Coronary Angiography Following Acute Myocardial Infarction in Ontario, Canada

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Background: The role of scientific evidence in shaping recommendations on capacity targets and cardiovascular technology utilization is unclear.

Methods: The temporal growth in the use of coronary angiography services and the use of statins after an acute myocardial infarction (AMI) was determined for all patients older than 65 years admitted to any hospital in Ontario, Canada, between 1992 and 2004. A Bayesian changepoint regression model was used to determine the rate of maximum uptake (inflection point) for use of cardiac catheterization service and statins after AMI. The inflection points were compared with the corresponding publication dates of the first positive evidence for outcome efficacy of use of cardiac catheterization service and statins after AMI as obtained from randomized control trials.

Results: The use of post-AMI coronary angiography closely mirrored overall temporal increases in cardiac catheterization capacity between 1992 and 2004 ($r=0.95$, $P<.001$). The inflection point for post-AMI angiography service use was September 1998, 11 months before the publication of the first positive randomized controlled trial demonstrating benefit of routine post-AMI angiography. Conversely, the inflection point for statin therapy occurred in October 1998, 47 months after the publication of the first positive randomized controlled trial demonstrating the benefits of statin therapy for the secondary prevention of coronary artery disease. These findings were consistent regardless of the presence of on-site cardiac catheterization facilities at the admitting AMI institution and patient illness severity levels.

Conclusion: The proliferation of cardiac catheterization in Ontario is attributable to factors other than the emergence of published scientific evidence.

Arch Intern Med. 2007;167:808-813

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THE FACTORS THAT ACCOUNT for the proliferation of technology in clinical medicine are complex. In the case of coronary artery disease, the growth of coronary angiography can be explained by increases in capacity,[1,2] which have outstripped changes in disease prevalence and necessitated significant resource expenditures in the United States and Canada.[3-5] Although population-based studies consistently fail to demonstrate a positive relationship between coronary angiography capacity and survival,[6-9] guideline developers and target-setting policy panels continue to rely on interjurisdictional capacities in addition to the publication of clinical trial evidence when justifying a more liberal use of angiography services.[10]

In Canada, the capacity for coronary angiography has historically been heavily constrained by prespecified volumes that have generally fallen well below perceived population needs and demands.[11,12] While many view the proliferation of cardiac catheterization as a direct policy response to emerging scientific evidence, the extent to which its proliferation has risen concordantly with scientific clinical trial evidence remains unclear. Indeed, the lack of clear associations between technology use (cardiac or otherwise) and survival have led some to remain skeptical about the importance of scientific evidence and its role in helping to shape recommendations on capacity and subsequent technology use.[13]

Accordingly, the objective of this study was to examine the temporal relationship between cardiac catheterization use in Ontario, Canada, and the publication of positive clinical trial results. The acute myocardial infarction (AMI) population is an ideal one to examine because the temporal use of coronary angiography after AMI in Ontario has been shown to mirror and, indeed, account for the vast majority of expanded cardiac catheterization service capacity in the previous decade.[2] Moreover, on-site procedural capacity at the admitting hospital has been demonstrated to be an important determinant of post-AMI coronary angiography.[1,6-8] Therefore, a comparison of hos-

pitals with vs those without on-site procedural capacity allowed for a natural experiment when evaluating the relationship among scientific evidence, cardiac catheterization capacity, and coronary angiography service use. In our study, we evaluate post-AMI statin use and its temporal relationship to scientific evidence as a nontechnology medical comparator. Given that data on drug prescriptions are available only for seniors, our study is limited to patients older than 65 years.

METHODS

DATA SOURCE

The Ontario Myocardial Infarction Database[14] contains information on patient demographics, comorbidity, vital statistics, procedures, and drug use for all patients hospitalized with an AMI in Ontario since March 1992 (data on drug use are only available for persons 65 years or older).

USE OF ANGIOGRAPHY AFTER AMI

Patients older than 65 years who were hospitalized with an AMI between March 1992 and December 2004 were identified. Those receiving angioplasty or dying within 24 hours of admission were excluded. Patients subsequently undergoing angiography within the index hospital admission were identified.

USE OF STATINS AFTER AMI

Patients older than 65 years receiving any statin within 30 days of hospital discharge were identified. We focused on new prescriptions and excluded individuals who received statins in the prior year and individuals discharged to a chronic care facility because of an inability to ascertain whether statins were dispensed.

