A vision for chronic disease prevention and intervention research: Report from a workshop

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ABSTRACT

The Population Studies Research Network of Cancer Care Ontario hosted a strategic planning workshop to establish an agenda for a prevention intervention research program in Ontario, including priority topics for investigation and design considerations.

The two-day workshop included: presentations on background papers developed to facilitate participants' preparation for and discussions in the workshop; keynote presentations on intervention research concerning primary prevention of chronic diseases, design and study implementation considerations; a dedicated session on critical and creative thinking to stimulate participation and discussion topics; breakout groups to identify, discuss and present study ideas, designs, implementation considerations; and a consensus process to discuss and identify recommendations for research priorities and next steps.

The retreat yielded the following recommendations: 1) develop an intervention research agenda that includes working with existing large-scale cohorts; 2) develop an intervention research agenda that includes novel research designs that could target individuals or groups; and 3) develop an intervention research agenda in which studies collect data on costs, define stakeholders, and ensure clear strategies for stakeholder engagement and knowledge transfer.

The Population Studies Research Network will develop options from these recommendations and release a call for proposals in 2014 for intervention research pilot projects that reflect these recommendations. Pilot projects will be evaluated based on their fit with the retreat's recommendations, and their potential to scale up to full studies and application in practice.

KEY WORDS: Research design; cohort studies; intervention studies; randomized controlled trials; prevention and control

La traduction du résumé se trouve à la fin de l'article.

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Canada's population is aging. About half of Canadian seniors report one or two chronic diseases and 24% have three or more long-term co-morbidities.¹ The coexistence of multiple chronic diseases causes disability and functional decline, high health care costs, and poor quality of life.² This is occurring despite the fact many chronic diseases can be effectively prevented and treated.³ If every Ontario resident changed only one risk factor, average life expectancy would increase by 3.7 years.⁴

Canada's population diversity, geographical dispersion, the federal-provincial split in responsibilities, and distinct provincial decision-making processes challenge a pan-Canadian chronic disease prevention strategy. Nevertheless, immediate action is needed to identify, evaluate, refine and implement cost-effective interventions to improve health. In Ontario, current research investments provide major opportunities for chronic disease prevention, and may provide a good model for Canada. However, in order to apply the evolving evidence base for prevention interventions^{5,6} to routine practice, we need:

- a) theory to guide the program's design and implementation;⁷
- b) advances in research designs and measurement tools to evaluate the efficacy or effectiveness of programs;⁸⁻¹⁰
- c) longer follow-up time to assess the duration of program effects;
- d) more detail to direct engagement and delivery, including: how to identify, recruit and retain the target audience, personnel training requirements, infrastructure needs, and incentives for adoption;^{11,12}

- e) reduction of the costs of intervention research; and
- f) knowledge translation/exchange to facilitate uptake of efficacious strategies.¹³

Cancer Care Ontario's Population Studies Research Network hosted a two-day workshop in January 2013, the objectives of

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which were to create a prevention intervention research agenda, including priorities for investigation and design considerations. This paper highlights the main issues that emerged, including the potential application of novel research designs, measurement tools, and new approaches for recruitment and follow-up, cost reduction, and outcomes assessment working with ongoing large-scale cohort studies that link records across databases and integrate biological samples. This paper discusses these issues in the context of the Ontario Health Study (OHS), a large, population cohort research platform.

Considerable investments have been made in cohort studies in many jurisdictions, including Canada. Examples include the Canadian Longitudinal Study of Ageing,¹⁴ a national study, and five provincial cohorts with explicit plans for harmonization of exposure and outcome information, brought together as the Canadian Partnership for Tomorrow (CPT) Project.¹⁵ An emerging trend in many jurisdictions is citizen science,¹⁶ and increasing attention is being given to participant engagement in research. The OHS, a component of the CPT Project, is a motivating example: a large cohort in which enrolment and data collection are Internet-based, it expends considerable effort to engage participants.

The Ontario Health Study

The OHS is designed to follow Ontario residents over many decades. Baseline data collection involves an online questionnaire, consent for re-contact, and consent to link the baseline data to provincial administrative health records to obtain detailed outcome information. The baseline data are wide-ranging, containing information on identified and potential risk factors for multiple chronic diseases, and personal and family health histories. The initial questionnaire is followed by in-depth investigation of a number of specific exposures, including psychosocial and mental health status, nutrition, sleep patterns, physical activity, and occupational and residential characteristics. Blood, urine samples and physical measures are being collected from large subsets of OHS participants.

