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Review

Canadian Women's Heart Health Alliance

Introducing the Canadian Women's Heart Health Alliance ATLAS on the Epidemiology, Diagnosis, and Management of Cardiovascular Diseases in Women

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ABSTRACT

Despite a global understanding that indicators and outcomes of cardiovascular disease (CVD) are known to differ between men and women, uptake of the recognition of sex and gender influences on the clinical care of women has been slow or absent. The Canadian Women's Heart Health Alliance (CWHHA) was established as a network of experts and advocates to develop and disseminate evidence-informed strategies to transform clinical practice and augment collaborative action on women's cardiovascular health in Canada. As an initial project, the CWHHA membership undertook an environmental scan of CVD in women in Canada from which a scientific statement could be developed to summarize critical sex- and gender-specific issues in CVD. This comprehensive review of the

RÉSUMÉ

Bien que l'on sache généralement que les indicateurs et les résultats des maladies cardiovasculaires (MCV) ne sont pas les mêmes chez les hommes et les femmes, la reconnaissance des différences entre les genres et les sexes dans la pratique clinique se fait lentement, voire pas du tout. L'Alliance nationale de la santé cardiaque des femmes (l'Alliance) est un réseau formé d'experts et d'intervenants ayant pour mission de formuler et de diffuser des stratégies fondées sur des faits afin de transformer la pratique clinique et de stimuler l'action concertée en matière de santé cardiovasculaire des femmes au Canada. Le premier projet des membres de l'Alliance a été de réaliser une analyse de la situation des femmes sur le plan des MCV au Canada, à partir de laquelle un énoncé scientifique pourrait être formulé pour

Cardiovascular disease (CVD) is the leading cause of premature death for women in Canada.[1] Despite a global understanding that manifestations and outcomes of CVD are known to differ between men and women, uptake of the recognition of sex and gender influences on the clinical care of women has been slow or absent.[2] The Canadian Women's Heart Health Alliance (CWHHA) was established as a network of experts and advocates to develop and disseminate evidence-informed strategies to transform clinical practice and augment collaborative action on women's cardiovascular (CV) health in Canada. The CWHHA membership identified as a high priority the need for an environmental scan of CVD in women in Canada from which a scientific statement could be developed to summarize critical sex- and gender-specific issues in CVD diagnosis, treatment and outcomes. Supported by the University of Ottawa Heart Institute (UOHI), the coordinating body of the CWHHA, the CWHHA along with the Heart and Stroke Foundation of Canada (HSFC) undertook a

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evidence focused on the sex- and gender-specific differences in comorbidity, risk factors, disease awareness, presentation, diagnosis, and treatment across the entire spectrum of CVD. In the process of creating the review, it was recognized that the team of CWHHA experts had also assembled an expansive collection of original research articles that were synthesized into detailed chapters reporting on the present state of the evidence unique to each cardiovascular condition in women. This work comprises an "ATLAS" on the epidemiology, diagnosis, and management of CVD in women. The overall goal of the ATLAS is to create a living document that will help clinicians and the public recognize the unique aspects of women's heart health care and provide policy makers with information they need to ensure equitable care for women with CVD.

résumer les différences entre les genres et les sexes en ce qui a trait aux MCV. Cette revue exhaustive des données probantes était axée sur les disparités entre les genres et les sexes sur les plans de la comorbidité, des facteurs de risque, des connaissances, des symptômes, du diagnostic et du traitement à l'égard de l'ensemble du spectre des MCV. Au cours des travaux nécessaires à cette revue, il est apparu que l'équipe des experts de l'Alliance avait aussi réuni une vaste collection d'articles sur la recherche de pointe, qui ont été synthétisés dans des chapitres détaillés faisant état des données actuelles sur la façon particulière dont chacune des maladies cardiovasculaires peut toucher les femmes. Un « atlas » de l'épidémiologie, du diagnostic et de la prise en charge des MCV chez les femmes a donc été ainsi créé. L'objectif global était de concevoir un document évolutif pour aider les cliniciens et le grand public à reconnaître les aspects particuliers des soins de santé cardiaque des femmes et fournir aux décideurs les renseignements dont ils ont besoin afin d'assurer que les femmes atteintes d'une MCV reçoivent des soins équitables.