DISEASE SEVERITY AND ADMITTING HOSPITAL CHARACTERISTICS

To evaluate whether the relationship between positive published evidence and population growth varied according to the characteristics of patients and/or their admitted hospitals, the cohort was stratified according to disease severity and the presence or absence of on-site coronary angiography capacity. The Ontario AMI mortality prediction rule[15] was used to stratify patients according to their predicted mortality rate. High-risk patients were those with a predicted mortality rate higher than the median predicted mortality rate for the overall cohort.

CLINICAL TRIALS

Randomized controlled trials (RCTs) were identified after searching the MEDLINE database for those published between 1966 and December 2004 using keywords related to cholesterol therapy, coronary artery disease, coronary angiography, unstable angina, and myocardial infarction. We also identified cross-references to original articles, review articles, and meta-analyses. We excluded RCTs evaluating the use of primary angioplasty. Only RCTs with a primary outcome of death or myocardial infarction or both were considered. Results of abstracts or presentations from large scientific meetings were not considered because discrepancies are frequently observed between results presented at meetings and those subsequently published in full-length articles.[16]

STATISTICAL ANALYSIS

Using a Bayesian change-point analysis,[17] we determined the point at which a change in the monthly rate of increase in the use of post-AMI angiography and statins (the "inflection point") occurred. We then determined the interval between each therapy's inflection point and first published positive RCT, as well as the probability that the inflection point occurred before the publication of the trial. Our regression model was defined as follows:

$$r_i = b_1 + b_2 time_i + b_3(time_i - a) * I(month_i > a) + \varepsilon_i,$$

where r_i is the rate of use of the therapy in the i^{th} month, ε_i is a normally distributed error term for the i^{th} month, and a is the change-point. $I(month_i>a)$ is defined to be 1 if $month_i$ is after the change-point, and zero otherwise. The regression parameter b_1 was constrained as nonnegative.

Diffuse proper prior distributions were assumed for the regression intercept and slopes of the model and a uniform prior distribution for the inflection point. The mean of the posterior distributions of the model parameters and associated 95% credible intervals (ie, estimated interval with 95% likelihood of encompassing the inflection point) were computed. The analysis was conducted using a Gibbs sampling algorithm.[18] An initial set of either 10 000 or 20 000 "burn-in" iterations were used to allow the Gibbs sampler to achieve stationarity. Subsequent monitoring for an additional 100 000 iterations, using a thinning interval of 10, was undertaken. The stationarity of the Gibbs sampler was assessed using the Geweke statistic.[19]

SENSITIVITY ANALYSES

The analysis of post-AMI angiography was repeated for individuals 65 years or younger. This analysis was not possible for post-AMI statin use because of a lack of data. The analysis of post-AMI angiography use was also repeated using risk-adjusted post-AMI angiography rates (rates adjusted for age, sex, and 30-day mortality). Finally, the analysis of statin use was repeated, examining the receipt of statins by 1 year after discharge.

SOFTWARE, ETHICS, AND FUNDING

The Bayesian Inference Using Gibbs Sampling Software (BUGS) version 0.603 for UNIX (MRC Biostatistics, Cambridge, England) was used. Ethics approval was obtained from the Sunnybrook and Women's College Health Sciences Centre Research Ethics Board. No external funding source was used for this study.

RESULTS

Cardiac catheterization capacity, as defined by the number of angiograms (for any cause) completed per month per 100 000 adults, rose from 296 per 100 000 adults in 1992 to 623 per 100 000 adults in 2005. The correlation between capacity and post-AMI coronary angiography service use was strong ($r=0.95$, $P<.001$).

