

CANCER PREVENTION RESEARCH IN CANADA

A STRATEGIC FRAMEWORK
FOR COLLABORATIVE ACTION

**CCRA
ACRC**

Canadian Cancer Research Alliance • Alliance
canadienne pour la recherche sur le cancer

CANADIAN PARTNERSHIP
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PARTENARIAT CANADIEN
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For additional information about this publication, please contact:

Canadian Cancer Research Alliance (CCRA)
1 University Avenue, Suite 300
Toronto, Ontario M5J 2P1 CANADA
Email: info@ccra-acrc.ca

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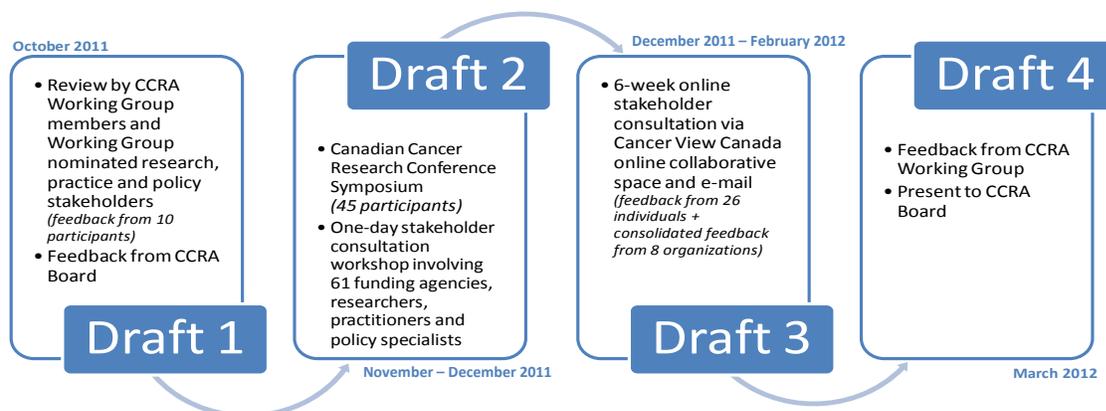
EXECUTIVE SUMMARY

In May of 2010, the Canadian Cancer Research Alliance (CCRA) published the first ever *Pan-Canadian Cancer Research Strategy*¹ framework report. This overall framework is grounded in the strengths of the Canadian cancer research community and is highly connected to emerging priorities in the international research landscape which will guide cancer research investment in Canada. This strategic framework sets an agenda of new collaborations between research funding agencies and aims to provide a vision for Canadian cancer research achievement over the next five years. The first action item that was proposed in this strategic framework led to the publication of a report² on the scope and nature of the investments in cancer risk factor and prevention research in Canada by CCRA member organizations. This then was to serve as the foundation for developing a pan-Canadian cancer prevention research framework to inform future CCRA funding priorities.

The purpose of this report is to provide a framework for collaborative action on and investment in cancer prevention research in Canada.

This framework is intended to cover a broad scope of research activities from risk factor identification and reduction through to intervention research, including individual behavior change as well as research to influence evidence-based public health/clinical practices and policies. Figure 1 reflects the multi-stage consultation process informing this report that involved research, practice, and policy experts from across Canada.

Figure 1: Stakeholder Consultation Process



The primary audience for this report is cancer research funding organizations working individually and collectively through the Canadian Cancer Research Alliance (CCRA). A secondary audience for the recommended actions in the report is other chronic disease research funders interested in partnering on risk factor reduction and prevention research initiatives focused on common non-communicable disease prevention priorities (e.g., tobacco, obesity, the environment).

The framework identifies needs and articulates opportunities for cancer risk identification and prevention research in Canada. It is expected that individual CCRA member organizations may have an

¹ http://www.ccra-acrc.ca/PDF%20Files/Pan-Canadian%20Strategy%202010_EN.pdf

² http://www.ccra-acrc.ca/PDF%20Files/Prev_2005-07_EN.pdf

interest in leading, working together with other CCRA members to support, and/or collaborating with research funding agencies focused on other chronic diseases that share many risk factors with cancer (e.g., cardiovascular, diabetes, lung). Thus, an anticipated outcome of the review and approval of this report by the CCRA Board includes the launch of new co-funded research funding opportunities in shared cancer prevention research priority areas.

Implications from Research Funding Review

The detailed May 2010 report³ of CCRA cancer prevention research investments from 2005-2007 was used to provide a benchmark of cancer prevention and risk reduction research activity in the country and served as a basis for some of the recommendations within the framework. An analysis of these research investment data indicated that cancer epidemiology is a relatively active field in Canada spanning a broad range of risk factors with provincially-based leadership indicated for a number of these known risk factors. The level of etiological investment in infectious agents suggests that this may be a particular area of strength in Canada that can help identify new viral agents and contribute to the development of new vaccines to prevent cancer. Conversely, the extremely low level of investment in alcohol research in Canada is a concern which may warrant further consideration by the CCRA.

Research on genetic susceptibilities (inherited and acquired cancer risk) represented the single largest investment (\$39.5M) among the 15 risk factors examined. Although genetic factors are not generally considered modifiable, understanding population variations in genetic predisposition to developing cancer and/or being affected by lifestyle and environmental/occupational risk factors may provide the foundation for more targeted prevention intervention approaches in the future.

Tobacco accounted for 40% of the total investment in intervention-related research. It has been argued that there is sufficient evidence to demonstrate that significant reductions in new cancer cases could be accomplished through lifestyle modification and population-based approaches to tobacco control. The relatively low level of investment in areas of cancer prevention research other than tobacco control substantiates previously reported research portfolio analyses conducted by the CCRA. Two examples where collective action by CCRA members might help address these funding limitations are in environmental and occupational exposure risk factor identification and risk reduction research and in obesity-related risk factor identification and risk reduction research focused on improved nutrition and increased physical activity.

With respect to environmental and occupational exposures, there was no funding from 2005-2007 for human intervention research and relatively limited funding for identifying new environmental and occupational exposures that may be causes of cancer. Thus, there is an opportunity for CCRA member organizations to expand prevention research funding to discover new environmental and occupational risk factors and develop and test interventions to reduce occupational exposures to carcinogens within the workplace. A multi-agency initiative by CCRA members to address this problem could have a substantial impact on this relatively understudied area, with only a relatively modest commitment of funds. Of note, the Canadian Cancer Society (CCS) and Cancer Care Ontario (CCO), in partnership with the Workplace Safety and Insurance Board (WSIB) have recently expanded their research investments in this area through funding the Occupational Cancer Research Centre (OCRC). CAREX Canada, largely funded by the Partnership, also has extensive surveillance data on environmental and occupational exposures. These provide valuable platforms upon which to build.

Turning to obesity-related research, intervention research funding was the largest category of spending among CCRA member organizations although it only amounted to \$2.7M over the three year period (2005-2007). While there were 18 CCRA member organizations which provided research funding for

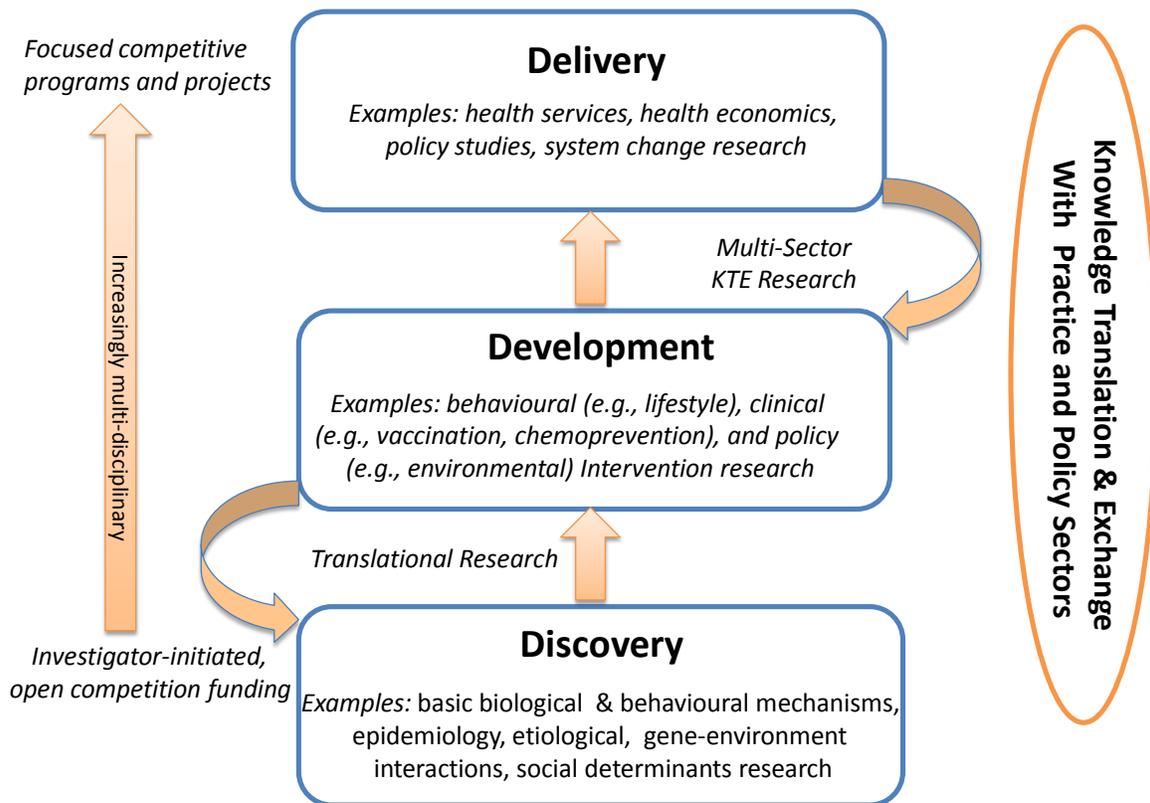
³ http://www.ccra-acrc.ca/PDF%20Files/Prev_2005-07_EN.pdf

obesity-related research between 2005 and 2007, the Canadian Institutes for Health Research (CIHR) and CCS alone accounted for 46.8% of the \$9.7M invested. In order to address the growing problem of obesity in Canada, CCRA member organizations could consider substantially increasing translational and intervention research investments and actively seek co-funding opportunities with non-cancer research funding agencies (e.g., Heart and Stroke Foundation, Canadian Diabetes Association) to leverage cancer-specific research funding with other chronic disease research funding agencies interested in reducing obesity and its deleterious health effects.

The 2005-2007 CCRA investment survey data⁴ suggest a significant barrier to progress may be limited research capacity due to the relatively small number of scientists engaged in cancer prevention research in Canada, particularly in intervention research. The importance of cancer risk reduction and prevention research is being recognized by Canadian cancer research funders and building scientific capacity in these gap areas is an overarching priority. In light of recent strategic investments in cancer prevention research by some CCRA member organizations, building prevention research capacity across Canada to take advantage of these new funding opportunities will be critical for their success. Future trend analyses of CCRA funding data will provide a valuable means to monitor the amounts and patterns of investment in this area.

A conceptual model for putting cancer prevention and risk research investment priorities in context is provided in Figure 2.

Figure 2: Prevention and Risk Research Strategic Funding Paradigm



⁴ http://www.ccra-acrc.ca/PDF%20Files/Prev_2005-07_EN.pdf

This graphical description displays the progression of research from basic discovery through intervention development to health services delivery research. As research moves from a foundation of discovery research to the study of the implementation of findings on population and health systems levels, the funding opportunities become proportionally less 'open' and increasingly focused, as well as increasingly multi-disciplinary. The proportion of investigator-initiated research evaluated through open competitions versus more focused research investments will differ in particular research topic areas and for different risk factors depending on the level of discovery, development and delivery research completed and synthesized to date. In more mature areas of study in which there has been significant investment in discovery and intervention development research, a higher proportion of strategic investments in delivery research may be warranted (e.g., tobacco control). Conversely, where the bulk of the research investments to date have been in discovery, and where the translational potential remains elusive, continued investments in investigator-initiated discovery and development research may be more appropriate.

However, as the translational research and KTE research arrows suggest, research evidence generated in any part of this research paradigm could and should inform resulting research questions, and investigator-initiated research should always be considered an important resource for the generation of new knowledge. For example, natural experiments and "real world" observational research may raise new questions that need to be investigated in "back to basics" discovery research. Knowledge translation and exchange is a critical activity throughout all phases of research and research funding priorities can and should be influenced in part by observations from the public health and clinical practice and policy communities.

One issue of concern raised during the framework consultation process, particularly among basic and etiological researchers, was the perceived trend that the proportion of research supported through open competitions relative to more focused investments by CCRA member organizations has been declining. Across the continuum of discovery, development and delivery research, open investigator-initiated grant opportunities are more frequently used for basic science and observational discovery research studies, with intervention (development), implementation and health services research (delivery) usually seeing a higher proportion of focused funding mechanisms (e.g., topic targeted requests for applications).

The CCRA investment data from 2007-2009⁵ indicate that while overall research dollars have grown by 27.4%, more focused research investments have only grown by 18.6%. Open competition funding for biology (31.5%), etiology (41.2%), early detection, diagnosis and prognosis (54.1%), and treatment (31.7%) have all grown more during the same time period. Only open competition funding for prevention intervention research (17.1%) and cancer control, survivorship, and outcomes research (13.0%) have grown by a lower percentage than the overall growth in more focused investments.

It should be noted that this concern regarding an appropriate balance between open and more focused funding extends beyond prevention and risk factor identification and reduction research across the cancer control continuum. As cancer research activities grow and evolve in Canada, more recent investment data will enable the CCRA to continue to monitor this important funding balance issue. The extent to which the collective investment by CCRA member organizations across the discovery, development, and delivery continuum is appropriate may be best understood in the context of the knowledge gained and the lessons learned from the research completed to date. Thus, the determination of an appropriate balance for different areas of research will depend in part on the ability to synthesize the emerging science.

⁵ Based on analysis of recent data (unpublished) from the Canadian Cancer Research Survey

Implications from Literature Reviews

There are a number of different sources that provide reviews of research evidence, including the peer-reviewed literature as well as organizational and expert opinion documents that make up what is often termed the grey literature. The number of reviews in the peer-reviewed literature alone is large and growing. For example, a simple search of the U.S. National Library of Medicine Pub Med website⁶ using the search terms ‘cancer prevention research’ yielded 10,240 review article citations dating back to 1970.

There are also well-recognized international and national organizations that lead the way in contributing to the systematic review of the research literature in general and the cancer research literature in particular. These include the WHO International Agency for Research on Cancer (IARC) monographs on the evaluation of carcinogenic risks to humans,⁷ the Cochrane library,⁸ The Canadian Task Force on Preventive Healthcare,⁹ The UK National Institute for Health and Clinical Excellence,¹⁰ The US Preventive Services Task Force,¹¹ and the US Community Preventive Services Task Force¹². All of these groups conduct regular reviews of the scientific literature and publish, update, and disseminate their findings and recommendations on a regular basis. While much of this work focuses on the practice and policy implications of the research reviews, a portion of some reviews is also devoted to elucidating research issues that remain to be addressed.

Recognizing that a systematic review of all the published documents, in addition to the many and varied grey literature documents, was beyond the scope and resources of this strategic framework development effort, the Canadian Partnership Against Cancer with its CCRA working group partners supported and worked with the Propel Centre for Population Health Impact at the University of Waterloo and the Canadian Cochrane Centre at the University of Ottawa to conduct a review of four sets of documents focusing on research issues or questions that need to be addressed in the future:

1. selected published and unpublished research strategy reports related to cancer risks and prevention (University of Waterloo)
2. cancer prevention relevant systematic reviews in the Cochrane Library (University of Ottawa)
3. cancer prevention relevant reviews in the Guide to Community Preventive Services (the Partnership)
4. cancer prevention research relevant policy documents in the Prevention Policies Directory (the Partnership).¹³

A number of potentially important research issues and questions were identified by this exercise and are described in the full report. However, while the effort to consider this information was appreciated by many of the reviewers of the earlier report drafts, particularly among the practice and policy reviewers, a number of research reviewers in the consultation process raised serious concerns about the inherent bias introduced by variable approaches to document identification and inclusion in the aforementioned review efforts. For example, almost all the documents reviewed focused on development or delivery related research issues and as such were largely silent on the important discovery research questions that remain to be addressed. Had it been possible to systematically review the over 100 WHO IARC

⁶ <http://www.ncbi.nlm.nih.gov/pubmed> (accessed February, 2012)

⁷ <http://www.iarc.fr/en/publications/list/monographs/> (accessed February, 2012)

⁸ <http://www.thecochranelibrary.com/view/0/index.html> (accessed September, 2011)

⁹ <http://www.canadiantaskforce.ca/> (accessed February, 2012)

¹⁰ <http://www.nice.org.uk/> (accessed February, 2012)

¹¹ <http://www.uspreventiveservicestaskforce.org/index.html> (accessed February, 2012)

¹² <http://www.thecommunityguide.org/index.html> (accessed November 2011)

¹³ <http://www.cancerview.ca/cv/portal/Home/PreventionAndScreening/PSProfessionals/PSPrevention/PreventionPoliciesDirectory> (accessed December 2011)

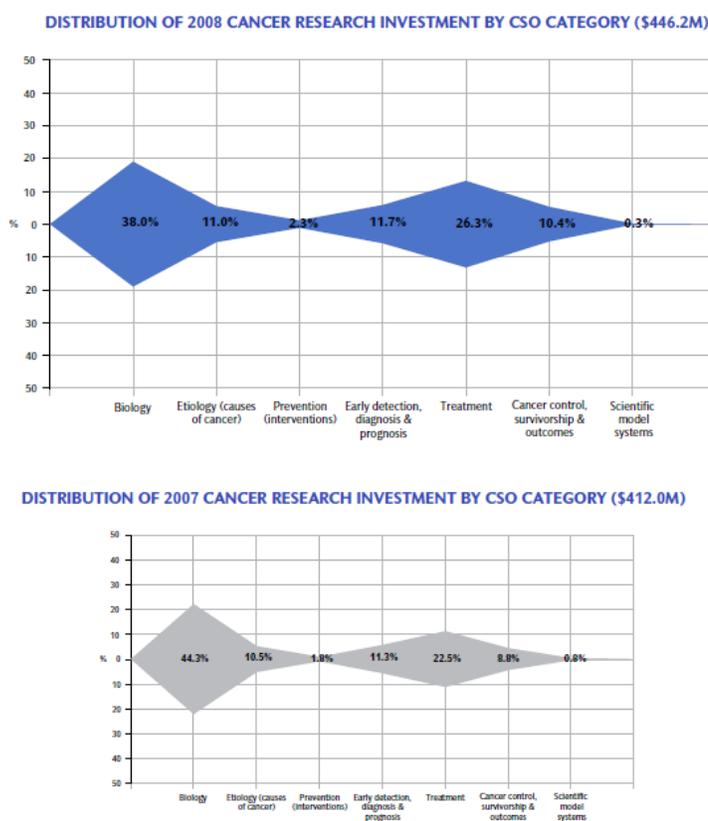
monographs on the evaluation of carcinogenic risks to humans, more discovery relevant research funding recommendations would no doubt have been identified.

A key recommendation in the framework that addresses the limitation of any ad hoc literature review process is that shared support by CCRA members should be garnered for cancer prevention research-focused knowledge synthesis efforts in order to conduct systematic reviews of risk factor and cancer prevention research review reports to inform future collectively funded request for proposals (RFPs). In this regard, there are a number of centres of knowledge synthesis excellence in Canada that could respond to RFPs to the CCRA to carry out such work on a timely and effective basis. This could dramatically increase the level of knowledge applied to the development of future cancer prevention research RFPs, and could help inform prevention research adjudication panels with the most up to date syntheses of findings relevant to the research proposals being reviewed. Moreover, once developed and evaluated, such an operation could be expanded to carry out similar knowledge synthesis efforts across the cancer control research continuum.

Where is Canada Taking the Lead in Cancer Prevention Research?

As can be seen from Figure 3 below, published in the most recent CCRA cancer research strategy investment report¹⁴, there has been an 8.3% increase in the total cancer research investments by CCRA members from 2007 to 2008, while there has been a 6.3 % relative percentage decrease in basic science biology investments in the same time period (a reduction of just under \$13M from 2007 to 2008).

FIGURE 3



While this reduction in basic science investments may reflect a change in priorities among some CCRA member organizations, basic science followed by treatment-related research remain the two largest

¹⁴ Canadian Cancer Research Alliance (2011). *Cancer Research Investment in Canada, 2008: The Canadian Cancer Research Alliance's Survey of Government and Voluntary Sector Investment in Cancer Research in 2008*. Toronto: CCRA. (Figure 3.2.1, page 20)

areas for cancer research investment in Canada. Compared with the overall growth observed for cancer research funding, the relatively small 1% increase in the combination of etiological and prevention intervention research from 2007 to 2008 highlights the importance of reviewing where Canada's risk factor identification and prevention research investments are being made and how both scientific opportunity and prevention practice and policy needs may inform prevention research priorities in the future. The importance of increased investment in cancer prevention and risk reduction research has been recognized by several CCRA member organizations, and examples of more current strategic investments not captured in the most recently available CCRA funding data are described in Appendix 1.

As previously noted, the cancer risk/causation component of Canada's cancer prevention research investments is relatively large. However, CCRA funding for genetic research accounts for a much larger share than the combined investments in lifestyle (e.g., alcohol use) and occupational/environmental risk factors. There are also significant opportunities to link basic science with population-based biomarker identification and molecular epidemiology. The multi-jurisdictional Canadian Partnership for Tomorrow Project represents an example of a collective investment where CCRA member organizations pooling resources can lead to a dramatic increase in our knowledge about cancer and other chronic disease risk factors.

Within Canada, there are prevention research capacity issues and recent CCRA data on the number and location of prevention scientists has revealed that there are very few researchers engaged in prevention research generally, and in intervention research specifically. Expanded capacity building resources should be considered by research funders to increase the field of qualified investigators in cancer prevention, risk reduction and intervention research. Above and beyond increased investments in training grants or nodes of research expertise, one model that may be worth examining to quickly attract new scientists into the field of cancer prevention research is the U.S. NIH career development K-awards.¹⁵ With respect to cancer prevention research, the NIH's National Cancer Institute has made and continues to make a significant investment in K-07¹⁶ five-year career development awards, which include significant salary support for research as well as training and travel funds. These investments led to significant growth in the number of cancer prevention and population scientists in the U.S.

