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Evidence for overuse of cardiovascular healthcare services in high-income countries: protocol for a systematic review and meta-analysis

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ABSTRACT

Introduction Overuse of cardiovascular healthcare services, defined as the provision of low-value (ineffective, harmful, cost-ineffective) tests, medications and procedures, may be common and associated with increased patient harm and health system inefficiencies and costs. We seek to systematically review the evidence for overuse of different cardiovascular healthcare services in high-income countries.

Methods and analysis We will search MEDLINE, EMBASE and Evidence-Based Medicine Reviews from 2010 onwards. Two investigators will independently review titles and abstracts and full-text studies. We will include published English-language studies conducted in high-income countries that enrolled adults (mean/median age ≥18 years) and reported the incidence or prevalence of overuse of cardiovascular tests, medications or procedures; adjusted risk factors for overuse; or adjusted associations between overuse and outcomes (reported estimates of morbidity, mortality, costs or lengths of hospital stay). Acceptable methods of defining low-value care will include literature review and multidisciplinary iterative panel processes, healthcare services with reproducible evidence of a lack of benefit or harm, or clinical practice guideline or Choosing Wisely recommendations. Two investigators will independently extract data and evaluate study risk of bias in duplicate. We will calculate summary estimates of the incidence and prevalence of overuse of different cardiovascular healthcare services across studies unstratified and stratified by country; method of defining low-value care; the percentage of included females, different races, and those with low and high socioeconomic status or cardiovascular risk; and study risks of bias using random-effects models. We will also calculate pooled estimates of adjusted risk factors for overuse and adjusted associations between overuse and outcomes overall and stratified by country using random-effects models. We will use the Grading of Recommendations, Assessment, Development and Evaluation to determine certainty in estimates.

Ethics and dissemination No ethics approval is required for this study as it deals with published data. Results will be presented at meetings and published in a peer-reviewed journal.

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Strengths and limitations of this study

► We seek to systematically review the evidence for overuse of different cardiovascular healthcare services (tests, medications or procedures) in high-income countries from 2010 onwards.

► Strengths of the study include our detailed prespecification of study methods in a study protocol; our comprehensive search strategy and inclusion of studies from all high-income countries (as defined by the World Bank) rather than just those located in North America; and our planned meta-analysis to create summary estimates of incidence and prevalence and risk factors for overuse of different cardiovascular healthcare services in high-income countries.

► Potential limitations of the study include the exclusion of non-English language and grey literature studies; further, our study may not provide information on whether newer cardiovascular healthcare services are overused in high-income countries.

INTRODUCTION

Low-value care has been defined as 'a healthcare service (procedure, test or medication) in which evidence suggests it confers no or very little benefit for patients, or risk of harm exceeds probable benefit, or more broadly, the added costs of the intervention do not provide proportional added benefits.'[1] Overuse (ie, provision of low-value care) is a well-recognised problem in high-income countries with substantial consequences for healthcare systems.[2–4] In North America, low-value care accounts for an estimated 30% or more of healthcare.[5 6] Overuse exposes patients to unnecessary harms and consumes critical human and financial resources needed to provide high-value healthcare services. It also threatens the financial sustainability of healthcare systems,[7 8] and potentially

contributes to climate change through increased healthcare waste and greenhouse emissions.[9–11]

Low-value cardiovascular healthcare services likely drive overuse in healthcare.[12] In a systematic review examining overuse in the USA between 1978 and 2010, most used low-value services were cardiovascular.[13] Estimated incidences of cardiovascular overuse varied from low (eg, coronary angiography for certain low-risk patients) to high (eg, carotid endarterectomy for certain high-risk patients), and many low-value services were persistently overused across the review period.[13] Cardiovascular service overuse has been highlighted by the Choosing Wisely campaign since its inception.[14] Among the first 'do not do' recommendations submitted by 25 American societies, 21% targeted cardiovascular testing.[15] These recommendations were provided not only by cardiovascular societies, but also other non-cardiovascular societies, indicating that overuse of cardiovascular services may be pervasive across healthcare in high-income countries.[15]

