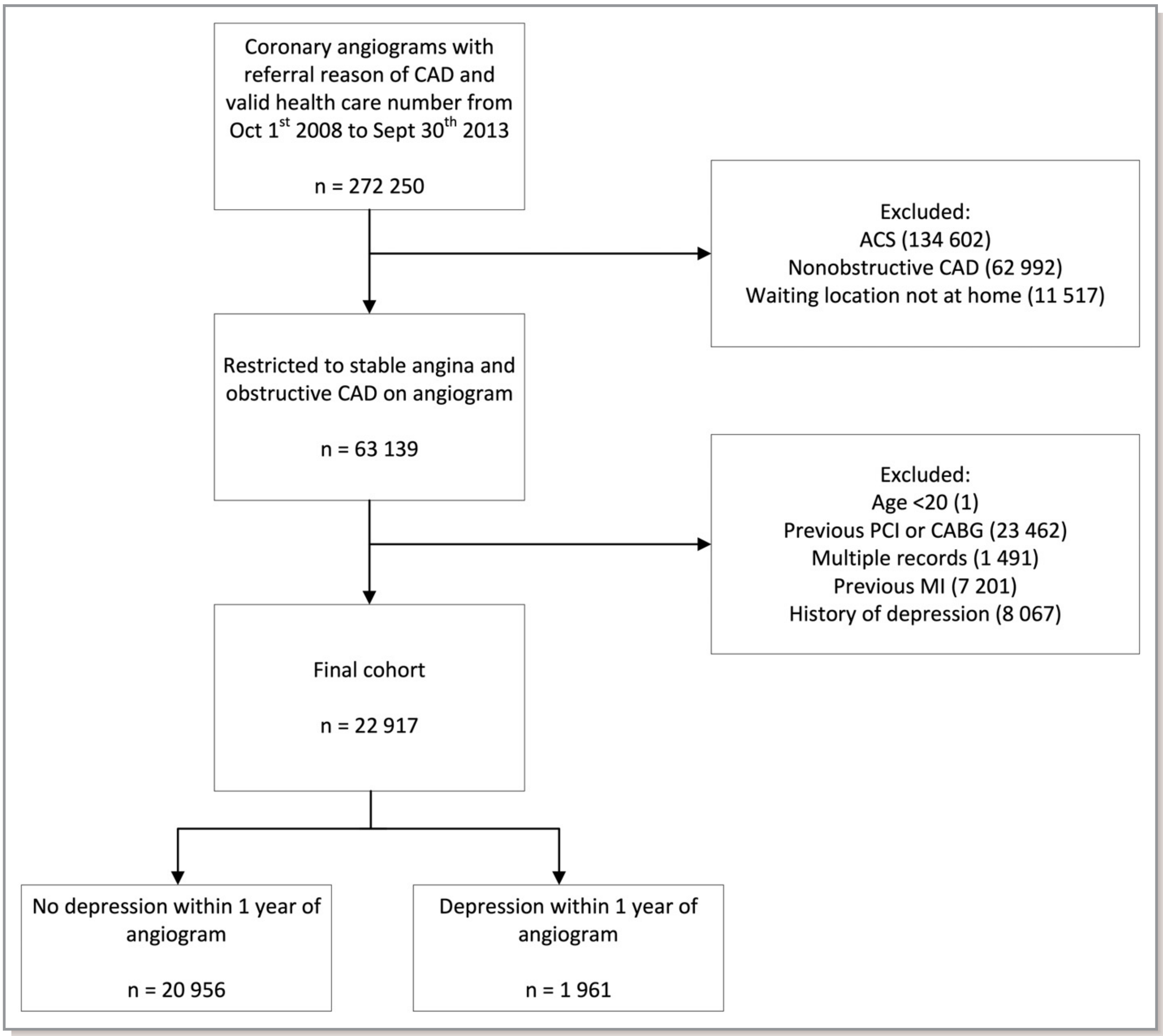


Figure 1. Cohort selection using the Cardiac Care Network registry. ACS indicates acute coronary syndrome; CABG, coronary artery bypass grafting; CAD, coronary artery disease; MI, myocardial infarction; and PCI, percutaneous coronary intervention.

Table 1. Baseline Characteristics of the Cohort According to Diagnosis of Depression Within 1 Year of Catheterization

Covariates	Total (N=22 917)	No Depression Within 1 Year (n=20 956)	Depression Within 1 Year (n=1961)	*P* Value
Patient-level factors				
Demographics				
Age, y (mean±SD)	65.6±10.2	65.7±10.1	65.0±10.7	0.007
Female	5280 (23.0)	4738 (22.6)	542 (27.6)	<0.001
Rural	3363 (14.7)	3145 (15.0)	218 (11.1)	<0.001
Income*				
1	3919 (17.1)	3530 (16.8)	389 (19.8)	0.006
2	4595 (20.1)	4211 (20.1)	384 (19.6)	
3	4779 (20.9)	4362 (20.8)	417 (21.3)	
4	4812 (21.0)	4412 (21.1)	400 (20.4)	
5	4698 (20.5)	4332 (20.7)	366 (18.7)	
Medical comorbidities				
Renal dysfunction	480 (2.1)	440 (2.1)	40 (2.0)	0.86
PVD	1526 (6.7)	1379 (6.6)	147 (7.5)	0.12
COPD	1194 (5.2)	1078 (5.1)	116 (5.9)	0.14
Previous stroke	241 (1.1)	211 (1.0)	30 (1.5)	0.03
Malignancy	587 (2.6)	534 (2.5)	53 (2.7)	0.68
Charlson score (mean±SD)	0.34±0.91	0.33±0.91	0.39±0.95	0.008
Charlson score >0	3913 (17.1)	3531 (16.8)	382 (19.5)	0.003
Cardiac risk factors				
Diabetes mellitus	9426 (41.1)	8593 (41.0)	833 (42.5)	0.21
Hypertension	19 070 (83.2)	17 415 (83.1)	1655 (84.4)	0.14
Hyperlipidemia	17 157 (74.9)	15 667 (74.8)	1490 (76.0)	0.23
Smoking				
Former smoker	6501 (28.4)	5951 (28.4)	550 (28.0)	0.74
Current smoker	4829 (21.1)	4394 (21.0)	435 (22.2)	0.21
CCS angina class				
0	4228 (18.4)	3862 (18.4)	366 (18.7)	0.17
1	3768 (16.4)	3428 (16.4)	340 (17.3)	
2	9382 (40.9)	8599 (41.0)	783 (39.9)	
3	5238 (22.9)	4802 (22.9)	436 (22.2)	
4	301 (1.3)	265 (1.3)	36 (1.8)	
Cardiac status/testing				
LV Function				
≥50%	12 769 (55.7)	11 611 (55.4)	1158 (59.1)	0.01
35–49%	1688 (7.4)	1546 (7.4)	142 (7.2)	
20–34%	534 (2.3)	487 (2.3)	47 (2.4)	
<20%	144 (0.6)	128 (0.6)	16 (0.8)	
NA	7782 (34.0)	7184 (34.3)	598 (30.5)	

