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Review

Guideline Alignment in Related Areas

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ABSTRACT

Clinical practice guidelines serve an important role in the primary and secondary prevention of cardiovascular disease. There is variability among guideline groups in the methods used to assess and grade clinical evidence, resulting in discrepancies in various guidelines. Multiple guidelines focused on different aspects of cardiovascular care can lead to recommendations that are out of sync. Discrepancies between a practice recommendation from 2 different Canadian guideline groups can lead to confusion among clinicians and patients, reducing the likelihood that the practice recommendation will be carried out. Assisting cardiovascular-focused guideline groups to align, to harmonize, and to score highly on appraisal has been a main function of the Canadian Cardiovascular Harmonized National Guidelines Endeavour (C-CHANGE). Validated appraisal tools, harmonized guideline initiatives, and continuous evaluation of the impact of guidelines on quality indicators and practice outcomes are crucial for improving cardiovascular care for all Canadians.

RÉSUMÉ

Les lignes directrices de pratique clinique jouent un rôle important dans la prévention primaire et la prévention secondaire des maladies cardiovasculaires. Les groupes de travail sur les lignes directrices utilisent des méthodes variées pour évaluer et classer les données cliniques, qui entraînent des divergences entre les diverses lignes directrices. Les nombreuses lignes directrices portant sur différents aspects des soins cardiovasculaires peuvent déboucher sur des recommandations qui sont en décalage. Les divergences entre les recommandations de pratique de deux différents groupes de travail sur les lignes directrices canadiennes peuvent semer la confusion parmi les cliniciens et les patients, et réduire la probabilité de mettre en œuvre les recommandations de pratique. La fonction principale de l'Initiative canadienne d'harmonisation des lignes directrices nationales (C-CHANGE pour *Canadian Cardiovascular Harmonization of National Guidelines Endeavour*) était d'aider les groupes de travail sur les lignes directrices sur les maladies cardiovasculaires dans l'alignement, l'harmonisation et l'octroi d'un score élevé à l'évaluation. Les outils d'évaluation validés, les initiatives d'harmonisation des lignes directrices et l'évaluation continue des répercussions des lignes directrices sur les indicateurs de qualité et les résultats de la pratique sont essentiels pour offrir de meilleurs soins cardiovasculaires à tous les Canadiens.

Clinical practice guidelines serve an important role in the primary and secondary prevention of cardiovascular disease. Competing guideline recommendations in similar areas are a contributing barrier to guideline adherence.[1] Discrepancies within guidelines in related fields may arise for a variety of reasons: varied frequency of updates, different target audiences, and nonuniform method of evaluating the evidence. Harmonization of Clinical Practice Guidelines may help to avoid confusion among primary health practitioners, specialists, medical trainees, and patients alike.

Hypertension control rates in Canada are superior to those of other developed countries, including the United States.[2] The establishment and dissemination of Canadian hypertension guidelines (Hypertension Canada Clinical Practice Guidelines, previously **C**anadian **H**ypertension **E**ducation **P**rogram [CHEP]) have coincided with vast improvements in blood pressure diagnosis, treatment, and control from 1990 to 2008.[2] One reason for the superior control rates in Canada may be the consistent nature of the hypertension recommendations over the last decade. In releasing annual updates by one guideline body, Hypertension Canada has promoted guideline accessibility and acceptance. Conversely, there have been variability in the recommendations by the Joint National Committee and the American College of Cardiology/American Heart Association in the United States. The American Academy of Family Physicians recently released their own

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guideline on the management of hypertension in adults aged more than 60 years and announced that they do not endorse the most recent American College of Cardiology/American Heart Association guideline.[3] The presence of contradictory guidelines has been cited as a major barrier to guideline adherence[1] and is likely to contribute to less than ideal hypertension management in the United States.

Competing guidelines also exist in Canada, as illustrated by discrepancies in dyslipidemia guidelines, a condition affecting more than one third of the Canadian population.[4] Clinical Practice Guidelines published in 2015 and endorsed by the College of Family Physicians of Canada recommend against the use of cholesterol targets in the treatment of dyslipidemia, suggesting that lipid levels should be checked for risk stratification before treatment initiation only.[5] Recommendations from the 2016 Canadian Cardiovascular Society (CCS) Guidelines for the Management of Dyslipidemia[6] and harmonized in the 2018 Diabetes Canada guidelines[7] call for a treat-to-target approach. Although international guidelines vary on this topic,[8,9] and the literature leaves room for individual physician interpretation, the inconsistency between Canadian guidelines is not helpful in providing cohesive care to an increasingly complex patient population. Furthermore, Hypertension Canada's recommendation for statin therapy in primary prevention of nondyslipidemic patients with hypertension is similar but not consistent with the 2016 CCS lipid recommendations, and in fact references the 2012 lipid guidelines.[6,10] Harmonization of guidelines overcomes the challenge for every guideline group to remain up-to-date in knowledge translation in the various domains of cardiovascular care.