comprehensive review of the evidence regarding sex- and gender-specific differences in comorbidity, risk factors, disease awareness, presentation, diagnosis, and treatment across the entire spectrum of CVD.[3]

The team that generated the review included clinicians, scientists, allied health, program managers, and patient partners with professional or personal experiences in women's heart health advocacy, education, knowledge translation, and policy. The intent of the review was to synthesize the state of the evidence for CVD in women, with a uniquely Canadian perspective, and identify significant knowledge gaps that hinder the transformation of clinical practice into one that is truly tailored for women—a significant health challenge that has only been recognized in Canada relatively recently.

In the process of creating the comprehensive and concise review on the evidence in women's heart health, it was recognized that the team of CWHHA experts had also assembled an expansive collection of original research articles that were synthesized into detailed chapters reporting on the present state of the evidence unique to each CV condition in women. This work comprises an ATLAS on the epidemiology, diagnosis, and management of CVD in women. The chapters of the ATLAS will be published serially in *CJC Open* over the next year, and subsequent updates will be incorporated as additional evidence becomes available. The overall goal of the ATLAS is to create a living document that will help clinicians and the public recognize the unique aspects of women's heart health care while providing policy makers with information they need to ensure equitable care for women with CVDs.

Specific aims of the ATLAS include the following: (1) report an environmental scan of the status of women's heart health and disease in Canada; (2) summarize the existing research on CVD in Canadian women; (3) identify importance of sex- and gender-specific differences and approaches to CV care in Canada; (4) identify knowledge gaps to guide future research; and (5) describe a unified approach to CV health promotion, disease management, and research in Canadian women with an ultimate goal of improving CV outcomes.

Methods

The writing groups comprised members of the Knowledge Translation and Mobilization, and Health Systems and Policy Working Groups of the CWHHA, a volunteer pan-Canadian professional organization powered by the Canadian Women's Heart Health Centre at UOHI, whose vision and mission is to improve women's CV health across their life span by supporting clinicians, scientists, patients, and decision-makers to work collaboratively to implement evidence to transform clinical practice and impact public policy related to women's CV health in Canada. In a key collaboration with CWHHA experts, HSFC staff complemented the writing group. The HSFC is dedicated to policy and advocacy, system change, knowledge translation, public awareness and education, and CVD research. In recent years, HSFC has identified women's heart and brain health as a priority, forming a Women's Research Network consisting of CV experts from across Canada and launching a women's awareness campaign in 2018. All writing group members have in-depth expertise on CVD in women. Following 2 national planning teleconferences of the CWHHA Knowledge Translation and Mobilization and Health Systems and Policy Working Groups, a topic outline based on the scope of the problem was developed. Chapter lead authors and writers were selected on the basis of experience and expertise to complete evidence-based summaries of their assigned topic areas. The chapter leads oversaw the compilation of the evidence and the writing of the chapter topic. All writing group members had opportunities to comment on, edit, and approve the chapters, which also underwent extensive peer review by members of Canadian Women's Heart and Brain Health Research Steering Committee and HSFC. Administrative data were obtained from the Canadian Institute for Health Information and analyzed by HSFC authors. Components of the demographic material are based on comparative data and information obtained from the Canadian Institute of Health Information for the most recently available years, 2016 to 2017.