There were 145 140 individuals older than 65 years hospitalized with an AMI between March 1992 and December 2004. Within the first 24 hours of admission, 11 312 patients died or received angioplasty and were excluded. Of the remaining 133 833, 20 833 (15.6%) received in-hospital angiography. There were 92 722 patients older than 65 years who had not previously been

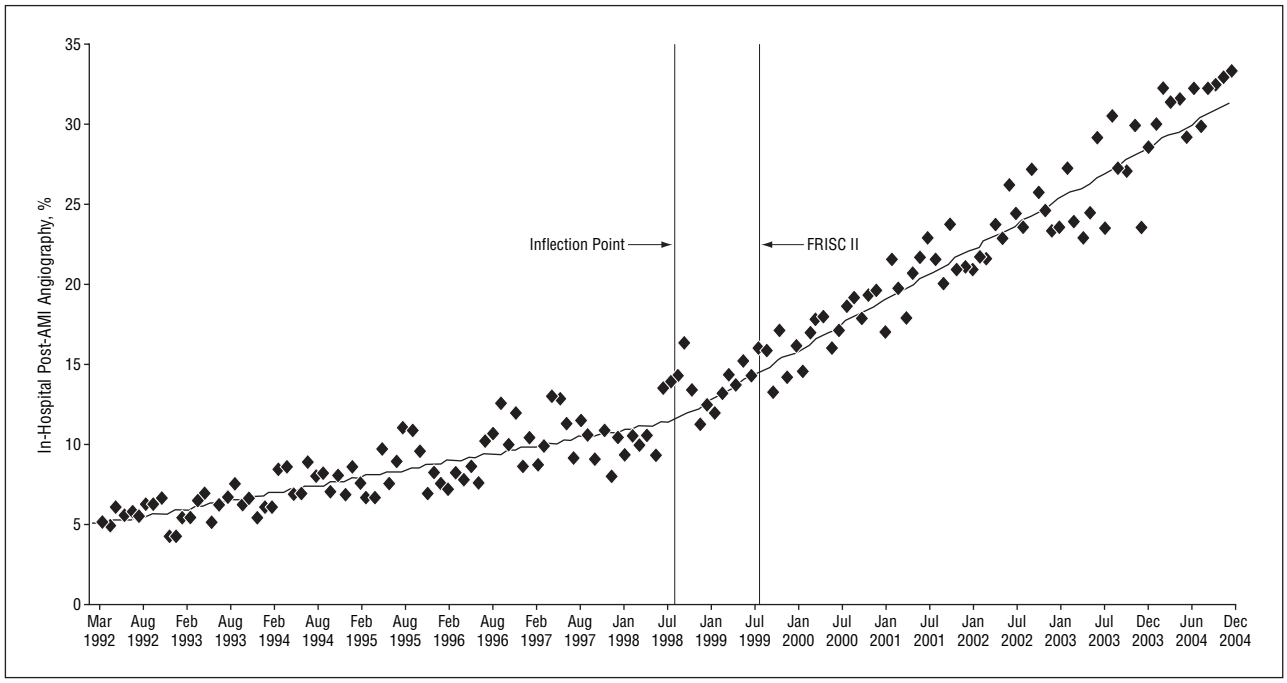

Figure 1. Adoption of angiography after acute myocardial infarction (AMI) in patients older than 65 years in Ontario, Canada. The relationship between the use of post-AMI angiography in patients older than 65 years and the publication of the first positive randomized controlled trial supporting this intervention (The Fragmin and fast Revascularization during InStability in Coronary artery disease [FRISC II] study). Line of best fit and inflection point for each data series were determined using a Bayesian change-point regression model. The inflection point and date of publication of FRISC II are indicated.