With respect to risk factor reduction and cancer prevention intervention research, a number of research recommendation documents and systematic reviews highlighted the dearth of cost data for interventions being collected as well as little or no cost effectiveness analyses in the intervention research conducted and published in the peer-reviewed literature. From the perspective of practice and policy, the absence of such data may make the decision to adapt or adopt a research-tested cancer prevention intervention more difficult. Program resources for health promotion and disease prevention in Canada are very limited in comparison to healthcare services for those who are already diagnosed with a disease. As such, CCRA member organizations that develop and disseminate RFPs for cancer prevention intervention research should consider including a requirement for the collection and analysis of intervention implementation cost data in relation to intervention effectiveness data. This may be particularly important in natural experiments, where the context in which a program or policy is being implemented may have profound cost implications for other jurisdictions considering a similar approach.

Research priorities for knowledge translation and exchange (KTE) research were under-developed from the documents reviewed and there was very limited risk factor or cancer prevention research funding focused on these topics. Given that these areas are critical to integrating the lessons learned from

¹⁵ <http://grants.nih.gov/training/careerdevelopmentawards.htm>

¹⁶ <http://grants.nih.gov/grants/guide/pa-files/PAR-09-078.html>

research with the lessons learned from policy and practice, and were identified as high priorities in many of the policy documents reviewed, another opportunity for collective CCRA research investment is in KTE research training and the support of pilot studies in this area. This would increase the number of Canadian cancer prevention researchers who may become interested in and capable of successfully competing for existing KTE research funding mechanisms both from Canada (CIHR) and the U.S. (NIH).

Finally, given the diversity of populations and the variation in risk factors and disease burden across Canada, both research recommendation/policy documents and systematic reviews identified research to help reduce cancer health disparities as high priorities. However, there are three conundrums that CCRA member organizations will need to consider should they choose to increase research investment in this important area. First and foremost is the role that social determinants play as “upstream” conditions that contribute greatly to health disparities across many diseases, including cancer. Given that many of these social determinants are endemic and, if modifiable, will only be changed looking outside of a health lens, it’s often difficult to address health disparities through a disease-specific research funding initiative.

Second, many vulnerable populations and underserved communities that have experienced cancer and other health disparities are reluctant to participate in research. From their perspective, research often represents simply another effort to “describe” what has been known to them for generations rather than studying how to “address” the problems. Research through the lenses of discrimination and deprivation may be viewed as exploitative rather than supportive. Should CCRA member organizations choose to invest in health disparities research, they should carefully examine the lessons learned from community-based participatory research approaches¹⁷ to better understand how to constructively engage those populations and communities being studied, and how best to share research design, analysis, and knowledge exchange responsibility and authority with the leaders of those communities in which the research is conducted.

Third, the cultural and socioeconomic diversity of underserved communities often moves research and practice into the development, delivery, and evaluation of targeted interventions tailored to the particular needs and circumstances of specific vulnerable populations. From a research perspective, it’s often difficult to generalize the lessons learned from these community-specific intervention studies. Even communities that share the same cultural heritage or socio-economic conditions may view the research findings as not relevant their particular community needs. From a program and practice perspective, the resources needed to implement multiple intervention programs and policies tailored to each community’s needs may be beyond the resources available for disease prevention and health promotion. The CCRA member organizations and other non-communicable disease research funders with program and policy arms (e.g., health charities) should explore sharing best practices and results in rigorous program evaluation of community-specific practice and policy interventions. This will help increase our knowledge base of what works for whom without trying to sort this out solely through the lens of intervention research.

Recommendations for Key CCRA Prevention Research Funding Priorities

The following recommendations represent the 10 highest priorities for prevention and risk research in Canada based on current strengths, gaps, and opportunities for coordination and collaboration among CCRA member organizations. They are presented in order of infrastructure, discovery, development and delivery research investment opportunities and, as such do not imply any funding priority order.

1. CCRA member organizations should individually and/or collectively support initiatives that will build capacity in gap areas of cancer prevention and risk reduction research including multi-disciplinary

¹⁷ Israel, B. A., Eng, E., Shulz, A. J., & Parker, E. A. (Eds.). (2005). *Methods in Community Based Participatory Research for Health*. San Francisco, CA: Jossey-Bass.

intervention development, KTE and health services delivery research. These initiatives may include training awards, mentorships, deliberate networks, nodes of expertise, career awards or other funding mechanisms to encourage existing researchers in Canada to apply their research acumen to cancer prevention. The success of these capacity building initiatives will result in an increase in the pool of excellent Canadian investigators in these under-represented fields who can successfully compete for both open competition and more focused investment RFPs.

2. With respect to expanding prevention research infrastructures, CCRA member organizations should work together to: a) network existing centres of excellence in risk factor and prevention related research across Canada to increase knowledge exchange across disciplines, sectors and jurisdictions, and b) expand investments in new centres of excellence in cancer risk factor and prevention research, particularly in jurisdictions where additional research expertise can expand the effectiveness of cancer prevention practice and policy initiatives.
3. A number of CCRA member organizations are heavily invested in investigator-initiated, open-competition discovery research, recognizing it as the foundation upon which intervention development and service delivery research are based. Where more focused investments in development and delivery research are needed, this growth should not lead to a decline in funding dollars for the critical foundation of discovery research.
4. Where substantial investments have and continue to be made in discovery research areas (e.g., genomics and cancer) CCRA organizations funding this research should take advantage of the opportunities for working together to provide strategic funding to explore the translational potential of discovery research to inform new prevention intervention development and testing.
5. Where evidence-based prevention interventions have shown limited impact on specific high-risk populations (e.g., heavy smokers), collaborative and targeted funding for multi-disciplinary discovery research should be increased to elucidate the mechanisms by which some people and populations benefit from evidence-based interventions and others do not.
6. The collective investment in prevention intervention development and testing research should be increased, particularly in areas where the population attributable benefit of reducing the risk factor (e.g., tobacco, obesity) and/or the prevalence of risk factors (occupational and environmental exposures) remains high. Common risk factor intervention research studies also provide a significant opportunity for CCRA members to leverage their funding with other non-communicable disease research funders and benefit the field through collaborative investments.
7. Health economics research and the routine collection of cost data should be considered a very high priority in all future intervention development and delivery research strategic investments.
8. CCRA member organizations should share resources to strategically fund ongoing knowledge synthesis efforts of published systematic reviews and unpublished research strategy reports to inform the development and the adjudication of future cancer risk identification and reduction RFPs. The CCRA secretariat should coordinate this shared investment initiative.
9. CCRA member organizations with at least two mission priorities of research, practice and policy should evaluate and share best practices for integrating development and delivery research (e.g., natural experiments, cancer health services research) with evidence-informed program implementation and policy change work.

10. For complex cancer prevention and control issues where endemic societal determinants play an overarching role (e.g., health disparities among culturally diverse and underserved populations), CCRA members should co-invest with government and non-government agencies in rigorous program and policy evaluation, linked with KTE research, to inform future research funding opportunities and program/policy actions.

It should be noted that increased investments in prevention intervention development research carry with it some special issues that may have contributed to the relatively low levels of past funding in Canada and will need to be considered as new intervention development research initiatives are planned in the future. The first is that, for comparative studies testing an intervention to reduce cancer cases, large numbers of subjects are required and long follow-up needed before answers are obtained. Thus, these types of trials can be quite costly, require multiple participating investigators and institutions, as well as involving a substantial infrastructure to manage. While the use of intermediate or surrogate endpoints (such as reduction in precancerous lesions or reduction in risk factor measures) can address problems of sample size, cost and time to complete studies, these approaches have their own complexities.

The second issue centres on studies where interventions are intended to modify the process of carcinogenesis and are evaluated by measuring intermediate pathological endpoints (such as the development of pre-neoplastic lesions like polyps). Here the challenge is whether the endpoint chosen is a necessary step in carcinogenesis or whether other pathways and steps can bypass it. If the former, its reduction should lead to reduction in invasive cancers; if the latter, its reduction may not have the anticipated impact on invasive cases. These methodological issues have made the field of prevention intervention research both challenging and complex, and initiatives in this area will need to include funding on methodological improvements in research design and endpoint specification.

Finally, the complexity of cancer prevention intervention research (e.g., outcomes measurement and multi-factorial designs) combined with the diversity of populations and service delivery contexts in which cancer and chronic disease prevention programs are targeted highlight the importance of building research, practice, and policy partnerships. This applies not only to the use of cancer and chronic disease prevention research knowledge (KTE), but also to the importance of the practice and policy communities working with research funders and scientists to help identify the highest priorities and opportunities for future cancer prevention research in Canada.

The Path Forward

This report was prepared for all CCRA organizations by a working group of representatives of several CCRA member agencies in response to Action Item #1 of the 2010 Pan-Canadian Cancer Research Strategy.¹⁸ The well documented observation that levels of funding for cancer prevention research in Canada have been and remain low relative to other areas of research led to the recommendation that a comprehensive review of cancer prevention research in Canada should be documented followed by a multi-agency effort to develop a cancer prevention research strategic agenda for Canada.

To solicit specific organizational interest and commitments to follow-up with the collective funding recommendations described herein, the CCRA should agree to sponsor a meeting in 2012 of CCRA member organizations interested in playing a leadership role and/or serving as funding partners. This should then lead to new collaborative RFPs beginning in 2013. In addition, in order to ensure continued relevance of the proposed framework for future cancer risk factor and prevention research funding in Canada, a regular review and update of this framework report, including an analysis of progress against the above priorities and funding trend data, should be conducted with support from the CCRA and should be presented at each biennial Canadian Cancer Research Conference beginning in 2013.

¹⁸ http://www.ccra-acrc.ca/PDF%20Files/Pan-Canadian%20Strategy%202010_EN.pdf

INTRODUCTION

In May of 2010, the Canadian Cancer Research Alliance (CCRA) published the first ever *Pan-Canadian Cancer Research Strategy*¹⁹ framework report. This overall framework is grounded in the strengths of the Canadian cancer research community and is highly connected to emerging priorities in the international research landscape that will guide cancer research investment in Canada. This strategic framework set an agenda of new collaborations between research funding agencies and aims to provide a vision for Canadian cancer research achievement over the next five years.

The CCRA is currently comprised of 31 organizations that together represent the custodians of the majority of taxpayer dollars and donations devoted to investing in research that will lead to better ways to prevent, diagnose and treat cancer. Its membership includes federal research funding agencies (such as the Canadian Institutes of Health Research), provincial research agencies (such as le Fonds de la recherche en santé du Québec), provincial cancer care agencies (such as Cancer Care Nova Scotia) and national cancer charities (such as the Canadian Cancer Society (CCS)). The CCRA secretariat is supported by the Canadian Partnership Against Cancer (the Partnership).

The first action item that was proposed in this strategic framework¹⁹ was to publish a report on the scope and nature of the investment in cancer risk factor and prevention research in Canada by CCRA member organizations and then to use the report as the foundation for developing a pan-Canadian cancer prevention research agenda. The investment in cancer risk factor and prevention research report, also published in May 2010, described the CCRA member organization funding from the years 2005 to 2007 of cancer etiologic studies, risk identification, risk reduction research, population interventions and other types of prevention research.²⁰ It also assessed the extent to which Canada has the researcher capacity (as of 2007) to effectively utilize increased funding in prevention research.

Following the publication of the investment report, the CCRA Board asked the Partnership to work with the CCS to co-lead (with the support of the Alberta Cancer Foundation, Canadian Breast Cancer Foundation, Cancer Care Ontario, the Ontario Institute for Cancer Research, and Prostate Cancer Canada) the development of the cancer prevention research strategic framework contained herein.

The purpose of this report is to provide a framework for collaborative action on and investment in cancer prevention research in Canada.

This framework is intended to cover a broad scope of research activities from risk factor identification and reduction through to intervention research, including individual behaviour change as well as research to influence evidence-based public health/clinical practices and policies.

The primary audience of this report is cancer research funders working individually and collectively through the CCRA. The goal of this framework is to articulate specific opportunities that individual CCRA member organizations may have an interest in leading, working together within the CCRA, and/or working together with research funding agencies focused on other chronic diseases that share many risk factors with cancer (e.g., cardiovascular, diabetes, lung). Acknowledging that CCRA member

¹⁹ http://www.ccra-acrc.ca/PDF%20Files/Pan-Canadian%20Strategy%202010_EN.pdf

²⁰ http://www.ccra-acrc.ca/PDF%20Files/Prev_2005-07_EN.pdf

organizations have well-established research funding priorities, this framework has been designed to identify where CCRA member organizations could partner to achieve scientific contributions above and beyond what any single member organization could do on its own. Thus, an anticipated outcome includes the launch of co-funded research funding opportunities in shared priority areas.

Building on the aforementioned cancer risk factor and prevention research investment report, the foundation for this strategic framework also includes:

1. a commissioned synthesis review report, by the Propel Centre for Population Health Impact at the University of Waterloo, of selected relevant research strategy documents, including peer-reviewed publications and unpublished reports, from Canadian and International sources, containing cancer and chronic disease prevention research priorities (see Appendix 2),
2. a synthesis, with the support of the Canadian Cochrane Centre, of the implications for research sections from Cochrane library systematic reviews; as well as Partnership staff reviews of the Prevention Policies Directory and the US Guide to Community Preventive Service systematic reviews relevant to cancer risk factor and prevention research (e.g., tobacco control, nutrition and physical activity), and
3. a three stage consultation process that involved research, practice, and policy experts from across Canada, in:
 - a. CCRA working group members reviewing and providing written feedback on the preliminary draft of this report,
 - b. a CCRA research conference symposium and a subsequent one-day workshop dedicated to reviewing a second draft of the report to identify and discuss strengths and limitations of the document, and
 - c. the posting (for six weeks) of a third draft of the report (reflecting feedback from a & b) on the Partnership's Cancer View Canada web portal inviting additional comments and suggestions for improvement from an even broader group of research, practice, and policy stakeholders in cancer prevention from across Canada.

It should be noted that the Propel summary review of cancer and chronic disease prevention research strategy documents specifically drafted to inform this strategic framework report is quite detailed, and the bulk of the text of this review was placed in Appendix 2.

There are several caveats and limitations to the strategic framework report that should be noted:

1. The report is primarily targeted to the CCRA member organizations and, as such, does not include a detailed description of research opportunities on general healthy living/chronic disease prevention;
2. It was beyond the scope of this report to specifically describe Canada's cancer prevention research strengths and weaknesses in relation to the international cancer prevention research community;
3. The 2005-2007 CCRA risk factor and prevention research investment report does not include information about length of investments (e.g., breakdowns of short-term, long-term, and rapid

funding schemes), nor does it reflect time trends in research investments or researcher capacity development;

4. It's important to note that while cancer shares a number of common risk factors (e.g., tobacco, obesity) with other major chronic diseases in Canada (e.g., heart, lung, and diabetes), the CCRA membership does not include the other Canadian disease-specific research funding agencies, which in their own right fund important risk factor identification and reduction research. As such, many cancer prevention research funding priorities may overlap with the research funding priorities of these other chronic disease research funding organizations.

CANADIAN INVESTMENTS IN CANCER RISK FACTOR AND PREVENTION RESEARCH

The data source for the CCRA *Investment Report in Cancer Risk Factor and Prevention Research, 2005-2007* was the Canadian Cancer Research Survey (CCRS) database. This database was composed of peer-reviewed cancer research projects funded by 37 organizations/programs within the federal government, provincial government, and voluntary sectors from January 1, 2005 to December 31, 2007. It included organizations that fund only cancer research (e.g., Canadian Cancer Society) and organizations that fund all types of health (e.g., Michael Smith Foundation for Health Research) and general science (e.g., Natural Sciences & Engineering Research Council) research.

There were 7,203 projects in the database at the time of the analyses for this report. All projects in the database are coded by: the Common Scientific Outline (CSO), cancer site (using International Statistical Classification of Diseases and Related Health Problems, ICD-10), and type of funding mechanism (definitions can be found in the sidebar). The CSO is an international standard for classifying cancer research. It is grouped into seven categories (1-Biology, 2-Etiology, 3-Prevention [interventions], 4-Early Detection, Diagnosis, and Prognosis, 5-Treatment, 6-Cancer Control, Survivorship, and Outcomes Research, and 7-Scientific Model Systems), which roll up from 38 codes. (Details about the CSO codes can be obtained at <http://www.cancerportfolio.org/cso.jsp>.)

A subset of 1,388 projects was selected for possible inclusion in this study. It included all projects with the CSO categories of 2-Etiology and 3-Prevention as well as selected codes within 4-Early Detection, Diagnosis, and Prognosis and 6-Cancer Control, Survivorship, and Outcomes Research. A primary coder reviewed these projects and excluded those with a focus on:

- cancer biology (research on model systems, however, was included if it directly related to specific cancer risk factors)
- preventing cancers in patients who have already had cancer, including studies focused on risks for secondary cancers associated with radiation treatment
- developing or testing lifestyle interventions aimed at improving symptom management or quality of life for cancer survivors
- screening or other tests intended to confirm a cancer diagnosis or determine prognoses in patients with cancer (screening of precursor lesions was, however, included)
- treatment of ductal carcinoma in situ (DCIS) if the intent was to inform breast cancer treatment (projects focused on risk reduction were, however, included)

- providing infrastructure support to research across the full continuum of cancer control – these projects may be relevant to cancer risk and prevention but lack the detail needed to be accurately classified

A total of 347 projects were excluded, leaving 1,040 projects in the final sample. To assess the reproducibility of the exclusion criteria, an independent coder reviewed a random sample of 200 projects (14.4% of the relevant projects). Observed agreement between the primary and secondary coders was 96%. Projects were classified according to the three-dimensional cancer risk and prevention research “cube” (see Figure 4). The cube consists of research focus (four categories), risk factor (15 categories), and research type (five categories). Detailed definitions can be found in the full report.²¹

FIGURE 4 **CANCER RISK AND PREVENTION CUBE**



The Funding Data

The overall investment in cancer risk and prevention research for 2005–07 was \$122.3M. This represents 10.7% of the investment in all cancer research funded by CCRA member organizations over this three-year period. As described on page 20 of the original report, Federal government agencies and programs made the largest investment in cancer prevention research within Canada (\$72.0M). The next largest funding source is from national voluntary organizations (\$33.3M) followed by provincial health research organizations (\$10.1M) and provincial cancer agencies (\$7.1M). Conversely, the largest percentage of sector specific research investments devoted to risk factor and cancer prevention research was by national voluntary organizations (13.4%) followed by provincial cancer agencies (12.2%), the federal government (10%) and provincial health research organizations (8.7%).

With respect to provincial cancer agency funding, no data were available from British Columbia, and of the four provincial cancer agencies that did report funding risk factor and cancer prevention research, Ontario (\$4.9M) and Alberta (\$2.0M) accounted for the overwhelming majority of this research funding.

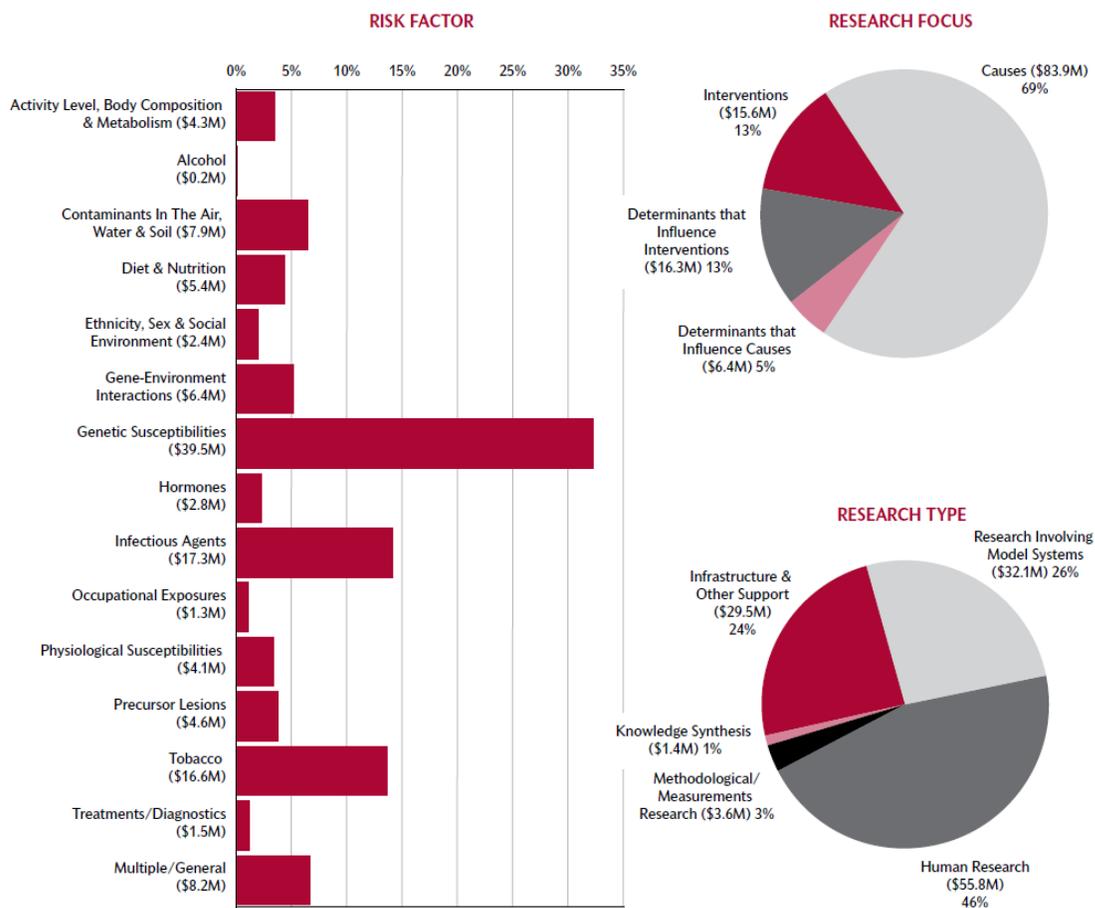
²¹ http://www.ccra-acrc.ca/PDF%20Files/Prev_2005-07_EN.pdf

Finally, while many aspects of cancer prevention are influenced by multiple sectors (e.g. public policies, private sector business models), no information is available on what if any relevant research funding comes from some sectors (e.g., the private sector) and to what extent, if any, different sectors work together to study how to reduce the risk of developing cancer.

Nearly eighty percent (79.4%) of the cancer prevention research was directed at specific cancer sites in contrast to the overall cancer research investment for which 48.0% was cancer site-specific. Most (83.5%) of the site-specific investment focused on nine cancer sites (see Table 3.1.1 of original report for details). Three sites had the largest cancer prevention investments: breast (\$22.4M), colorectal (\$19.4M), and lung (\$11.0M). Relative to the overall cancer research investment, research on cervical cancer had a strong prevention focus (i.e., 56.6% of the total investment in cervical research fell into the prevention basket). More than 40% of the oral cancer and colorectal cancer investments were also prevention-focused. On the other end of the spectrum was prostate cancer where less than 6% of this investment was for prevention research.