Continued

Table 1. Continued

Covariates	Total (N=22 917)	No Depression Within 1 Year (n=20 956)	Depression Within 1 Year (n=1961)	*P* Value
Exercise ECG risk				
Low risk	5821 (25.4)	5349 (25.5)	472 (24.1)	0.02
High risk	7478 (32.6)	6876 (32.8)	602 (30.7)	
Uninterpretable	1141 (5.0)	1042 (5.0)	99 (5.0)	
NA	8477 (37.0)	7689 (36.7)	788 (40.2)	
Functional imaging risk				
Low risk	5745 (25.1)	5221 (24.9)	524 (26.7)	0.20
High risk	7850 (34.3)	7199 (34.4)	651 (33.2)	
Unknown	9322 (40.7)	8536 (40.7)	786 (40.1)	
Native stenosis†				
LM	2707 (11.8)	2452 (11.7)	255 (13.0)	0.09
Proximal LAD	6958 (30.4)	6371 (30.4)	587 (29.9)	0.67
Mid/distal LAD	11 803 (51.5)	10 766 (51.4)	1037 (52.9)	0.20
Circumflex	11 123 (48.5)	10 138 (48.4)	985 (50.2)	0.12
RCA	13 063 (57.0)	11 918 (56.9)	1145 (58.4)	0.19
Treatment within 90 d				
CABG	6741 (29.4)	6039 (28.8)	702 (35.8)	<0.001
MED	6415 (28.0)	5918 (28.2)	497 (25.3)	
PCI	9761 (42.6)	8999 (42.9)	762 (38.9)	
Hospital-level factors				
Availability				
Cath, PCI, and CABG	16 908 (73.8)	15 498 (74.0)	1410 (71.9)	0.13
Cath only	3467 (15.1)	3153 (15.0)	314 (16.0)	
Cath and PCI only	2542 (11.1)	2305 (11.0)	237 (12.1)	
Physician-level factors				
Referring physician				
Cardiology	12 849 (56.1)	11 771 (56.2)	1078 (55.0)	0.46
GP/FP	5611 (24.5)	5109 (24.4)	502 (25.6)	
Other	4457 (19.4)	4076 (19.5)	381 (19.4)	
Physician performing cath				
PCI physician	10 965 (47.8)	10 074 (48.1)	891 (45.4)	0.03

Data are shown as n (%) except as noted. CABG indicates coronary artery bypass grafting; Cath, catheterization; CCS, Canadian Cardiovascular Society; COPD, chronic obstructive pulmonary disease; GP/FP, general practitioner/family physician; LAD, left anterior descending; LM, left main; LV, left ventricular; MED, medical therapy; NA, not done or missing; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; RCA, right coronary artery

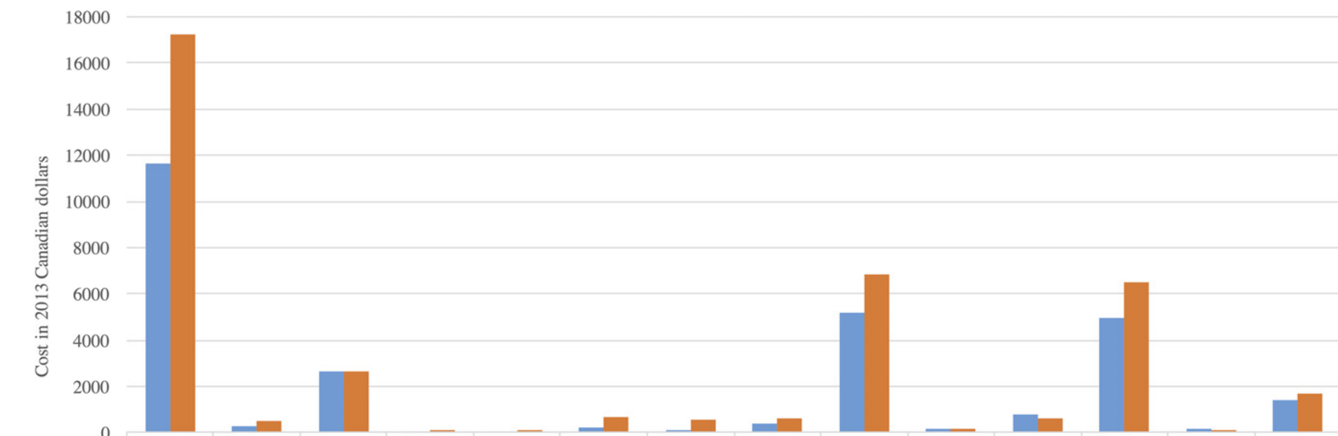
*Income quintile: 1, lowest; 5, highest.