Evidence on CVD in women

For the purpose of the chapters included in the ATLAS, CVD refers to diseases, disorders, syndromes, and conditions that affect the heart and blood vessels. Vital Canadian statistics and hospitalization administrative data were extracted using International Classification of Diseases, 10th Revision, and codes (Supplemental Table S1). When available, studies with Canadian data were prioritized for inclusion to provide a Canadian perspective. When unavailable, studies with data from outside of Canada were included. Because of the lack of evidence covering the full scope of topics included in the ATLAS, it was not possible to perform a systematic literature review unique to CVDs in women. On the basis of the specific areas and the level of evidence, various search strategies were used to review the chapter topics. Please see the Supplemental Table S2 for listing of keywords used for literature searches to identify articles selected for inclusion in each chapter.

One of the first steps in moving past a one-size-fits-all approach to CVD treatment and management involves ensuring that studies systematically account for each patient's biologic sex, as well as other intersecting factors over and above sex that are associated with outcomes such as gender, age, race, and socioeconomic status.[4] New policies implemented at research funding agencies along with the implementation of editorial guidelines at peer-review journals include sex and gender analysis as one benchmark among many when evaluating grants or publications. The overarching goal is to increase transparency, promote inclusion, and ensure the research community carefully considers sex and gender, where appropriate. The terms "sex" and "gender" are often incorrectly used interchangeably despite clear and distinct definitions. Sex refers to biological constructs that are primarily associated with physical and physiological features, including hormones, genes, anatomy, and physiology typically categorized as female or male. Gender refers to socially constructed roles, behaviors, expressions, and identities, and typically categorized as woman/girl or man/boy. Although Tannenbaum et al.[5] report that CV medicine is arguably the most advanced specialty in its understanding of clinically significant biological differences between the sexes, from prevention to treatment, the lag time between discovery and implementation of sex-specific considerations accounts for disparities in CV morbidity and mortality.

Sex differences unique to women with CVD

It has been long recognized that age reduces many estrogen-related vascular responses. The increasing evidence indicates that as women's vessels spend considerable time under widely fluctuating hormonal influence, including puberty, pregnancy, peripartum, and menopause, women's vessels may be preset for more severe functional alterations compared with men.[6] The structural findings in the vasculopathy of women with ischemic heart disease demonstrate that both macro and micro vessels are smaller in size, have increased stiffness including fibrosis and remodeling, and have more diffuse disease whereby erosion is greater than plaque rupture.[5] Sex hormones are known to exert effects on the vascular reactivity via the endothelium and directly on smooth muscles. Very recently reported is the intriguing finding from longitudinal sex-specific analyses of blood pressure that women, compared with men, exhibit a steeper increase in blood pressure beginning as early as in the third decade and continuing through the life course, which suggests sex-unique biological characteristics of the vasculature, even independent of hormonal influence.[7] Women in the **W**omen's **I**schemia **S**yndrome **E**valuation (WISE) study had coronary endothelial dysfunction that independently predicted adverse outcomes. Bugiardini and Merz[8] reported that in the large arteries of women presenting with chest discomfort, endothelial dysfunction is an indication of early atherosclerosis before structural changes to the vessel wall are seen on angiography. Furthermore, endothelial dysfunction of the microvasculature has significant potential to limit myocardial perfusion.

Another sex difference unique to women relates to adverse pregnancy outcomes (APOs). APOs are disorders caused by placenta dysfunction and maternal vascular abnormalities, including platelet activation, inflammation, and vasospasm. Pregnancy, now commonly referred to as a "women's first stress test" and related APOs put women at increased risk for future CVD.[9] In a recent comprehensive review on the long-term CV risk associated with APOs, Lane-Cordova et al. report that the vascular abnormalities that are present during an APO (e.g., hypertension, pre-eclampsia, or gestational diabetes) also underlie common, difficult-to-treat forms of CVD in women as they age, including coronary microvascular disease, suggesting shared mechanistic pathways for APOs and CVD.[9] At present, there are no studies addressing the impact of APOs on ischemia and no obstructive coronary artery disease.