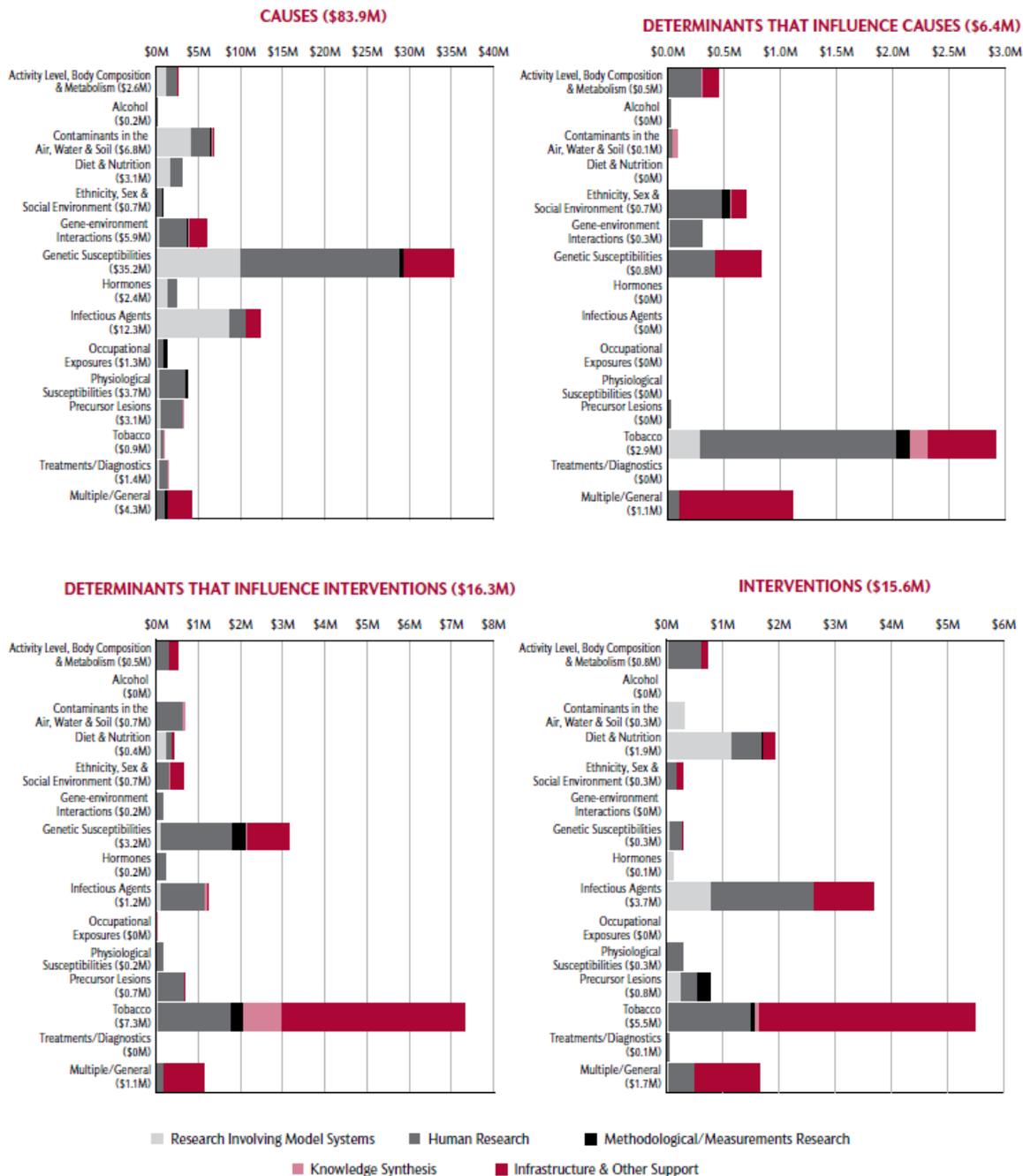
Figure 5 shows the distribution of the investment for each dimension of the cancer risk and prevention cube. The top three risk factors, in terms of investments, were Genetic Susceptibilities, Infectious Agents, and Tobacco. Together, they accounted for 60% of the overall cancer prevention research investment. On the other end of the spectrum, investment in Alcohol represented 0.1% of the overall investment. In terms of research focus, 68.6% of the investment was for projects focused on cancer causation/etiology; 12.8% was for intervention research. For research focus, research on causes of cancer accounted for the largest proportion of investment while human research accounted for the largest proportion of the investment by research type.

FIGURE 5 **DISTRIBUTION OF INVESTMENT BY THREE DIMENSIONS OF THE CANCER RISK AND PREVENTION CUBE, 2005–07**



Another view of the investment distribution is provided in Figure 6. Here the distribution of the investment data by risk factors and research types are shown for each research focus. For Causes, Genetic Susceptibilities had the largest risk factor-specific investment, with the majority of research conducted on humans. In terms of both types of determinants research, Tobacco represented the largest risk factor-specific investment. Much of this research was focused on social factors influencing smoking, genetic factors affecting nicotine addiction, and variables affecting the efficacy of tobacco prevention/control interventions. For Interventions, Tobacco and Infectious Agents had the largest risk factor-specific investments. In terms of research type, Infrastructure & Other Support comprised large proportions of both determinants categories and Interventions.

FIGURE 6
CANCER RISK AND PREVENTION RESEARCH INVESTMENT BY RISK FACTOR AND RESEARCH TYPE FOR EACH RESEARCH FOCUS, 2005–07



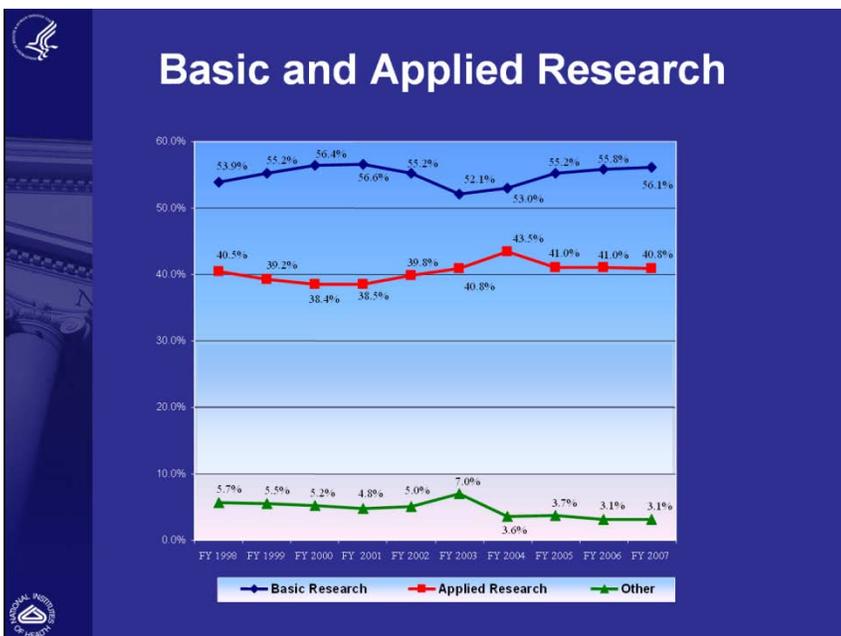
Implications for Research, Practice, and Policy

The analyses from this report represented a point in time assessment between the years 2005 and 2007 of CCRA prevention research investments. As such it doesn't capture more recent changes in funding priorities. Moreover, while the report documented CCRA member organization prevention research investments in Canada, as previously noted, it does not address the research investments made by other Canadian chronic disease research funding agencies nor does it address the prevention research investments made by other countries.

With respect to other Canadian chronic disease funding agency investments related to cancer prevention, the Canadian Partnership Against Cancer as part of its Nutrition and Physical Activity Alignment in Action Initiative²² is currently conducting a portfolio analysis of all obesity related research in Canada (e.g., nutrition and physical activity) with the cooperation of a number of chronic disease research funding agencies including the Heart and Stroke Foundation of Canada, the Canadian Diabetes Association, the Canadian Lung Association, and CIHR institutes including the Institute for Prevention & Public Health, and the Institute for Nutrition, Metabolism, & Diabetes. The Canadian Obesity Research Investment report will be available in July 2012 and will expand our knowledge of the research investments addressing these important risk factors.

In terms of international comparisons, while specific prevention research investment data from other countries are not available, overall research investment data from the U.S. National Institutes of Health (see Figure 7) reflect that about 55% of all research at the NIH focuses on basic science (discovery) while about 40% focuses on applied research (intervention development, testing, implementation, and health services delivery research).

FIGURE 7²³



²² <http://www.partnershipagaincancer.ca/wp-content/uploads/AIA-FINAL-REPORT-NOV-23-3.pdf>

²³ NIH at the Crossroads: Myths, Realities, and Strategies for the Future. Presentation by Dr. E. Zerhouni, Director of the NIH <http://www.drugabuse.gov/about/organization/nacda/powerpoint/NIHCrossroads506.ppt#369,5,Slide 5> (accessed 18/2/12)

With respect to the role of research in promoting population health and preventing disease in individuals, the research investments in basic science and epidemiological/etiological investigations of potential genetic, lifestyle, and environmental risk factors for cancer constitute the foundation of cancer prevention research upon which intervention development, testing and preventive health services and policy delivery research is based. The continuum of discovery, development, and delivery research²⁴ is a paradigm (see Figure 2) through which CCRA member organizations can coordinate activities. An analysis of collective investment in discovering new cancer risk factors and the mechanisms by which they work relative to translating these discoveries into the development of evidence based risk reduction intervention practices and policies will provide a framework for future research investment. It will also be important to evaluate how best to deliver these new prevention approaches in real world settings.

A concern raised in the consultation feedback by the scientific community, particularly from the more basic biological and epidemiological scientists, was that funding support through open competitions is declining while more focused funding is increasing. Because this concern extends beyond prevention research per se, the CCRA conducted a special analysis of the most recent CCRA funding data across the cancer research continuum from 2007-2009, grouping open competition funding on any topic with open competition site-specific funding compared to funding initiatives focused on one or more specific research areas (see Figure 4). To estimate the amount and percentage invested in Discovery, Development, and Delivery Research, Common Scientific Outline (CSO) codes 1 -biology, 2-etiology, and 7-model systems research were grouped as Discovery, CSO codes 3 -prevention interventions, 4-early detection, diagnosis & prognosis, 5- treatment research were grouped as Development, while CSO code 6-cancer control, survivorship & outcomes research was used as a proxy for Delivery. Table 1 displays these data.

TABLE 1

Research investments by CSO/year

	Open to all areas of research				Focused on 1 or more specific research areas			
	CSO 1+2+7	CSO 3+4+5	CSO 6	TOTAL	CSO 1+2+7	CSO 3+4+5	CSO 6	TOTAL
	Discovery	Development	Delivery		Discovery	Development	Delivery	
2007	\$92,690,170	\$41,648,532	\$10,581,780	\$144,920,481	\$34,192,265	\$38,489,674	\$8,657,446	\$81,339,384
2008	\$99,069,474	\$50,358,226	\$11,645,535	\$161,073,235	\$33,501,360	\$44,301,564	\$12,266,399	\$90,069,323
2009	\$103,894,123	\$58,375,126	\$13,237,870	\$175,507,119	\$33,423,053	\$55,055,142	\$13,829,085	\$102,307,280

Percent of research type per year

	Open to all areas of research				Focused on 1 or more specific research areas			
	CSO 1+2+7	CSO 3+4+5	CSO 6	TOTAL	CSO 1+2+7	CSO 3+4+5	CSO 6	TOTAL
	Discovery	Development	Delivery		Discovery	Development	Delivery	
2007	64.0	28.7	7.3	100	42.0	47.3	10.6	100
2008	61.5	31.3	7.2	100	37.2	49.2	13.6	100
2009	59.2	33.3	7.5	100	32.7	53.8	13.5	100

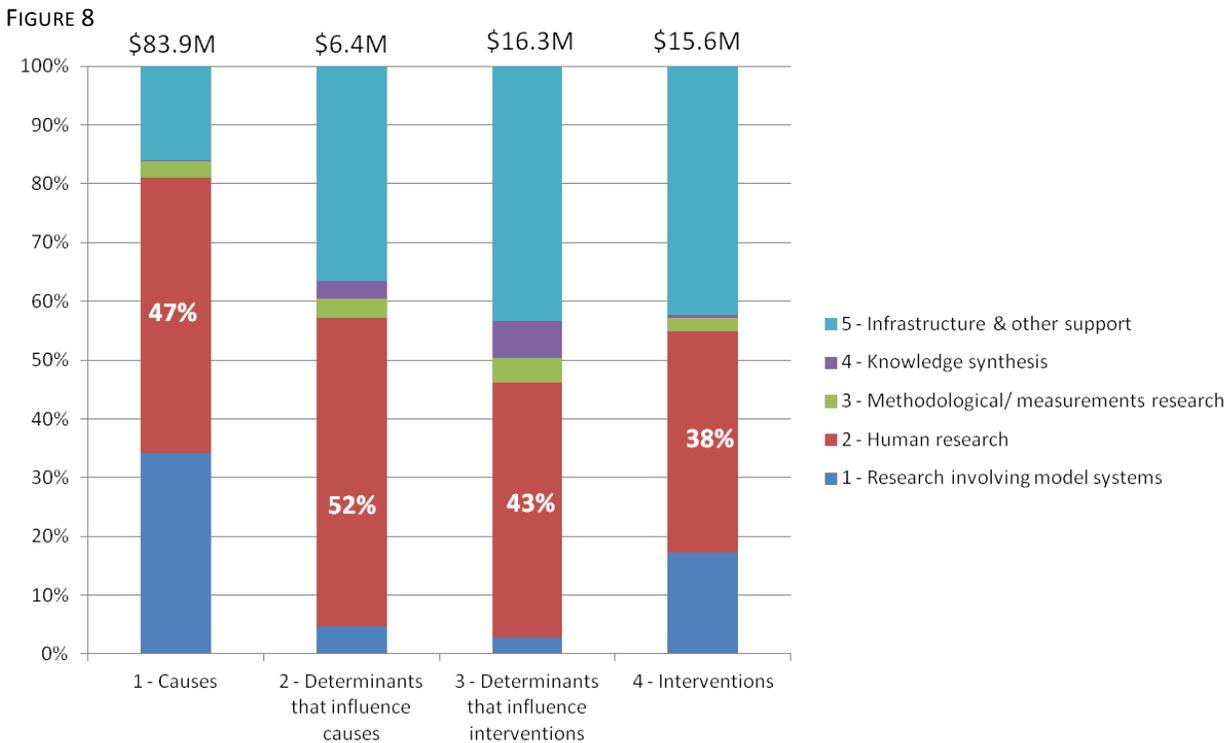
As can be seen in Table 1, while the total research dollars for open competition research grew overall in all three groupings of CSO codes (Discovery, Development, and Delivery), the percentage dropped for

²⁴ Von Eschenbach AC. NCI sets goal of eliminating suffering and death due to cancer in 2015. J of the Nat Med Assoc. 2003; 95(7): 637-39.

basic discovery research by about 5% and grew by approximately 5% for intervention development research. For more focused research areas, the basic science dollar amount dropped slightly and the percentage dropped by 9.3%, while Development and Delivery research increased by 6.5% and 2.9% respectively. Thus, at least through 2009, total dollar investments in biological and etiological open competition Discovery research continued to grow while the percentage dropped in relation to Development and Delivery research. It will be important for the CCRA to continue monitor this overall trend in future years, and examine the trends specifically within prevention, to ensure that the foundation of basic science discovery research remains strong even as the investments in more translational intervention development and health services delivery research grows.

RECOMMENDATION 3

Turning back to the practice and policy implications of the 2005-2007 CCRA member organization prevention research data, Figure 8 identifies the percentage of each of the four research foci, including intervention research, involving human subjects. The total dollar amount for each research focus from Figure 5 is displayed again in Figure 8 above each stacked bar.



If we multiply the total funding allocated to research on interventions (\$15.6M) by the 38% we see in Figure 8, from 2005 to 2007 \$5,920,000 was invested in Canadian human intervention cancer prevention research. This represents 4.8% of the total of \$122.3M invested in prevention research for the three year period of 2005-2007.

This compares to \$39,433,000 (32.2% of all prevention research) for research on causes involving human subjects, \$3,328,000 (2.7% of all prevention research) for determinants that influence causes research in humans, and \$7,009,000 (5.7% of all prevention research) for determinants that influence interventions research in humans. Thus, 10.5% (4.8% + 5.7%) of all Canadian prevention research funding was related to testing or understanding the factors that influence cancer prevention interventions for Canadians, while about 35% of all cancer prevention research funding in Canada has focused on etiological factors

and the factors that influence the determinants of which Canadians are more likely or less likely to develop cancer.

Cancer Prevention Researcher Capacity in Canada

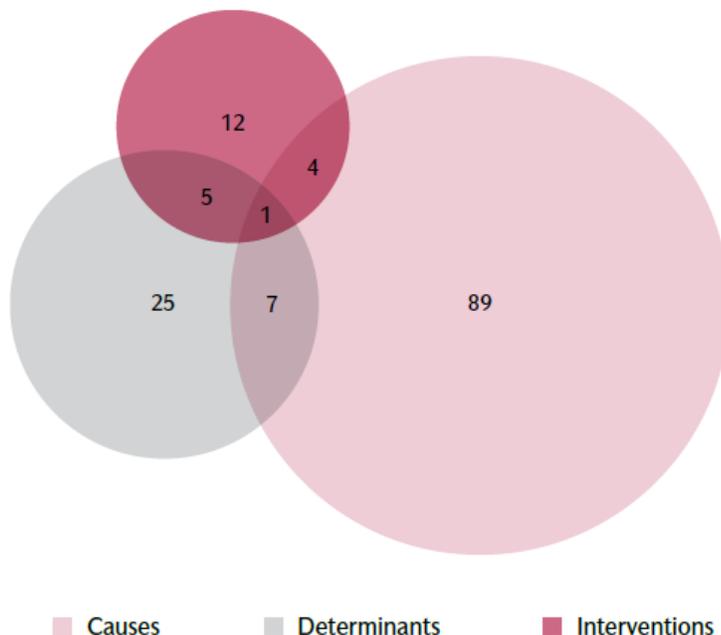
To better understand who in Canada is doing what research work funded by CCRA member organizations, the analysis of the prevention research portfolio report determined that there were 820 researchers (excluding trainees) involved in a funded cancer prevention research project during the 2005–07 period. To identify the number of **active** researchers working in cancer prevention, the following criteria were applied:

- the researcher must be the nominated principal investigator
- the researcher must be working in a Canadian institution
- the researcher must have either a career award or operating grant that is weighted at 100% cancer prevention
- at least one career award/operating grant identified above was active on December 31, 2007

On the basis of these criteria, 143 researchers were identified. These individuals represented 17.4% of the 820 researchers described above. A breakdown of 143 researchers in terms of areas of focus is provided in Figure 9. In this Venn diagram, the two determinants categories were combined. Of note, only 12 researchers were exclusively conducting human intervention research.

FIGURE 9

CANCER PREVENTION RESEARCHERS BY RESEARCH FOCUS [1] (N=143)



[1] Reflects researchers with operating grants or career awards active on December 31, 2007. Project budgets had to be weighted at 100%.

Within Canada, there appears to be a researcher capacity issue – the report revealed that there were very few researchers engaged in cancer prevention intervention research. The importance of cancer risk and prevention research has been recognized by research funders. In light of recent strategic investments, future trend data may provide a valuable means to monitor amounts and patterns of investment in this area. Figure 10 provides a 2005-2007 snap shot of cancer prevention researchers by province and across risk factors.

RECOMMENDATION 1

As can be seen in Figure 10, the four provincial jurisdictions with the largest number of prevention researchers from 2005- 2007 were Ontario, Quebec, British Columbia, and Alberta. The four risk factor areas with the largest concentration of cancer prevention researchers were genetic susceptibilities, infectious agents, tobacco, and contaminants in the air, water, and soil. Assuming the relative investments across provinces has not changed recently, provincial cancer and health agencies where cancer and chronic disease prevention practice and policy priorities are high but where cancer prevention research capacity is very limited (e.g., the Atlantic Provinces, Saskatchewan and Manitoba) may wish to consider pooling limited resources or networking with researchers from other Provinces to support cancer prevention research capacity development on an inter-provincial collaborative basis.

RECOMMENDATION 2

FIGURE 10

CANCER PREVENTION RESEARCHERS BY RISK FACTOR AND PROVINCE [1]

PROVINCE	Activity Level, Body Composition & Metabolism	Alcohol	Contaminants in the Air, Water & Soil	Diet & Nutrition	Ethnicity, Sex & Social Environment	Gene-environment Interactions	Genetic Susceptibilities	Hormones	Infectious Agents	Occupational Exposures	Physiological Susceptibilities	Precursor Lesions	Tobacco	Treatments/Diagnostics	Multiple/General
B.C.	2		5	1	3	1	6	1	4	1	3	1	4	1	1
Alta.	1		2	1		2	2	1	1		1		1	1	1
Sask.															
Man.															1
Ont.	5		9	7	5	3	17	4	3	2	4	5	12	2	3
Que.	2		3	2	3	4	12	1	14	3	2	1	5	1	2
N.B.				1											
N.S.									2			1			
P.E.I.													1		
N.L.							1								
Canada	10	0	19	12	11	10	38	7	24	6	10	8	23	5	8

[1] Researchers are counted for each risk factor for which their projects have been coded. The numbers are not weighted. Total shown is 191.

Should CCRA member organizations choose to consider increased investment in cancer prevention research in risk factors (e.g., alcohol, hormones, occupational exposures, viruses) or foci (e.g., intervention research) where research capacity is limited, a critical issue would be how to grow the field of qualified investigators in Canada who could and would choose to compete for new cancer prevention research funding. For example, CCRA member organizations may wish to examine, in the short-term, attracting intervention researchers focused on reducing common risk factors (e.g., tobacco, obesity, environmental and occupational exposures) who receive funding from other chronic disease research funding agencies by exploring joint funding of cancer and chronic disease prevention intervention research.

RECOMMENDATIONS

1 + 6

In the longer-term, expanded training grant resources may need to be considered to expand the field of qualified investigators in cancer prevention intervention research. One model worth examining is the U.S. NIH K-awards.²⁵ With respect to cancer prevention research, the NIH’s National Cancer Institute has made and continues to make a significant investment in K-07²⁶ five-year career development awards to grow the number of cancer prevention and population scientists in the U.S. From 1990 to the present, this investment in cancer prevention research career development awards dramatically increased both the number of cancer prevention researchers and the number of cancer research centres in the US with robust cancer prevention research programs.