†Significant stenosis ≥70%, except ≥50% stenosis significant for LM.

depression were female, resided in urban areas, and had an income in the lowest quintile. Compared with nondepressed patients, depressed patients had a higher mean Carlson comorbidity index, indicating a greater number of comorbidities, and a higher rate of previous stroke. With respect to other patient-level factors, more patients with depression within 1 year of index catheterization had a left ventricular ejection fraction >50% and underwent CABG as an initial treatment strategy. Last, fewer patients with depression underwent catheterization by a percutaneous coronary intervention physician.

Healthcare Costs

Healthcare service sectors and their corresponding costs according to diagnosis of depression during the first year following angiogram are shown in Figure 2 and Table S2. The



	Hospital-izations	Emergency Department Visits	Same Day Surgery	Inpatient Mental Health	Long-Term Care	Rehab	Complex Continuing Care	Home Care Serivces	Outpatient Clinics	Laboratory	Dialysis	Fee-for-service visits	Physician capitation	Medication
No Depression within 1 year	11,617	280	2,671	13	25	206	85	380	5,211	164	785	4,977	147	1,426
Depression within 1 year	17,245	502	2,675	138	103	685	545	634	6,844	195	625	6,525	129	1,679

Figure 2. Mean 1-year healthcare sector costs according to diagnosis of depression within 1 year of catheterization. ED indicates emergency department.

mean cumulative 1-year healthcare cost was substantially greater for patients with depression (\$32 072±\$41 963) than for patients without depression (\$23 021±\$25 741, P<0.001). Depressed patients had higher mean 1-year costs across nearly all healthcare sectors, including acute inpatient care, chronic care, outpatient care, physician costs, and medications.

For the cohort as a whole, acute inpatient care represented the largest contributor to the aggregate 1-year cost. In this sector, mean costs related to acute hospitalizations and inpatient mental health care were significantly greater for patients with depression compared with patients without depression. In the chronic care sector, average costs related to long-term care, rehabilitation, complex continuing care, and home care services were all significantly higher for depressed patients. In the outpatient care sector, costs associated with outpatient clinics, emergency department visits, and laboratory services were significantly higher for patients with depression, but there was no difference in terms of average dialysis and same-day surgery costs compared with nondepressed patients. Expenditures related to fee-for-service visits and medication prescriptions were significantly higher for depressed patients.

Table 2 shows the unadjusted and adjusted CRs of 1-year cumulative healthcare costs within 1 year of index angiogram. A diagnosis of depression was a statistically significant predictor of increased healthcare expenditures, with an adjusted CR of 1.33 (95% confidence interval [CI], 1.29–1.37; P<0.001). This CR corresponds to a mean 33% increase in 1-year healthcare costs in patients with depression compared with nondepressed patients. There was no statistically significant relationship between healthcare costs and female sex or rurality; however, greater income was associated with lower healthcare expenditures. Other significant drivers of cumulative 1-year cost included a greater number of comorbidities denoted by the Charlson score (adjusted CR: 1.15; 95% CI, 1.14–1.17; P<0.001), as well as peripheral vascular disease (CR: 1.18; 95% CI, 1.14–1.22; P<0.001) and chronic obstructive pulmonary disease (CR: 1.08; 95% CI, 1.04–1.13; P<0.001). Previous stroke (CR: 0.87; 95% CI, 0.80–0.95; P=0.002) and malignancy (CR: 0.93; 95% CI, 0.87–0.99; P=0.023) were associated with lower cumulative 1-year healthcare expenditures. Cardiac risk factors that were significant predictors of increased healthcare expenditures were diabetes mellitus (CR: 1.11; 95% CI, 1.09–1.13; P<0.001) and hypertension (CR: 1.07; 95% CI, 1.04–1.10; P<0.001), whereas hyperlipidemia (CR: 0.96; 95% CI 0.94–0.98; P<0.001) was associated with lower costs. More severe angina symptoms (Canadian Cardiovascular Society class 4) were associated with reduced healthcare costs, whereas worse left ventricular function and stenosis in any of the major coronary vessels were associated with higher 1-year mean costs. One-year costs were significantly greater for patients with CABG (CR: 2.54; 95% CI, 2.48–2.61; P<0.001) and percutaneous coronary intervention (CR: 1.29; 95% CI, 1.26–1.32; P<0.001) as the initial treatment strategy compared with medical therapy. Hospital capacity to perform catheterization, percutaneous coronary intervention, and CABG was associated with lower costs (CR: 0.89; 95% CI, 0.82–0.97; P=0.012) compared with hospitals that had the capacity to perform only catheterization. Finally, 1-year