In discussing harmonization, it is important to review the role that Clinical Practice Guidelines play in improving patient outcomes. Rather than serving as a "rule book," guidelines can help health practitioners incorporate evidence-based medicine into patient care.[11] The application of an individual guideline recommendation in clinical practice must remain at the discretion of the individual clinician who best knows their patient or client. For example, for a patient with higher cardiovascular risk, the target blood pressure is < 120 mm Hg systolic based on the **S**ystolic Blood **Pr**essure **In**tervention **T**rial (SPRINT). However, a clinician may have a patient with coronary artery disease and diastolic blood pressure of only 60 mm Hg, and the clinician does not want to lower the blood pressure further to preserve diastolic coronary filling. The recommendations are all "should do's and should not do's," and the practitioner is not obligated to blindly follow them. They would likely explain to their patient why the practice recommendation does or does not apply and set a treatment plan.

Given variations in the patient population of Canada, specific regions or systems may be motivated to create clinical practice guidelines for a specific patient population. We suggest that regional- or institution-specific guidelines in Canada should reference back to the corresponding Canadian guideline group and should be considered as implementation efforts to aid in guideline dissemination through tailoring of the national guideline to meet local and regional needs. A complete guideline harmonization process should include coordination of implementation tool development with regional tailoring, involving guideline developers to mitigate the need for an entire new regional guideline and remain true to the evidence. Competing guidelines lead to redundancy and confusion. There are several possible ways to address the redundancies in Canadian cardiovascular guidelines. Harmonization can take place during the guideline development process by preemptively distributing clinical topics and promoting cross-collaboration across topics. This is easier said than done, considering the many involved stakeholders and need for timely guideline updates when new evidence becomes available. The complexities of cardiovascular care in Canada make it imperative for guideline developers to prioritize collaboration over "ownership" of a clinical domain. Harmonized guidelines, with identically worded recommendations in 2 or more national guideline documents, help to reinforce important practice recommendations.

For example, specific and consistent guidelines in the comanagement of atrial fibrillation and heart failure are important, given up to 50% of patients with heart failure may develop atrial fibrillation.[12] In response to the 2017 CCS Heart Failure Guidelines, McClure and colleagues[13] suggest that the "guideline's significant scope and redundancy may reduce the reader's confidence in them." The authors note that the heart failure guidelines make recommendations on topics overlapping with other CCS guidelines such as atrial fibrillation.[13] Although criticized for redundancy,[13] the 2017 CCS Heart Failure Guidelines do attempt to harmonize with existing CCS guidelines.[12] In the clinical domain of oral anticoagulation, the CCS heart failure guidelines simplify the recommendations and state they are following the updated 2016 CCS Atrial fibrillation guidelines. Regarding rate and rhythm control, the 2017 Heart Failure guidelines make more specific recommendations, but do mention they are consistent with CCS Atrial Fibrillation guidelines. Some redundancy in guidelines may be necessary to provide up-to-date evidence in a clinical domain. Future decisive collaborations between the CCS Atrial Fibrillation and the Heart Failure groups would promote better harmonization between guidelines and avoid perceived redundancies. Precise and uniform wording and citations to existing guidelines would promote confidence in the strength and consistency of the recommendations. Further, identical wording of harmonized recommendations appearing in 2 or more guidelines documents will reinforce and strengthen confidence.

Adding new recommendations at each cycle without removing outdated recommendations by each of the guideline bodies may hamper awareness with high guideline volume acting as a barrier to guideline adherence.[1] Consistency is also important beyond recommendations and applies to implementation strategies as well. There are both redundancies and inconsistencies in the physical activity recommendations by various Canadian organizations.[14] Given the high rates of inactivity among Canadians, challenges exist in the effective implementation of physical activity recommendations.[15] Expecting everyone to walk briskly for at least 150 minutes per week misses the fact that many people with frailty or disabilities cannot manage this, and that the greatest benefit comes from moving someone from sedentary behaviour to any movement. Although targeting sedentary behaviour reduction at a policy level may have more chance of success,[16] targeting inconsistencies and promoting simplification of guidelines may promote better physician and patient uptake. Providing

goal-oriented implementation strategies is especially important for guidelines on behavioural counselling regarding diet, physical activity, and smoking cessation. A lack of "outcome expectancy," a belief about the likelihood of the behaviour leading to a specific outcome, has been reported as a significant barrier in preventative health counseling.[1] Physicians may not implement guideline recommendations, for example, to reduce dietary sodium or to promote weight loss, where the benefits of counselling on outcomes may be difficult to appreciate on a patient-to-patient level.[1] Few guidelines, for example, recommend simple implementation strategies to exercise counselling; one exception is Diabetes Canada's individualized "exercise prescription," which can be modified in real-time in the clinical setting.[17]