RECOMMENDATION 1

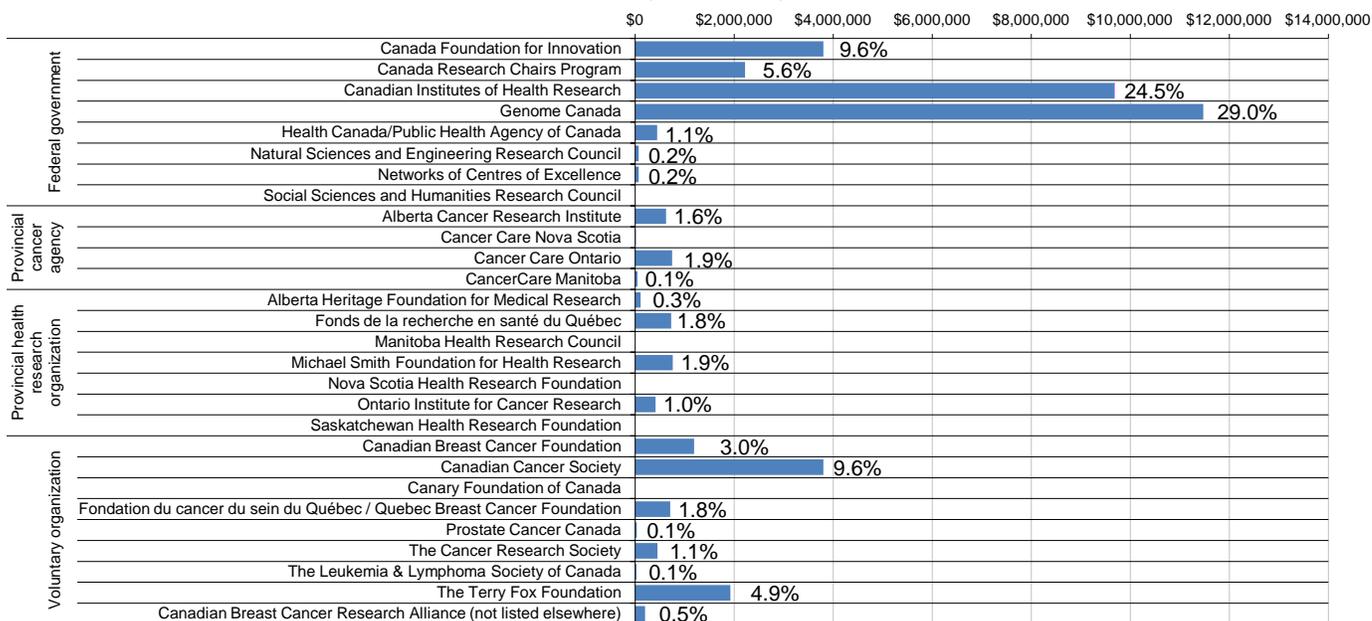
Summary of Findings from the Investment in Cancer Risk & Prevention Research Report 2005-2007

The cancer risk/causation component of the cube formed the largest proportion of the investment. The data suggest that cancer epidemiology is a relatively active field in Canada (Figure 4), and that research activity spans a broad range of risk factors with provincially-based research leadership indicated for a number of risk factors. The level of etiological investment in infectious agents suggests that this may be key area of strength in Canada that can help identify new viral agents and develop vaccines to prevent cancer. The low level of investment in alcohol research, a shared modifiable risk factor for noncommunicable diseases²⁷, may warrant further consideration.

RECOMMENDATION 3

FIGURE 11

Investment in genetic susceptibilities research by funding organization, 2005-2007 (% of \$39.5M)



²⁵ <http://grants.nih.gov/training/careerdevelopmentawards.htm>

²⁶ <http://grants.nih.gov/grants/guide/pa-files/PAR-09-078.html>

²⁷ http://whqlibdoc.who.int/publications/2009/9789241597418_eng.pdf

Research on genetic susceptibilities (inherited and acquired cancer risk) represented the single largest investment (\$39.5M) among the 15 risk factors examined in the report. Although genetic factors are not generally considered mutable, understanding population variation in the genetic predisposition to developing cancer and the potential interaction with lifestyle and environmental risk factors may provide the foundation for more targeted prevention intervention approaches in the future. As reflected in Figure 11, 23 of the 28 research funders had some investment in genetic susceptibilities research.

RECOMMENDATION 4

However, the ultimate value of genetic susceptibilities research for cancer prevention is an open question.²⁸ Thus, one opportunity for a new direction in CCRA cancer prevention research funding could be to have either the largest funders of this type of research (e.g., Genome Canada, CIHR, CFI) individually, or the smaller funders collectively, devote an increased percentage of their funding to translational research with a focus on developing prevention interventions targeted to groups of individuals genetically at higher than average risk of being impacted by behavioural, biological, environmental, or occupational risk factors for developing cancer.

RECOMMENDATIONS
4 + 5

Tobacco accounted for 40% of the combined investments in Interventions and Determinants that Influence Interventions. It has been argued that there is sufficient evidence to demonstrate that significant reductions in new cancer cases could be accomplished through lifestyle modification and population-based approaches, but that translating research results and providing compelling evidence of cost-effectiveness may be barriers.²⁹ Within Canada, there may also be a researcher capacity issue – the report revealed that there were a relatively small number of researchers engaged in cancer prevention intervention research.

RECOMMENDATIONS
1 + 7

The relatively low level of investment in other areas of cancer prevention research substantiates previously reported findings by the CCRA. Two examples of where collective action by CCRA members might help address this limitation are in environmental and occupational exposure risk factor identification and risk reduction research and obesity related risk factor identification and risk reduction research focused on nutrition and physical activity. With respect to environmental and occupational exposures, there was no funding for human intervention research and relatively limited funding for identifying new environmental and occupational exposures that may be causes of cancer (see Figure 6) from 2005-2007.

RECOMMENDATION 6

As with genetic susceptibilities research (Figure 11), there were a few large funders of this type of research (e.g., CIHR, CCS, Terry Fox Foundation) but only a very small percentage of this investment went to discovering new occupational exposures and nothing went to addressing the ones about which we know. Thus, if there was an interest among CCRA member organizations to expand prevention research funding to discover new occupational risk factors and develop and test interventions to reduce occupational exposures to carcinogens, creating a multi-agency initiative to address this problem could have a substantial impact in this relatively understudied area for a potentially small increase in the cost to each participating CCRA member. CCS and CCO have recently expanded their research investments in the area of occupational risk factor research in partnership with the Workplace Safety Insurance Board of Ontario (WSIB).

RECOMMENDATION 6

²⁸ Rennert, G. (2007) Cancer prevention: from public health interventions to individual tailoring. *European Journal of Cancer Prevention*, 16(3), 165-166.

²⁹ Colditz GA, Sellers TA, Trapido E. Epidemiology – identifying the causes and preventability of cancer? *Nature Reviews Cancer*. 2006; 6(1): 75-83.

Turning to obesity related research, intervention research was the largest category of spending among CCRA member organizations (see Figure 6) although it only amounted to \$2.7M over three years (2005-2007). As noted in the introduction of this report, in 2012 the Partnership will complete a portfolio analysis of all obesity related research funding in Canada for the years 2006-2008. However, this new analytic report will not be limited to CCRA member organizations, but will include all Canadian research funding agencies with an interest in addressing the growing problem of obesity in Canada and its concomitant health problems. While there were 18 CCRA member organizations which provided funding for obesity-related research between 2005 and 2007, CIHR and CCS accounted for 46.8% of the \$9.7M invested over three years. If CCRA member organizations wanted to substantially increase intervention research funding to address the growing problem of obesity in Canada, they could choose to co-fund new research funding opportunities with non-cancer research funding agencies (e.g., HSFC, CDA) and thus leverage their cancer research funding with other research funding agencies concerned with obesity.

RECOMMENDATION 6

The importance of cancer risk and prevention research has been recognized by research funders. In light of recent strategic investments in cancer prevention research, future trend data will provide a valuable means to monitor amounts and patterns of investment in this area. The CCRA has committed to providing these data in future reports.

CANCER PREVENTION RESEARCH FUNDING PRIORITIES FROM LITERATURE REVIEWS

There are a number of different sources that provide reviews of research evidence, including the peer-reviewed literature as well as organizational and expert opinion documents that make up what is often termed the grey literature. The number of reviews in the peer-reviewed literature alone is large and growing. For example, a simple search of the U.S. National Library of Medicine Pub Med website³⁰ using the search terms 'cancer prevention research' yielded 10,240 review article citations dating back to 1970.

There are also well-recognized international and national organizations that lead the way in contributing to the systematic review of the research literature in general and the cancer research literature in particular. These include the WHO International Agency for Research in Cancer (IARC) monographs on the evaluation of carcinogenic risks to humans,³¹ the Cochrane library,³² the Canadian Task Force on Preventive Healthcare,³³ the UK National Institute for Health and Clinical Excellence,³⁴ The US Preventive Services Task Force,³⁵ and the US Community Preventive Services Task Force³⁶. All of these groups conduct regular reviews of the scientific literature and publish, update, and disseminate their findings and recommendations on a regular basis. While much of this work focuses on the practice and policy implications of the research reviews, a portion of most reviews is also devoted to elucidating research issues that remain to be addressed.

³⁰ <http://www.ncbi.nlm.nih.gov/pubmed> (accessed February, 2012)

³¹ <http://www.iarc.fr/en/publications/list/monographs/> (accessed February, 2012)

³² <http://www.thecochranelibrary.com/view/0/index.html> (accessed September, 2011)

³³ <http://www.canadiantaskforce.ca/> (accessed February, 2012)

³⁴ <http://www.nice.org.uk/> (accessed February, 2012)

³⁵ <http://www.uspreventiveservicestaskforce.org/index.html> (accessed February, 2012)

³⁶ <http://www.thecommunityguide.org/index.html> (accessed November 2011)

Recognizing that a systematic review of all the published reviews, in addition to the many and varied grey literature documents, was beyond the scope and resources of this strategic framework development effort, the Canadian Partnership Against Cancer with its CCRA working group partners supported and worked with the Propel Centre for Population Health Impact at the University of Waterloo and the Canadian Cochrane Centre at the University of Ottawa to conduct a review of four sets of documents focusing on research issues or questions that need to be addressed in the future: 1) selected published and unpublished research strategy reports related to cancer risks and prevention (University of Waterloo), 2) cancer prevention relevant systematic reviews in the Cochrane Library (University of Ottawa), 3) cancer prevention relevant reviews in the Guide to Community Preventive Services (the Partnership), and 4) cancer prevention research relevant policy documents in the Prevention Policies Directory (the Partnership).³⁷

The synthesis of selected published and unpublished documents containing cancer and chronic disease prevention research priorities was conducted by the Propel Centre for Population Health Impact at the University of Waterloo (see Appendix 2 for their full report). While almost all individual research project reports include suggestions for future research, the effort made herein was to find and summarize recommendations from documents that were not focused on the implications of individual research study findings, but rather reviewed a content area of research and described more strategic priorities by content area. Detailed findings from the synthesis report described in Appendix 2 include the criteria and process for setting research priorities, and the research priorities themselves. Where possible, CCRA categories for research focus, type and risk factor were used to synthesize findings.

In addition, at the December 1st, 2011 stakeholder consultation workshop that reviewed and discussed the second draft of the strategic framework report, the suggestion was made to add Canadian policy documents to the document review portion of this report. In response, the Partnership's Prevention Policies Directory³⁸ was examined by Partnership staff using the search term "research." The Prevention Policies Directory is a regularly updated, searchable database of Canadian policies as well as legal instruments (e.g., statutes, regulations, codes, etc) relating to the key modifiable risk factors for cancer and related chronic diseases including nutrition, physical activity, alcohol consumption, tobacco control, infectious agents, environmental and occupational exposures, and UV/ionizing radiation. The search produced a listing of 59 documents that were scanned for relevance of which 24 were reviewed. A list of the included documents can be found in Appendix 3.

Propel Centre for Population Health Impact's Knowledge Synthesis

At the outset, general parameters for document selection were to select up to 30 Canadian and relevant international prevention research framework, strategy and recommendation documents, including peer-reviewed and grey literature. In this context grey literature includes report, web-based materials, and other documents that have not been published in a peer-reviewed scientific journal. The document selection process was iterative and incremental, whereby the results of each step in the selection process informed the next step. Inclusion and exclusion criteria were refined progressively and are described below. Figure 1 within the Propel report (see Appendix 2, page 8) depicts a flowchart of the article selection process.

The following parameters guided the initial search:

- 1991 to 2011

³⁷<http://www.cancerview.ca/cv/portal/Home/PreventionAndScreening/PSPProfessionals/PSPPrevention/PreventionPoliciesDirectory> (accessed December 2011)

³⁸<http://www.cancerview.ca/preventionpolicies>

- English language
- Grey and peer-reviewed
- Cancer and chronic disease prevention research
- Other specific diseases: heart disease, diabetes; selected only as they are relevant in documents about chronic disease prevention research

The search strategy was as follows:

- The initial searches were conducted using the following databases: Scopus, PubMed, Google, Google Scholar
- The following search terms were used for the initial searches: cancer, Neoplasms[MeSH], chronic disease, chronic disease[MeSH], prevention, research, framework*, strat*, recommend*, priorities, agenda*. Three search terms were tried and rejected: chronic illness, plan*, model*

One hundred and six documents (95 articles and 11 grey literature documents) were selected initially based on relevance of the title and abstract (if available) between the years 1991 to 2011. The initial selection was to include articles with **general cancer prevention and chronic disease prevention research priorities**, and additional articles from the following topic areas:

- Alcohol
- Chemoprevention
- Clinical prevention
- Environmental health
- Genomics
- Nutrition
- Obesity
- Occupational health
- Physical activity
- Social disparities
- Sun safety
- Tobacco
- Viral HPV/viral HBV

In order of priority, the following decision rules were used to select articles:

- Canadian content
- Specific prevention research priorities described
- Documents from leading health research organizations and coalitions³⁹
- Unique prevention research content areas
- Most recent within a particular content area
- Research priorities based in a priority on work groups, followed by literature reviews, workshops or conferences and other ways of developing research priorities (e.g., editorial).

³⁹ Canadian Cancer Society, Chronic Disease Prevention Alliance of Canada, Canadian Institutes of Health Research, Canadian Strategy for Cancer Control, Heart and Stroke Foundation, National Association for Health Research Foundations, National Cancer Institute, World Health Organization

Applying the above filters and additional exclusion criteria (see Appendix 2) resulted in the selection of 34 documents (23 articles and 11 grey literature documents). The 34 documents were read carefully to examine their appropriateness in detailing specific research priorities (i.e., rather than a high level research framework document), in representing relevant topic areas, and in adding research recommendations that were still relevant (based on date article was written, and the topic).

An additional search of related articles and grey literature was conducted to seek out sources of research strategy documents in areas that were identified as gaps (i.e., alcohol, tobacco, clinical prevention, viral HPV, viral HBV, sun safety), and more recent sources in the area of environmental and occupational health. This was done through a Google search for the gaps and a website search of organizations that had not been previously searched.

Overall, 23 documents were included in the knowledge synthesis. Of those, 13 were from peer-reviewed sources and 10 were from the grey literature. The list of peer-reviewed articles and grey literature used to inform the report can be found in Appendix 3 of the report. The full Propel report in Appendix 2 documented any framework (e.g., criteria, process) used to set priorities, and proposed specific research priorities. The research priorities were coded and summarized by CCRA research focus and CCRA research type (CCRA, 2010).

Research Priorities

The review revealed a very wide-range of cancer prevention research priorities, including areas that are well-established and others that are in their infancy. As seen in the full report in Appendix 2, the articles on *obesity* had the largest number of research priorities documented (n=148), followed by *general cancer prevention* (n=65), *occupational/environmental health* (n=59), *physical activity* (n=27) and *tobacco* (n=17).

The selected grey literature identified more priorities overall (221 vs. 155) and in the areas of infrastructure, funding, and dissemination (n=50 priorities) than peer reviewed sources (n=11 priorities). The numbers of priorities by other CCRA research types were similar for grey and peer reviewed sources (Table 2).

TABLE 2: NUMBER OF RESEARCH PRIORITIES IDENTIFIED BY CCRA RESEARCH TYPE

	Research Involving Model Systems	Human Research	Methodological/Measurements Research	Knowledge Synthesis	Infrastructure	Dissemination	Funding	Overall
Grey (n=10)	29	87	55	0	21	18	11	221
Peer reviewed (n=13)	28	73	43	0	4	5	2	155
Overall	57	160	98	0	25	23	13	376

Grey literature sources emphasized interventions in the number of research priorities they identified (n=37 priorities) compared to peer reviewed sources (n=19 priorities); whereas peer reviewed sources emphasized causes (n=33 priorities) compared to grey literature sources (n=19 priorities) (Table 3).

TABLE 3: NUMBER OF RESEARCH PRIORITIES IDENTIFIED BY CCRA RESEARCH FOCUS

	Causes	Determinants that Influence Causes	Determinants that Influence Interventions	Interventions	Overall
Grey literature (n=10)	19	58	35	37	149
Peer reviewed (n=13)	33	32	32	19	116
Overall	52	90	67	56	265

While the detailed results of the review of research priorities appear in Propel's full report in Appendix 2 (see section 3.0), listed below are a number of examples describing the types of research opportunities raised in the documents by selected research types.

Research Involving Model Systems: Representative Sample of Research Priorities Identified *Obesity*

Explore the role of novel gut-derived signals on regulation of energy balance and the effect of gut micro biome on gut absorption, signaling, and metabolism; investigate the underlying neurobiology of appetite, energy balance, and obesity using rare single gene and syndromic obesity disorders as a means to understand mechanisms promoting obesity in the general population; determine the specific genes, biological pathways, and epigenetic factors leading to increased food intake, obesity, and body composition abnormalities in genetic obesity syndromes; use global approaches (such as GWAS, exome or whole genome sequencing, genomics, metabolomics) to define novel molecules and pathways that participate in regulating energy balance and therefore may provide new therapeutic approaches to prevention or treatment of obesity.

RECOMMENDATION 3

Tobacco

Additional research is needed in the characterization of nicotine dependence (genetic, brain mechanisms, bio-behavioral, pharmacologic, economic, and social aspects), so that we can develop improved strategies to reduce smoking initiation and prevalence, especially in high-risk groups targeted by the tobacco industry.

RECOMMENDATION 6

Occupational + Environmental Carcinogens

Use of molecular biology advances to permit identification of persons particularly susceptible to these contaminants together with markers of exposure may help to identify subpopulations suitable for research that may clarify the need for intervention. Develop animal models to assess toxicological differences between children and adults and to evaluate toxicity to developing organ systems; conduct research to study developmental changes in metabolism, immune function, and proliferative activity, and how these changes may affect susceptibility to cancer.

RECOMMENDATIONS
3 + 5

Human Research: Representative Sample of Research Priorities Identified *General*

Biomonitoring of environmental exposures is recognized as a key element to success in this field for generating baseline data on levels of environmental contaminants in the Canadian population, and would allow tracking of exposure levels over time, geographical comparisons that may be linked to environmental exposures and quantitative assessment of cancer risk associated with exposure to selected compounds; specific research initiatives would be able to compare biological levels determined

in study populations to the distribution found within the Canadian population, to assess factors determining high or low exposures to chemical carcinogens and to link biomarker levels with health outcomes; human studies of substances suspected of causing cancer based on experimental studies, where no or inadequate human data are available, was also emphasized; mechanisms and efficacy of chemoprevention agents and the use of supplements or clinical interventions, studying both risks and benefits and the full range of outcomes (good and bad).

RECOMMENDATION 4

Physical Activity

Determine whether mixed-use development actually increases walking and biking; assess how perceptions of barriers interact with the built environment to predict physical activity behaviour; identify what low-income young people and their parents cite as the greatest barriers to physical activity in urban areas; study communities with successful programs that enable citizens to easily engage in physical activity; identify groups of individuals who might be at high risk for developing cancer and who would be likely to benefit from adopting an exercise program. Such groups might include persons who are sedentary, overweight or obese, or who have other characteristics of risk that might be affected by physical activity.

RECOMMENDATION 6

Genomics

The potential for genomic risk stratification to enable efficiencies in prevention program delivery that reduce cost without compromising care; evaluating different counseling delivery models that have been shown in previous health promotion research to be effectively incorporated into primary care or community health settings; evaluating the interventions that might be most cost-effective upstream of genomic technology development.

RECOMMENDATION 4

Skin Cancer

Assess the impact of message framing in changing behaviour (e.g. projected wrinkling); assess the efficacy of an internet portal for skin cancer prevention and investigate the use of YouTube.com for dissemination of skin cancer prevention messages to the adolescent audience.

Nutrition

Expand research examining the influence of the environment on individuals' food choices may benefit from a realization that, across populations or communities, the physical environment, the social environment, and personal choice may have differential influences on the foods that people choose to eat.

RECOMMENDATION 6

Occupational + Environmental Carcinogens

Demanding work schedules, such as those requiring mandatory overtime or shift work, should receive priority; research should examine long work hours in occupations involving public safety (e.g., health care, law enforcement, transportation, utilities) since the consequences of errors due to fatigue can be especially great; the extent to which the identification and control of occupational carcinogens has reduced risk sufficiently and if there are important risks still to be identified. For example, the risks of lung cancer among asbestos-exposed workers appears to be diminishing; to develop better mechanisms to understand the overall risks and benefits of HRT; examine the association between childhood cancer incidence and birth defects; define and characterize the child's environment by studying exposure patterns.

RECOMMENDATION 6

Infrastructure, Dissemination + Funding: Representative Sample of Research Priorities Identified

General

The establishment of a Cancer Prevention Research Coordinating Committee to provide a vision for cancer prevention research within and across CCRA partnerships; implement targeted funding mechanisms for cancer prevention research, i.e., a rapid response mechanism and targeted RFAs; promote collaborative research across Canada in cancer epidemiology and prevention; the creation of a fast-track policy or program evaluation funding stream where applications can be submitted at any time and be subjected to peer review as quickly as is feasible (so natural experiments can be conducted).

RECOMMENDATION 2

Obesity

Develop public-private partnerships to provide access to samples and data from clinical studies supported by industry; develop infrastructure and methods to integrate surveillance research across individual, family, community, state, and national levels, using valid measures of behaviors, environments, and policies to gain a better understanding of the interplay among behaviors and influencing factors; support multilevel research within the context of primary care, using advances in e-Health technologies in combination with electronic medical records (EMRs); use research networks within healthcare systems to document obesity outcomes related to implementing processes of care, such as screening for obesity and delivering obesity interventions care within the healthcare setting.

RECOMMENDATIONS
2 + 7

Dissemination/Communication

Research that engages the community, assesses the context, needs, and resources and plans programs in response to those needs; research is needed to understand the characteristics of groups that exert their influence at different points in the dissemination process, e.g., who are the champions/pioneers and how do we best identify and train them, what is the impact of using champions in terms of their personal and professional growth and other positive/negative consequences.