Table 2. CRs for Mean 1-Year Healthcare Costs

Covariates	Unadjusted CR (95% CI)	*P* Value	Adjusted CR (95% CI)	*P* Value
Depression within 1 y	1.39 (1.34–1.44)	<0.001	1.33 (1.29–1.37)	<0.001
Patient-level factors				
Demographics				
Female	0.98 (0.96–1.01)	0.21	1.02 (1.00–1.04)	0.05
Age index	1.01 (1.01–1.02)	<0.001	1.01 (1.01–1.01)	<0.001
Rural	0.99 (0.96–1.03)	0.7	1.00 (0.98–1.03)	0.93
Income*				
1	Referent		Referent	
2	0.96 (0.93–1.00)	0.04	0.95 (0.92–0.98)	<0.001
3	0.93 (0.89–0.96)	<0.001	0.94 (0.92–0.97)	<0.001
4	0.95 (0.92–0.99)	0.01	0.96 (0.94–0.99)	0.01
5	0.91 (0.87–0.94)	<0.001	0.93 (0.91–0.96)	<0.001
Medical comorbidities				
Renal dysfunction	2.92 (2.71–3.14)	<0.001	2.10 (1.96–2.26)	<0.001
PVD	1.46 (1.40–1.52)	<0.001	1.18 (1.14–1.22)	<0.001
COPD	1.24 (1.18–1.30)	<0.001	1.08 (1.04–1.13)	<0.001
Previous stroke	1.21 (1.09–1.34)	<0.001	0.87 (0.80–0.95)	0.002
Malignancy	1.36 (1.27–1.45)	<0.001	0.93 (0.87–0.99)	0.023
Comorbidities: Charlson score	1.23 (1.22–1.25)	<0.001	1.15 (1.14–1.17)	<0.001
Cardiac risk factors				
Diabetes mellitus	1.29 (1.27–1.32)	<0.001	1.11 (1.09–1.13)	<0.001
Hypertension	1.31 (1.27–1.35)	<0.001	1.07 (1.04–1.10)	<0.001
Hyperlipidemia	1.04 (1.02–1.07)	<0.001	0.96 (0.94–0.98)	<0.001
Smoking				
Nonsmoker	Referent		Referent	
Former smoker	1.04 (1.01–1.06)	0.008	1 (0.98–1.02)	0.83
Current smoker	0.99 (0.97–1.02)	0.71	1.03 (1–1.05)	0.04
CCS angina class				
0	Referent		Referent	
1	0.86 (0.83–0.89)	<0.001	0.91 (0.88–0.94)	<0.001
2	0.86 (0.83–0.88)	<0.001	0.91 (0.88–0.93)	<0.001
3	0.93 (0.90–0.96)	<0.001	0.93 (0.90–0.96)	<0.001
4	0.87 (0.79–0.96)	0.006	0.86 (0.79–0.93)	<0.001
Cardiac status/testing				
LV function				
≥50%	Referent		Referent	
35–49%	1.40 (1.09–1.19)	<0.001	1.01 (0.97–1.04)	0.77
20–34%	1.33 (1.24–1.43)	<0.001	1.19 (1.12–1.27)	<0.001
<20%	1.32 (1.15–1.52)	<0.001	1.28 (1.15–1.43)	<0.001
NA	0.98 (0.96–1.01)	0.221	0.97 (0.95–0.99)	0.01

Continued

Table 2. Continued

Covariates	Unadjusted CR (95% CI)	*P* Value	Adjusted CR (95% CI)	*P* Value
Exercise ECG risk				
Low risk	Referent		Referent	
High risk	1.13 (1.10–1.16)	<0.001	0.98 (0.96–1.01)	0.24
Uninterpretable	1.15 (1.09–1.21)	<0.001	1.04 (0.99–1.08)	0.12
NA	1.42 (1.28–1.46)	<0.001	1.17 (1.14–1.2)	<0.001
Functional imaging risk				
Low risk	Referent		Referent	
High risk	1.12 (1.09–1.16)	<0.001	1.02 (1.00–1.05)	0.08
Unknown	1.12 (1.09–1.15)	<0.001	1.04 (1.02–1.07)	0.002
Native stenosis†				
LM	1.68 (1.63–1.74)	<0.001	1.14 (1.11–1.17)	<0.001
Proximal LAD	1.29 (1.26–1.32)	<0.001	1.13 (1.11–1.16)	<0.001
Mid/distal LAD	1.20 (1.17–1.23)	<0.001	1.11 (1.09–1.13)	<0.001
Circumflex	1.38 (1.36–1.41)	<0.001	1.13 (1.11–1.15)	<0.001
RCA	1.34 (1.31–1.37)	<0.001	1.13 (1.11–1.15)	<0.001
Treatment within 90 d				
MED	Referent		Referent	
CABG	2.42 (2.34–2.49)	<0.001	2.54 (2.48–2.61)	<0.001
PCI	1.05 (1.03–1.08)	<0.001	1.29 (1.26–1.32)	<0.001
Hospital-level factors				
Availability				
Cath only	Referent		Referent	
Cath and PCI only	0.92 (0.85–1.00)	0.043	0.93 (0.84–1.04)	0.18
Cath, PCI, and CABG	0.89 (0.84–0.95)	<0.001	0.89 (0.82–0.97)	0.012
Physician-level factors				
Referring physician				
GP/FP	Referent		Referent	
Cardiology	1.05 (1.02–1.08)	<0.001	1.04 (1.02–1.06)	0.001
Other	1.16 (1.12–1.20)	<0.001	1.1 (1.07–1.13)	<0.001
Physician performing cath				
PCI physician	0.96 (0.94–0.98)	<0.001	0.97 (0.95–0.99)	0.007

CABG indicates coronary artery bypass grafting; Cath, catheterization; CCS, Canadian Cardiovascular Society; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CR, cost ratio; GP/FP, general practitioner/family physician; LAD, left anterior descending; LM, left main; LV, left ventricular; MED, medical therapy; NA, not done or missing; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; RCA, right coronary artery

*Income quintile: 1, lowest; 5, highest.

†Significant stenosis ≥70%, except ≥50% stenosis significant for LM.

healthcare costs were lower if the index catheterization (CR: 0.97; 95% CI, 0.95–0.99; *P*=0.007) was performed by an interventional cardiologist with subspecialty training in percutaneous coronary intervention. In the sensitivity analysis that excluded medication costs (Table S3), depression remained a statistically significant predictor of 1-year cumulative healthcare costs (CR: 1.35; 95% CI, 1.31–1.39; *P*<0.001). Other predictors of healthcare costs also remained statistically significant following the exclusion of drug costs.

Discussion

This population-based study demonstrated that an occurrence of depression within 1 year of receiving a diagnosis of chronic stable angina was associated with an increase in mean cumulative 1-year healthcare costs. This increase remained significant after adjusting for other drivers of cost, such as medical comorbidity and cardiac status. Patients diagnosed with depression incurred greater expenditures in almost all healthcare domains, affecting both acute and ambulatory care including medication costs.

Previous evaluations of the implications of depression for healthcare costs among patients with cardiovascular disease have focused predominantly on populations with acute coronary syndrome, CABG, and heart failure. In contrast, a few small studies have examined resource utilization associated with depression in the setting of chronic stable angina and provided limited data on medical expenditures.[15–17] The current study differs in that comprehensive healthcare cost information and clinical data on chronic stable angina patients with depression have been captured at a population level. In particular, this study estimates total and sector-specific healthcare costs, including an illustration of overall resource utilization with respect to outpatient and inpatient services. Our findings underscore the important role of depression in the pattern of healthcare consumption in CAD patients; this study demonstrates that receiving a diagnosis of depression can intensify healthcare expenditures as soon as 1 year following diagnosis of chronic stable angina.

