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1 **Relationship between Initial Treatment Strategy in Stable Coronary Artery Disease**
2 **and 1-Year Costs**

3
4 Short title: Stable angina and 1 year costs

5
6 Jaskaran S Kang MD¹, Maria C Bennell MSc MPH¹, Feng Qiu MSc², Merrill L
7 Knudtson MD³, Peter C Austin PhD^{2,4}, Dennis T Ko MD MSc^{1,2,4}, Harindra C
8 Wijeyesundera MD PhD^{1,2,4}

9
10 **Affiliations:** ¹Schulich Heart Centre, Division of Cardiology, Sunnybrook Health
11 Sciences Centre, University of Toronto, Ontario, Canada; ²Institute for Clinical
12 Evaluative Sciences (ICES), Ontario, Canada; ³Libin Cardiovascular Institute,
13 University of Calgary, Calgary, Alberta; ⁴Institute of Health Policy, Management and
14 Evaluation, University of Toronto, Ontario, Canada.

15
16 **Address for Correspondence:**

17 Harindra C Wijeyesundera
18 2075 Bayview Avenue, Suite A202
19 Toronto, Ontario M4N3M5
20 Tel: (416)480-4527 Fax: (416)480-4657
21 Email: harindra.wijeyesundera@sunnybrook.ca

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3 25 **ABSTRACT**

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5 26 **Background:**

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8 27 Cardiovascular disease is one of the most costly chronic diseases, with annual
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10 28 expenditures projected to continue to increase. The relationship between initial treatment
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12 29 strategy and cumulative costs is unknown. Our objective was to examine the variation in
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14 30 patient-level costs and identify drivers of cost in patients with stable coronary artery
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16 31 disease (CAD).

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20 32 **Methods:**

21
22 33 In this retrospective cohort study using administrative databases in Ontario, Canada, we
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24 34 identified all patients with stable coronary artery disease identified after index
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26 35 angiography. We categorized hospitals into low, medium or high revascularization ratio
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28 36 centers. The primary outcome was the cumulative 1-year health care costs. We used a
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30 37 hierarchical generalized linear model to identify patient and hospital characteristics
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32 38 associated with patient costs. Our model included two main co-variates of interest: (1) the
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34 39 treatment allocation (medical vs. PCI vs. CABG) and (2) the hospital revascularization
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36 40 ratio. The model was adjusted for patient, physician and hospital factors.

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41 41 **Results:**

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43 42 Our cohort consisted of 39,126 patients (15,138 medical therapy, 23,988 revascularized).
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45 43 The mean 1-year cost was \$24,026 (range: \$54 to \$985,600). The mean cost for medical
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47 44 management versus revascularization was \$18,069 and \$27,786 respectively. The
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49 45 strongest predictor of 1-year costs was revascularization (PCI: RR 1.27, 95% CI 1.24-
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51 46 1.31; CABG: RR 2.62, 95% CI 2.53-2.71). Hospital revascularization ratio did not
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3 47 significant impact costs, and there was no significant interaction between treatment and
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6 48 revascularization ratio.

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8 **49 Conclusions:**

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10 50 Revascularization is a major predictor of 1-year cumulative health care costs,
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12 51 highlighting the resource utilization impact of decisions regarding initial treatment
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15 52 strategy.

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17 53 **Key Words:** Cardiac disease – coronary, Health economics

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55 **Introduction**

56 Coronary artery disease (CAD) is a leading cause of morbidity and mortality,[1]
57 and as such represents a major economic burden on healthcare expenditures.[2] In 2005,
58 it was estimated that the cost of cardiovascular disease was \$20.9 billion in the United
59 States, with annual expenditures projected to triple by 2030.[1-3]

60 The treatment for stable CAD includes medical therapy alone or in combination
61 with revascularization by either percutaneous coronary intervention (PCI) or coronary
62 artery bypass grafting (CABG). There is ongoing controversy as to the best initial
63 treatment strategy despite numerous landmark trials, suggesting that the two treatment
64 choices are equivalent in regards to death and major adverse cardiovascular events as
65 well as symptom relief.[4-6] This debate has resulted in significant variation in clinical
66 practice.[7] Understanding the potential impact of such practice variation on resource
67 utilization is important. This is especially relevant given the current era of substantial
68 budgetary constraints, where there is high priority for the efficient use of scarce health
69 care resources. Indeed, recent guidelines from professional cardiovascular societies
70 reinforce the importance of incorporating value and resource implications into health care
71 decisions.[8]