RECOMMENDATION 9

Community-based Research

The shift from intervention-centered to context-centered frameworks for community intervention heightens the importance of elaborating key constructs related to community impact; further elaboration of the multiple ways that capacity can be defined and measured is needed, particularly with respect to their use in diverse sociocultural communities; developing new research designs as well as strengthening existing designs.

RECOMMENDATION 10

Genomics

Evaluate new and different approaches to recruitment for genetic studies that augment minority and population-based participation.

Social Disparities

Evaluate specific grant and contract processes to determine what additional steps are needed to enhance the cultural competence, representative composition, and methodological expertise of peer review panels for cancer health disparities research; increase the proportion of support targeted specifically to disease prevention, health promotion, evaluation, and translational research on cancer health disparities.

RECOMMENDATION 10

Skin Cancer

Identify relevant research organizations and build a working partnership for skin cancer prevention research; undertake dissemination studies on sunscreen and sun protective clothing.

RECOMMENDATION 2

Nutrition

Funders and researchers will need to develop more expeditious systems for proposal generation and review to take advantage of naturally occurring experiments and be open to less tightly controlled experimental conditions.

RECOMMENDATION 6

Occupational + Environmental Carcinogens

A national childhood cancer registry should be established; develop a national database for environmental exposure data in children.

Review of Policy Documents from the Prevention Policies Directory

As noted previously, during the December 1st stakeholder consultation workshop that reviewed draft two of the strategic framework report, there was a recommendation to include policy documents in this report. Based on a search of the Partnership's Prevention Policies Directory, 24 out of 59 documents identified using "research" as a search term were reviewed. The included documents yielded a total of 80 cancer prevention related research recommendations from six Canadian jurisdictions. As outlined in Table 4, the number and presence of research priorities varied by risk factor and jurisdiction.

TABLE 4

Risk Factor/Condition	National	Alberta	British Columbia	Nova Scotia	Ontario	Prince Edward Island	
Nutrition	5						5
Physical Activity	3					1	4
Obesity	18				3		21
Alcohol	6		8	1	2		17
Tobacco	15			4	1		20
Occupational + Environmental Carcinogens	12	1					13
Infectious Agents	2				1		3
General Chronic Disease Prevention	1			1		2	4
OVERALL	62	1	8	6	7	3	

Note: Jurisdictions or modifiable risk factors not represented in this table were omitted as the review did not uncover any relevant research priorities for these jurisdictions/risk factors.

Review of the included policy documents indicated that the majority of future research priorities were related to obesity, tobacco, alcohol, and occupational and environmental carcinogens. Each of these research priorities were then analyzed according to their alignment with the Discovery-Development-Delivery model. In keeping with the model, research priorities related to knowledge translation and exchange, and increasing collaboration between researchers and practice or policy stakeholders were also considered. Table 5 illustrates the alignment of research priorities by cancer prevention risk factor/condition to the Discovery-Development-Delivery model. According to this analysis, the majority of research priorities reviewed aligned with the Development and Discovery aspects of the model.

TABLE 5

Risk Factor/Condition	Discovery	Development	Delivery	Knowledge Translation and Exchange	Collaboration
Nutrition	1				1
Physical Activity		1		1	
Obesity	4	15		2	
Alcohol	3	6	2	2	1
Tobacco	5	9	5	1	1
Occupational + Environmental Carcinogens	8	5	1	1	1
Infectious Agents	1	1		1	
General Chronic Disease Prevention		2	1		1
OVERALL	22	39	9	8	5

Within the Discovery component of the model, research priorities within the reviewed policy documents were related to better understanding the interaction between the various risk factors and the development of cancer and chronic disease to address knowledge gaps and influence practice and policy. Below are a couple of example priorities from Discovery:

- Conduct Canadian longitudinal cohort research on child health-environment linkages in general⁴⁰
- Develop a national alcohol research program that is informed by a determinants of health approach and is directed at gaining a better understanding of the risk and protective factors surrounding alcohol use⁴¹

Research priorities related to Development ranged from descriptions of the types of behavioural research needed to understand determinants of disease and health to the development of interventions to support cancer and chronic disease prevention efforts, often with an emphasis for interventions to be developed with attention given to cost-effectiveness and applicability to a broad population. The majority of priorities related to the need for obesity intervention research, and given the complexity of addressing obesity and the growing prevalence in Canada, this was not a surprising finding. The following are example priorities for Development:

RECOMMENDATIONS
6 + 7

- Undertake research to develop cost-effective and outcome-effective interventions, policies and environmental changes to promote healthy eating and physical activity⁴²
- Research to increase the knowledge base related to creating children-, youth-, and adolescent-friendly environments that facilitate healthy living⁴³

⁴⁰ Canadian Partnership for Children's Health and Environment. (2008). *First steps in lifelong health – A vision and strategy for children's health and environment in Canada*. Retrieved from:

http://www.opha.on.ca/resources/docs/CPCHE_FirstSteps_VisionStrategy-EN.pdf

⁴¹ British Columbia Office of the Provincial Health Officer. (2008). *Public health approach to alcohol policy: an updated report from the Provincial Health Officer*. Retrieved from:

<http://www.health.gov.bc.ca/library/publications/year/2008/alcoholpolicyreview.pdf>

⁴² Centre for Science in the Public Interest. (2005). *Proposal for an effective integrated pan-Canadian healthy living strategy*. Retrieved from: http://www.cspinet.org/canada/pdf/PanCdn_EffectiveLivStrat.pdf

- Behavioural research about the development of unhealthy lifestyles and best ways to effect changes that can provide information on which to base cost-effective and evidence-based interventions⁴⁴

Priorities related to Delivery, or health services research, were less prevalent than the former types of research. Tobacco-related research priorities were the most numerous here, which may be due to the well-established links already discovered between tobacco and cancer, as well as a myriad of effective tobacco control interventions tested in research, in comparison with other modifiable risk factor domains. The focus of the majority of priorities within this Delivery domain related to policy research or policy evaluation research. Clearly, policy stakeholders are interested in understanding the effectiveness of policies implemented on health outcomes. Examples of priorities indicated for Delivery include:

RECOMMENDATION 9

- Evaluate existing and new tobacco control policies in order to better understand the impact of these policies on tobacco use in subpopulations and the population as a whole in the province⁴⁵
- Research into effective program models and program planning approaches for diabetes education in the Aboriginal population⁴⁶
- Conduct research into effectiveness of current restrictions on advertising and exposure of BC youth to alcohol promotions, including internet promotions⁴⁷

RECOMMENDATION 10

Of utmost importance to practice and policy stakeholders is the relevance of research to their work. Practitioners and policy specialists need research that can fill knowledge gaps, and need the best available evidence at their fingertips to influence program and policy development. As indicated in the model, knowledge translation and exchange is and should be integral to the research process. This includes involvement in the research process and consideration of practice and policy needs when developing research questions. As such, collaboration and knowledge translation and exchange, including clear needs for knowledge syntheses relevant to practice and policy, surfaced within the research priorities reviewed. Examples of these include:

RECOMMENDATION 8

- Facilitate access to and develop knowledge to inform policies, program and practices that will prevent and reduce alcohol-related harm⁴⁸
- Conduct research to draw from evidence/experience in other countries, including identifying models for developing cost/benefit analyses of different tax policies⁴⁹

RECOMMENDATION 7

⁴³ Heart and Stroke Foundation of Canada. (2005). *Addressing obesity in Canada: A think tank on selected policy research priorities*. Retrieved from: <http://www.cdpac.ca/media.php?mid=239>

⁴⁴ Prince Edward Island Cancer Control Strategy Advisory Committee. (2004). *Partners taking action: A cancer control strategy for Prince Edward Island 2004-2015*. Retrieved from: http://www.gov.pe.ca/photos/original/hss_ccs.pdf.pdf

⁴⁵ Nova Scotia Department of Health and Wellness. (2011). *Moving toward a tobacco-free Nova Scotia: Comprehensive tobacco control strategy for Nova Scotia*. Retrieved from: <http://www.gov.ns.ca/hpp/publications/Moving-toward-Tobacco-Free-NS-Strategy.pdf>

⁴⁶ Coordinating Committee for the National Diabetes Strategy. (2005). *Building a national diabetes strategy: Synthesis of research and collaborations*. Retrieved from: http://www.phac-aspc.gc.ca/publicat/bnds-bsnd/pdf/bnds-bsnd-vol_1-eng.pdf

⁴⁷ British Columbia Office of the Provincial Health Officer. (2008). *Public health approach to alcohol policy: an updated report from the Provincial Health Officer*. Retrieved from: <http://www.health.gov.bc.ca/library/publications/year/2008/alcoholpolicyreview.pdf>

⁴⁸ Nova Scotia Department of Health Promotion and Protection. (2007). *Changing the culture of alcohol use in Nova Scotia: an alcohol strategy to prevent and reduce the burden of alcohol-related harm in Nova Scotia*. Retrieved from: http://www.gov.ns.ca/ohp/publications/Alcohol_Strategy.pdf

⁴⁹ Canadian Centre on Substance Abuse. (2005). *Key messages emerging from the National Thematic Workshop on Alcohol Policy*. Retrieved from: http://www.ccsa.ca/2004_CCSA_Documents/ccsa-011136-2004.pdf

- Develop and implement a strategic research agenda to engage researchers, institutions, and agencies in working collaboratively to address gaps in knowledge of chronic disease and underlying determinants⁵⁰
- Support and capitalize on opportunities to work with multisectoral partners on health promotion research initiatives⁵¹

Implications for Cancer Prevention Research from Systematic Review Summaries

This section of the report highlights work by staff from the Partnership, a graduate student and staff at the Canadian Cochrane Centre. Cochrane reviews by and large focus on clinical interventions although some population based intervention studies are included in the library. Table 6 summarizes the number of systematic reviews found in the Cochrane Library by risk factor and with the search terms used for cancer in general (column 2) and for prevention in particular (column 3).

TABLE 6

Risk Factor	Retrieved Results	Search Terms Used in addition to cancer and/or prevention
Activity Level, Body Composition and Metabolism	93	(activit* OR exercis* OR "body composition*" OR BMI or metabolism OR obes* OR adipos*)
Alcohol	19	(alcohol OR "alcohol use" OR "alcohol dependence")
Contaminants in the Air, Water and Soil (includes exposure to sun as a risk factor)	11	(contaminant* OR air OR water OR soil OR environmental OR carcinogen OR rad* OR sun OR UVA OR UVB OR "ultraviolet")
Diet & Nutrition	107	(diet* OR nutrition*)
Ethnicity, Sex and Social Environment	4	(ethnic* OR race OR sex OR gender OR "social environment"* OR "social determinant"*)
Gene Environment Interactions	6	((gene* AND environment) OR (gene* AND interaction) OR ("gene* environment interaction") OR (gene* AND environment) OR (gene* AND lifestyle) OR epigen*)
Genetic Susceptibilities	5	("gene* susceptib*" OR "family hist*" OR fam* OR "familial cancer*")
Hormones	0	(hormon*)
Infectious Agents	18	(infect* OR "infectious disease*" OR "infectious agent" OR Hepatitis OR HPV OR papilloma OR HCV OR "Hep C" OR HBV or "Hep B" OR HIV OR "Human immunodeficiency virus")
Occupational Exposures	0	("occupational exposure" OR occupation* OR workplace)
Precursor Lesions	8	(lesion* OR "precursor lesion*" OR adenom* OR "oral leukoplakia*" OR keratosis* OR basal OR squamous OR crohn* OR IBD OR "irritable bowel disorder" OR GERD OR "Gastroesophageal reflux*" OR polyp* OR dyslpasia* OR dyspepsia*)
Tobacco	47	(tobacco OR smok* OR cigar* OR "second-hand" OR "second hand" or "2nd hand")
Treatments/Diagnostics	36	(treatment* OR diagnos*)

⁵⁰ Nova Scotia Department of Health. (2003). *Nova Scotia chronic disease prevention strategy*. Retrieved from: http://www.gov.ns.ca/hpp/publications/CDP_Strategy_Report_Final_October30.pdf

⁵¹ Nova Scotia Department of Health and Wellness. (2011). *Moving toward a tobacco-free Nova Scotia: Comprehensive tobacco control strategy for Nova Scotia*. Retrieved from: <http://www.gov.ns.ca/hpp/publications/Moving-toward-Tobacco-Free-NS-Strategy.pdf>

The Cochrane Library currently houses 4791 reviews (current and withdrawn). Searching using the term 'Cancer' in the title, abstract or keywords identified 595 reviews as of November 2011. The following synthesis is based on a total of 75 reviews. Of the 75 reviews, one examined four risk factors, seven examined two, and the remainder examined one. Dates of reviews included in this synthesis ranged from 2006 -2011.

Synthesis of Authors' Implications for Research from Cochrane Reviews

In general, the degree of specificity and number of research recommendations varied greatly between reviews. In order to get a sense of where authors were recommending further work, research implications were grouped into methodological, population, economic, intervention, observational and etiological categories.

Methodological recommendations

A methodological recommendation was one that focused primarily on the conduct and quality of studies, whether observational or clinical. These types of recommendations are focused on, for example, random allocation concealment, blinding, sample size, study type, etc.

By far, the largest number of recommendations reflected the view by authors that the quality of those studies available to include in reviews was variable. Most frequently mentioned recommendations included: conduct a RCT or further RCTs in the topic area (n = 23), increase sample size or number of clusters (n=12), perform longer term interventions and/or follow up (n=9), ensure blinding (n=5), ensure that appropriate outcomes are considered (n=5), ensure adequate control or reference groups are used (n=5), ensure studies are well designed (n=4), ensure that reporting is done according to standards, e.g., CONSORT (n=4), ensure that interventions are well defined and standard definitions are used where possible (n=4), and use an appropriate unit of analysis (e.g., community vs. individual) (n=4). Other suggestions were to hold multicentre trials, use validated tools where they exist, use previous research or theory to guide interventions, and include more details regarding the intervention, participant selection, refusal, dropout etc.

Population recommendations

A population recommendation is a recommendation that suggests further research on specific populations or sub-populations of interest to address certain limitations of findings in the studies surveyed.

Of those authors that included population recommendations, the main trend was to recommend more specificity, that is, looking at the influence of interventions in particular populations (n=18). Depending on the intervention, this could refer to sex or gender, populations with different exposures to a therapy, sub groups considered more at risk or who could benefit the most from an intervention, and populations bearing a larger cancer burden. While the majority of authors recommended looking more deeply at specific populations, one review recommended looking at approaches that have been successful at the individual level to determine how to scale up interventions toward a population level intervention.

RECOMMENDATION 10

Economic recommendations

An economic recommendation looks to inform future research on questions of cost utility of certain interventions or findings.

Only nine reviews made recommendations to consider an economic analysis (e.g., cost effectiveness of different interventions, financial implications of legislation to modify fat intake) as a component of further research including the cost of incorporating an intervention into routine practice.

RECOMMENDATION 7

Intervention recommendations

An intervention recommendation is focused on the development of new intervention studies to address limitations of included studies, or to further developing research evaluated by the review.

“Further research is needed” was a common statement with authors of most of the reviews providing suggestions for ongoing work (n=60). The two most common suggestions were with respect to: 1) study design – to replicate, improve or use a different study design for continued work in the same area, as well as 2) ongoing work to explore specific components or different combinations of interventions to understand effect on outcomes (e.g., drilling down to look either at specific sub categories of an intervention [e.g., specific forms of smokeless tobacco] or sub populations; variation in the intervention [e.g., combining therapies or different combinations of therapies]; looking at the use of a therapy in a different application [e.g., metastatic disease]). Authors of two reviews recommended waiting for the results of ongoing trials that might provide clearer answers with respect to an intervention. In only one review did authors suggest that further research in a particular area - use of silver acetate for smoking cessation - was unlikely to add any further understanding.

RECOMMENDATION 6

Observational recommendations

An observational recommendation provides recommendations for future observational studies to address questions that were raised in the course of the review.

While RCTs were recommended study designs for most reviews, four reviews identified observational studies as relevant designs for further research.

Etiological recommendations

An etiological recommendation provides research recommendations to support a better etiological understanding of the cancer in question, or its precursor condition.

Two reviews suggested further work in this area – one with respect to potential agents to be investigated for prevention of progression of cervical intra-epithelial neoplasia as well as the development of vaccines for high-risk HPV subtypes, and the second in assessing the potential in modifying the endocannabinoid system to reduce urges to smoke.

RECOMMENDATIONS
4 + 5

With respect to risk factor specific findings Table 7 lists the finding from eight Cochrane reviews related to nutrition and cancer.

TABLE 7

Review	Cancer Relevant Nutrition Topic	Cochrane Review Finding
1	Selenium for preventing cancer	Little evidence for impact on cancer risk for women. Regular intake cannot be recommended to either selenium replete or deficient populations. But suggestions for further research e.g., gender differences, different cancers, high burden of cancer and differing selenium exposure levels.
2	Antioxidant supplements for preventing gastrointestinal cancers	No convincing evidence that antioxidant supplements have an effect on GI cancers. RCTs of selenium use are ongoing and more trials may be needed.
3	Dietary calcium supplementation for preventing colorectal cancer and adenomatous polyps	Sufficient evidence does not exist to recommend the general use of calcium supplements. Further research needed on individual susceptibilities to determine which subgroups might benefit.
4	Dietary fibre for the prevention of colorectal and adenomas carcinomas	No evidence from RCTs to suggest that increased dietary fibre intake will reduce the recurrence of adenomatous polyps within a two to four year period
5	Interventions for preventing non melanoma skin cancers in high risk groups	Data are from single studies so can't be conclusive but saw no difference in the effectiveness of beta carotene, selenium or reduced fat/ insufficient evidence to support use of retinols/ isotretinoin increases risk. Need to do further research in population with Xeroderma pigmentosum – huge impact on QOL and life expectancy. Also RCTs for people with albinism, people with trauma or burns, with basal cell naevus syndrome, people exposed to arsenic, people with RDEB or those treated using PUVA.
6	Green tea (Carmellia sinesis) for the prevention of cancer	Data insufficient to suggest use. RCTs in this area are nearly nonexistent.
7	Retinoids for preventing the progression of cervical intra-epithelial neoplasia	Retinols currently have no place in the clinical management of patients with CIN- no consistent effect in preventing the progression or enhancing regression. Authors state that many other potential agents require investigation.
8	Vitamin D supplementation for the prevention of mortality in adults	More evidence needed before drawing final conclusions on the effect of Vitamin D on cancer – need more RCTs testing efficacy alone or in combination with calcium and comparing different doses

Synthesis from the Guide to Community Preventive Services Systematic Review Research Gaps

The US Guide to Community Preventive Services conducts state-of-the-art systematic reviews that analyze all available scientific evidence on what works to promote health and prevent disease, injury and disability in community settings; assess the economic benefits of the interventions found to be effective; and identify research gaps. With respect to research gaps, Partnership staff reviewed the summaries from the Community Guide website⁵² that addressed risk factors focused on or shared with cancer prevention. These included adolescent health, alcohol, cancer, diabetes, health communication, nutrition, obesity, physical activity, social environment, tobacco, vaccines, and worksite. Only those reviews with insufficient evidence finding commonly describe research gaps to be addressed.

⁵² <http://www.thecommunityguide.org/index.html>

Review summaries where prevention research gaps were explicitly articulated included: increasing tobacco use cessation; preventing skin cancer; obesity prevention and control – interventions to reduce screen time; and promoting physical activity. The research questions described through the Community Guide reviews are by and large Development and Delivery research issues.

Increasing Tobacco Use Cessation Research Gaps

While the effectiveness of increasing the unit price for tobacco products and mass media campaigns (as part of a multi-component approach) is established, research issues remain regarding these interventions. Exemplar research questions that remain to be addressed include:

- What intervention components are most effective in multi-component intervention approaches? RECOMMENDATION 6
- What is the most effective combination of messages for mass media campaigns?
- What are the rates of participation in these interventions?
- What are the differential effects of mass media campaigns among populations that differ culturally? RECOMMENDATION 10
- What are the effects of these interventions on environmental tobacco smoke?
- What is the cost benefit, cost-utility, or cost per illness averted of these interventions? RECOMMENDATION 7

Increasing Tobacco Use Cessation: Health Care System-Level Research Gaps

While the effectiveness of a number of clinically-based approaches (e.g., multi-component health care provider reminder plus provider education with or without patient education materials, provider reminder systems alone) is established, research issues remain regarding these interventions. Exemplar research questions that remain to be addressed include:

- What characteristics of provider-based interventions contribute to increased or decreased effectiveness? RECOMMENDATION 6
- What are the effects of provider assessment and feedback interventions on provider delivery of advice to quit to tobacco-using patients? On patient tobacco use cessation?
- What frequency, duration, and format of provider education efforts are required to obtain consistent improvements in provider performance and patient response?
- Do provider-based interventions differ in effectiveness in different populations? RECOMMENDATION 10
- Do provider-based interventions for tobacco use cessation interfere with office flow or efficiency? Do they increase or decrease the delivery of other preventive services.
- What is the cost-effectiveness for provider interventions that target tobacco alone compared with provider interventions that target multiple preventive services? RECOMMENDATION 7

Preventing Skin Cancer

While the effectiveness of preventing skin cancer through education and policy in primary school and recreational settings is established, there is insufficient evidence from systematic reviews for other approaches (e.g., interventions targeting parents and care-givers of children; community-wide intervention such as mass media) or settings (e.g., secondary schools and universities, outdoor occupational settings, healthcare settings and providers). Given the limited number of approaches and settings where efficacy/effectiveness data have been published for preventing skin cancer, there are a number of higher-level research gaps that future studies will need to address. These include:

- Design and analysis considerations (e.g., rigorous analytic methods are needed that control for relevant confounders such as risk levels and weather conditions)
- Adequate description of target population and context (e.g., better descriptions of annual UV exposure in the places in which intervention studies are conducted)

- Improved intervention descriptions (e.g., more detailed descriptions of intervention characteristics would help practitioners replicate successes)
- Duration of interventions and length of follow-up
- Intervention level and quality (e.g., development of measures of environmental and policy change strategies)
- Measurement of outcomes (e.g. how do different sun-protective behaviours interact?)

RECOMMENDATION 9

Obesity Prevention and Control in Community Settings

While the effectiveness of preventing and controlling obesity through behavioural interventions to reduce screen time, multi-component counseling interventions, and workplace programs to promote physical activity is established, there is insufficient evidence from systematic reviews for other approaches (e.g., mass media interventions to reduce screen time) or settings (e.g., school-based programs, health care provider-oriented interventions). Exemplar research questions that remain to be addressed include:

- Further differentiation of sedentary from non-sedentary screen time behaviours is needed.
- What is the relationship between screen time and other sedentary behaviours (e.g., reading)?
- What are the mechanisms for screen time being associated with weight-related outcomes (e.g., advertising of food, snacking/eating while watching TV, etc.)?
- Are behavioral interventions aimed at reducing screen time as effective in different socioeconomic, gender, or ethnic subgroups?
- Many workplace studies lack information to determine differential effects according to blue or white collar job status. Those that do report occupational status included predominantly white collar workers.
- Information on the feasibility of implementing programs across small to very large workplace settings is hampered by missing workplace size data in a majority of studies.