The original design of the OHS incorporated both observational and experimental components, with the focus in the first few years on the former to develop the cohort and to collect participant data. The longitudinal nature of the OHS and the rich sources of administrative and medical records maintained by several provincial entities allow measurement of health behaviours and outcomes unique to OHS participants. Collection of community-level factors, including the built environment, nutrition and tobacco policies, is also planned over the course of follow-up. Now, with more than 225,000 participants enrolled, the time is ripe to test interventions aimed at altering the exposure patterns of the participants to optimize health and lessen their risk of adverse outcomes. Indeed, some workshop participants suggested that the OHS and other cohort research platforms offer an opportunity to embed and test interventions that are designed to address population health problems. Discussion of the potential for intervention research in cohort studies precipitated some debate in that the design implies the interventions would be individual-based, but previous studies have found limited impact for such interventions. Furthermore, much emphasis is given to the need for community-based interventions.^{17,18} However, it might also be argued that the Internet and related technologies to facilitate

recruitment and retention of participants and to aid data capture have resulted in the “personalization” of the community, thereby contributing to citizen science.

New approaches to intervention research within cohort studies

In addition to large sample sizes and informed consent protocols to facilitate follow-up and record linkage, cohort research platforms have other virtues: enabling longer-term follow-up to assess health outcomes and the sustainability of effects; allowing comparison of participants in an intervention with those who do not participate, during recruitment and through follow-up; providing higher recruitment and adherence than in *de novo* studies; and the potential for conducting intervention research across jurisdictions because of harmonization efforts.¹⁹

Furthermore, cohort studies can facilitate a wide variety of randomized controlled trial (RCT) designs. Cluster and stepped wedge RCT designs randomize groups (e.g., hospitals, districts, provinces, and schools) rather than individuals. In the latter design, each group receives the intervention at a randomly allocated point in time. Other RCT designs tend to randomize individuals rather than groups. Participants in a “patient preference” RCT design are asked which treatment they prefer and are then allocated according to their preference. Those without preferences have their treatment group allocated randomly. The Multi-LIFE design²⁰ extends this design by allowing participants to choose from a large number of possible randomizations and generates a factorial trial where joint effects can also be assessed. Zelen (single randomized consent) designs randomize individuals and then seek their consent to treatment. Those who are randomized to usual care are not informed about trial treatments they will not receive. The “cohort multiple” (cmRCT) design²¹ facilitates multiple Zelen-type RCT designs within a longitudinal cohort of participants with the characteristics of interest. For each RCT, eligible cohort participants are identified and a proportion are randomly selected and offered the intervention. This process is repeated for multiple further RCTs for the duration of the cohort study. The cmRCT design is especially suited to open trials with “treatment as usual” as the comparator²¹ where outcomes are easily collected. Both Multi-LIFE and cmRCT designs can accommodate multiple RCTs within cohorts. The cmRCT is advantageous when the interventions are highly desired in the wider population; most participants will choose the interventions if they are allocated to them, otherwise the treatment effects are weak. For interventions that are clearly desired by a fraction of the population, the multi-LIFE design may maintain a stronger treatment effect, since participants are willing to try either the experimental intervention or the comparator without having a strong preference. In the context of working with the OHS or any large cohort, investigators will develop intervention research ideas that can target either individuals or groups, and weigh the advantages and limitations of different randomized designs to evaluate the reach, efficiency and effectiveness of the proposed interventions.

Also, to enable the longer-term assessment of outcomes of intervention research based on hybrid or alternative designs embedded in existing cohorts, it is imperative that access be available to different data sources that can be linked. The Institute for Clinical Evaluative Sciences (ICES) is the repository for several

databases funded and maintained by the Province of Ontario, including OHIP billings, hospital discharge data, all-causes mortality, cancer registry data, and outcomes encounters, and other data. ICES has research agreements with many agencies and groups, including the OHS. ICES makes data available (in anonymized format) to researchers to investigate social and health questions. Furthermore, there is a long history of probabilistic record linkage in Ontario in circumstances where deterministic record linkage is not possible. The record-linkage methods for resolving uncertainties are well developed,²² and, as such, intervention studies are possible in existing large-scale cohorts where deterministic record linkage is not available.

Challenges and open questions for intervention research

A number of important challenges and questions require consideration when developing intervention research studies. First, most intervention studies have excluded measures of cost and utility. Stakeholders need cost parameters to determine priorities for intervention funding within existing budgets.

Second, interventions potentially have implications for health inequalities. Intervention research could target disadvantaged groups with a view to reducing disparities or to improving health status. Targeting disadvantaged populations would compensate for participation biases that tend to result in the preferential inclusion of the advantaged. However, even if inequities in health outcomes were to occur,²³ could the results be considered successful if a net gain for all health groups in a jurisdiction were achieved?