Although many of the cardiovascular services examined in the overuse literature are valuable when used appropriately, they are not when used for certain indications. For example, percutaneous coronary intervention (PCI), carotid endarterectomy and endovascular abdominal aortic aneurysm repair (EVAR) are all efficacious when appropriately indicated. However, PCI may be overused in stable coronary artery disease[16 17] and carotid endarterectomy and EVAR may be overused in asymptomatic, high-risk patients with limited life expectancy.[18–20] Cardiovascular diagnostic testing similarly provides useful and sometimes necessary clinical information, but its overuse can lead to a cascade of additional healthcare.[21] For example, one study found that patients who received a low-value ECG were five times more likely to have further testing or appointments than patients who did not.[22] The resulting cascade of healthcare involved specialist consultations, additional testing (eg, transthoracic echocardiograms and nuclear stress tests) and cardiac catheterisations.[22]

Overuse of cardiovascular tests, procedures or medications may be costly and harmful to patients.[23] Although the downstream effects of overuse are incompletely understood, frameworks suggest that they include direct medical costs (eg, prolonged hospitalisation), non-medical costs (eg, travel costs for unforeseen medical appointments) and indirect costs (eg, lost productivity).[23] Overuse of cardiovascular procedures may lead to increased morbidity and mortality and unanticipated hospital admissions with an average length of stay of 2 days.[18] In one study, 1 in 7 low-value EVARs, 1 in 13 low-value carotid endarterectomies, and 1 in 12 low-value renal artery angioplasties were associated with hospital-acquired complications, most commonly healthcare-associated infections.[18]

Overuse is estimated to cost between $75.7 and $101.2 billion dollars annually in the USA,[8] and cardiovascular testing in asymptomatic or low-risk patients may represent some of the highest cost low-value services.[24] For certain overused cardiovascular services, such as low-value ECGs, the cost of the test is low, but the high rates of overuse contribute to substantial costs.[24] Other cardiovascular services are more expensive, but have lower documented rates of overuse. For example, overuse of carotid artery disease screening (a low-cost test) in asymptomatic patients and PCI (a high-cost test) in those with stable coronary artery disease is estimated to cost $274 and $212 million dollars per year in the USA, respectively.[19] Importantly, these estimates likely underestimate the financial burden of overuse on healthcare systems as they do not take into consideration the costs of the downstream effects of overuse.[21 25]

Both indirect and direct methods have been used to measure overuse.[26] Indirect measurement examines geographical variations in the use of healthcare services independent of differences in patient or population characteristics.[2] For example, the finding of a ninefold variation in rates of elective PCI across countries suggests potential PCI overuse.[27] The problem with indirect measurement, however, is that divergent rates of use do not necessarily represent inappropriate utilisation in the high-use areas.[28] In comparison, direct measurement uses an evidence-informed definition of a low-value service to detect overuse.[2]

This low-value care definition may be sourced from Choosing Wisely recommendations, clinical practice guidelines or outputs from expert consensus processes.[2] Using this definition, researchers study overuse in administrative databases, insurance claims data or national registries.[29 30] Using a Delphi approach, a 17-member expert panel judged that 11.6% of PCIs for non-acute indications in the US National Cardiovascular Data Registry were low value.[17] Direct measurements are considered to be the most reliable indicator of overuse and can be used to guide de-implementation research and interventions.[2]

Objectives

The primary objective of this systematic review is to summarise reported direct estimates of the incidence and prevalence of overuse of different cardiovascular healthcare services (procedures, tests or medications) in adults who received care in high-income countries (as defined by the World Bank[31]) from 2010 to present. We will also determine whether overuse of these services varies by country; method of defining low-value care; the percentage of included females, different races, and those with low and high socioeconomic status or cardiovascular risk; and study risks of bias. The secondary objectives are to identify and summarise risk factors for overuse of different cardiovascular healthcare services and determine whether their overuse is associated with increased morbidity, mortality, costs or lengths of hospital stay. These data will be used to identify those low-value cardiovascular services that de-implementation interventions may have the greatest potential to improve quality of care, patient outcomes and healthcare spending.