72 Although there are studies examining the predictors of initial treatment strategy in
73 patients with stable CAD, there is a paucity of literature on the impact of the different
74 treatment strategies on health care costs. Accordingly, we sought to address this gap in
75 knowledge by studying the cumulative 1-year health care costs in patients diagnosed with
76 stable CAD after a coronary angiogram, using a population-based clinical registry of
77 patients in Ontario, Canada. Ontario is Canada's largest province with approximately 14

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3 78 million residents, all of whom receive universal health coverage, provided by a single 3rd
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5 79 party payer, the Ministry of Health and Long Term Care (MOHTLC). Our objectives
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8 80 were to determine the degree of variation in health care costs, and understand the
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10 81 predictors of cumulative healthcare costs. In particular, we were interested in the
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12 82 relationship between initial treatment strategy (medical management versus
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14 83 revascularization) as well as the impact of hospital revascularization ratio on subsequent
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16 84 health care utilization.
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22 86 **Methods**

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25 87 This study was approved by the institutional review board at Sunnybrook Health
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27 88 Sciences Centre, Toronto, Canada. Under Ontario's Personal Health Information
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29 89 Protection Act (PHIPA), the need for patient consent was waived.
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32 90 *Study Type*

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34 91 Observational cohort study
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36 92 *Setting*

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39 93 Our primary data source was the Cardiac Care Network (CCN) of Ontario.
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41 94 CCN is comprised of 19 member hospitals that provide adult cardiac services, and
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43 95 includes a clinical registry of patients who undergo cardiac angiography, PCI, or
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45 96 CABG.[9,10] Its accuracy has been validated by retrospective chart review.[11,12] We
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47 97 linked CCN data to population-level administrative databases using unique, encoded
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49 98 identifiers and analyzed it at the Institute for Clinical Evaluative Sciences (ICES).[13-
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55 100 We used several administrative databases in our study. The Canadian Institute
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3 101 for Health Information Discharge Abstract Database (CIHI-DAD) contains data on all
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5 102 hospitalizations. The CIHI-DAD includes a “most responsible” diagnosis and up to 24
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8 103 additional diagnoses codes that can be used to estimate comorbidity. We used the
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10 104 Ontario Registered Persons Database to ascertain death. We obtained data on
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12 105 physician visits/consultation from the fee-for-service claims history in the Ontario
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14 106 Health Insurance Program (OHIP) database, and the National Ambulatory Care
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16 107 Reporting Service database for administrative, clinical, financial, and demographic
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18 108 data for hospital-based ambulatory care, including emergency department visits,
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20 109 outpatient surgical procedures, medical day/night care, and high-cost ambulatory
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22 110 clinics such as dialysis, cardiac catheterization, and oncology. We obtained medication
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24 111 information from the Ontario Drug Database, which has comprehensive drug
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26 112 utilization information on patients over 65 years of age, for whom full drug coverage
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28 113 is provided for by the Ontario Ministry of Health and Long Term Care of Ontario
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30 114 (MOHLTC).

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36 115 *Patients*

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39 116 The cohort consisted of patients who received an angiogram between October
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41 117 1st 2008 and September 30th 2011, for the indication of stable CAD, and had obstructive
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43 118 coronary stenosis. During this period, there were only 18 CCN member hospitals. For
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45 119 patients who received multiple angiograms during the study period, we considered only
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47 120 the initial angiogram. Refer to Figure 1 for additional inclusion and exclusion criteria.
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49 121 We allocated patients revascularized within 90 days of their index angiogram to the
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51 122 revascularization strategy (and into PCI or CABG subgroups), as is consistent with the
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53 123 literature and known procedural wait-times,[10,11] and all remaining patients to the
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3 124 medical therapy strategy. We categorized patients that received multiple angiograms
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5 125 within this timeframe on the basis of the first procedure they received.
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8 126 *Revascularization to Medical Therapy Ratio*