RECOMMENDATION 3

RECOMMENDATION 10

RECOMMENDATION 7

It should be noted that increased investments in prevention intervention development and delivery research carry with it some special issues that may challenge how large an expansion of funding in Canada will be needed for development and delivery research initiatives in the future. The first is that questions addressing the differential impact of separate components in multi-component interventions require multifactorial research designs that involve larger sample sizes and more resources for implementing and evaluating multiple individual and combinations of intervention components. Second, efforts to test interventions with different populations and evaluate the barriers to delivery of prevention services in diverse contexts are complicated by the complexity of being able to generalize from population-specific or context-specific studies to other populations or settings. This external validity issue often limits the interest in and use of evidence-based cancer prevention approaches for populations and in settings that may similar but not identical to the ones included in the studies. Finally, the lack of cost data, cost effectiveness/benefit analyses, and sensitivity analyses in cancer prevention intervention research related to implementation feasibility, can limit the applicability of prevention intervention research findings for potential practice and policy knowledge users.

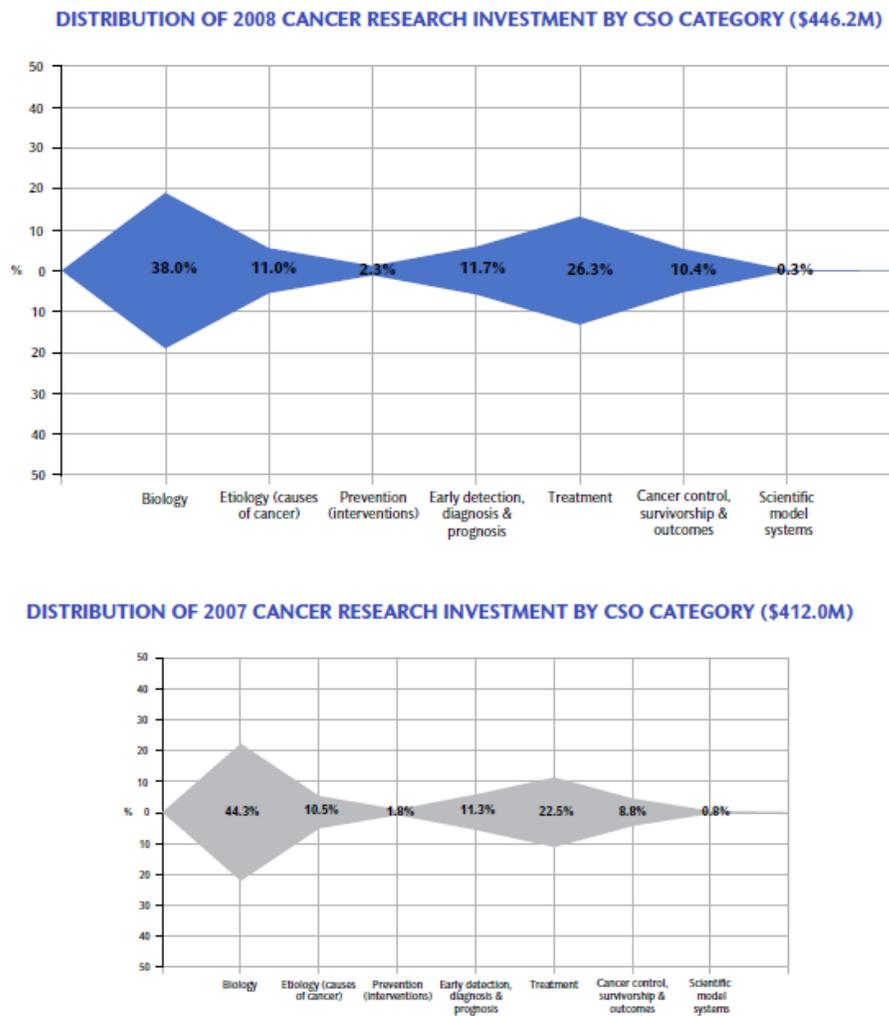
RECOMMENDATION 10

RECOMMENDATION 7

WHERE IS CANADA TAKING THE LEAD IN CANCER PREVENTION RESEARCH?

As can be seen from the figure below, published in the most recent CCRA cancer research strategy investment report⁵³, while there has been an 8.3% increase in the total of CCRA member organization cancer research investments from 2007 to 2008, and a 6.3 % percentage decrease in basic science biology investments in the same time period. Basic science, followed by treatment-related research, remain the two largest cancer research investment envelopes in Canada.

FIGURE 12



The small 1% increase in the combination of etiological and prevention intervention research from 2007 to 2008 highlights the importance of reviewing where Canada’s risk factor identification and prevention

⁵³ Canadian Cancer Research Alliance (2011). *Cancer Research Investment in Canada, 2008: The Canadian Cancer Research Alliance’s Survey of Government and Voluntary Sector Investment in Cancer Research in 2008*. Toronto: CCRA. (Figure 3.2.1, page 20)

research investments are being made and how both scientific opportunity and prevention practice and policy needs may inform prevention research priorities in the future.

Canada's Prevention Research Foundation Upon Which to Build

The cancer risk/causation component of the prevention research investment cube formed the largest proportion of the investment. The level of etiological investment in infectious agents suggests that this may be key area of strength in Canada upon which to build. The 2005-2007 CCRA funding data suggest that cancer epidemiology is an active field in Canada and that research activity spans a broad range of risk factors with provincially-based research leadership indicated for a number of risk factors. Opportunities to link basic science with population-based biomarker identification and molecular epidemiology abound, and the multi-jurisdictional Canadian Partnership for Tomorrow Project represents an excellent example of collective investment in this important area of research.

RECOMMENDATION 3

Cancer risk factor and prevention research capacity in Canada clearly varied by jurisdiction. Thus, provincial cancer and health agencies, where cancer and chronic disease prevention practice and policy priorities are high but where cancer prevention research capacity is very limited, may wish to consider pooling limited resources to support cancer prevention research capacity development and/or networking with researchers in provinces where more prevention research is funded in order to expand on an inter-provincial collaborative basis.

RECOMMENDATION 2

Research on genetic susceptibilities (inherited and acquired cancer risk) represented the single largest investment (\$39.5M) among the 15 risk factors examined in the report. However, given the limited number of prevention intervention protocols that have been developed to date from this substantial investment, a new opportunity in CCRA cancer prevention research funding could be to have either the largest funders of this type of research (e.g., Genome Canada, CIHR, CFI) individually, or the smaller funders collectively, devote an increased percentage of their funding to translational research with a focus on developing prevention interventions biologically targeted to groups of individuals genetically at higher than average risk of developing cancer.

RECOMMENDATIONS
4 + 5

Prevention Research Funding Development Needs

Tobacco accounted for 40% of the combined research investments in Interventions and Determinants that Influence Interventions. It has been argued that there is sufficient evidence to demonstrate that significant reductions in new cancer cases could be accomplished through lifestyle modification and population-based approaches but that translating research results and providing compelling evidence of cost-effectiveness may be barriers. Within Canada, there may also be a researcher capacity issue – the report revealed that there were very few researchers engaged in intervention research.

RECOMMENDATIONS
1 + 7

The relatively low level of investment in other areas of cancer prevention intervention research substantiates previously reported findings by the CCRA. Should CCRA member organizations choose to consider increased investment in cancer prevention research in risk factors (e.g., alcohol, hormones, occupational exposures) or intervention research where research investment and researcher capacity is limited, a critical issue would be how to grow the field of qualified investigators in Canada who could and would choose to compete for new cancer prevention research funding. For example, with respect to the limited number of cancer prevention intervention researchers in Canada, CCRA member organizations may wish to examine, in the short run, attracting intervention researchers focused on

reducing common risk factors (e.g., tobacco, obesity, environmental and occupational pollutants) who receive funding from other chronic disease research funding agencies by exploring joint funding of cancer and chronic disease prevention intervention research.

RECOMMENDATIONS
1 + 6

Two examples of where collective action by CCRA members might help address limited research investment in risk factor reduction are in environmental and occupational exposure intervention research and obesity related intervention research focused on nutrition and physical activity. If there was an interest among CCRA member organizations to expand prevention research funding to develop and test interventions to reduce occupational exposures to carcinogens, creating a multi-agency initiative to address this problem could have a substantial impact in this understudied area for potentially a small increase in the marginal costs to each participating CCRA member. If CCRA member organizations wanted to substantially increase intervention research funding to address the growing problem of obesity in Canada, they could also choose to co-invest in new research funding opportunities with non-cancer research funding agencies (e.g., HSF, CDA) and thus leverage their cancer research funding with other disease-specific research funders that share a concern about the growing problem of obesity.

RECOMMENDATION 6

With respect to risk factor reduction and cancer prevention intervention research, a number of research recommendation documents and systematic reviews highlighted the dearth of cost effectiveness data in the intervention research conducted and published in the peer-reviewed literature. From the perspective of practice and policy, the absence of such data makes the decision to adapt or adopt a research-tested cancer prevention intervention very difficult to make. Program resources for health promotion and disease prevention in Canada, are very limited in relation to healthcare services for those who are ill. As such, CCRA member organizations who develop and disseminate RFPs for cancer prevention intervention research should consider including a requirement for the collection and analysis of intervention implementation cost data in relation to intervention effectiveness data. This may be particularly important in natural experiments, where the context in which a program or policy is being implemented may have profound cost implications for other jurisdictions considering a similar approach.

RECOMMENDATION 7

Research priorities for knowledge synthesis and knowledge translation and exchange (KTE) research were under-developed from the documents reviewed and there was very limited risk factor or cancer prevention research funding focused on these topics. Given that these areas are critical to integrating the lessons learned from science with the lessons learned from policy and practice, and were identified as high priorities in many of the policy documents reviewed, another opportunity for collective CCRA member organization research investment could be:

1. Shared support for a CCRA-focused knowledge synthesis operation tasked with conducting systematic reviews of risk factor and cancer prevention original research reports in preparation for future collectively funded CCRA member organization RFPs.
2. Collective investment in KTE research training and pilot studies to increase the number of Canadian cancer prevention researchers interested in and capable of successfully competing for existing KTE research funding mechanisms both in Canada (CIHR) and the U.S. (NIH).

RECOMMENDATION 8

RECOMMENDATION 1

With respect to collective investment in knowledge synthesis to improve the quality of CCRA risk factor and prevention research RFPs and adjudication panel considerations, there are a number of centres of knowledge synthesis excellence in Canada that could respond to an RFP to carry out such work on a

timely and effective basis. Moreover, once developed and evaluated, such an operation could be expanded to carry out similar knowledge synthesis efforts across the cancer control continuum.

RECOMMENDATION 8

Finally, given the diversity of populations and the variation in risk factors and disease burden across Canada, both research recommendation/policy documents and systematic reviews identified research to help reduce cancer health disparities as high priorities. However, there are three conundrums that CCRA member organizations will need consider should they choose to increase research investment in this important area.

First and foremost is the role that social determinants play as “upstream” conditions that contribute greatly to health disparities across many diseases, including cancer. Given that many of these social determinants are endemic, and if mutable will only be changed looking outside of a health lens, it’s difficult to address health disparities through any disease-specific research funding initiative.

Second, many vulnerable populations and underserved communities that have experienced cancer and other health disparities are reluctant to participate in research. From their perspective, research often represents simply another effort to “describe” what has been known to them for decades and sometimes centuries, rather than studying how to “address” the problems. Research through the lenses of discrimination and deprivation may be viewed as exploitative rather than supportive. Should CCRA member organizations choose to invest in health disparities research they should examine carefully the lessons learned from community-based participatory research approaches to better understand how to constructively engage those being studied, and how best to share research design, analysis, and knowledge exchange responsibility and authority with the leaders of these communities in which the research is conducted.

RECOMMENDATION 10

Third, the cultural and socioeconomic diversity of underserved communities often moves research and practice into the development, implementation, and evaluation of targeted interventions tailored to the particular needs and circumstances of specific vulnerable populations. From a research perspective, it’s difficult to generalize the lessons learned from these community-specific intervention studies, and even communities that share the same cultural heritage or socio-economic conditions may view the research findings as not relevant their particular community needs. From a program and practice perspective, the resources needed to implement multiple intervention programs and policies tailored to each communities needs may be beyond the resources available for disease prevention and health promotion. The CCRA member organizations with program and policy arms (e.g., health charities) may wish to explore how expanding resources for more rigorous program evaluation of community-specific practice and policy interventions, and the sharing of the results of these evaluations, can help increase our knowledge base of what works for whom without trying to sort this out solely through intervention research.

RECOMMENDATION 9

The aforementioned research agency investment opportunities represent only a partial list of prevention research investment actions that CCRA member organizations may choose to implement either individually or collectively. As noted in the introduction, it is recognized that each CCRA member organization has its own research funding priorities driven by scientific interests and expertise, as well as public, practice and policy priorities. This strategic framework is designed to help the *CCRA membership consider collective funding opportunities* where the limited resources for risk factor and cancer prevention research in Canada could and perhaps should focus in the next five years. Opportunities for collective investment within and outside the CCRA abound should the CCRA members be inclined to act

to leverage their individual organizational investments so as to make whole of risk factor and cancer prevention research greater than the sum of its parts.

RECOMMENDATIONS FOR CCRA ACTION

The following recommendations represent the 10 highest priorities for prevention and risk research in Canada based on current strengths, gaps, and opportunities for coordination and collaboration among CCRA member organizations. They are presented in order of infrastructure, discovery, development and delivery research investment opportunities and, as such do not imply any funding priority order.

1. CCRA member organizations should individually and/or collectively support initiatives that will build capacity in gap areas of cancer prevention and risk reduction research including multi-disciplinary intervention development, KTE and health services delivery research. These initiatives may include training awards, mentorships, deliberate networks, nodes of expertise, career awards or other funding mechanisms to encourage existing researchers in Canada to apply their research acumen to cancer prevention. The success of these capacity building initiatives will result in an increase in the pool of excellent Canadian investigators in these under-represented fields who can successfully compete for both open competition and more focused investment RFPs.
2. With respect to expanding prevention research infrastructures, CCRA member organizations should work together to: a) network existing centres of excellence in risk factor and prevention related research across Canada to increase knowledge exchange across disciplines, sectors and jurisdictions, and b) expand investments in new centres of excellence in cancer risk factor and prevention research, particularly in jurisdictions where additional research expertise can expand the effectiveness of cancer prevention practice and policy initiatives.
3. A number of CCRA member organizations are heavily invested in investigator-initiated, open-competition discovery research, recognizing it as the foundation upon which intervention development and service delivery research are based. Where more focused investments in development and delivery research are needed, this growth should not lead to a decline in funding dollars for the critical foundation of discovery research.
4. Where substantial investments have and continue to be made in discovery research areas (e.g., genomics and cancer) CCRA organizations funding this research should take advantage of the opportunities for working together to provide strategic funding to explore the translational potential of discovery research to inform new prevention intervention development and testing.
5. Where evidence-based prevention interventions have shown limited impact on specific high-risk populations (e.g., heavy smokers), collaborative and targeted funding for multi-disciplinary discovery research should be increased to elucidate the mechanisms by which some people and populations benefit from evidence-based interventions and others do not.
6. The collective investment in prevention intervention development and testing research should be increased, particularly in areas where the population attributable benefit of reducing the risk factor (e.g., tobacco, obesity) and/or the prevalence of risk factors (occupational and environmental exposures) remains high. Common risk factor intervention research studies also provide a significant opportunity for CCRA members to leverage their funding with other non-communicable disease research funders and benefit the field through collaborative investments.

7. Health economics research and the routine collection of cost data should be considered a very high priority in all future intervention development and delivery research strategic investments.
8. CCRA member organizations should share resources to strategically fund ongoing knowledge synthesis efforts of published systematic reviews and unpublished research strategy reports to inform the development and the adjudication of future cancer risk identification and reduction RFPs. The CCRA secretariat should coordinate this shared investment initiative.
9. CCRA member organizations with at least two mission priorities of research, practice and policy should evaluate and share best practices for integrating development and delivery research (e.g., natural experiments, cancer health services research) with evidence-informed program implementation and policy change work.
10. For complex cancer prevention and control issues where endemic societal determinants play an overarching role (e.g., health disparities among culturally diverse and underserved populations), CCRA members should co-invest with government and non-government agencies in rigorous program and policy evaluation, linked with KTE research, to inform future research funding opportunities and program/policy actions.

It should be noted that increased investments in prevention intervention development research carry with it some special issues that may have contributed to the relatively low levels of past funding in Canada and will need to be considered as new intervention development research initiatives are planned in the future. The first is that, for comparative studies testing an intervention to reduce cancer cases, large numbers of subjects are required and long follow-up needed before answers are obtained. Thus, these types of trials can be quite costly, require multiple participating investigators and institutions, as well as involving a substantial infrastructure to manage. While the use of intermediate or surrogate endpoints (such as reduction in precancerous lesions or reduction in risk factor measures) can address problems of sample size, cost and time to complete studies, these approaches have their own complexities. In the context of intervention trials using an endpoint of risk reduction, a key question in understanding the impact of this measure on cancer risk will be robustness of the cause-effect relationship between the “risk” and the development of cancer.

The second issue centres on studies where interventions are intended to modify the process of carcinogenesis and are evaluated by measuring intermediate pathological endpoints (such as the development of pre-neoplastic lesions like polyps). Here the challenge is whether the endpoint chosen is a necessary step in carcinogenesis or whether other pathways and steps can bypass it. If the former, its reduction should lead to reduction in invasive cancers; if the latter, its reduction may not have the anticipated impact on invasive cases. These methodological issues have made the field of prevention intervention development research both challenging and complex, and initiatives in this area will need to include funding on methodological improvements in research design and endpoint specification.

Finally, the complexity of cancer prevention intervention research designs (e.g., multi-factorial) combined with the diversity of populations and service delivery contexts to which cancer and chronic disease prevention programs are targeted highlight the importance of building research, practice, and policy partnerships. This applies not only to the use of cancer and chronic disease prevention research knowledge (KTE), but also to the importance of the practice and policy communities working with research funders and scientists to help identify the highest priorities and opportunities for future cancer

prevention research in Canada. If a growing investment in cancer prevention research in Canada is to be supported by CCRA member organizations linking science with service will be critical.

The Path Forward

This report was prepared for all Canadian Cancer Research Alliance members by representatives of several CCRA member agencies in response to Action Item #1 of the 2010 Pan-Canadian Cancer Research Strategy.⁵⁴ The well documented observation that levels of funding for cancer prevention research in Canada have been and remain low relative to other areas of research led to the recommendation that a comprehensive review of cancer prevention research in Canada should be documented followed by a multi-agency effort to develop a cancer prevention research strategic agenda for Canada.

To solicit specific organizational interest and commitments to follow-up with the collective funding recommendations described herein, the CCRA should agree to sponsor a meeting in 2012 of CCRA member organizations interested in playing a leadership role and/or serving as funding partners. This should then lead to new collaborative RFPs beginning in 2013. In addition, in order to ensure continued relevance of the proposed framework for future cancer risk factor and prevention research funding in Canada, a regular review and update of this framework report, including an analysis of progress against the above priorities and funding trend data, should be conducted with support from the CCRA and should be presented at each biennial Canadian Cancer Research Conference beginning in 2013.

⁵⁴ http://www.ccra-acrc.ca/PDF%20Files/Pan-Canadian%20Strategy%202010_EN.pdf

APPENDIX 1

Examples of CCRA Member Organization recent strategic investments in cancer prevention research

The Canadian Cancer Society (CCS) has made several strategic investments in cancer prevention research since the CCRA cancer risk and prevention investment report was prepared.

Within CCS' 5-year nationwide strategic plan (approved in 2010), a key priority is to lead research to better prevent cancers. The Society aims to improve policy and practice through prevention and risk reduction research by focusing on the following areas: tobacco control, occupational and environmental carcinogens, obesity, healthy eating, physical activity, and fundamental research to improve our understanding of cancer etiology and prevention. One of the ways CCS plans to achieve this is through the establishment of a Canadian Cancer Society Centre for Cancer Prevention that will better network cancer prevention research across Canada and provide a platform to link research, policy and practice activities. The priorities for CCS cancer prevention and risk reduction research are:

- build Canadian capacity in strategic areas of risk reduction and prevention research
- facilitate knowledge translation in the research-practice-policy continuum
- integrate the Canadian Cancer Society Research Institute's (CCSRI) core research programs and major initiatives with CCS' divisional activities to form a more cohesive and impactful program
- expand (with partners) CCS' national leadership in cancer risk reduction and prevention research

In support of these priorities, CCS has already made several new investments in cancer prevention research since the CCRA cancer risk and prevention investment report (2005-2007) was prepared.

In 2009 CCSRI launched a Prevention Initiative to support strategic investments in the area of cancer prevention and risk reduction research. The Initiative was guided by the advice of a National Advisory Committee on Research in Prevention and supported new research that reduced the risk of cancer, with a particular focus on prevention interventions.

In the last two years the Initiative has launched four Requests for Applications focused on the areas of modifiable risk factors, interventions to prevent cancer, and a translation supplement award program. Through these programs, 13 new grants have been awarded representing a total commitment of over \$4.6M. The Initiative has also launched several capacity building programs that are currently supporting two senior research scientists, five junior investigators, and a studentship representing a commitment of almost \$2M. In addition, three new funding programs are in progress; specifically a multi-sector team grant program to leverage linkages between research and other programs delivered by CCS, a reissuance of the translation supplement award program, and a fast track grant program launched in partnership with CIHR and other funders to create a mechanism to allow researchers to respond to emerging opportunities where changes to programs, events and/or policies have the potential to impact healthy living and cancer prevention and/or risk reduction at the population level. Taken together, CCS expects to commit \$4.7M to these new programs.

CCSRI continues to dedicate significant resources to cancer prevention and risk reduction research through investments in its major initiatives. CCS is investing in the Propel Centre for Population Health Impact (formerly the Centre for Behavioural Research and Program Evaluation) which has a major focus

on tobacco control and healthy living. CCS' investment in the NCIC Clinical Trials Group also supports a limited amount of chemoprevention activities.