METHODS AND ANALYSIS
Protocol, reporting and registration

We prespecified our methods following recommendations for conducting systematic reviews and meta-analyses of incidence, prevalence and prognostic factor studies.[32–34] The protocol is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) statement (see online supplemental file 1 for the completed PRISMA-P checklist). It was registered on PROSPERO, the international prospective register of systematic reviews (registration number: CRD42021257490).[35 36] The sponsor, the University of Ottawa, had no role in protocol development. The start date for the study was 1 July 2021 and the planned end date is 1 June 2022.

Clinical questions

We formulated study clinical questions using suggested frameworks for posing clinical questions for systematic reviews of incidence, prevalence and prognostic factor studies.[32 33 37]

Primary clinical question

► In adults (mean/median age ≥18 years) who received healthcare in a high-income country, what is the cumulative incidence, incidence rate, and point or period prevalence of overuse of different cardiovascular healthcare services overall and stratified by country; method of defining low-value care; the percentage of included females, different races, and those with low and high socioeconomic status or cardiovascular risk; and study risks of bias (as outlined below)?

Secondary clinical questions

1. In adults (mean/median age ≥18 years) who received healthcare in a high-income country, which factors increase the adjusted odds of overuse of different cardiovascular healthcare services?
2. In adults (mean/median age ≥18 years) who received healthcare in a high-income country, is overuse of a certain cardiovascular healthcare service associated with an increased adjusted mortality, morbidity, cost and length of hospital stay?

Definitions

A high-income country will be defined according to the World Bank as a country with a gross national income per capita >US$12 696 in the 2022 fiscal year, calculated using the World Bank Atlas Method (see table 1 for a list of these countries).[31] We will define overuse as a direct measurement of the provision of low-value care. Low-value care will be defined as a healthcare service (procedure, test or medication) 'in which evidence suggests it confers no or very little benefit for a particular patient population, or risk of harm exceeds probable benefit, or more broadly, the added costs of the intervention do not provide proportional added benefits.'[1] Acceptable direct methods of defining low-value care will include: (1) recommendations from literature review and multidisciplinary iterative panel processes (eg, the RAND/University of California at Los Angeles

Table 1	High-income countries as defined by the World Bank[31]		
Andorra	Denmark	Kuwait	San Marino
Antigua and Barbuda	Estonia	Latvia	Saudi Arabia
Aruba	Faroe Islands	Liechtenstein	Seychelles
Australia	Finland	Lithuania	Singapore
Austria	France	Luxembourg	Sint Maarten (Dutch part)
Bahamas, The	French Polynesia	Macao SAR, China	Slovak Republic
Bahrain	Germany	Malta	Slovenia
Barbados	Gibraltar	Monaco	Spain
Belgium	Greece	Nauru	St Kitts and Nevis
Bermuda	Greenland	Netherlands	St Martin (French part)
British Virgin Islands	Guam	New Caledonia	Sweden
Brunei Darussalam	Hong Kong SAR, China	New Zealand	Switzerland
Canada	Hungary	Northern Mariana Islands	Taiwan, China
Cayman Islands	Iceland	Norway	Trinidad and Tobago
Channel Islands	Ireland	Oman	Turks and Caicos Islands
Chile	Isle of Man	Palau	United Arab Emirates
Croatia	Israel	Poland	UK
Curaçao	Italy	Portugal	USA
Cyprus	Japan	Puerto Rico	Uruguay
Czech Republic	Korea, Rep	Qatar	Virgin Islands (US)

Appropriateness Rating Method[38]), (2) healthcare services with reproducible evidence of a lack of benefit or harm (with supporting literature supplied by study authors), or (3) clinical practice guideline or Choosing Wisely recommendations from the study's country or region of origin.[2 13] Cardiovascular healthcare services will be defined as cardiac or extracranial peripheral vascular (ie, aortic, extracranial carotid or other peripheral arterial) tests, medications or procedures. Tests may include laboratory tests, ECGs or diagnostic imaging tests, while procedures may include interventional (eg, PCI) or surgical (eg, carotid endarterectomy) procedures.