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10 127 We calculated revascularization to medical therapy ratio (referred to herein as
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12 128 revascularization ratio), defined as the number of patients who were categorized as
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14 129 revascularization patients divided by the number of patients who underwent medical
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16 130 therapy. We then allocated the hospitals into one of three categories, high, medium, or
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18 131 low, based on equal tertiles of revascularization ratio.
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21 132 *Main Outcomes*

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24 133 The primary outcome was the total cumulative cost per patient in the one year
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26 134 following the index angiogram. Complete cost profiles were available for all patients for
27
28 135 1 year or until death. As such, we did not have to consider censored costs in our
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30 136 analyses. The categories of costs were all-cause physician visits and laboratory tests,
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32 137 acute care and chronic care hospitalizations, emergency department visits, same day
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34 138 surgeries, and CAD-related medication use for patients ≥ 65 years of age.[15,16]
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39 139 We determined costs associated with physician visits and laboratory tests using
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41 140 data from the claims history of the OHIP database.[14] The OHIP database also
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43 141 included shadow billings from providers of organizations covered by alternate payment
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45 142 arrangements. We estimated the cost of hospitalization using the Resource Intensity
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47 143 Weight (RIW) methodology.[16] We multiplied the RIW associated with the case-mix
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49 144 group for each hospitalization in the CIHI-DAD by the average provincial cost per
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51 145 weighted case for all Ontario acute and chronic care hospitals for that year.[16] This
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53 146 method yields a mean cost per hospitalization for cases assigned to a particular case-
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3 147 mix group category. We used a similar RIW methodology to determine the costs for
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5 148 emergency department visits and same day surgeries, both using the National
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8 149 Ambulatory Care Reporting Service database. We adjusted costs to 2013 Canadian
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10 150 dollars using the Consumer Price Index.

11 12 13 151 *Statistical Analyses*

14
15 152 We used hierarchical generalized linear models, with a logarithmic link and
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17 153 gamma distribution. The models incorporated hospital-specific random effects to account
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19 154 for within-hospital homogeneity in outcomes. The logarithmic link function is
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21 155 advantageous, as it restricts predicted costs to positive values. In addition, final model
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23 156 coefficients are straightforward to interpret; specifically, the exponential of the
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25 157 coefficient provides a rate ratio (RR), or the relative increase in the mean cost for a one
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27 158 unit change in the predictor variable. We used the gamma distribution because of the
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29 159 skewed distribution of health care costs.[17] Our models included 2 main co-variables of
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31 160 interest: 1) the treatment allocation (medical vs PCI vs CABG) and 2) the
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33 161 revascularization ratio (high vs medium vs low). In addition, the models included an
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35 162 interaction between treatment allocation and revascularization ratio. We adjusted the
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37 163 models for patient, physician and hospital factors, as listed in Table 1. We fit the
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39 164 hierarchical generalized linear models using Proc GLIMMIX using SAS Version 9.3
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41 165 (SAS Institute Inc., Cary, NC).

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49 167 **Results**

50 51 168 *Patients*

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3 169 Between October 1st, 2008 and September 30th, 2012, a total of 183,630
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5 170 angiograms were performed in Ontario. The final cohort was compromised of 39,126
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7 171 stable CAD patients, of which 15,138 were medically treated and 23,988 were treated
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9 172 with revascularization (PCI: 15,601 patients, CABG: 8,387 patients; Figure 1). There
10
11 173 were substantial differences in the baseline characteristics between medical therapy and
12
13 174 revascularized groups (Table 1), with medically treated patients being older, more likely
14
15 175 to be female, having greater co-morbidity and less severe anginal symptoms based on
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17 176 Canadian Cardiovascular Society (CCS) class.
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20 177 *Revascularization Ratio*

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22 178 The average revascularization ratio across the 18 Ontario hospitals was 1.58,
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24 179 ranging from 1.09 to 2.31 (Appendix Figure 1).
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27 180 *Variation in Cumulative 1-Year Health Care Cost*