In addition to CCSRI's central research programs, individual divisions have also made significant targeted prevention and risk reduction research investment in recent years. CCS' British Columbia/Yukon division established a research chair in Cancer Primary Prevention in partnership with the University of British Columbia and the Government of British Columbia. The recruitment of this chair was Phase I of a multi-staged vision to further develop CCS' cancer prevention activities. Phase II of this initiative consists of developing and implementing cancer prevention research. Projects funded by CCSRI, CIHR, and CBCF are currently in progress, focusing on diverse topics in cancer prevention including workplace health promotion, protection from worksite carcinogens, and reducing breast cancer risks.

CCS' Nova Scotia division has also established a research chair in Population Cancer Research in partnership with Cancer Care Nova Scotia, QEII Hospital, and Dalhousie University. Many of the current and proposed activities of this chair position build on Atlantic PATH – the Atlantic component of the CPAC and provincially-funded national cancer cohort study, Canadian Partnership for Tomorrow.

In 2009 the Occupational Cancer Research Centre (OCRC) was established to fill gaps in knowledge of work-related cancers and to translate these findings into preventive programs to control exposures and improve the health of workers. The OCRC is jointly funded by the Workplace Safety and Insurance Board, Cancer Care Ontario, and the CCS Ontario Division, in collaboration with the United Steelworkers Union.

Importantly, CCSRI has recently redesigned its research portfolio around the CCS' three long term goals: to reduce cancer incidence rates, reduce cancer mortality rates, and to enhance the quality of life for Canadians living with and beyond cancer. CCS' strategic intent over the next five years is to increase its relative investment in risk reduction and prevention research. Dedicated and targeted funding mechanisms are being developed through this newly structured portfolio that will build on and expand the scope of CCSRI's Prevention Initiative. A major goal of this newly structured program is to better link and leverage the central prevention and risk reduction funding opportunities through CCSRI with specific CCS divisional programs and other relevant activities across the country, in addition to the promotion of knowledge translation. An End 1 development committee, composed of research, policy and program experts, has been struck to oversee program development in cancer prevention and risk reduction research.

The Canadian Partnership Against Cancer, although not primarily a research funding agency, has provided some resources supporting cancer prevention research since 2007. CAREX Canada began collecting data and geographically mapping the presence of workplace and environmental carcinogens across the country in 2007. The Partnership's continued investment in CAREX Canada through March 2017 ensures that cancer prevention researchers interested in studying and reducing the prevalence of these cancer risk factors will have an ever growing data set for such studies.

The Canadian Partnership for Tomorrow Project was launched in 2008 and will provide a cohort platform of 300,000 Canadians and enable, using the collected datasets and further participant follow-up, a number of prevention-related research projects. The project involves the BC Cancer Agency, Alberta Health Services, Cancer Care Ontario with the Ontario Institute for Cancer Research, Quebec's CARTaGENE project, and Cancer Care Nova Scotia with Dalhousie University collaborating for work in the Atlantic Provinces. It is co-funded by the Partnership and its regional partners.

Canadian Breast Cancer Foundation (CBCF) funding for research and fellowships focusing on prevention and risk factors related to breast cancer are funded primarily through regional open competitions. CBCF funding has and continues to support research that includes investigations of workplace, dietary and environmental factors that influence breast cancer development and the discovery of genetic or familial factors contributing to breast cancer development. Other work of the Foundation has supported the prevention of breast cancer recurrence.

In 2010, the BC/Yukon Region invested in the creation of a Breast Cancer Prevention and Risk Assessment clinic (now open), which is part of supporting the BC/Yukon Division Cancer Primary Prevention Chair at BC Women's Hospital.

Given the relatively low application level of prevention research to open competitions, CBCF is considering increasingly targeted approaches to encouraging breast cancer prevention research. CBCF is also interested in early action on prevention priorities outlined in the National Breast Cancer Research Framework.

Cancer Care Ontario continues to expand its support for research and program evaluation tools related to cancer prevention including:

- Continue research program in etiologic studies of cancer and other chronic diseases
- Enhance research programs to conduct geospatial analysis
- Development of a research program in complex chronic disease in collaboration with other local institutions
- Develop a research program to support risk factor modification
- Establish an innovative Ontario researcher network in occupational and environmental cancer.
- An occupational cancer research program established – the Occupational Cancer Research Centre
- Enable action against CCO/Public Health Ontario Chronic Disease Prevention Blueprint
- Build a cancer prevention performance measurement framework that can serve as a resource for all partners who have a role in prevention

Cancer Care Nova Scotia (CCNS) continues to support research through investments in sharing data, contributing expertise in primary prevention and analytic resources. Projects and initiatives of note include:

- Physical Activity Research Study at Dalhousie University looking at physical activity in young adult cancer survivors – tertiary prevention. CCNS was a facilitator of this acting as a source of cohort for research sample.
- Evaluation research to determine the effectiveness of a public health program intervention on youth tanning behaviour targeted to junior and senior high school students. The program titled

The Truth About Tanning takes a youth-centered approach to de-normalize active tanning behaviour (natural and artificial) in the school community.

- Using the cancer survivor cohort, sharing data and analytic expertise to assess physical activity behaviours over a 5 year period to determine how to apply strategies to encourage increased activity levels in the survivors of breast, colorectal and prostate cancer.
- Research in progress looking into risks related to urinary cancers and arsenic exposure in the Nova Scotia water supply.
- Atlantic PATH study with CCNS infrastructure support will inform and direct investment in cancer prevention in the future.
- Study in progress looking into cancer risk resulting from outdoor air pollution in the Halifax Regional Municipality. CCNS is an enabler of this research providing linkage to the cancer registry.
- CCNS pilot study to determine a methodology to conduct a case control study on arsenic exposure and urinary tract cancer.
- Tui'kn Project - funded by Aboriginal and Northern Affairs to allow Cape Breton-based Aboriginal communities to develop a range of health indicators for their communities (inclusive of cancer indicators and cervical screening).
- CCNS supporting research into the risk of second malignant neoplasms among people diagnosed with certain embryonal tumours during childhood.
- Baseline and comparative data on youth utilization of tanning beds in Nova Scotia begin coordinated through CCNS on behalf of N.S. Department of Health and Wellness, Doctors Nova Scotia and Canadian Cancer Society. Data will provide insight into the impact of the N.S. Tanning Beds Act proclaimed in May 2011.
- CCNS registry data shared with C-NET - the CPAC Analytic Network. This includes survival and prevalence methodologies and projection methodologies.

A new initiative to be launched by CCNS in the winter of 2012 will facilitate research through access to the cancer registry for identification of cancer survivor survey respondents. This is a cancer survivor cohort. The focus will be on gynecological cancer survivors over the past five years and their physical activity behaviours to determine what might encourage increased physical activity levels in this Nova Scotian population.

Prostate Cancer Canada's (PCC) mandate includes funding research in support of improved diagnostic strategies, risk assessment tools, improved prognosis of response to preventive interventions, differentiation between cancers from low malignant disease and improving diagnostic yield and evidence-based prevention strategies.

PCC has historically utilized open-competition research programs (e.g., Pilot Grants and Clinician Scientist Awards) to provide financial support for basic and translational research. The focus of the existing grants and awards is investigator driven. Over the past few years, very few of the applications received have been in the area of prevention and even fewer have been granted. Prostate cancer prevention knowledge (prevention of both primary and progression) is lacking. Prostate cancer patients, families and donors have proposed primary prevention and prevention of progression as research priorities.

PCC is taking a leadership role in establishing prostate cancer research priorities within Canada. A CCRA Working Group has been formed to collaborate in the development and implementation of a National Prostate Cancer Research Strategy. Environmental scans, including consultation with patients, donors and the research/medical community, will be conducted and analyzed. This report will inform the national research strategy. It is envisioned that the Implementation of the strategy will be the goal of a Prostate Cancer Research Alliance.

In order to prioritize/monitor/evaluate projects of this nature, a prostate cancer research alliance will:

1. be driven by collaborative, national research projects,
2. serve as a facilitator of institutional collaboration, project development and funding,
3. oversee project reviews, catalogue development and document prostate cancer biobank activities,
4. create opportunities for sharing information, technology, experimental models and tissue and for technician exchanges.

A Prostate Cancer Canada Research Alliance (PCCRA), which will implement the National Prostate Cancer Research Strategy, may comprise private and government research funding agencies which have the capacity to participate in funding national prostate cancer research projects. The projects will be patient-centered, will have the potential of improving the quality of patient care, and will include the search for better prevention, diagnostics and prognostics. The projects will also be multi-institutional and multi-disciplinary.

PCC will seek funding partners for each of the directed research programs and projects. Prevention (of prostate cancer and prostate cancer progression) will undoubtedly be one of the initial focused research strategies supported by the Prostate Cancer Research Alliance.

APPENDIX 2

KNOWLEDGE SYNTHESIS OF PREVENTION

RESEARCH PRIORITIES

FINAL REPORT

September 30, 2011

Prepared for the Canadian Partnership Against Cancer

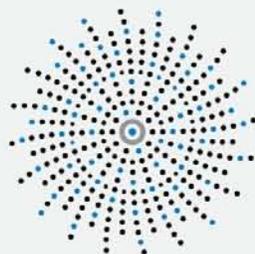
Prepared by the Propel Centre for Population Health Impact

Jennifer Yessis, PhD

Erin Smith, MIPH

Stephanie Filsinger, MSc

Barbara Riley, PhD



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Prepared by

Jennifer Yessis, PhD, Erin Smith, MIPH, Stephanie Filsinger, MSc, Barbara Riley, PhD

With library science support from Heather McGrath, MLIS

For further information regarding this report, please contact: Dr. Jennifer Yessis

Propel Centre for Population Health Impact
Lyle S. Hallman Institute
University of Waterloo
200 University Avenue West
Waterloo ON Canada
N2L 3G1
Telephone: 519-888-4567 x 32860
Fax: 519-886-6424
Email: [jyessis@uwaterloo.ca](mailto: jyessis@uwaterloo.ca)

Report funded by

Canadian Partnership Against Cancer

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EXECUTIVE SUMMARY

Context and Overview of the Report

The Canadian Cancer Research Alliance (CCRA) is leading development of a cancer prevention research agenda for Canada. As part of the development process, a synthesis of selected documents containing cancer and chronic disease prevention research priorities was commissioned. Findings from this synthesis are the focus of this report. Findings include the criteria and process for setting research priorities, and research priorities themselves. Where possible, CCRA categories for research focus, type and risk factor were used to synthesize findings. The report concludes with some considerations for a prevention research agenda.

The knowledge synthesis was done over a two month period with a tightly defined scope and limited resources. A collaborative approach was used with the Partnership Program Manager and the Partnership lead (on behalf of the Partnership and CCS leads) throughout the project.

Documents in the Synthesis

The synthesis includes 23 documents – 15 from peer reviewed sources and 8 from the grey literature. Documents were selected intentionally to cover a wide spectrum of cancer and chronic disease prevention research topics, include Canadian content to the extent possible, and represent the most recent sources the research team could locate in specific topic areas. See Figure 1 (page 8) for a flowchart that shows the document selection process.

The synthesis documented any framework (e.g., criteria, process) used to set priorities, and proposed specific research priorities. The research priorities were coded and summarized by CCRA research focus and CCRA research type (CCRA, 2010).

Criteria and Process for Setting Research Priorities

With three exceptions, criteria guiding the development of research priorities were not included in the articles reviewed. The NCIC report (2008) used the following criteria:

- **Impact criteria:** Potential for research recommendations to reduce the public health burden, to impact the cancer burden when implemented, research should be conducted in areas where evidence indicates that exposure will impact cancer burden.
- **Diversity criteria:** Recommendations should be diverse to ensure a comprehensive strategy.
- **Alignment with existing policy priorities:** Recommendations should take advantage of current/emergent trends, policies that may lend themselves to natural experiments.
- **Other criteria:** In the context of the identified priority areas greater weight should be given to those recommendations that have an impact on other diseases, have the potential to resonate with end users (including CCS and the public), and develop cancer prevention research capacity.

Additional criteria considered by McKinnon et al. (2009) included the feasibility of research implementation, the impact of the research in general and in priority subpopulations, the impact of the research on health outcomes, the costs of the recommendations to society, and cost effectiveness of doing the research. Brownson et al. (2008) ranked research recommendations based on feasibility and importance.

Research priorities from the articles reviewed were determined using different processes such as expert working groups, literature reviews and workshops or conferences that gathered a group of experts together. Although several articles described membership on working groups tasked with setting research priorities, none of the descriptions mentioned the relative emphasis given to different perspectives, and the extent policy, program and research perspectives were reflected.

Articles were silent on plans for updating research priorities. In the rapidly evolving area of cancer prevention, this is particularly important. For example, in the next six months the U.S. National Cancer Institute is releasing a series of papers referred to as research gaps in policy measures of the framework convention on tobacco control (D. Hammond, personal communication, September 22, 2011).

Research Priorities

The synthesis revealed a very wide-range of cancer prevention research priorities, including areas that are well-established and others that are in their infancy. The detailed results appear in section 3.0 of this report. Below are a few observations that examine similarities and differences across research focus and research type.

- From the selected articles, the number of obesity research priorities far exceeded other research topics. Research priorities for general cancer prevention research, and environmental/occupational health were a distant second according to the number of research priorities in research type and research focus respectively. This may reflect varying degrees of momentum in different research areas. It might also mostly be a result of the types of articles in the synthesis. For example, both the NIH Strategic Plan and the NCIC Cancer Prevention Initiative Strategy and Working Group Reports were not peer reviewed journal articles and were not limited by space constraints. In developing the research agenda, caution should be taken in comparing the number of research priorities identified in one article to the number identified in another.
- Most research priorities were determinants that influence causes. Fewest priorities were related to causes of cancer. This may also be partially a reflection of the articles included in the knowledge synthesis. The research priorities in the obesity articles often used obesity as an outcome and not cancer which was required to be considered a cause according to CCRA's definition of cause.
- Research priorities for knowledge synthesis, dissemination / communication, and community-based research appear under-developed. Fewer research priorities in these areas may also be a reflection that research priorities in these topic areas are not easily classified into CCRA's analytical framework of risk factors, research type and focus. For example, research priorities identified by Trickett et al. (2011) could not be classified into the research focus categories and were all categorized as "other". Furthermore, priorities for knowledge syntheses may emerge once specific research initiatives are underway.

- Reviewed articles included Canadian content to the extent possible (CCRA, 2010, NCIC, 2008, NCIC, 2007a, NCIC 2007b, NCIC, 2007c, NCIC, 2007d, Miller, 1995). In most cases, research priorities are applicable in a variety of settings (e.g., in both the United States and in Canada). However, caution should be taken in applying research priorities to the Canadian setting in some cases. For example, the article by Cummings and Orleans (2009) was focused on tobacco policy research priorities. While many of the specific research priorities are likely applicable in both the United States and Canada, some may not be relevant in the Canadian policy context.
- *Natural experiments*: These were recommended across research areas, focus and type. Funding mechanisms may need to be flexible with fairly quick turnaround in order to be responsive to the opportunities afforded by naturally occurring variation in environments or other conditions.
- *Cancer disparities*: Examining cancer disparities in different subgroups was identified in many articles and seen as a cross-cutting theme for consideration in the research agenda.
- *Methodologies*: A common emphasis was on ensuring measures are psychometrically sound (reliable, valid, specific and sensitive to change), particularly those used for surveillance purposes. The importance of surveillance of risk factors using these valid and reliable measures was also recommended. With respect to researcher controlled interventions, the importance of internal validity, and cohort studies was mentioned across research type and in the interventions section. Another theme that was highlighted across research type and research focus was encouraging alternatives to randomized trials that focus on a plurality of methods and developing a context-sensitive science of prevention.
- *Study of biomarkers*: The development, study, validation and use of biomarkers for examining intermediate end-points and outcomes was recommended for use in qualitative and quantitative risk assessments, across research type, and research focus and as a focus for methodological research.
- *Molecular epidemiology*: This theme emerged particularly in the area of research involving model systems, infrastructure and the research focus of causes.

Use of this Synthesis

The above observations are a modest start to what may be gleaned from the detailed data extraction spreadsheet. Some decisions about the boundaries (e.g., audience, desired results, criteria and process for setting priorities, etc.; see section 4.1) will help to discern how findings may be best used to inform the CCRA cancer prevention research agenda.

INTRODUCTION

Purpose and Overview of the Report

The Canadian Cancer Research Alliance (CCRA) is leading development of a cancer prevention research agenda for Canada. As part of the development process, a synthesis of selected documents containing cancer and chronic disease prevention research priorities was commissioned. Findings from this synthesis are the focus of this report. Findings include the criteria and process for setting research priorities, and research priorities themselves. Where possible, CCRA categories for research focus, type and risk factor were used to synthesize findings. The report concludes with some considerations for a prevention research agenda.

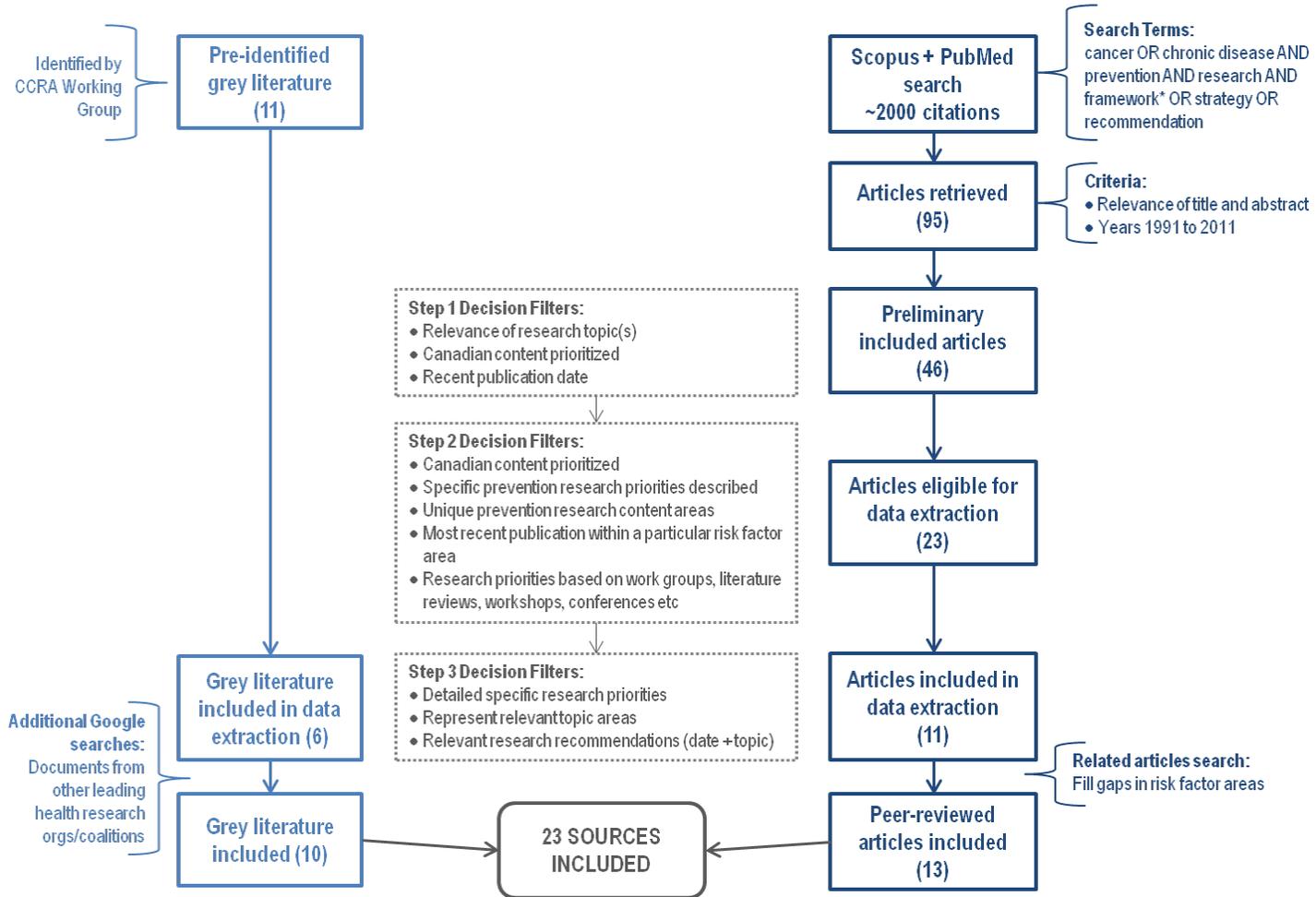
Throughout the project, Propel worked closely with the Partnership Program Manager and the Partnership lead (on behalf of the Partnership and CCS leads) from the CCRA working group to complete each milestone.

METHODS

Document Selection Process

At the outset, general parameters for document selection were to select up to 30 Canadian and relevant international prevention research framework, strategy and recommendation documents, including peer reviewed and grey literature. The document selection process was iterative and incremental, whereby the results of each step in the selection process informed the next step. Inclusion and exclusion criteria were refined progressively and are described below. Figure 1 depicts a flowchart of the article selection process.

Figure 1: Flowchart of Knowledge Synthesis Document Selection Process



Initial Parameters

The following parameters guided the initial search:

- 1991 to 2011
- English language
- Grey and peer reviewed
- Cancer and chronic disease prevention research
- Other specific diseases: heart disease, diabetes; selected only as they are relevant in documents about chronic disease prevention research

Search Strategy

- The initial searches were conducted using the following databases: Scopus, Pubmed, Google, Google Scholar
- The following search terms were used for the initial searches: cancer, Neoplasms[MeSH], chronic disease, chronic disease[MeSH], prevention, research, framework*, strat*, recommend*, priorities, agenda*. Three search terms were tried and rejected: chronic illness, plan*, model*

The initial searches resulted in very high yields (7,000 to over 10,000 articles for each of four different searches) (Appendix A). To limit the scope of the search and retrieve more relevant articles in each search, the search terms used for article selection were focused considerably. See Appendix B for an overview of the yield from more focused searches.

Document Selection

One hundred and six articles were selected initially based on relevance of the title and abstract (if available) between the years 1991 to 2011. From this initial pool of eligible documents, we aimed to select approximately 20 documents for a more detailed review and extraction. The initial selection was to include articles with **general cancer prevention and chronic disease prevention research priorities**, and additional articles from the following topic areas:

Alcohol	Nutrition	Sun safety
Chemoprevention	Obesity	Tobacco
Clinical prevention	Occupational health	Viral HPV/viral HBV
Environmental health	Physical activity	
Genomics	Social disparities	

The titles, year and abstracts (if available) were reviewed for the 106 articles. Fifty seven were selected based on relevance of the title and abstract (if available), relevance of the research topic(s), recent publication date, and (to the extent possible) Canadian content. Information from the 57 articles was entered into a spreadsheet including: citation, purpose of the article, the abstract, and notes from a review of the article.