Information sources

We will search MEDLINE; EMBASE; and the databases contained within Evidence-Based Medicine Reviews (ACP Journal Club; the Cochrane Central Register of Controlled Trials, Database of Systematic Reviews, and Methodology Register Database; Database of Abstracts of Reviews of Effects; Health Technology Assessment Database; and National Health Service Economic Evaluation Database) from 1 January 2010 without restrictions. We will begin our search in 2010 because recommendations regarding low-value care may have changed considerably over a time period beyond a decade in length. To identify additional citations, we will use the PubMed 'related articles' feature, and manually search bibliographies of included studies and relevant systematic and narrative review articles identified during the search. As we anticipate that the systematic review will identify a large number of peer-reviewed published studies, we will not search or include grey literature as this may challenge the feasibility of completing the evidence synthesis.

Search strategy

With the assistance of an information-scientist/medical librarian (RS), we created the initial MEDLINE and EMBASE search strategies. We first extracted Medical Subject Heading (MeSH) terms used to index studies known to meet inclusion criteria for our systematic review as well as those used in a previous systematic review on overuse of healthcare services in the USA.[13] We then used those terms to search for additional relevant studies in PubMed and extracted MeSH terms those studies were indexed under.[13] This process was repeated until we did not find any additional relevant MeSH indexing terms.[13] Finally, we searched for Emtree terms that were similar to the above MeSH terms in EMBASE and created a list of non-MeSH/non-Emtree keywords for cardiovascular healthcare services and overuse. Using a combination of these MeSH/Emtree terms and keywords, we then constructed search filters covering the search themes *cardiovascular healthcare services* and *overuse*. After the MEDLINE search strategy was created, we submitted it to another information-scientist/medical librarian to peer review it using the Peer-Review of Electronic Search Strategies (PRESS) guideline[39] (see box 1 for our PRESS'd MEDLINE search strategy).

> **Box 1 PRESS'd MEDLINE search strategy**
>
> 1. exp Health Services Misuse/
> 2. ((overuse* or unnecessary or ineffective or overtreat* or overdiagnos* or overutilis* or overutiliz* or low-value or or wasteful* or appropriateness or inappropriate) adj10 (test* or imaging or procedure* or drug* or medication* or therapy or service* or intervention*)).tw,kf.
> 3. (overuse* or unnecessary or ineffective or overtreat* or overdiagnos* or overutilis* or overutiliz* or low-value or wasteful* or appropriateness or inappropriate).tw,kf. and ("in data review" or in process or publisher or "pubmed not medline").st.
> 4. choos* wisely.mp.
> 5. or/1–4
> 6. exp Cardiovascular Surgical Procedures/
> 7. exp heart diseases/di, dg, su, th or exp vascular disease/di, dg, su, th
> 8. ((cardiovascular or cardiac or vascular or heart) adj2 disease*).ti.
> 9. exp Cardiac Imaging Techniques/ or exp Diagnostic Techniques, Cardiovascular/
> 10. (angiogra* or echocardiogra* or electrocardiogra* or myocardial perfusion imaging or duplex ultrasound or lower extremity arterial duplex ultrasound or carotid duplex ultrasound).kf,tw.
> 11. (percutaneous coronary intervention* or cabg or coronary arter* bypass or renal arter* angioplast* or carotid endarterectom* or endovascular abdominal aortic aneurysm repair* or peripheral arter* bypass or coronary revasculari?ation*).tw,kf.
> 12. ((cardiac or cardiovascular) adj2 (test* or imaging or procedure* or drug* or medication* or therapy or service* or intervention*)).tw,kf.
> 13. exp Troponin/bl
> 14. (troponin adj2 test*).tw,kf.
> 15. Defibrillators, Implantable/
> 16. or/6–15
> 17. 5 and 16
> 18. (overuse* or unnecessary or ineffective or overtreat* or overdiagnos* or overutilis* or overutiliz* or low-value or wasteful* or appropriateness or inappropriate).tw,kf. adj10 (angiogra* or echocardiogra* or electrocardiogramECG* or myocardial perfusion imag* or duplex ultrasound or lower extremity arterial duplex ultrasound or carotid duplex ultrasound).kf,tw.
> 19. (overuse* or unnecessary or ineffective or overtreat* or overdiagnos* or overutilis* or overutiliz* or low-value or wasteful* or appropriateness or inappropriate).tw,kf. adj10 (percutaneous coronary intervention* or cabg or coronary arter* bypass or renal arter* angioplast* or carotid endarterectom* or endovascular abdominal aortic aneurysm repair* or peripheral arter* bypass or coronary revasculari?ation* or implant* cardioverter* or implant* defibrillator*).kf,tw.
> 20. (overuse* or unnecessary or ineffective or overtreat* or overdiagnos* or overutilis* or overutiliz* or low-value or wasteful* or appropriateness or inappropriate).tw,kf. adj10 (cardiac test* or cardiovascular test* or cardiac imaging or cardiovascular procedure* or cardiovascular drug* or cardiovascular medication*).kf,tw.
> 21. or/17–20
> 22. exp animals/ not humans/
> 23. 21 not 22
> 24. limit 23 to yr="2010 -Current"
> 25. limit 24 to english language
> PRESS, Peer-Review of Electronic Search Strategies.