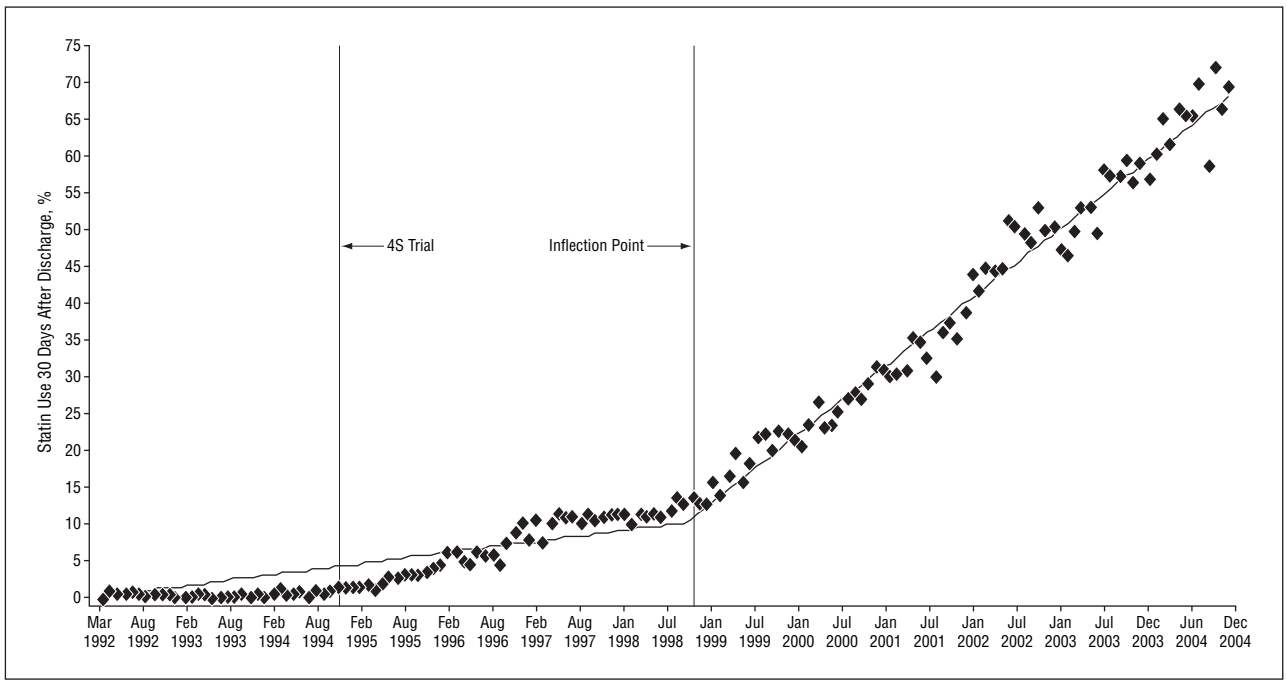

Figure 2. Adoption of statin use after acute myocardial infarction (AMI) in patients older than 65 years in Ontario, Canada. The relationship between the use of statins by 1 year after AMI in patients older than 65 years and the publication of the first positive randomized controlled trial supporting this intervention (Scandinavian Simvastatin Survival Study [4S]). Line of best fit and inflection point for each data series were determined using a Bayesian change-point regression model. The inflection point and date of publication of 4S are indicated.

dispensed any statin and were not discharged to a chronic-care facility; 19 144 (20.6%) received a statin within 30 days of hospital discharge. **Figure 1** and **Figure 2** illustrate the monthly rates of use of post-AMI angiography and statins, respectively, in patients older than 65 years admitted with AMI during the study period.

The Fragmin and fast Revascularization during InStability in Coronary artery disease (FRISC II) trial[20] was the first RCT supporting a role for routine post-AMI angiography. The Scandinavian Simvastatin Survival Study (4S)[21] was the first RCT supporting the use of statins for secondary prevention of coronary artery disease. The over-

Table. Comparison of the Inflection Point for Post-AMI Statin and Angiography Use With the Publication of the First Positive RCT Supporting Each Intervention*

Variable	Publication Date of First Positive RCT	Inflection Point (95% Credible Interval)	Probability That the Inflection Point (Time of Maximum Rate of Change) Occurred *After* First Positive RCT, %	Probability That the Inflection Point (Time of Maximum Rate of Change) Occurred *Before* First Positive RCT, %
Coronary Angiography (Patients Aged >65 y)				
All hospitals	Aug 1999	Sep 1998 (Mar 1998-May 1999)	0.1	99.9
On-site diagnostic catheterization facilities available	Aug 1999	Oct 1997 (Jan 1996-June 1999)	1.4	98.6
On-site diagnostic catheterization facilities not available	Aug 1999	May 1999 (Nov 1998-Nov 1999)	5.2	94.8
High-risk patients	Aug 1999	Aug 1998 (Feb 1998-Feb 1999)	0.2	99.8
Low-risk patients	Aug 1999	Aug 1998 (Jun 1998-Nov 1998)	0	100
Statins (Patients Aged >65 y)				
All hospitals	Nov 1994	October 1998 (Aug 1998-Jan 1999)	100	0
On-site diagnostic catheterization facilities available	Nov 1994	May 1998 (Nov 1997-Oct 1998)	100	0
On-site diagnostic catheterization facilities not available	Nov 1994	Dec 1998 (Sept 1998-Mar 1999)	100	0
High-risk patients	Nov 1994	Apr 1999 (Feb 1999-Jun 1999)	100	0
Low-risk patients	Nov 1994	Mar 1998 (Dec 1997-Jul 1998)	100	0

Abbreviations: AMI, acute myocardial infarction; RCT, randomized controlled trial.