These results are consistent with previous literature on resource utilization in the context of depression and chronic medical illnesses, including cardiovascular diseases. Heart failure patients with depression, for instance, have been shown to have a 2-fold greater likelihood of hospitalization and emergency department visits over a mean follow-up of 1.6 years,[14] and following myocardial infarction, depressive symptoms are associated with a 24% increase in total hospitalization days during an 18-month follow-up period.[9] In our cohort of chronic stable angina patients, mean 1-year expenditures among individuals diagnosed with depression within 1 year of angiogram were 33% higher compared with patients without depressive illness. These higher costs were related to acute inpatient care services, including acute hospitalizations and inpatient mental health care, as well as nonacute healthcare services such as outpatient visits, rehabilitation, home care services, and medications. This suggests that depression can have a wide-ranging impact on healthcare utilization. Given the chronic and recurrent nature of depression, this cost difference may possibly persist or diverge even further after a 1-year time period. Indeed, understanding the drivers of the acute phase following an occurrence of depression versus those of the chronic phase in patients with stable angina is the logical next step in future research in this area.

There are several possible explanations for the propensity toward higher healthcare costs among patients with depression and chronic stable angina. Depressed patients are recognized to have a higher rate of deleterious behaviors that may have important repercussions on the clinical trajectory of CAD. These behaviors include lifestyle habits such as decreased physical activity and tobacco use, as well as lower adherence to treatments, especially medications.[7] Such impairments in self-care may result in adverse effects over the short and long term, leading to hospital readmissions and protracted lengths of stay. From a physiological standpoint, depression may exert various biological effects on the cardiovascular system including increased sympathetic activity and platelet adhesion, resulting in a higher risk of cardiac events that require heightened medical care.[7] Depressive illness may also exacerbate somatic symptoms associated with medical comorbidities, including chronic stable angina, leading patients to have more contact with their healthcare providers. In addition, patients with depression may present to their physicians for complaints specifically related to mental health.

Given the findings of this study, therapeutic strategies to attenuate costs associated with depression deserve further attention. Depression is often underrecognized by clinicians, and efforts toward improving its detection through screening may be beneficial. The integration of psychiatric interventions into cardiovascular care also warrants consideration. Examples include the participation of mental health professionals in a multidisciplinary team or involvement in cardiac rehabilitation centers. In such settings, patients may derive benefit from the support of case managers and psychiatrists who work alongside medical professionals.

Our study must be interpreted in the context of several limitations that merit discussion. First, we had medication costs only for patients aged ≥65 years, given that full coverage is available only for this age group. We would expect, however, that this would bias to the nondepressed group, given that they had older age. In addition, we lacked information about nonpharmacological approaches to depression such as psychotherapy because those are not captured in the available administrative databases. As such, we may be underestimating the incremental cost associated with depression in terms of the full range of therapeutic options. Second, we allocated patients to the depression group if they had a diagnosis at any point within 1 year. Consequently, some of the costs in this group were incurred before the formal diagnosis of depression and cannot be attributed to the diagnosis of depression itself. We chose this study design because our primary research question studied the impact of depression on 1-year healthcare costs following an index diagnosis of coronary disease; as such, this time frame is appropriate for cost evaluation. Furthermore, our study utilizes an observational data set, and as such, there are baseline covariates that we were not able to account for; therefore, we cannot discount residual confounding. Finally, we used administrative databases and diagnostic codes to identify patients with depression, whereas previous studies have used structured psychiatric assessment tools. As a result, severity of depression was not determined, and patients with milder mood disturbances besides major depressive disorder may have been included in the cohort; however, this underscores that even potentially milder forms of mood disorders are associated with increased costs.

In summary, our results demonstrate that the occurrence of depression within 1 year of diagnosis of chronic stable angina is a significant independent predictor of mean 1-year healthcare costs. This trend toward greater healthcare utilization among depressed patients echoes the findings of previous work in the area of depression and chronic medical diseases. The effect of depressive illness on cost permeates nearly all healthcare domains, including both ambulatory and hospital-based care, resulting in an overall increase in medical expenditures. Depression is prevalent and a major driver of cost among patients with chronic stable angina. At this time, it is not known whether screening or treatment for depression improves cardiovascular outcomes and reduces healthcare consumption in patients with CAD. Further investigations are warranted to evaluate these aspects of care.

Acknowledgments

The authors acknowledge that the clinical registry data used in this publication are from participating hospitals through the Cardiac Care Network of Ontario, which serves as an advisory body to the Ministry of Health and Long-Term Care (MOHLTC), is funded by the MOHLTC, and is dedicated to improving the quality, efficiency, access and equity in the delivery of the continuum of adult cardiac services in Ontario, Canada. Parts of this material are based on data and information compiled and provided by CIHI. However, the analyses, conclusions, opinions and statements expressed herein are those of the author, and not necessarily those of CIHI. We thank IMS Brogan Inc for use of their Drug Information Database. The following databases required acknowledgement for their use in this publication: Canadian Institute for Health Information Discharge Abstract Database, National Ambulatory Care Reporting System, Registered Persons Database, Ontario Mental Health Reporting System, and Ontario Drug Benefit database.

Sources of Funding

Wijeysundera is supported by a Distinguished Clinician Scientist award for the Heart and Stroke Foundation of Canada.

Disclosures

None.