Data management and selection process

The titles and abstracts of citations identified during the search will be imported into Covidence (https://www.covidence.org/). Thereafter, two investigators will

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use Covidence to remove duplicates and independently review the titles and abstracts of articles identified by the search and select any article deemed potentially relevant by either investigator for full-text review. Finally, two investigators will review the full-text of all potentially relevant citations and select studies for inclusion in the systematic review. Disagreements regarding study inclusion will be resolved via consensus or arbitration by a third investigator. Chance-corrected agreement between investigators regarding full-text article inclusion will be calculated using a kappa statistic.[40]

Eligibility criteria and outcomes

We will use the following study inclusion criteria[33 37]:

► The study included adults (mean/median age ≥18 years) who received healthcare in a high-income country (as defined by the World Bank[31]).

► The study reported one or more of the following outcomes (or these outcomes could be calculated from the data provided):

– Cumulative incidence, incidence rate or point or period prevalence of overuse of a cardiovascular healthcare service or services.[41]

– Odds ratios (ORs), risk ratios (RRs) or hazard ratios (HRs) (and surrounding standard errors (SEs) or 95% confidence intervals (CIs)) adjusted for the presence of other risk factors or confounding variables and relating one or more potential risk factor of interest to overuse of a cardiovascular healthcare service or services.

– ORs, RRs, HRs or other measures (and surrounding SEs or 95% CIs) describing differences in mortality, morbidity, costs or lengths of hospital stay associated with overuse of a certain cardiovascular healthcare service or services instead of no overuse and adjusted for the presence of other risk factors or confounding factors.

► The study design was observational (ie, cohort, case–control or cross-sectional[41 42]) and used an acceptable method of defining low-value care as outlined above.[13] We will also include studies of interventions to decrease overuse if sufficient data on overuse were reported for the control group.[13]

Disagreements between investigators as to whether a healthcare service is cardiovascular or not will be resolved via consensus or arbitration by a third investigator. We will exclude studies: (1) published in non-English languages; (2) published only as an abstract; (3) published before the year 2010 or those that only enrolled patients before 2010; (4) that reported only unadjusted risk factors for overuse or unadjusted associations between overuse and outcomes; or (5) that measured inefficient care (eg, use of a brand name instead of equivalent generic drug).[13]