*Comparison of the inflection point reflecting the time at which the rate of increase of post-AMI statin use and post-AMI angiography use changed with the publication of the Scandinavian Simvastatin Survival Study (4S; November 1994) and the Fragmin and fast Revascularization during InStability in Coronary artery disease (FRISC II; August 1999) trials, respectively. The credible interval reflects an estimated interval with 95% likelihood of encompassing this inflection point. The probability that the inflection point occurred after the published landmark trial is indicated (probability = 100% indicates an extremely high likelihood that the inflection point occurred after the landmark trial).

all inflection point for in-hospital coronary angiography occurred approximately 11 months before the publication of FRISC II (**Table**). Conversely, the overall inflection point for statin use by 30 days after AMI occurred approximately 47 months after the publication of the 4S trial (Table).

The inflection point for both angiography and statin use occurred earlier in hospitals with on-site catheterization facilities than in those without (Table). Fewer high-risk patients received post-AMI angiography or statins (data not shown). The inflection point for angiography use was similar in both high- and low-risk patients, but paradoxically later for statin use in high-risk patients (Table).

The inflection point for post-AMI angiography use in patients 65 years or younger was similar to that for patients older than 65 years. In addition, the risk-adjusted rates of post-AMI angiography use mirrored the unadjusted rates of post-AMI angiography use. Finally, the inflection point for statin use at 1 year, rather than at 30 days post-AMI, also occurred subsequent to the publication of 4S (1 year: November 1999, probability inflection after 4S = 100%).

COMMENT

Our study demonstrated that the proliferation of post-AMI coronary angiography service use accelerated before the emergence of any positive published clinical trial evidence demonstrating survival benefits. The pre–scientific evidence rise in cardiac catheterization services occurred among high- and low-risk AMI populations admitted to hospitals with or without on-site procedural capacity, and contrasted with post-AMI statin prescribing patterns, a nontechnology medical therapy comparator whose rates rose nearly 4 years after the emergence of published scientific evidence.

Available evidence has demonstrated that the relative increases in the use of cardiovascular technologies in Canada is similar to that in the United States, with direct annual expenditures now exceeding $400 million in Ontario alone.[3-5] Some have viewed the proliferation in cardiac technologies as a challenge to the sustainability of Canadian Medicare, especially given that growth rates have outstripped temporal changes in demographics and disease prevalence.[2,5] Higher utilization rates of coronary interventions have not translated into clear population survival advantages beyond optimization of medical therapy.[6-9] However, proponents of increased use of cardiovascular technology have countered by drawing on the emergence of clinical trial evidence demonstrating improved outcomes among patients with acute coronary syndromes who are randomized to aggressive coronary interventions. The acceleration in capacity-driven cardiac catheterization service use, which predated the publication of any positive clinical trials, suggests that increased use of coronary angiography was explained by factors other than scientific evidence alone.

While the publication of positive clinical trial evidence could not account for rapid increases in the population-based rates of coronary angiography after AMI, proliferation in cardiac catheterization capacity and subsequent service use may have been driven by "perceived" population needs, as evidenced by lengthy coro-

nary angiography waiting lists during the mid and late 1990s. Indeed, increases in capacity during periods of lenthy waiting lists are important. However, even if one were to assume that cardiac catheterization capacity expansion was an appropriate short-term response to queue delays, such policy responses do not address why service demands for coronary angiography proliferated so rapidly before the publication of scientific evidence demonstrating efficacy.

Non–evidence-based diagnostic technology proliferation is not unique to cardiac services. For example, since its introduction in 1970, the application of the balloon-tipped flotation right heart catheter has expanded. It is estimated that 1.5 million patients in the United States receive this diagnostic intervention each year, many for shock or acute respiratory distress syndrome, at an estimated annual cost of almost US $2 billion. The proliferation of this technology occurred despite the absence of evidence supporting its clinical benefit (and demonstrating possible harm) and calls for a moratorium on its use by experts in the field.[22] In addition, the proliferation of discretionary, non–evidence-based imaging has also been documented. For example, increased use of magnetic resonance imaging and computed tomography for assessment of acute low back pain in Medicare beneficiaries in Pennsylvania between 2000 and 2002 was likely due to widespread availability of advanced imaging technologies rather than an epidemic of low back pain; a 5.5% increase in patients with low back pain was associated with a 20% increase in the use of magnetic resonance imaging or computed tomography. Applying published guidelines would negate the need for most of these scans.[23]