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29 181 Individual patient 1-year cost varied substantially, from a minimum of \$54 to a
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31 182 maximum of \$985,600. As seen in Figure 2, the overall cost was heavily skewed, with an
32
33 183 overall median of \$15,707 and overall mean of \$24,026. The mean (and median) costs for
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35 184 medical and revascularization treatments were \$18,069 (\$7,867) and \$27,786 (\$21,428)
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37 185 respectively. The mean cost by hospital ranged from \$19,749 to \$28,473.
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40 186 *Components of Health Care Costs*

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42 187 The majority of healthcare costs were due to acute care hospitalization with a
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44 188 significantly higher cost for patients undergoing revascularization than patients managed
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46 189 with medical therapy (Table 2). This was primarily driven by the cost of CABG.
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49 190 *Predictors of Health Care Costs*

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3 191 The results of the fully adjusted model are found in Table 3. In so far as our 2
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5 192 primary co-variables of interest, there was no significant difference in cost associated with
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8 193 the hospital tertile revascularization ratio. In contrast, revascularization was a significant
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10 194 predictor of mean cost regardless of the modality (PCI: RR 1.27, 95% CI 1.24-1.31;
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12 195 CABG: RR 2.62, 95% CI 2.53-2.71; $P<0.001$ for both).

15 196 In addition, sex was a statistically significant predictor of mean cost, with a RR of
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17 197 0.96 (95% CI 0.95-0.98) for males ($P<0.001$), indicating that the mean per-patient cost
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19 198 was 4% less for males compared to females (Table 3). Peripheral vascular disease (RR
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21 199 1.25, 95% CI 1.21-1.28, $P<0.001$), hypertension (RR 1.11, 95% CI 1.08-1.13, $P<0.001$),
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23 200 and higher Charlson score (RR 1.17, 95% CI 1.16-1.17, $P<0.001$) were associated with
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25 201 higher mean cost. Previous cardiac surgery was associated with a 17% reduction in mean
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27 202 cost. Symptom severity, as measured by CCS class, had an impact on mean cost, with
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29 203 more symptomatic patients, in general, having lower mean cost. The specialty of the
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31 204 referral physician was a predictor of cost, with patients who were referred by either
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33 205 cardiologists or other physicians having an increased 1-year cumulative cost compared to
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35 206 those referred by their family physicians. In general, busier hospitals (as measured by
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37 207 their annual cardiac catheterization volume) had lower cost, although the magnitude of
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39 208 this effect was small.

45 209 In our interaction model (see Appendix Table 1), we were able to compare the
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47 210 cost of each initial strategy, stratified by the type of hospital (low, medium or high
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49 211 revascularization ratio). We found that, on average, there was no difference in cumulative
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51 212 1-year health care cost for patients treated medically compared to those undergoing
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53 213 revascularization at the different strata defined by the hospital revascularization ratio.
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3 214 Similarly, patients treated initially by PCI had similar costs at high vs medium vs low
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5 215 revascularization hospitals, as did CABG patients.
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10 217 **Interpretation**

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12 218 In this study we found significant variation in the 1-year cumulative health care
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14 219 costs among stable CAD patients treated at different hospitals. Patients with greater co-
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16 220 morbidity had higher cost, as did patients treated with either type of revascularization.
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19 221 Our analysis suggests that the majority of the variation in cost was attributable to the
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21 222 differences in treatment strategy. Importantly, the variation observed between-hospitals
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23 223 based on revascularization ratio was not associated with a statistically significant
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25 224 difference in cumulative health care costs, regardless of the management strategy.
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29 225 To the best of our knowledge, ours is the first study to evaluate cumulative health
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31 226 care costs associated with differing initial treatment strategies among stable CAD patients
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33 227 in over a decade and the first to look at the drivers of these costs. It has previously been
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35 228 reported that the direct cost of stable CAD accounted for 1.3 % of the UK national health
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37 229 expenditures.[18] The vast majority of this cost was related to revascularization
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39 230 procedures (35% of cost) and hospital bed occupancy (31% of cost). Additionally, drug
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41 231 treatment accounted for 12% of total expenditures. Similar findings were found in several
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43 232 other UK and European studies.[19,20]
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47 233 In our study, the major driver for 1-year cumulative costs was the receipt of
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49 234 revascularization. If revascularization offers no impact on mortality and if symptom relief
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51 235 is equivocal, as previous RCTs have shown, then our study suggests that the decision to
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53 236 pursue a revascularization strategy will translate into a substantial impact on healthcare
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3 237 resources. It follows that revascularization in patients with minimal symptoms in whom
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5 238 clinical benefit may be marginal may concurrently place an important financial burden on
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8 239 the healthcare system. This reinforces the importance of appropriate selection of patients
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10 240 who should receive PCI or CABG. Interestingly, the cumulative cost for each of the
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12 241 treatment strategies did not vary with hospital revascularization ratio – i.e. the cost of a
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14 242 strategy was similar regardless of the sites tendencies to favor revascularization or
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17 243 medical management. This implies a similar degree of efficiency for hospitals at different
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19 244 revascularization strata, which is a reassuring finding.