Data items and collection process

Once we have established consensus on which studies should be included in the systematic review, two investigators will independently extract data in duplicate using a predesigned electronic data extraction spreadsheet. This spreadsheet will be piloted on a representative sample of five included studies. We will extract the following data from included studies: (1) design, data source and setting of the study (country, region and rural vs urban[13]); (2) patient recruitment period; (3) the direct method of defining overuse of different cardiovascular healthcare services (eg, clinical practice guideline) and the year it was published (where relevant); (4) sample size; (5) included patient characteristics (for descriptive purposes), including percentages of patient sex, race and socioeconomic status and patients with coronary, cerebrovascular and peripheral artery disease; pulmonary disease; diabetes; chronic kidney disease; cancer; and a smoking history; (6) reported estimates of the included patients' risk of cardiovascular events or their estimated life expectancy (as reported by the authors); (7) reported cumulative incidences, incidence rates and point or period prevalences of overuse of cardiovascular healthcare services; (8) reported adjusted risk factors for overuse of cardiovascular healthcare services (and their surrounding 95% CIs); (9) reported adjusted associations between overuse of cardiovascular healthcare services and estimates of morbidity, mortality, costs and lengths of hospital stay (and their surrounding 95% CIs or standard deviations (SDs)); and (10) which other prognostic or confounding factors were adjusted for when evaluating associations between potential risk factors and overuse or between overuse and morbidity, mortality, costs, and lengths of hospital stay. Three investigators will independently extract data when they are only presented visually (eg, within a bar graph) and then their results will be averaged.[13] If more than one method of defining low-value care or overuse was used, we will extract each of the estimates and report and analyse them separately.[13]

Risk of bias assessment

Two investigators will independently evaluate the risk of bias of studies reporting incidence and prevalence estimates using the Joanna Briggs Institute's critical appraisal checklist of studies reporting prevalence data.[32] The Joanna Briggs checklist includes questions about whether the sample frame was appropriate to address the target population, participants were sampled in an appropriate way, sample size was adequate, study subjects and setting were described in detail, the data analysis was conducted with sufficient coverage of the identified sample, valid methods were used for the identification of the condition, the condition was measured in a standard and reliable way and statistical analyses were appropriate.[32] Those studies that reported risk factors for overuse or associations between overuse and outcomes will also be independently evaluated by two investigators using the Quality in Prognosis Studies tool.[43 44] This tool includes questions regarding study participation and attrition; potential risk factor and outcome description and measurement; confounding measurement and account; and methods and reporting of statistical analyses.[43 44] For those studies

that used administrative data, we will also examine whether the study authors considered the accuracy (sensitivity and specificity) of the codes used to define variables. Disagreements regarding risk of bias assessments will be resolved by consensus.

Qualitative data synthesis

We will perform a narrative synthesis of the included studies and their reported data before considering meta-analyses.[45] We will first tabulate characteristics of the included studies, including their design; data source; setting; recruitment period; included patients; studied low-value cardiovascular healthcare service or services; direct method of defining overuse of each service; reported incidences, incidence rates, and point or period prevalences of overuse of different services; and reported risk factors for overuse of different services or associations between overuse and estimates of morbidity, mortality, costs and lengths of stay. This tabulation will allow us to cluster the low-value cardiovascular healthcare services by test, medication or procedure and identify potentially duplicate data. It will also allow us to determine if any definitions of low-value care may have changed over the 10-year study period and to identify which studies provided similar enough information be included in meta-analyses.

Quantitative data synthesis and statistical analyses

Where it was not reported, we will calculate the cumulative incidence, incidence rate and point or period prevalence of overuse of different cardiovascular healthcare services. Cumulative incidence will be calculated using the following formula:

$$\text{Cumulative incidence} = \frac{\text{Number of new cases of overuse of a cardiovascular healthcare service}}{\text{Total population at risk}}$$

where the total population at risk will be defined as the number of adults who have not been exposed to the low-value cardiovascular healthcare service. Incidence rate will be determined using the formula:

$$\text{Incidence rate} = \frac{\text{Number of new cases of overuse of a cardiovascular healthcare service}}{\text{Total person - time at risk}}$$

Point or period prevalence will be determined using the formula:

$$\text{Point or period prevalence} = \frac{\text{Number of existing cases of overuse of a cardiovascular healthcare service at a point in time or over a period of time}}{\text{Total defined population at that time or over that period of time}}$$

The SE and 95% CI of these proportions will then be determined using the Clopper-Pearson exact binomial method.