References

1. Economic Burden of Illness in Canada. 2008. Available at: http://www.phac-aspc.gc.ca/publicat/ebic-femc/2005-2008/index-eng.php. Accessed November 28, 2016.
2. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, Das SR, de Ferranti S, Després JP, Fullerton HJ, Howard VJ, Huffman MD, Isasi CR, Jiménez MC, Judd SE, Kissela BM, Lichtman JH, Lisabeth LD, Liu S, Mackey RH, Magid DJ, McGuire DK, Mohler ER III, Moy CS, Muntner P, Mussolino ME, Nasir K, Neumar RW, Nichol G, Palaniappan L, Pandey DK, Reeves MJ, Rodriguez CJ, Rosamond W, Sorlie PD, Stein J, Towfighi A, Turan TN, Virani SS, Woo D, Yeh RW, Turner MB. Heart disease and stroke statistics-2016 update: a report from the American Heart Association. *Circulation*. 2016;133:e38–e360.
3. Heidenreich PA, Trogdon JG, Khavjou OA, Butler J, Dracup K, Ezekowitz MD, Finkelstein EA, Hong Y, Johnston SC, Khera A, Lloyd-Jones DM, Nelson SA, Nichol G, Orenstein D, Wilson PW, Woo YJ. Forecasting the future of cardiovascular disease in the United States: a policy statement from the American Heart Association. *Circulation*. 2011;123:933–944.
4. Bock JO, Luppa M, Brettschneider C, Riedel-Heller S, Bickel H, Fuchs A, Gensichen J, Maier W, Mergenthal K, Schafer I, Schon G, Weyerer S, Wiese B, van den Bussche H, Scherer M, Konig HH. Impact of depression on health care utilization and costs among multimorbid patients—from the MultiCare Cohort Study. *PLoS ONE*. 2014;9:e91973.
5. Bankier B, Januzzi JL, Littman AB. The high prevalence of multiple psychiatric disorders in stable outpatients with coronary heart disease. *Psychosom Med*. 2004;66:645–650.
6. Lichtman JH, Froelicher ES, Blumenthal JA, Carney RM, Doering LV, Frasure-Smith N, Freedland KE, Jaffe AS, Leifheit-Limson EC, Sheps DS, Vaccarino V, Wulsin L. Depression as a risk factor for poor prognosis among patients with acute coronary syndrome: systematic review and recommendations: a scientific statement from the American Heart Association. *Circulation*. 2014;129:1350–1369.
7. Carney RM, Freedland KE, Miller GE, Jaffe AS. Depression as a risk factor for cardiac mortality and morbidity: a review of potential mechanisms. *J Psychosom Res*. 2002;53:897–902.
8. Frasure-Smith N, Lesperance F, Gravel G, Masson A, Juneau M, Talajic M, Bourassa MG. Depression and health-care costs during the first year following myocardial infarction. *J Psychosom Res*. 2000;48:471–478.
9. Kurdyak PA, Gnam WH, Goering P, Chong A, Alter DA. The relationship between depressive symptoms, health service consumption, and prognosis after acute myocardial infarction: a prospective cohort study. *BMC Health Serv Res*. 2008;8:200.
10. Myers V, Gerber Y, Benyamini Y, Goldbourt U, Drory Y. Post-myocardial infarction depression: increased hospital admissions and reduced adoption of secondary prevention measures—a longitudinal study. *J Psychosom Res*. 2012;72:5–10.
11. Baumeister H, Haschke A, Munzinger M, Hutter N, Tully PJ. Inpatient and outpatient costs in patients with coronary artery disease and mental disorders: a systematic review. *Biopsychosoc Med*. 2015;9:11.
12. Rodwin BA, Spruill TM, Ladapo JA. Economics of psychosocial factors in patients with cardiovascular disease. *Prog Cardiovasc Dis*. 2013;55:563–573.
13. Oxlad M, Stubberfield J, Stuklis R, Edwards J, Wade TD. Psychological risk factors for cardiac-related hospital readmission within 6 months of coronary artery bypass graft surgery. *J Psychosom Res*. 2006;61:775–781.
14. Moraska AR, Chamberlain AM, Shah ND, Vickers KS, Rummans TA, Dunlay SM, Spertus JA, Weston SA, McNallan SM, Redfield MM, Roger VL. *Circ Heart Fail*. 2013;6:387–394.
15. Rutledge T, Vaccarino V, Johnson BD, Bittner V, Olson MB, Linke SE, Cornell CE, Eteiba W, Sheps DS, Francis J, Krantz DS, Bairey Merz CN, Parashar S, Handberg E, Vido DA, Shaw LJ. Depression and cardiovascular health care costs among women with suspected myocardial ischemia: prospective results from the WISE (Women's Ischemia Syndrome Evaluation) Study. *J Am Coll Cardiol*. 2009;53:176–183.
16. Versteeg H, Hoogwegt MT, Hansen TB, Pedersen SS, Zwisler AD, Thygesen LC. Depression, not anxiety, is independently associated with 5-year hospitalizations and mortality in patients with ischemic heart disease. *J Psychosom Res*. 2013;75:518–525.
17. Palacios JE, Khondoker M, Achilla E, Tylee A, Hotopf M. A single, one-off measure of depression and anxiety predicts future symptoms, higher healthcare costs, and lower quality of life in coronary heart disease patients: analysis from a multi-wave. Primary Care Cohort Study. *PLoS ONE*. 2016;11:e0158163.
18. Szpakowski N, Bennell MC, Qiu F, Ko DT, Tu JV, Kurdyak P, Wijeysundera HC. Clinical impact of subsequent depression in patients with a new diagnosis of

stable angina: a Population-Based Study. *Circ Cardiovasc Qual Outcomes*. 2016;9:731–739.