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22 245 Our findings should be interpreted in the context of several limitations that merit
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24 246 discussion. First, we were limited to administrative databases, and thus do not have
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27 247 information on several important factors, such as intensity of medical optimization that
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29 248 may influence cost. Second, we were unable to calculate the indirect costs, such as
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31 249 productivity losses, which has been reported to account upwards to 75% of the total cost
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33 250 of CAD.[19] Third, based on our allocation of treatment strategy, there is a risk of
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36 251 survivorship bias, in that patients who died within 90 days were allocated to the medical
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38 252 therapy group and thus have lower costs. This risk is mitigated by the fact that our cohort
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40 253 was a stable CAD population with very low mortality – indeed, our previous work
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42 254 showed a 90 day mortality that was <1%.[21] Finally, we limited our analyses to health
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44 255 care costs over a restricted 1 year time-horizon in a cohort of patients post coronary
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47 256 angiography. As such, our results cannot be generalized to stable CAD patients who have
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49 257 not undergone angiography.
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3 258 In conclusion, the majority of costs associated with stable CAD are due to acute
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5 259 care hospitalization, with the primary driver being revascularization. Our study highlights
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8 260 the resource implications of an initial revascularization strategy.
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17 264

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282 access to all of the data in the study and takes responsibility for the integrity of the data
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284

285 **CONFLICTS**

286 The authors do not have any potential conflicts of interest or industry relationships to
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359 FIGURE LEGENDS

360 Figure 1. Study population

361 Figure 2. Variation in individual and hospital level costs

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Table 2. Components of 1-year mean costs

Cost category	Total cost	Medical	Revascularization	p-value
Acute care hospitalization	\$11,373	\$7,038	\$14,109	<0.001
ER	\$372	\$367	\$375	0.262
Surgery	\$2,691	\$2,090	\$3,071	<0.001
Physician visits	\$5,449	\$4,079	\$6,313	<0.001
Medication*	\$1,810	\$1,857	\$1,780	0.004
Laboratory	\$194	\$195	\$193	0.326
Long term care	\$54	\$93	\$29	<0.001

ER = emergency room

* For patients over 65 years of age

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CABG	PCI	p-value
\$25,927	\$7,755	<0.001
\$403	\$361	<0.001
\$1,901	\$3,699	<0.001
\$10,086	\$4,284	<0.001
\$1,476	\$1,944	<0.001
\$217	\$180	<0.001
\$47	\$19	<0.001

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Table 3. Predictors of 1-year cumulative health care costs

Covariates	RR (95% CI)	p-value
Treatment		
Medical management	referent	
PCI	1.27 (1.24-1.31)	<0.001
CABG	2.62 (2.53-2.71)	<0.001
Hospital revascularization ratio		
Low	referent	
Medium	1.03 (0.93-1.15)	0.560
High	1.08 (0.97-1.21)	0.130
Patient-level factors		
Demographics		
Age, yrs	1.01 (1.01-1.01)	<0.001
Male gender	0.96 (0.95-0.98)	<0.001
Rural	0.97 (0.95-0.99)	<0.001
Income*		
5	referent	
1	1.10 (1.07-1.12)	<0.001
2	1.04 (1.02-1.07)	<0.001
3	1.02 (1.00-1.05)	0.072
4	1.02 (1.00-1.05)	0.036
Medical comorbidities		
PVD	1.25 (1.21-1.28)	<0.001
Previous MI	0.95 (0.93-0.97)	<0.001
COPD	1.10 (1.07-1.13)	<0.001
Charlson score	1.17 (1.16-1.17)	<0.001
Cardiac risk factors		
Diabetes	1.00 (0.99-1.02)	0.640
Hypertension	1.11 (1.08-1.13)	<0.001
Hyperlipidemia	0.95 (0.93-0.97)	<0.001
History smoking	1.00 (0.99-1.02)	0.930
Cardiac status/testing		
Native stenosis [†]		
LM	1.12 (1.09-1.15)	<0.001
Prox LAD	1.10 (1.08-1.11)	<0.001
Mid/distal LAD	1.08 (1.06-1.09)	<0.001
Circumflex	1.11 (1.09-1.12)	<0.001
RCA	1.09 (1.07-1.11)	<0.001
Previous CABG	0.83 (0.82-0.85)	<0.001
LV function		