The nonalignment between use of diagnostic technology and evidence of health outcomes has many explanations. First, scientific evidence of diagnostic technologies has historically concentrated on "accuracy." Second, the systematic evaluation and synthesis of diagnostic technology evaluations are complex and may not always be applicable to an assessment of survival outcomes per se.[24] Third, human or societal attributes or both[25] may enhance decision-making preferences, thereby biasing patients, physicians, and policymakers toward the pursuit of new and evolving technologies over established medical therapies—an observation supported by our study demonstrating discordance between the adoption of technologies and medical therapies in response to scientific evidence. Finally, physicians, many of whom comprise health policy committees, also have a tendency to accept interventions without critical assessment when the proponents are prestigious and prominent and the interventions well remunerated.[26]

The delay in adoption of effective pharmacologic therapy is not unique to our study and is also likely due to a complex interaction between scientific and nonscientific factors, including local practice style, habit, commercial detailing, or other marketing strategies.[27] Enhanced knowledge of factors affecting the adoption of non–technology-based therapies is necessary to ensure the effective use of evidence-based therapies.

The poor alignment between technology proliferation and scientific evidence may conspire to erode resource allocation efficiency and undermine the use of less costly and more proven interventions. In addition, rapid adoption of technology before making adequate health care assessments may challenge the ability and impetus for future unbiased assessments. While system monitoring and surveillance may mitigate inappropriate resource utilization, clinical decision leaders must continue to advocate for health technology evaluations to ensure that optimal community treatment patterns concordant with evidence and efficiency are realized.[28]

Our study has noteworthy limitations. First, the lack of available clinical detail (such as post-AMI angina, shock, mechanical complications, or high-risk stress testing) precluded our ability to examine the appropriateness of coronary angiography. While such details are unlikely to have reversed our conclusions given that angiography inflection points were similar for both low- and high-risk patients, the absence of positive published clinical trial data does not necessarily imply that utilization was inappropriate. Second, we were unable to assess the effect of positive trials supporting the use of primary angioplasty on angiography capacity target setting. A consistent absence of evidence demonstrating a reduction in death and/or AMI in the non-primary angioplasty population before the publication of FRISC II and the fact that more than 90% of all post-AMI angiography was performed in a non-primary angioplasty setting suggests that the positive trials supporting primary angioplasty are unlikely to have driven changes in overall angiography capacity. Third, our study was confined to the population of Ontario. Although the absolute rates of post-AMI coronary angiography are approximately 2½ times higher in the United States than in Canada,[11] our findings are likely applicable to the United States. Previous literature has demonstrated that the relative rate of coronary angiography growth in Ontario mirrors growth rates in other regions throughout North America.[3,4] Furthermore, our data were comprehensive and reflected the treatment patterns of Canada's largest province. Finally, the robustness of our results is further supported by the consistency in findings across younger and older subgroups, across higher and lower risk groups, early and late use of statins, and between hospitals with and without onsite cardiac catheterization facilities.

In conclusion, the rapid growth of post-AMI coronary angiography was strongly correlated with increases in cardiac catheterization capacity but predated the publication of positive clinical trial evidence demonstrating outcome benefit. Cardiovascular technology proliferation is likely attributable to factors other than the emergence of published scientific evidence. The extent to which greater implementation of health technology assessments can successfully curtail the proliferation of non–evidence-based technologies requires further study.

Accepted for Publication: December 15, 2006.
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Author Contributions: *Study concept and design:* Singh, Austin, Chong, and Alter. *Analysis and interpretation of*

data: Singh, Austin, Chong, and Alter. *Drafting of the manuscript:* Singh and Alter. *Critical revision of the manuscript for important intellectual content*: Singh, Austin, Chong, and Alter. *Statistical analysis:* Austin. *Obtained funding:* Alter. *Administrative, technical, and material support:* Singh. *Study supervision:* Alter.

Financial Disclosure: None reported.

Funding/Support: This study was supported by grant 153472 from the Canadian Institutes of Health Research.

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