19. About Cardiac Care Network. 2016. Available at: http://www.ccn.on.ca/ccn_public/FormsAboutCCN/about.aspx. Accessed November 25, 2016.
20. Cardiac Care Network Annual Report 2015-2016. 2016. Available at: http://www.ccn.on.ca/ccn_public/uploadfiles/files/CCN_Annual_Report_2015_16.pdf. Accessed November 25, 2016.
21. Ko DT, Guo H, Wijeysundera HC, Natarajan MK, Nagpal AD, Feindel CM, Kingsbury K, Cohen EA, Tu JV. Assessing the association of appropriateness of coronary revascularization and clinical outcomes for patients with stable coronary artery disease. *J Am Coll Cardiol*. 2012;60:1876–1884.
22. Schwalm JD, Wijeysundera HC, Tu JV, Guo H, Kingsbury KJ, Natarajan MK. Influence of coronary anatomy and SYNTAX Score on the variations in revascularization strategies for patients with multivessel disease. *Can J Cardiol*. 2014;30:1155–1161.
23. Bradley SM, Maddox TM, Stanislawski MA, O'Donnell CI, Grunwald GK, Tsai TT, Ho PM, Peterson ED, Rumsfeld JS. Normal coronary rates for elective angiography in the Veterans Affairs Healthcare System: insights from the VA CART program (Veterans Affairs Clinical Assessment Reporting and Tracking). *J Am Coll Cardiol*. 2014;63:417–426.
24. Levine GN, Bates ER, Blankenship JC, Bailey SR, Bittl JA, Cercek B, Chambers CE, Ellis SG, Guyton RA, Hollenberg SM, Khot UN, Lange RA, Mauri L, Mehran R, Moussa ID, Mukherjee D, Nallamothu BK, Ting HH. 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. *Circulation*. 2011;124:e574–e651.
25. Hiller W, Dichtl G, Hecht H, Hundt W, Mombour W, von Zerssen D. Evaluating the new ICD-10 categories of depressive episode and recurrent depressive disorder. *J Affect Disord*. 1994;31:49–60.
26. Kessing L. A comparison of ICD-8 and ICD-10 diagnoses of affective disorder - a case register study from Denmark. *Eur Psychiatry*. 1998;13:342–345.
27. Fiest KM, Jette N, Quan H, St Germaine-Smith C, Metcalfe A, Patten SB, Beck CA. Systematic review and assessment of validated case definitions for depression in administrative data. *BMC Psychiatry*. 2014;14:289.
28. Gurevich Y, McFarlane A, Morris K, Jokovic A, Peterson GM, Webster GK. Estimating the number of coronary artery bypass graft and percutaneous coronary intervention procedures in Canada: a comparison of cardiac registry and Canadian Institute for Health Information data sources. *Can J Cardiol*. 2010;26:e249–e253.
29. Jacobs P, Yim R. Using Canadian administrative databases to derive economic data for health technology assessments. Ottawa: Canadian Agency for Drugs and Technologies in Health; 2009. Available at: https://www.cadth.ca/media/pdf/H0483_Canadian_Admin_Databases_mg_e.pdf. Accessed December 5, 2016.
30. Blough DK, Ramsey SD. Using generalized linear models to assess medical care costs. *Health Serv Outcomes Res Method*. 2000;1:185–202.
31. Kelley AS, Ettner SL, Morrison RS, Du Q, Wenger NS, Sarkisian CA. Determinants of medical expenditures in the last 6 months of life. *Ann Intern Med*. 2011;154:235–242.
32. Kang JS, Bennell MC, Qiu F, Knudtson ML, Austin PC, Ko DT, Wijeysundera HC. Relation between initial treatment strategy in stable coronary artery disease and 1-year costs in Ontario: a population-based cohort study. *CMAJ Open*. 2016;4:e409–e416.

SUPPLEMENTAL MATERIAL

Table S1. International Classification of Diseases, 10th Revision (ICD-10-CA) codes for depression

ICD-10-CA Code	Description
F32	Depressive episode
F32.0	Mild depressive episode
F32.1	Moderate depressive episode
F32.2	Severe depressive episode without psychotic symptoms
F32.3	Severe depressive episode with psychotic symptoms
F32.8	Other depressive episodes
F32.9	Depressive episode, unspecified
F33	Recurrent depressive disorder
F33.0	Recurrent depressive disorder, current episode mild
F33.1	Recurrent depressive disorder, current episode moderate
F33.2	Recurrent depressive disorder, current episode severe without psychotic symptoms
F33.3	Recurrent depressive disorder, current episode severe with psychotic symptoms
F33.4	Recurrent depressive disorder, currently in remission
F33.8	Other recurrent depressive disorders
F33.9	Recurrent depressive disorder, unspecified
F34.1	Dysthymia
F34.8	Other persistent mood [affective] disorders
F34.9	Persistent mood [affective] disorder, unspecified
F38.0	Other single mood [affective]disorders
F38.1	Other recurrent mood [affective] disorders
F38.8	Other specified mood [affective] disorders
F39	Unspecified mood [affective] disorder
F41.2	Mixed anxiety and depressive disorder

Table S2. Mean 1-year health care sector costs according to diagnosis of depression during first year following index catheterization.

Variables	Value	Total (n=22,917)	No Depression within 1 year (n=20,956)	Depression within 1 year (n=1,961)	p-value
Total	Mean ± SD	23,796 ± 27,621	23,021 ± 25,741	32,072 ± 41,963	<.001
	Median (IQR)	16,230 (9,059-30,353)	15,744 (8,869-29,900)	25,205 (11,713-36,115)	<.001
Acute Inpatient Care Sectors					
Acute Hospitalization	Mean ± SD	12,098 ± 19,723	11,617 ± 18,108	17,245 ± 31,829	<.001
	Median (IQR)	7,346 (0-17,595)	7,346 (0-17,359)	12,762 (1,792-20,977)	<.001
Inpatient Mental Health	Mean ± SD	24 ± 1,954	13 ± 1,806	138 ± 3,126	0.007
	Median (IQR)	0 (0-0)	0 (0-0)	0 (0-0)	<.001
Chronic Care Sectors					
Long-Term Care	Mean ± SD	32 ± 884	25 ± 833	103 ± 1,310	<.001
	Median (IQR)	0 (0-0)	0 (0-0)	0 (0-0)	<.001
Rehabilitation	Mean ± SD	247 ± 2,490	206 ± 2,185	685 ± 4,608	<.001
	Median (IQR)	0 (0-0)	0 (0-0)	0 (0-0)	<.001
Complex Continuing Care	Mean ± SD	125 ± 2,851	85 ± 2,415	545 ± 5,696	<.001
	Median (IQR)	0 (0-0)	0 (0-0)	0 (0-0)	<.001
Home Care Services	Mean ± SD	402 ± 1,692	380 ± 1,659	634 ± 1,992	<.001
	Median (IQR)	0 (0-0)	0 (0-0)	0 (0-274)	<.001
Outpatient Care Sectors					
Outpatient clinics	Mean ± SD	5,351 ± 4,112	5,211 ± 3,966	6,844 ± 5,202	<.001
	Median (IQR)	3,893 (2,238-7,953)	3,745 (2,184-7,840)	5,949 (3,044-9,122)	<.001