Third, time horizon, specificity of mechanisms, and appropriate measures are interconnected questions that require further debate. The large size of cohort studies allows small effect sizes that have substantial population impact to be detected. Funders, however, may resist waiting for longer-term outcomes, such as mortality reduction, and therefore may insist on proxy measures (e.g., BMI or blood pressure). Moreover, policy-making favours interventions whose specific mechanisms of effect are known. Yet, if longer-term outcomes follow a non-specific intervention, such as enrolling participants in an activity, does it matter if etiological pathways are unknown or the effects of postulated mechanisms remain uncertain?

Should interventions be tested at the individual or community level (or both)? Numerous literature reviews invite skepticism about interventions targeting individuals. Yet, technologies such as smartphones may open up novel delivery options. OHS participants, for example, who adopt technologies early, may become advocates for the desired health change. Scaling up individual-level interventions to a population level is very expensive. Translating community-level interventions into cohort platforms requires large investments in strategies to achieve participant buy-in and complex decision-making protocols for intervention randomization designs. Yet, difficulties in scaling up interventions should not discourage innovative designs. Inspiration can be drawn from the success and subsequent scaling-up of the North Karelia Project on CVD reduction and the more recent European EPODE project to change environments and behaviour to reduce childhood obesity. Effective stakeholder engagement strategies will help clarify what questions can be addressed, what information is needed and how that information is to be packaged, to aid decision-making.

It is certainly appropriate to recognize that interventions, particularly those embedded within cohort research platforms such as the OHS, will be complex^{24,25} and that interventions are more likely to succeed when theory-based.^{26,27} The recent increased penetration of social media as a channel to influence knowledge, attitudes and behaviours may have implications for theory development. As yet, it appears that intervention research projects to date have not incorporated the potential for social media and other internet technologies to enable dynamic tailoring, interactive education, and self-monitoring.²⁸

CONCLUSION

A prevention intervention research agenda is critically needed. Ontario's current investments in and infrastructure for research, including the Ontario Health Study large-scale population cohort, should be leveraged to identify, evaluate, modify and implement cost-efficient interventions to reduce the incidence, morbidity and mortality of chronic diseases. Embedding research questions into existing cohorts such as the OHS can optimize the advantages of these platforms to: identify group and/or individual interventions; reduce the costs of research; allow for the application of novel designs, including randomized trials; embrace innovative delivery options that take advantage of e-mobile and e-health initiatives; optimize participant recruitment and retention; enable longer-term follow-up; and assess impacts on health outcomes and measure cost-effectiveness. In addition, strategies should be developed that identify and engage key stakeholder groups to facilitate refinement of questions, delivery approaches, and application of results. The proposed research agenda is anticipated to yield relevant, scalable recommendations to achieve improved health.

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RÉSUMÉ

Le réseau de recherche « Étude de la population » d'Action Cancer Ontario a organisé un atelier de planification stratégique afin de fixer l'agenda d'un programme de recherche d'intervention sur la prévention en Ontario, y compris les thèmes prioritaires à aborder et les éléments à considérer dans le plan d'étude.

L'atelier de deux jours incluait : des présentations sur les documents de base élaborés pour faciliter la préparation des participants et leurs discussions durant l'atelier; des allocutions sur la recherche d'intervention axée sur la prévention primaire des maladies chroniques, le plan d'étude et les éléments à considérer dans la mise en œuvre de l'étude; une séance consacrée à la pensée critique et créatrice pour stimuler la participation et les sujets de discussion; la formation de petits groupes pour cerner, discuter et présenter des idées d'étude, des plans d'étude et des éléments à considérer pour la mise en œuvre; et un exercice de consensus pour discuter des priorités de recherche et de la suite des choses et formuler des recommandations.

Ces journées de réflexion ont produit les recommandations suivantes : 1) élaborer un agenda pour la recherche d'intervention incluant l'utilisation des cohortes à grande échelle existantes; 2) élaborer un agenda pour la recherche d'intervention incluant des plans de recherche novateurs qui pourraient cibler des particuliers ou des groupes; et 3) élaborer un agenda pour la recherche d'intervention avec des études pour recueillir des données sur les coûts, identifier les acteurs du milieu et présenter des stratégies claires pour la mobilisation des acteurs et le transfert des connaissances.

Le réseau de recherche « Étude de la population » formulera des options à partir de ces recommandations et lancera un appel de propositions en 2014 pour des projets-pilotes de recherche d'intervention qui reflètent ces recommandations. Les projets-pilotes seront évalués selon leur degré de correspondance avec les recommandations de l'atelier, leur potentiel de transformation en études complètes et leurs possibilités de mise en pratique.

MOTS CLÉS : plan de recherche; études de cohortes; études d'intervention; essais comparatifs randomisés; prévention et contrôle