Aligning cardiovascular guidelines in Canada can also help outline the current gaps in knowledge and variations in practice. One challenge for guideline bodies is to address areas of clinical importance in which high-quality evidence does not exist even though intuitively the answer seems obvious. Although Hypertension Canada recommends initiation of antihypertensive therapy for adults with uncomplicated hypertension without cardiovascular risk factors at a treatment threshold of > 160/100 mm Hg, there is no clear recommendation for what to do below that threshold.[10] Clinicians would like guidance for patients who are at lower risk and have not been studied with controlled cardiovascular outcomes trials. In this example, most clinicians would correctly start therapy if there was not a response to a period of health behaviours change over 4 to 6 months, which is in accordance with consensus recommendations in Europe and the United States.[18,19] Extrapolating guidelines to these areas must be done carefully, because ethics bodies, payers, and research funding agencies may refuse to allow research studies of practice gaps if they are already covered by a guideline recommendation, even if it is only a consensus recommendation.

Relevant clinical gaps in current guidelines should be addressed by increasing the involvement of a large scope of specialists, primary care providers, and patients. For example, involving experts in the common genetic condition of familial hypercholesterolemia in the development of dyslipidemia guidelines may lead to increased identification and earlier therapy of patients with this disorder.[20] Primary care physicians provide most of the preventative cardiovascular care in Canada, and their involvement and buy-in are instrumental to promoting population health. Including patients in the guideline development process is instrumental to identifying, studying, and improving patient-related outcomes.

Although inconsistencies between Canadian guideline group recommendations pose a challenge, there have been efforts to harmonize and align guidelines. Discrepancies between the Canadian Task Force for Preventative Health Care screening recommendations and other Canadian guideline groups have been cited as a challenge in primary care practice.[21] The approach taken for hypertension screening recommendations is an example of how harmonization efforts can lead to a successful outcome. In this case, a process developed between the Canadian Task Force for Preventative Health Care and the Hypertension Canada Clinical Practice Guidelines led to an agreement to put guidelines developers together to jointly review the evidence and bound each group to use the same recommendation wording with successfully aligned results.[22] Another example of successful harmonization is that between Diabetes Canada and Hypertension Canada concerning hypertension management among diabetic patients. The groups developed a memorandum of understanding to use the same methods binding on both groups and identical wording.[7] The result is more than 15 years of uniform recommendations, including targeted blood pressure of less than 130/80 mm Hg in patients with diabetes, with specific and consistent indications for renin-angiotensin system inhibition.[7,10]

The **C**anadian **C**ardiovascular **Ha**rmonized **N**ational **G**uidelines **E**ndeavour (C-CHANGE) was established in 2011 in response to concerns that discrepancies between guidelines on cardiovascular risk prevention are affecting quality of care in Canada.[11] The C-CHANGE effort to synthesize various guideline bodies and provide a uniform guideline for primary care professionals regarding cardiovascular care in Canada has been successful in this regard.[14,23,24] Nine individual guideline groups participated in the most recent update in 2018,[23] with the process involving collaboration among primary care physicians, specialists, allied health care providers, and expert methodologists in evidence-based medicine.

C-CHANGE has attempted to address many of the previously outlined discrepancies in clinical practice guidelines (see Table 1). For example, C-CHANGE includes the CCS Lipid Guideline's recommendation for treatment of dyslipidemia and will ask the Hypertension Canada Clinical Practice Guidelines committee to review its older lipid management guideline. With closer ties to the Canadian College of Family Practice for implementation (Canadian College of Family Practice's Prevention in Hand Program, available at https://www.cfpc.ca/Prevention_in_Hand/), it is hoped that C-CHANGE can influence a reevaluation of the Canadian College of Family Practice's Prevention's dyslipidemia recommendations based on the new evidence. Whether the C-CHANGE initiative solves the problems related to guideline discrepancies is dependent on healthcare practitioners' awareness and acceptance of the guidelines across the spectrum of specialties. It is necessary to continuously evaluate the implementation and to establish the effectiveness of the dissemination of the harmonized guidelines to the target population.