Where we identify more than one study that provided estimates of overuse of the same low-value healthcare practice, incidence or prevalence estimates for overuse of that practice will be pooled using DerSimonian and Laird random-effects models.[46] As suggested by Barendregt *et al*, we will transform these proportional estimates using a double arcsine transformation prior to meta-analyses.[32 47] The data will then be back-transformed to incidence and prevalence estimates after meta-analysis.[32]

We will use the OR (for dichotomous outcomes) or standardised mean difference (for continuous outcomes) as the summary measures of choice for pooled risk factor and outcome analyses. Similar adjusted risk factor estimates and outcome associations will be pooled using DerSimonian and Laird random-effects models.[46] Where the OR was not reported, we will pool log-transformed RRs or HRs instead. When adjusted estimates were calculated from the same data source across several studies, we will include the estimate derived from the largest study. As a sensitivity analyses, we will also recalculate the estimate using that derived from the other, smaller studies as studies may have variably adjusted their estimates for potentially confounding factors.

We will inspect forest plots, calculate I^2 inconsistency statistics and conduct tests of homogeneity ($p<0.10$ considered significant given the low power of these tests) to assess for between-study heterogeneity in the above estimates.[48–50] We will consider I^2 statistics >25%, >50% and >75% to represent low, moderate and high degrees of heterogeneity, respectively.[49] In the presence of at least low between-study heterogeneity in our pooled estimates of incidence and prevalence, we will conduct subgroup meta-analyses and meta-regression using DerSimonian and Laird random-effects models. We will use the following predictor variables in these stratified meta-analyses and meta-regressions: (1) country; (2) direct method of defining low-value care; (3) whether the study was population-based versus not; (4) the percentage of included females, different races, and those with low and high socioeconomic status or low and high cardiovascular risk (as defined by the authors); and (5) whether there was a high or lower risk of bias relating to measuring overuse. Where different countries disagree regarding the definition of low-value care, we will allow the local setting to make the decision about what is low value and only report summary estimates of low-value care per country rather than across all studies. We will also report stratified analyses within country-level estimates rather than across all studies.

We will evaluate for evidence of small study effects potentially due to publication bias by visually inspecting funnel plots of incidence and prevalence of overuse and using Begg's and Egger's tests ($p<0.05$ considered significant).[51] We will use the study sample size instead of the inverse of the SE on the y-axis as this may perform more favourably in these analyses.[32 52] Statistical analyses will be performed by a PhD-trained meta-analyst using Stata MP V.13.1 (Stata Corporation, College Station, Texas, USA).

Certainty in the cumulative evidence

We will use the Grading of Recommendations, Assessment, Development and Evaluation for assessment of evidence about prognostic factors to determine the certainty in the estimates of association between the

reported risk factors and overuse or between overuse and estimates of morbidity, mortality and costs.[53] To do this, we will first assess the risk of bias, imprecision, inconsistency, indirectness and publication bias associated with the evidence for the reported risk factors.[54–58] The overall certainty in these estimates will then be adjudicated as high (further evidence is high) ('further research is very unlikely to change our confidence in the estimate'), moderate ('further research is likely to have an important impact on our confidence in the estimate and may change the estimate'), low ('further research is very likely to have an important impact on our confidence in the estimate and is likely to change the estimate') or very low ('very uncertain about the estimate').[36]

Patient and public involvement

Patients and the public were not involved in the creation of the protocol. Patients will be involved in subsequent studies examining barriers and facilitators to reducing overuse of cardiovascular healthcare.

ETHICS AND DISSEMINATION

No ethics approval is required for this study as it deals with published data. Results of the systematic review will be presented at cardiovascular and other relevant meetings and published in a peer-reviewed journal. Potential limitations of the study include the exclusion of non-English language and grey literature studies. Further, our study may not provide information on whether newer cardiovascular healthcare services are overused in high-income countries. Outputs of the study will include summary estimates of the incidence and prevalence of overuse of different cardiovascular healthcare services in high-income countries, risk factors for their overuse and pooled estimates of the burden of overuse of different cardiovascular healthcare services on patients and healthcare systems. Through the involvement of several international stakeholders in cardiovascular medicine and surgery and de-implementation science, our results will hopefully be of immediate interest and use to guide discussion regarding prioritisation of services.