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4	≥50%	referent	
5	35-49%	1.03 (1.00-1.05)	0.020
6	≤34%	1.14 (1.10-1.18)	<0.001
7	NA	0.95 (0.93-0.97)	<0.001
8			
9	Exercise ECG risk		
10	Low risk	referent	
11	High risk	1.04 (1.02-1.06)	0.003
12	Uninterpretable	1.09 (1.05-1.14)	<0.001
13	NA	1.24 (1.21-1.27)	<0.001
14			
15	Functional imaging risk		
16	Low risk	referent	
17	High risk	1.01 (0.99-1.03)	0.280
18	Unknown/NA	1.05 (1.03-1.08)	<0.001
19			
20			
21	CCS class		
22	0	referent	
23	1	0.90 (0.87-0.92)	<0.001
24	2	0.88 (0.85-0.90)	<0.001
25	3	0.90 (0.88-0.92)	<0.001
26	4	0.86 (0.82-0.90)	<0.001
27			
28			
29	Physician factors		
30	Referral physician		
31	Family physician	referent	
32	Cardiology	1.02 (1.01-1.05)	0.005
33	Internal medicine	1.00 (0.98-1.03)	0.680
34	Other	1.22 (1.19-1.27)	<0.001
35	Missing	1.03 (1.00-1.05)	0.023
36			
37			
38	Hospital factors		
39	Annual cath volume	0.99 (0.99-0.99)	<0.001

CABG= coronary artery bypass grafting, Cath = catheterization, CI = confidence interval,

COPD = chronic obstructive pulmonary disease, ECG = electrocardiogram,

LAD = left anterior descending, LM = left main, LV = left ventricular, MI = myocardial infarction,