Gender differences in women with CVD

Beyond biological sex, gender is increasingly recognized as a pivotal determinant of health and outcomes. However, there is a lack of standardized gender measurement. In a seminal white paper summarizing the findings and recommendations for the development of and integrated approach to identifying and managing patients with ischemia and no obstructive coronary artery disease, it is recognized that the knowledge gaps related to patient phenotypes (including the expressions and influences of sex and gender), mechanistic understanding, and treatment of patients with CVD are numerous.[10] Specifically, there is a need for improved understanding of the biopsychosocial factors that may influence the development and treatment of women with CVD. In a recent editorial, Dr Wenger,[11] a pioneer in women's heart health, persuasively elucidates that the CV health of women requires more than sex-specific research. Furthermore, she argues that to truly understand the complicated interdependence of sex and gender on outcomes, research going forward must include the domains of women's beliefs and behaviours as well as the sociocultural (gender) forces that affect women's lives and ultimately women's heart health.

Clinical Practice Guidelines for women with CVD

Canada. Guidelines and Position statements for CV care are developed by and available through the Canadian Cardiovascular Society (CCS) in the Guidelines and position statements library on the CCS website (www.ccs.ca). These guidelines, developed through literature review, evidence, and clinical experience, represent the consensus of a multidisciplinary panel of "experts" who are charged with the mandate of formulating

disease-specific recommendations. To date, these guideline recommendations have been assumed to be applicable to both men and women, and have not been reported by sex; when thought to be relevant, a section on "special populations" may include sex-specific statements. A singular sex-specific document addressing ischemic heart disease in women was published in 2000, as a result of a CCS-initiated consensus conference.[12] Canadian Clinical Practice Guideline (CPG) developers have yet to endorse a consistent and systematic approach for considering sex-specific CV information in the CPG.

However, an initiative led by the CCS in 2018 was undertaken to determine the feasibility and outcomes of a structured process for considering sex and gender in CPGs, specifically for managing ST-segment elevation myocardial infarction. A sex and gender champion was appointed to the guideline development committee. The feasibility of tailoring the CPG to sex was ascertained by recording (1) the male−female distribution of the study population; (2) the adequacy of sex-specific representation in each study using the participation/prevalence ratio; and (3) whether data were disaggregated by sex. The outcome was to determine whether CPG recommendations based on an assessment of the evidence should differ by sex. It was concluded that implementation of a systematic process for critically appraising sex-specific evidence for CPGs was straightforward and feasible; however, inadequate enrollment and reporting by sex hindered comprehensive sex-specific assessment of the quality of evidence and strength of CPG recommendations on the management of ST-segment elevation myocardial infarction.[2] Although gender-specific analyses were deemed not feasible at this time, it was emphasized that going forward it is imperative that results be stratified by sex for clinicians to have the ability to provide sex-specific care. A recognition of the importance of ensuring female participation in CV trials is supported by recently mandated policies of the Canadian Institutes of Health Research[13] and the HSFC requiring sex- and gender-based analysis in funded research.[1] Moreover, equitable representation in research of high CVD risk groups, such as indigenous and ethnic women, is additionally required.

United States. With the support of the American Heart Association, women-specific CV prevention guidelines were first published in 2004,[14] updated in 2007,[15] and subsequently updated as "effectiveness-based" guidelines in 2011.[16] Over the past decade, additional published guidelines, scientific statements, and advisories have increasingly addressed the following aspects of CVD in women: peripheral artery disease (2012),[5,17] trends in awareness of heart disease in women (2013),[18] stroke prevention in women (2014),[19] role of noninvasive testing in the clinical evaluation of women with suspected ischemic heart disease (2005) and updated in 2014,[20,21] acute myocardial infarction (2016), prevention and experience of ischemic heart disease (2016),[22] spontaneous coronary artery dissection (2018),[23] and promotion of risk identification and reduction of CVD in women through collaboration with obstetricians and gynecologists (2018).[24] All of these documents consistently report that the level of evidence is not available at this time to provide sex-based guidelines for treatment of heart events in women. It is also interesting to note that there are no women-focused statements/guidelines on heart failure, arrhythmias, or valve diseases. Women are considered "special populations" within the few guideline documents that address sex-specific issues on these topics.