Table 1. Best practice for guideline harmonization

- Funding should be industry-free and achieved through public and institutional sources
- Memoranda of understanding between guidelines groups on how harmonization will work
- Harmonization efforts begun before guidelines developers use their systematic reviews to update or craft new recommendations
- A variety of medical practitioners with academic appointments and recognized expertise in the area, including methodology experts with no conflicts of interest, should have a seat at the table
- Collaboration between existing guideline bodies in areas with overlapping clinical domains
- Use of a scientifically sound appraisal tool such as AGREE II
- Implementation and dissemination of guideline harmonization efforts should be studied and continuously improved
- Evaluation of the impact of the guidelines on patient outcomes
- Methodology experts with no conflicts of interest to par

AGREE II, **A**ppraisal of **G**uidelines, **Re**search and **E**valuation II.

C-CHANGE is also working to strengthen cardiovascular prevention guidelines in Canada by promoting use of a strong methodology in the guideline development process. The **A**ppraisal of **G**uidelines, **Re**search and **E**valuation (AGREE) Collaboration, established in 2003 and revised in 2010 with AGREE II, has published an internationally relevant tool to evaluate guideline development. Such a tool has important implications in understanding inconsistencies across guidelines and provides a framework for adjudicating the quality of guideline development.[25,26] The AGREE II framework incudes 6 domains that cover the scope and purpose of the guideline, stakeholder involvement including patient involvement, rigour of development, clarity, applicability, and editorial independence.[27] C-CHANGE assesses the AGREE II score for each of the 9 partner guideline groups as part of a continuous quality-improvement process.[14]

Although AGREE II is an important step forward toward the standardization of the quality of guideline development, it does not assess the strength of the clinical content of the guidelines.[25] The quality of such evidence was addressed in a Canadian study in 2007,[28] with the authors evaluating 9 different cardiovascular risk management guidelines. Although 231 recommendations (68%) of the guidelines were based on randomized-controlled trial evidence, only 105 of those (45%) received a "Grade A or high grade" recommendation by these authors. These data strengthen the argument for guideline bodies to use extended grading systems and make specific citations to the supporting evidence within the guideline.[28] The 2018 C-CHANGE guideline addresses this problem, "[working] with the guideline groups to ensure that the evidence cited, and systematic reviews are of the highest quality."[23] Only 10.5% of the recommendations in the C-CHANGE guidelines are based on consensus, with zero consensus recommendations for drug or device therapies.[23]

The 2018 C-CHANGE guideline emphasizes the importance of a strong methodology by including a table specifically outlining the grading system or methodology used by each of the contributing guideline groups.[10] Given the involvement of a multitude of guideline bodies representing different specialties and disease processes, the appraisal processes are not identical among them.[23] There are obvious theoretical advantages to prospectively using one uniform appraisal process such as AGREE II in clinical practice guideline development, in that uniformity may increase physician and patient uptake.[11] The CCS guidelines have emphasized the use of the AGREE II in guideline development. However, it may not be realistic for every guideline body to adhere to AGREE II in a prospective manner, given the associated time and cost.[11] Perhaps more important than the appraisal process itself is adherence and documentation of the process with emphasis on evidence rather than eminence-based medicine.

The alignment and strengthening of the Canadian clinical practice guideline enterprise are integral steps to ensure best practice in cardiovascular risk prevention in primary care. One potential step looking forward could be to integrate a greater variety of medical disciplines with the C-CHANGE process and create a truly uniform multisystem guideline to address the major noncommunicable chronic diseases of the patient population. For example, chronic obstructive pulmonary disease and cardiovascular disease often coexist in the same patient.[29] In addressing the issue of beta-blocker use in patients with chronic obstructive pulmonary disease or asthma with concomitant cardiovascular disease, involvement of the Canadian Thoracic Society would allow a more synthesized and patient-centered recommendation. Similar initiatives could be undertaken for recommendations for nonsteroid anti-inflammatory medications in patients with coexisting osteoarthritis cardiovascular disease, as well as the well-recognized linkage between mental health conditions and cardiovascular disease.[30]

Conclusions

Overall, Canada deserves its international recognition for excellence in evidence, critical appraisal, and guidelines development. There is even greater potential from linking together guidelines from the major chronic diseases, coordinating implementation tool development including regional tailoring, and monitoring the impact on health with a national population-based guidelines surveillance program.

Disclosures

The authors have no conflicts of interest to disclose.

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