NA implies not done or missing, PCI = percutaneous coronary intervention,

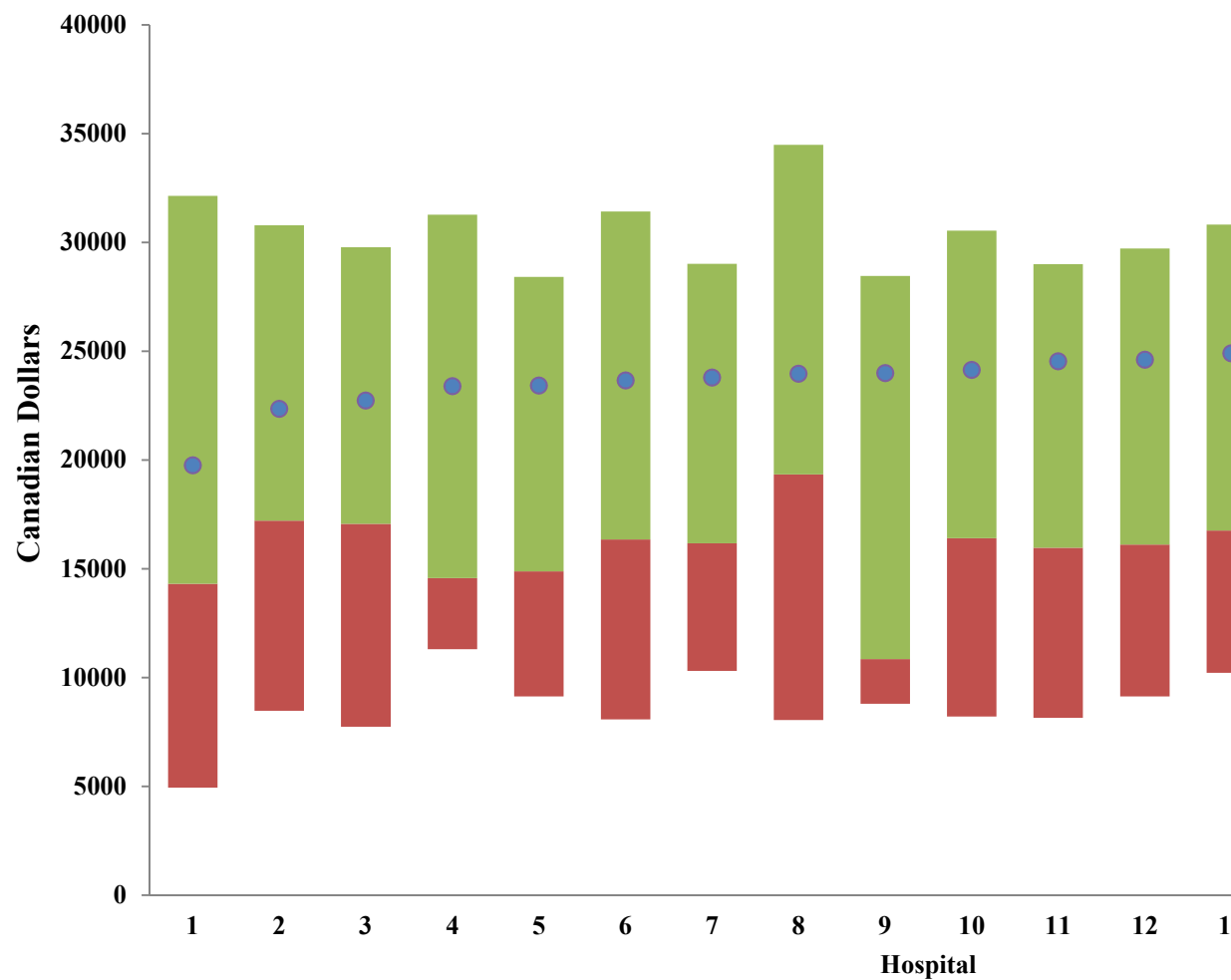
PVD = peripheral vascular disease, RCA = right coronary artery, RR= rate ratio.

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

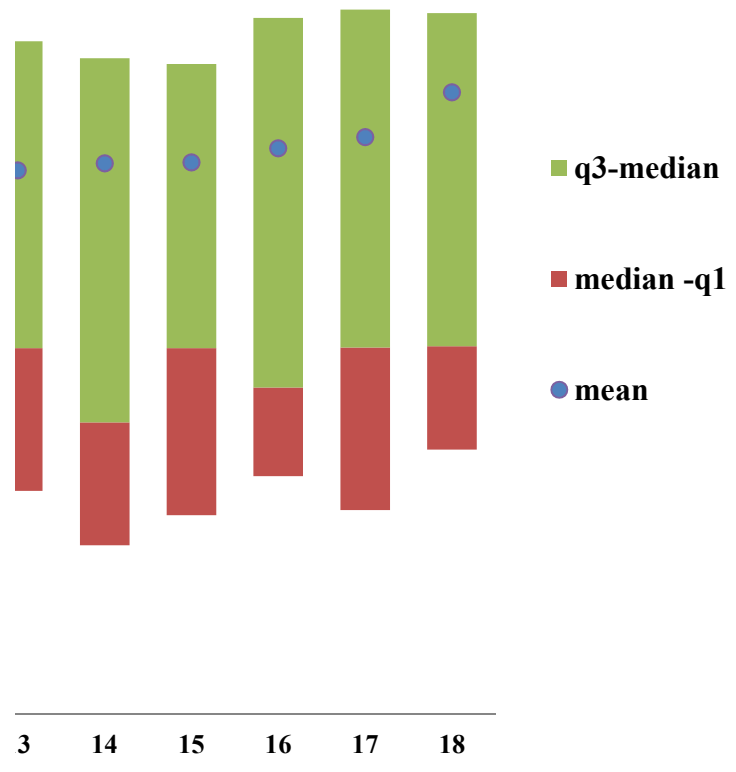
†LM if ≥50% stenosis, Prox LAD if ≥70% stenosis, Mid/distal LAD if ≥70% stenosis,

Circumflex if ≥70% stenosis, RCA if ≥70% stenosis.