Global. Similar to documents in Canada, there are no specific documents dedicated to CV guidelines in women, largely because of a lack of adequate evidence base.[25] Within the 2016 European Guidelines for Cardiovascular Prevention, a few recommendations tailored specifically for women are provided and advise against assessing CVD risk in women aged < 50 years with no risk factors, although it may be beneficial to assess CVD risk in women before prescribing combined oral contraception; screening of women aged > 50 years, or postmenopause, may be considered in the same way that it is for men, that is, for those at increased risk of CVD, for example, family history of CVD or hyperlipidemia, or presenting with major risk factors, including pre-eclampsia. These recommendations are based on an evidence base using 8 risk estimation systems (Framingham,[26] SCORE,[27] ASSIGN − SCORE,[28] QRISK1,[29] QRISK2,[30] PROCAM,[31] Pooled Cohort Studies Equations,[32] CUORE,[33] and Globorisk[34]) with a percentage of women ranging from 32% to 64% (median 52%, mean 49%) and recommend several sex-specific cutoffs for CVD risk factors, including waist circumference (target value for women is < 80 cm and < 94 cm for men), high-density lipoprotein cholesterol (>1.2 mmol/L indicates lower risk in women, whereas for men the value is > 1.0 mmol/L), and alcohol consumption (limits are 1 glass per day for women and 2 glasses/day for men).

The stunning lack of research specifically oriented to women and the under-representation of women in CVD research studies are significant contributing factors to the underdiagnosis, undertreatment, and current absence of CPGs for women with CVD in Canada. CPGs are developed using national guideline committees made up of groups of experts in the treatment of specific clinical disorders and are a key step in translating evidence into clinical practice. Despite a general understanding that appearances and outcomes of diseases may contrast for male and female patients, the uptake of sex and gender factors into CPGs has been slow, with only 20% of CPGs recommending sex-specific diagnostic or treatment strategies.[35,36] Tannenbaum et al. offer a number of clinical examples in which the consequences of not including evidence separately in CPGs about women and men can range from missed opportunities to incorrect prescription of drugs.[5] If quality of care for both male and female patients is to be enhanced, sex and gender differences must be incorporated into CPG development. Our own research into the lack of sex- and gender-specific guidelines identified the following barriers to the addition of sex and gender considerations in the process of guideline development: (1) an inclination for working groups to develop recommendations for the "general" patient population; (2) a lack of cognizance that attention to sex- and gender-related factors may improve the quality of the guidelines; and (3) the absence of a organized process for identifying and systematically evaluating the evidence on sex and gender differences.[2]

CWHHA Women's Cardiovascular ATLAS Project

The need for a dedicated compilation of articles addressing the state of the science of women's CV health in Canada is

clear and heretofore unmet. The CWHHA Women's Cardiovascular ATLAS project aims to fill this void and begins with the present installment that provides a critical appraisal of the currently inadequate evidence base to support female-specific clinical guidelines and recommendations for CVD in Canada. This will be followed by a series of chapters examining in detail the fundamental issues regarding CV health and disease in Canadian women, including an assessment of the burden of CVD on women in Canada, a statement on "the patient's perspective" written by women with lived experiences of CVD, and examination of the sex- and gender-specific differences in comorbidity, risk factors, and a lack of awareness on the part of women and their healthcare providers. The final chapters will include a discussion of future directions and the action needed on multiple fronts to achieve sex and gender equity for women's CV health to correct the glaring "unders" of CVD for women in Canada: under-awareness, underdiagnosis, undertreatment, under-researched, and under-supported. Once all of the chapters of the ATLAS have been published in this series, we anticipate that we will have created a living document that can be refreshed annually as the evidence base grows and can provide a ready resource and reference for the development of CPG and synthesis of state-of-the art knowledge in women's CV health and disease. Most important, it is our intention that the CWHHA *Women's Cardiovascular Atlas* will help clinicians and the public recognize the unique aspects of women's heart health care while at the same time provide policy makers with information they need to ensure equitable care for women with CVDs.