De-implementation of healthcare services should begin with the identification and prioritisation of low-value services.[59 60] Perhaps the most well-known example of this is the Choosing Wisely campaign, where lists of low-value services are published by individual societies that are disseminated to healthcare providers (eg, in academic journals) and the public (eg, public-facing campaigns).[61 62] However, evidence suggests that simply identifying a low-value service has little impact on overuse overall.[63–66] Prioritisation of specific low-value services by systematically identifying factors such as rates of overuse and the associated economic burden and risk of harm to patients and healthcare systems (as in this study) may help focus de-implementation efforts.

Systematic review methodology may be used to synthesise evidence on cardiovascular healthcare service overuse

that could be used to help guide prioritisation decisions. A systematic review of overuse in the USA across all areas of medicine was published in 2012.[13] This study included a narrative description of the published evidence for overuse up until 2010. Subsequent narrative updates have been published annually from 2016 to 2019.[4 67–69] These reviews provide valuable narrative syntheses of the rapidly emerging evidence on medical overuse. However, because they examined all studies of medical overuse, they did not provide detailed information on each of the included studies and their findings. They also included studies published across variable time periods with different and important risks of bias. Finally, they did not provide data from other high-income countries or summary estimates of the frequency of overuse across the included studies. Therefore, these evidence syntheses are likely not able to help with prioritisation decisions regarding overuse of cardiovascular healthcare services.

The outputs of this systematic review will be used to inform a research programme that aims to reduce overuse of cardiovascular healthcare services. Subsequent steps will include cohort studies designed to determine whether the priority low-value cardiovascular healthcare services identified in the systematic review are those that are also overused in Canada. This will be followed by an interview-based study to determine barriers and facilitators to overuse and de-implementation of low-value cardiovascular Canadian healthcare services. We will use this information to design de-implementation randomised controlled trials that aim to reduce overuse of priority low-value cardiovascular healthcare services across different Canadian regions. These studies may serve as a template to inform similar programmes of work in other countries.

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Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

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PRISMA-P 2015 Checklist

This checklist has been adapted for use with systematic review protocol submissions to BioMed Central journals from Table 3 in Moher D et al: Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews* 2015 **4**:1

An Editorial from the Editors-in-Chief of *Systematic Reviews* details why this checklist was adapted - Moher D, Stewart L & Shekelle P: Implementing PRISMA-P: recommendations for prospective authors. *Systematic Reviews* 2016 **5**:15

Section/topic	#	Checklist item	Information reported Yes	Information reported No	Page
ADMINISTRATIVE INFORMATION					
Title					
Identification	1a	Identify the report as a protocol of a systematic review	☒	☐	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	☒	☐	Not applicable
Registration	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract	☒	☐	5 and 11
Authors					
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author	☒	☐	1-3
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	☒	☐	33
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	☒	☐	Not applicable
Support					
Sources	5a	Indicate sources of financial or other support for the review	☒	☐	33
Sponsor	5b	Provide name for the review funder and/or sponsor	☒	☐	11
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	☒	☐	11
INTRODUCTION					
Rationale	6	Describe the rationale for the review in the context of what is already known	☒	☐	6-9

Section/topic	#	Checklist item	Information reported Yes	Information reported No	Page
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	☒	☐	10-12
METHODS					
Eligibility criteria	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as criteria for eligibility for the review	☒	☐	15-16
Information sources	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage	☒	☐	13
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	☒	☐	13-14
STUDY RECORDS					
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	☒	☐	14
Selection process	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)	☒	☐	14
Data collection process	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	☒	☐	16-17
Data items	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications	☒	☐	16-17
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	☒	☐	15-16
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	☒	☐	17-18
DATA					
Synthesis	15a	Describe criteria under which study data will be quantitatively synthesized	☒	☐	18-21
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., I^2, Kendall's tau)	☒	☐	18-21

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Section/topic	#	Checklist item	Information reported		Page
			Yes	No	
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)	☒	☐	20
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	☒	☐	Not applicable
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)	☒	☐	21
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)	☒	☐	21