Figure 2. Variation in individual and hospital level costs



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Appendix table 1. Predictors of 1-year cumulative health care costs*

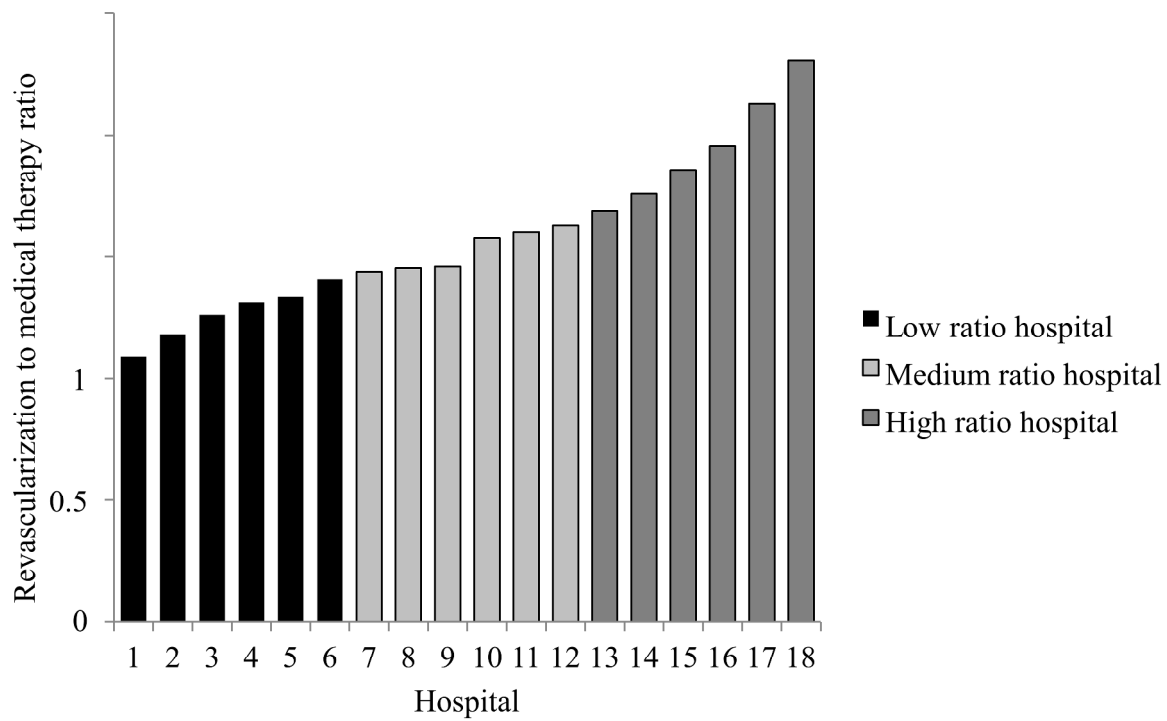
Covariates	RR (95% CI)	p-value
Treatment:		
Medical management:		
High vs. low	1.08 (0.98-1.20)	0.127
Medium vs. low	1.03 (0.93-1.13)	0.562
High vs. medium	1.05 (0.95-1.16)	0.318
PCI:		
High vs. low treatment	1.04 (0.94-1.15)	0.415
Medium vs. low treatment	1.06 (0.96-1.17)	0.237
High vs. medium treatment	0.98 (0.89-1.08)	0.719
CABG:		
High vs. low	1.00 (0.90-1.10)	0.964
Medium vs. low	1.00 (0.91-1.11)	0.929
High vs. medium	0.99 (0.90-1.10)	0.893

CABG = coronary artery bypass graft, CI = confidence interval,
 PCI = percutaneous coronary intervention, RR= rate ratio.

*Fully adjusted model for patient characteristics

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Appendix figure 1. Variation in initial treatment strategy across Ontario



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