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References

1. Heart and Stroke Foundation of Canada. 2018 Heart Report: Ms. Understood. 2018. Available at: https://www.heartandstroke.ca/-/media/pdf-files/canada/2018-heart-month/hs_2018-heart-report_en.ashx. Accessed August 17, 2019.
2. Norris CM, Tannenbaum C, Pilote L, et al. Systematic incorporation of sex-specific information into clinical practice guidelines for the management of ST-segment–elevation myocardial infarction: feasibility and outcomes. J Am Heart Assoc 2019;8:e011597.
3. Norris CM, Yip CYY, Nerenberg KA, et al. State of the science in women's cardiovascular disease: a Canadian perspective on the influence of sex and gender. J Am Heart Assoc 2020;9:e015634.
4. Tannenbaum C, Ellis RP, Eyssel F, Zou J, Schiebinger L. Sex and gender analysis improves science and engineering. Nature 2019;575:137-46.
5. Tannenbaum C, Norris CM, McMurtry MS. Sex-specific considerations in guidelines generation and application. Can J Cardiol 2019;35:598-605.
6. Pepine CJ, Anderson RD, Sharaf BL, et al. Coronary microvascular reactivity to adenosine predicts adverse outcome in women evaluated for suspected ischemia: results from the National Heart, Lung and Blood Institute WISE (Women's Ischemia Syndrome Evaluation) study. J Am Coll Cardiol 2010;55:2825-32.
7. Ji H, Kim A, Ebinger JE, et al. Sex differences in blood pressure trajectories over the life course. JAMA Cardiol 2020 Jan 15 [Epub ahead of print].
8. Bugiardini R, Merz CNB. Angina with "normal" coronary arteries: a changing philosophy. JAMA 2005;293:477-84.
9. Lane-Cordova AD, Khan SS, Grobman WA, et al. Long-term cardiovascular risks associated with adverse pregnancy outcomes: JACC review topic of the week. J Am Coll Cardiol 2019;73:2106-16.
10. Bairey Merz CN, Pepine CJ, Walsh MN, Fleg JL. Ischemia and No Obstructive Coronary Artery Disease (INOCA): developing evidence-based therapies and research agenda for the next decade. Circulation 2017;135:1075-92.
11. Wenger NK. Adverse cardiovascular outcomes for women—biology, bias, or both? JAMA Cardiol 2020 Jan 15 [Epub ahead of print].
12. Canadian Cardiovascular Society 2000 Consensus Conference: Women and Ischemic Heart Disease. Can J Cardiol 2001;17(Suppl D):3D-69D.
13. Canadian Institutes of Health Research and Institute of Gender and Health. Sex, gender and health research. Available at: http://www.cihr-irsc.gc.ca/e/50833.html. Accessed July 8, 2019.
14. Mosca L, Appel LJ, Benjamin EJ, et al. Evidence-based guidelines for cardiovascular disease prevention in women. Circulation 2004;109:672-93.
15. Mosca L, Banka CL, Benjamin EJ, et al. Evidence-based guidelines for cardiovascular disease prevention in women: 2007 update. J Am Coll Cardiol 2007;49:1230-50.
16. Mosca L, Benjamin EJ, Berra K, et al. Effectiveness-based guidelines for the prevention of cardiovascular disease in women—2011 update. A guideline from the American Heart Association. J Am Coll Cardiol 2011;57:1404-23.
17. Hirsch AT, Allison MA, Gomes AS, et al. A call to action: women and peripheral artery disease. Circulation 2012;125:1449-72.
18. Mosca L, Hammond G, Mochari-Greenberger H, et al. Fifteen-year trends in awareness of heart disease in women. Circulation 2013;127:1254-63.