Emergency Department visits	Mean ± SD	299 ± 581	280 ± 549	502 ± 823	<.001
	Median (IQR)	0 (0-387)	0 (0-368)	172 (0-715)	<.001
Same Day Surgery	Mean ± SD	2,671 ± 2,259	2,671 ± 2,257	2,675 ± 2,290	0.91
	Median (IQR)	2,004 (1,722-3,601)	2,004 (1,722-3,618)	2,004 (1,722-3,435)	0.34
Laboratory	Mean ± SD	167 ± 169	164 ± 167	195 ± 187	<.001
	Median (IQR)	127 (58-222)	125 (56-218)	149 (74-266)	<.001
Dialysis	Mean ± SD	771 ± 7,949	785 ± 8,042	625 ± 6,882	0.39
	Median (IQR)	0 (0-0)	0 (0-0)	0 (0-0)	0.23
Physician costs					
Fee-for-service visits	Mean ± SD	5,109 ± 3,992	4,977 ± 3,848	6,525 ± 5,081	<.001
	Median (IQR)	3,668 (2,088-7,684)	3,557 (2,046-7,581)	5,630 (2,807-8,844)	<.001
Physician capitation	Mean ± SD	146 ± 140	147 ± 141	129 ± 135	<.001
	Median (IQR)	65 (32-262)	65 (32-264)	52 (31-225)	<.001
Medications	Mean ± SD	1,448 ± 2,284	1,426 ± 2,258	1,679 ± 2,531	<.001
	Median (IQR)	905 (0-2,099)	891 (0-2,076)	1,079 (25-2,353)	<.001

SD = standard deviation, IQR = interquartile range

Table S3. Adjusted cost ratios for mean 1-year healthcare costs (with medication costs excluded)

Co-Variates	**Cost Ratio (95% CI)**	**p-value**
Depression within 1 year	1.35 (1.31-1.39)	<.001
Patient-level Factors		
Demographics		
Female	1.01 (0.99-1.03)	0.398
Age Index	1.01 (1.01-1.01)	<.001
Rural	1 (0.97-1.02)	0.757
Income*		
1	Referent	
2	0.96 (0.93-0.99)	0.006
3	0.95 (0.93-0.98)	0.003
4	0.98 (0.95-1.01)	0.118
5	0.95 (0.92-0.97)	<.001
Medical Comorbidities		
Renal dysfunction	2.17 (2.02-2.34)	<.001
PVD	1.19 (1.15-1.24)	<.001
COPD	1.06 (1.02-1.11)	0.007
Previous stroke	0.86 (0.78-0.94)	0.001
Malignancy	0.93 (0.86-0.99)	0.026
Comorbidites: Charlson score	1.15 (1.14-1.17)	<.001
Cardiac Risk Factors		
Diabetes	1.08 (1.06-1.1)	<.001
Hypertension	1.06 (1.03-1.09)	<.001
Hyperlipidemia	0.95 (0.93-0.97)	<.001
Smoking		
Non smoker	Referent	
Former smoker	1 (0.98-1.02)	0.87
Current smoker	1.02 (1-1.05)	0.074
CCS Angina Class		
0	Referent	
1	0.91 (0.88-0.94)	<.001
2	0.9 (0.87-0.92)	<.001
3	0.92 (0.89-0.94)	<.001
4	0.84 (0.78-0.92)	<.001
Cardiac Status/Testing		
LV Function		
>=50%	Referent	
35-49%	1.01 (0.97-1.04)	0.693
20%-34%	1.21 (1.14-1.29)	<.001
<20%	1.33 (1.18-1.49)	<.001
NA	0.97 (0.95-0.99)	0.011
Exercise ECG Risk		
Low risk	Referent	
High risk	0.98 (0.96-1.01)	0.193

Uninterpretable	1.03 (0.98-1.08)	0.216
NA	1.17 (1.14-1.2)	<.001
Functional Imaging Risk		
Low risk	Referent	
High risk	1.02 (1-1.05)	0.091
Unknown	1.05 (1.02-1.08)	<.001
Native Stenosis†		
LM	1.16 (1.12-1.19)	<.001
Prox LAD	1.15 (1.12-1.17)	<.001
Mid/distal LAD	1.12 (1.1-1.15)	<.001
Circumflex	1.14 (1.12-1.16)	<.001
RCA	1.14 (1.12-1.16)	<.001
Treatment within 90 days		
MED	Referent	
CABG	2.69 (2.61-2.76)	<.001
PCI	1.31 (1.28-1.34)	<.001
Hospital-level Factors		
Availability		
Cath only	Referent	
Cath and PCI only	0.93 (0.83-1.04)	0.207
Cath, PCI and CABG	0.88 (0.81-0.97)	0.012
Physician-level Factors		
Referring Physician		
GP/FP	Referent	
Cardiology	1.04 (1.02-1.06)	0.002
Other	1.1 (1.07-1.13)	<.001
Physician performing Cath		
PCI physician	0.97 (0.95-0.99)	0.005

CI = confidence interval, COPD = chronic obstructive pulmonary disease, PVD = peripheral vascular disease, CCS = Canadian Cardiovascular Society, LV = left ventricular, ECG = electrocardiogram, NA= not done or missing, LM = left main, LAD = left anterior descending, RCA = right coronary artery, MED = medical therapy, CABG= coronary artery bypass grafting, Cath = catheterization, PCI = percutaneous coronary intervention, GP/FP = General practitioner/Family physician

* Income quintile: 1=lowest, 5 = highest

†Significant stenosis ≥70%, except ≥50% stenosis significant for LM