19. Bushnell C, McCullough LD, Awad IA, et al. Guidelines for the prevention of stroke in women. Stroke 2014;45:1545-88.

20. Mieres JH, Gulati M, Bairey Merz N, et al. Role of noninvasive testing in the clinical evaluation of women with suspected ischemic heart disease. Circulation 2014;130:350-79.

21. Mieres JH, Shaw LJ, Arai A, et al. Role of noninvasive testing in the clinical evaluation of women with suspected coronary artery disease: consensus statement from the Cardiac Imaging Committee, Council on Clinical Cardiology, and the Cardiovascular Imaging and Intervention Committee, Council on Cardiovascular Radiology and Intervention, American Heart Association. Circulation 2005;111:682-96.

22. McSweeney JC, Rosenfeld AG, Abel WM, et al. Preventing and experiencing ischemic heart disease as a woman: state of the science. Circulation 2016;133:1302-31.

23. Hayes SN, Kim ESH, Saw J, et al. Spontaneous coronary artery dissection: current state of the science: a Scientific Statement from the American Heart Association. Circulation 2018;137:e523-57.

24. Brown HL, Warner JJ, Gianos E, et al. Promoting risk identification and reduction of cardiovascular disease in women through collaboration with obstetricians and gynecologists: a presidential advisory from the American Heart Association and the American College of Obstetricians and Gynecologists. Circulation 2018;137:e843-52.

25. Piepoli MF, Hoes AW, Agewall S, et al. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts) Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). Eur Heart J 2016;37:2315-81.

26. D'Agostino RB Sr, Vasan RS, Pencina MJ, et al. General cardiovascular risk profile for use in primary care. Circulation 2008;117:743-53.

27. Conroy RM, Pyörälä K, Fitzgerald AP, et al. Estimation of ten-year risk of fatal cardiovascular disease in Europe: the SCORE project. Eur Heart J 2003;24:987-1003.

28. Woodward M, Brindle P, Tunstall-Pedoe H. Adding social deprivation and family history to cardiovascular risk assessment: the ASSIGN score from the Scottish Heart Health Extended Cohort (SHHEC). Heart 2007;93:172-6.

29. Hippisley-Cox J, Coupland C, Vinogradova Y, et al. Derivation and validation of QRISK, a new cardiovascular disease risk score for the United Kingdom: prospective open cohort study. BMJ 2007;335:136.

30. Hippisley-Cox J, Coupland C, Vinogradova Y, et al. Predicting cardiovascular risk in England and Wales: prospective derivation and validation of QRISK2. BMJ 2008;336:1475-82.

31. Assmann G, Cullen P, Schulte H. Simple scoring scheme for calculating the risk of acute coronary events based on the 10-year follow-up of the prospective cardiovascular Munster (PROCAM) study. Circulation 2002;105:310-5.

32. Goff DC Jr, Lloyd-Jones DM, Bennett G, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014;63(25 Part B):2935-59.

33. Giampaoli S. CUORE: A Sustainable Cardiovascular Disease Prevention Strategy. London, England: SAGE Publications, 2007.

34. Hajifathalian K, Ueda P, Lu Y, et al. A novel risk score to predict cardiovascular disease risk in national populations (Globorisk): a pooled analysis of prospective cohorts and health examination surveys. Lancet Diabetes Endocrinol 2015;3:339-55.

35. Keuken DG, Haafkens JA, Hellema MJ, Burgers JS, Moerman CJ. Incorporating a gender perspective into the development of clinical guidelines: a training course for guideline developers. Implement Sci 2007;2:e1-7.

36. Tannenbaum C, Clow B, Haworth-Brockman M, Voss P. Sex and gender considerations in Canadian clinical practice guidelines: a systematic review. CMAJ Open 2017;5:E66-73.

Supplementary Material

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