In order of priority, the following decision rules were used to select the next set of articles:

- Canadian content
- Specific prevention research priorities described
- Documents from leading health research organizations and coalitions⁵⁵
- Unique prevention research content areas
- Most recent within a particular content area
- Research priorities based in a priority on work groups, followed by literature reviews, workshops or conferences and other ways of developing research priorities (e.g., editorial).

The annotations allowed for a more in-depth application of the inclusion criteria. They also allowed for specific exclusion criteria to emerge. Articles were excluded for several reasons:

- Broad research frameworks were described without specific research recommendations (e.g., Best et al., 2003, Emmons, 2000, Hiatt and Rimer, 1999).
- Articles focused only on the process of developing research priorities (O’Fallon et al., 2003).

⁵⁵ Canadian Cancer Society, Canadian Disease Prevention Alliance of Canada, Canadian Institutes for Health Research, Canadian Strategy for Cancer Control, Heart and Stroke Foundation, National Association for Health Research Foundations, National Cancer Institute, World Health Organization

- The article was an editorial that focused on methods more than research priorities (Prentice, 2004).
- Articles did not include specific research priorities (e.g., O'Callaghan, 2011; Khoury and Mensah, 2005).⁵⁶

Applying the above filters and exclusion criteria resulted in the selection of 34 articles. The 34 articles were read carefully to examine their appropriateness in detailing specific research priorities (i.e., rather than a high level research framework document), in representing relevant topic areas (as identified in section 2.1.3), and in adding research recommendations that were still relevant (based on date article was written, and the topic).

Based on this detailed review, 14 articles were selected. An additional 13 were considered for selection.

Of the 13 articles for consideration:

- One article was identified as having important content (Owen et al., 2004) for inclusion, but was considered dated. A related articles search of Owen et al (2004) was conducted to attempt to find a more recent research agenda in this area. The article that replaced this article was: Brownson et al., 2008.
- Several articles that were initially selected were introductions to a more detailed research agenda (McKinnon et al., 2009) or referred to a more comprehensive research agenda that was developed as part of a work group (Krieger et al., 2005). The more specific articles were selected for the synthesis (Lytle, 2009; Report of the Trans-HHS Cancer Disparities Progress Review Group, 2004).
- The content of the Bowen et al. (2009) article (i.e., dissemination research in cancer control) was considered important by the Propel/CPAC team and was selected for inclusion in the synthesis.
- Katmarzyk et al. (2008) was not selected because it did not add unique content, and obesity was already well-represented in the other articles.
- Hawk et al. (2008) was not selected because it described the process/framework and steps in conducting research on lifestyle alternatives, but did not describe specific research priorities.
- Lioy et al (2010) was not selected because the research priorities were too high a level.
- Based on expert consultation Miller (1995) was selected for inclusion.
- Although dated, we were unable to locate more recent articles that provide occupational and environmental health prevention research priorities (for children). Carroquino et al. (1998) was selected.
- Based on additional searches for more recent occupational and environmental health prevention research articles that were not fruitful, Carroquino et al. (1998) was selected.
- McBride (2005) was selected for genomic content.

⁵⁶ There is one exception to this rule. We selected a detailed article by CCRA, 2010 that referred to funding of prevention in great detail and was used as a lens to frame the data extraction.

- Three articles were specific to conducting research in low to middle income countries (i.e., Baris et al, 2000; Bousquet et al., 2010; Mendes ad Alwan, 2011) and were excluded on that basis.

An additional search for grey literature was conducted to seek out sources of research priorities in areas that were identified as gaps (i.e., alcohol, tobacco, clinical prevention, viral HPV, viral HBV, sun safety), and more recent sources in the area of environmental and occupational health. This was done through a Google search for the gaps and a website search of organizations that had not been previously searched. The following websites were searched: Canadian Diabetes Association, Cancer Council Australia, Cancer Council Victoria, Cancer Research UK, Centre for Addiction and Mental Health, Centers for Disease Control and Prevention, David Suzuki Foundation, The Lung Association, the National Institute of Environmental Health Sciences, and the National Institutes of Health.

The results of the grey literature search were selecting two documents: Cummings and Orleans, 2009 and Skin Cancer Prevention Working Group, 2007. Others were excluded because they did not include specific research priorities (National Lung Health Framework, 2008; National Diabetes Strategy, 2003).

A next step was consulting with two content experts who were asked about articles in specific content areas. David Hammond was consulted in the tobacco policy research area to examine the selected tobacco policy research agenda document (Cummings and Orleans, 2009). The article was identified as relevant for tobacco policy research in general. One drawback of the selected article is that it is U.S. based which will need to be considered, since some of the proposed policy research priorities are not relevant in a Canadian policy context (D. Hammond, personal communication, August 2011). Anthony Miller was contacted to ask if he was aware of an update to the article he published (Miller, 1995) on the primary prevention of cancer with specific focus in the area of environmental health. Miller had not updated his article. He was also not aware of a more recent, comparable article from other authors (A. Miller, personal communication, August 2011).

Additional articles selected from new searches:

- Cummings and Orleans (2009) was selected after finding the article through a Google search, and consulting with an expert.
- Gritz et al. (2007) added valuable and unique content in the area of tobacco research.
- The Skin Cancer Prevention Working Group report (n.d.) selected from a Google search added valuable content that was missing from the selection of articles.

A subset of articles that was excluded appears in Appendix C. The articles are grouped according to their focus and may provide useful perspectives and information for the CCRA research agenda that are outside of the scope of this synthesis of research priorities.

Data Extraction

The purpose of the data extraction process was to classify the main processes used to develop research priorities, and to identify proposed research priorities, organized by pertinent topic areas and types of research.

Data Extraction Process

The process was conducted using a data extraction template that was created in Microsoft Excel. First, relevant information from each of the selected articles was compiled into the template according to fields identified at the start of the process. Next, a content analysis of those fields was conducted in order to identify the main processes and broad categories for filtering and synthesizing research priorities. During the process, additional fields were added to the extraction template.

In a special report from CCRA on investment in cancer risk and prevention research 2005-2007, research was classified according to a three-dimensional risk and prevention “cube” (CCRA, 2010). The cube consists of research type (5 categories), research focus (4 categories) and risk factor (15 categories). The data extraction template used the analytical framework (e.g., research focus, risk factor and research type) developed by the CCRA to organize the research priorities identified in each article. Definitions of the categories from the CCRA cube are found in Appendix D.

The data extraction template also included fields used to sort articles by year of publication, type of article, and citation. The main content extracted from each article included the following fields: purpose of the article (as it relates to developing research priorities), process/methods to develop research priorities, and the research priorities categorized by research type, research focus and risk factor.

Each article was documented on a row in the extraction template. Individual research priorities were extracted from each article onto the spreadsheet. Each priority was categorized into research type (e.g., research involving model systems, human research, etc.), research focus (e.g., causes, determinants that influence causes, etc.) or risk factor (e.g., activity level, body composition & metabolism, alcohol, etc.) categories.

Several decision rules were applied to the extraction process:

- Research priorities may have been included in more than one risk factor category, and research type. Rather than extract the priority into the “multiple/general” risk factor category, it was felt that it would be more informative to include a single priority in more than one risk factor category. Some priorities were relevant for more than one research type (e.g., methodological/measurements research and infrastructure categories).
- The CCRA research type infrastructure was separated into infrastructure, dissemination and funding on the spreadsheet since these categories were distinct themes that emerged with a number of priorities.

- The CCRA research focus definition of “causes” refers to the causes of cancer, factors associated with cancer risks and possible mechanisms/modulators involved in carcinogenesis. We referred to this definition when categorizing “causes”. For specific articles, such as articles related to the topic of obesity, many of the research priorities on obesity were not related to causes because they referred to the cause of obesity, not the cause of cancer.
- For research focus, some research priorities related to infrastructure (e.g., capacity building, training programs, funding recommendations, etc.) were categorized into an “other” category on the spreadsheet. These were not reported in detail in this report because they were not related to the research focus categories.

Research priorities were categorized by one member of the research team (E.S.), and reviewed in detail by another (J.Y.). Questions about categorization and the classification of priorities were discussed and resolved.

Description of Selected Documents

Overall, 23 articles were included in the knowledge synthesis. Of those, 15 were from peer reviewed sources and 8 were from the grey literature. The complete list of articles is included in the reference list in section 5.0. The main focus of each of the 23 articles is shown in Table 1 by the reference and the number of articles in each category.

Initially we wanted to select articles related to general cancer prevention research, in addition to articles with specific areas of focus. We searched for and selected articles on each of the identified topic areas of interest except for the following topics: alcohol, chemoprevention, clinical prevention, and viral HPV/viral HBV. These topics are covered in the general articles and in another article that used an environmental lens to look at primary prevention (i.e., Miller, 1995). Two articles on the research topics of community-based research and cancer communication/dissemination research were also included in the selected articles, since these topics were considered gaps even though they were not identified a priori as topics to include.

We provide details of the search methods above (and in related Appendices), so that boundaries for the synthesis are transparent. Gaps may be apparent in key words, databases, websites or pages searched, content areas, or other dimensions.

Table 1: Main Focus and Process Used for Articles Extracted

ARTICLE FOCUS	Number of Articles	Reference	Process Used				
			Workshop / Conference	Working Group	Literature Review	Editorial	Findings based on database
General Cancer Prevention	6 *article did not include research priorities, but did include a detailed description of funding	CCRA, 2010 * NCIC, 2008 (with 2011 update) + 4 workgroup reports		✓			✓
Obesity	2	McKinnon et al., 2009 Strategic Plan for NIH Obesity Research, 2011		✓ ✓			
Nutrition	2	Milner, 2003 Lytle, 2009			✓ ✓		
Dissemination or Communication	2	Kreuter et al., 2007 Bowen et al., 2009		✓	✓		
Occupational/ Environmental	3	Miller, 1995 ⁵⁷ Carroquino et al., 1998 Caruso et al., 2006	✓ ✓		✓		
Tobacco	2	Gritz et al., 2007 Cummings & Orleans, 2009		✓		✓	
Physical Activity	2	McTiernan, 1999 Brownson et al., 2008		✓		✓	
Community-based research	1	Trickett et al., 2011	✓				
Genomics	1	McBride, 2005				✓	
Sun Safety	1	Queensland Skin Cancer Prevention Working Group, n.d.		✓			
Social disparities	1	Report of the Trans-HHS Cancer Health Disparities Review Group, 2004		✓			

⁵⁷ This article was a general cancer prevention research article using an environmental health lens so it was categorized in occupational/environmental health.

SUMMARY OF FINDINGS

Findings were based on an analysis of the data extraction template which can be found in an accompanying file⁵⁸. Findings are summarized according to the major dimensions of interest (e.g., CCRA classifications). The continued relevance of research priorities in the documents was not assessed; it is possible that the priorities are no longer relevant if investments have already been made, research has been conducted in those areas or it's no longer considered relevant for other reasons (e.g., alignment with prevention policy priorities).

Criteria and Process to Develop Priorities

Research priorities from the selected articles were identified using different processes including: working groups established to identify research priorities (working groups often included a series of meetings (e.g., face-to-face, teleconferences), review of background material, and identification of research priorities); literature reviews to provide context to research priorities that may have a number of experts involved; workshops or conferences that gathered a group of experts to identify research priorities; and an editorial on a particular topic of interest that included research priorities. The level of detail related to the processes used to develop priorities varied in each article. Table 1 presents the processes used to develop research priorities in each of the groupings of articles.

- Twelve of the selected articles were the products of working groups (NCIC, 2008 + 4 working groups: Working Group 1 - Modifiable Risk Factors Group (NCIC, 2007a); Working Group 2 – Intervention Group (NCIC, 2007b); Working Group 3 – Knowledge Exchange, Media and Policy Group (NCIC, 2007c); Working Group 4 – Clinical Medicine and Basic Biology Group (NCIC, 2007d); Kreuter et al., 2007; Trans-HHS Cancer Disparities Progress Review Group, 2004; Cummings & Orleans, 2009; Brownson et al., 2008; McKinnon et al., 2009; Strategic Plan for NIH Obesity Research, 2011; Skin Cancer Prevention Working Group, n.d.).
- Four of the articles presented literature to help clarify the research priorities identified (Lytle, 2009; Milner, 2003; Bowen et al., 2009; Caruso et al., 2006). The reviews were not “systematic reviews”; the literature primarily provided context for the priorities identified.
- Two articles resulted from workshops that were held to identify research priorities for community level interventions (Trickett et al., 2011), and preventable causes of cancer in children (Carroquino et al., 1998). One article was the result of a presentation at the President’s Cancer Panel Conference on Avoidable Causes of Cancer in Bethesda Maryland (Miller, 1995).
- Editorial articles were selected when research priorities added unique information (n=3). McBride (2005) wrote an editorial that included a discussion of the role of genomics in chronic disease prevention, and identified research priorities for consideration. McTiernan and colleagues (1999) provided a narrative on research

⁵⁸ Filename: CPAC KnowledgeSynthesisExtractionTemplate_20110930

priorities for exercise clinical trials related to cancer prevention research. Gritz and colleagues (2007) described research priorities to bring together tobacco control, lung cancer research and policy.

The criteria used to develop recommendations were explicitly stated in three articles (NCIC, 2008; McKinnon et al., 2009; Brownson et al., 2008). The NCIC (2008) report identified a number of criteria for identifying priorities related to the potential for impact, diversity, alignment with existing policy priorities, and other criteria. More specifically:

- **Impact criteria:** Potential for research recommendations to reduce the public health burden, to impact the cancer burden when implemented, research should be conducted in areas where evidence indicates that exposure will impact cancer burden.
- **Diversity criteria:** Recommendations should be diverse to ensure a comprehensive strategy.
- **Alignment with existing policy priorities:** Recommendations should take advantage of current/emergent trends, policies that may lend themselves to natural experiments.
- **Other criteria:** In the context of the identified priority areas greater weight should be given to those recommendations that have an impact on other diseases, have the potential to resonate with end users (including CCS and the public), and develop cancer prevention research capacity.

Additional criteria considered by McKinnon et al (2009) included the feasibility of research implementation, the impact of the research in general and in priority subpopulations, the impact of the research on health outcomes, the costs of the recommendations to society, and cost effectiveness of doing the research. Brownson et al. (2008) ranked research recommendations based on feasibility and importance.

Research Priorities

Research priorities identified in each article were organized according to the risk factors identified in the search strategy and cross-referenced with the dimensions and categories of the cancer risk and prevention cube (i.e., risk factors, research type and research focus). See Appendix D for operational definitions of the CCRA dimensions and categories (CCRA, 2010) and decision rules for categorizing research priorities.

The types of recommendations presented in the selected articles varied by article. In some articles the recommendations were specific and in others they were high level. When reporting on the numbers of research priorities in particular areas this should be kept in mind.

Research Type

Table 2 identifies the number of research priorities identified by CCRA research type category according to the main focus of each article. As seen in the table, the articles on obesity had the largest number of research priorities documented (n=148), followed by general cancer

prevention (n=65), occupational/environmental health (n=59), physical activity (n=27) and tobacco (n=17). As well, human research had the largest number of research priorities documented (n=160), followed by methodological measurements research (n=98) and research involving model systems (n=57). The number of research priorities identified in the selected articles could be an indicator of momentum in an area. They may also reflect different levels of granularity for research priorities, and/or different space constraints for articles. The main research priorities identified by CCRA research type are described below. General risk factor themes for each of the groupings of articles by research type are found in Appendix E.

Research Involving Model Systems

- For the general cancer prevention research article (NCIC, 2008) the broad areas for priorities identified in the article and the 4 workgroups include: developing biomarkers and intermediate end points, conducting molecular epidemiological studies, epidemiological studies of cancer, and investigations across all cancer sites.
- The Strategic Plan for NIH Obesity Research identified research priorities in several areas with priorities listed in each of these areas (2011). The NIH Strategic Plan (2011) identified 11 priorities related to biological mechanisms in regulating energy balance: specific roles of organs, tissues and molecules in the development of obesity, 12 priorities related to genes, epigenetics and critical periods in human development and 2 priorities related to the consequences of obesity.
- Milner (2003) suggested the following priorities: relationships of bioactive food components and genetic pathways linked with cancer, critical intake and duration to result in a physiological change in cancer incidence and tumor behaviour, temporal relationships between gene-nutrient interactions, information needed to examine the influence of genetic profiles, temporal effects of foods and components on gene expression patterns, and a better understanding of how bioactive food components may influence processes.
- McBride (2005) indicated that one priority would include conducting research related to understanding the human genome across time, settings, and populations to inform the discussion about what is genetic and what is social/environmental.
- In the environmental/occupational area, Miller (1995) identified the following priorities: to examine the available monitoring mechanisms to examine the impact aspirin has on cancer, research to understand when information is sufficient to justify reductions in exposure, research into alternatives to water chlorination, molecular biology studies to determine people most at risk for various cancers, study of cancer risks on those who have been exposed to particular contaminants. Carroquino (1998) also identified topics of interest with specific research priorities for each of the topics: studying biomarkers generally (and specific questions related to biomarkers were identified), research using animal models to assess toxicological differences between adults and children, and examination of developmental changes from gestation through to adulthood, and how these changes may affect susceptibility to cancer.

- Gritz et al. (2007) suggested that the characterization of nicotine dependence (e.g., genetic, brain mechanisms, biobehavioural, etc.) to develop improved strategies to reduce smoking initiation and prevalence is an important research priority.
- McTiernan (1999) recommended that a series of small clinical trials be conducted to measure exercise change effects on biomarkers to understand the risk/protective effect of exercise for cancer and as a feasibility study for a larger clinical trial.

Human Research

- Priorities identified by NCIC (2008) are broadly grouped into social determinants of health (and the understanding of underserved populations), environmental and occupational factors, and modifiable risk factors. The Modifiable Risk Factors workgroup identified several priorities including behavioural and epidemiological research to examine obesity, diet and physical activity interventions, understanding of diet supplementation and cancer risk (particularly through randomized control trials), understand the nature of the causal association between vitamin D and cancer risk, understand the cancer risk of exposure to pesticides and other toxins, and human studies of substances that may be suspected of causing cancer (NCIC, 2007a). The Intervention group identified the following priorities: facilitators and barriers to primary prevention in diverse communities, understanding of modifiable and non-modifiable factors with subgroups within the population expected to have differing cancer risks, risk factor interventions in underserved populations, and the cost effectiveness of interventions (NCIC, 2007b). The Clinical Medicine and Basic Biology work group identified three broad areas: optimization and effectiveness of prevention techniques such as screening for specific cancers or precancerous lesions, mechanisms and efficacy of chemopreventive agents and understanding the nature of physician-patient communication during a patient visit (factors that contribute to its success) (NCIC, 2007d).
- Three key areas were identified in the NIH Strategic Plan for Obesity Research (2011) including understanding the impact of SES on development of obesity (disparities), understanding the correlates, determinants and consequences of obesity, the consequences of obesity and the research to design and test interventions. McKinnon et al. (2009) identified priorities in the following areas: capacity development, agriculture and food supply, economic research, built environment and transportation, youth settings and education policies, media and marketing and economic research of incentives and disincentives.

Table 2: Number of Research Priorities Identified by CCRA Research Type

	Research Involving Model Systems	Human Research	Methodological/ Measurements Research	Knowledge Synthesis	Infrastructure	Dissemination	Funding	Overall
General (n=5)	4	18	16	0	15	2	10	65
Community-based research (n=1)	0	0	3	0	0	0	0	3
Obesity (n=2)	25	65	41	0	2	15	0	148
Nutrition (n=2)	6	3	5	0	0	0	1	15
Genomics (n=1)	1	8	4	0	0	0	0	13
Dissemination Communication (n=2)	0	8	2	0	0	5	0	15
Disparities (n=1)	0	0	3	0	3	0	1	7
Occupational/ Environment (n=3)	17	23	17	0	2	0	0	59
Tobacco (n=2)	1	16	0	0	0	0	0	17
Physical Activity (n=2)	3	15	6	0	2	0	1	27
Sun Safety (n=1)	0	4	1	0	1	1	0	7
Overall	57	160	98	0	25	23	13	376

- Carroquino (1998) specifically recommended priorities to understand dietary factors in infants that result in cancer and obesity, the impact of maternal nutrition on intermediate outcomes and cancer, understand factors that influence the exposure of the child especially during critical periods, exposure of the fetus during gestation and the impact of paternal exposure on outcomes in the child. Caruso et al. (2006) also recommended greater understanding of demanding work schedules, studying the impact of long work hours and outcomes in specific vulnerable populations. Unique priorities identified in Miller (1995) include the sociological determinants of smoking and how to intervene, determinants to get people to quit smoking, greater understanding of the determinants of heavy drinking on cancer risk, hazard surveillance and dissemination, extent to which identification and control of occupational carcinogens has reduced risk, and the risks and benefits of HRT, sunscreen, and various diets on risks of cancer and other outcomes.
- Cummings & Orleans (2009) identified research priorities in specific tobacco policy areas: tax and price policies (n=5 priorities), product regulation policies (n=5), policies to limit marketing (n=5), policies to assure counter marketing and public education campaigns (n=5), policies to expand clean indoor air laws and restrictions (n=4), and policies to increase demand for access to and use of evidence-based cessation techniques (n=5). Gritz et al. (2007) documented priorities in the area of lung cancer research, the impact of continued smoking on patients with smoking-related diseases, understanding the nature of nicotine addiction, and tobacco related illness prevention, prevention of initiation and cessation of tobacco-use.
- Research priorities identified by Brownson et al. (2008) were related to the following broad categories: population subgroups, schools and the community, transportation and recreational physical activity, community design, policy implementation, and economic evaluations. McTiernan (1999) suggested that cancers most likely to be related to physical activity from observational studies should be tested using an intervention and suggested conducting studies on individuals most at risk.
- The impact genomics may have on chronic disease prevention is unclear. McBride (2005) identified research priorities to help clarify the role of genomics for chronic disease prevention including the target group for genetic testing, the most effective methods to increase public skills for evaluating the contribution of genomics research, genomic risk stratification, and examining cost effectiveness of interventions.
- Kreuter et al. (2007) identified research priorities related to narrative forms of communication such as whether narrative communication is more effective than non-narrative forms of communication in delivering messages about cancer risks, specific questions about the impact on the message depending on the characteristics of the target audience and the person delivering the message, whether narrative forms of communication work when a comprehensive message is needed, and whether mechanisms of narrative communication work differently for individuals in different stages of the cancer continuum.

- Specific research priorities related to sun safety identified by the Skin Cancer Prevention Working Group (n.d.) include the evaluation of sun safety programs, the impact of messages in changing behaviour, the impact of vitamin D levels on skin cancer risk and the efficacy of an internet portal to disseminate information.
- Three priorities were identified by Lytle (2009) in the area of human studies: conduct pilot or effectiveness studies where the environment is manipulated to see the impact of the change; examine food purchasing behaviours, along with the physical environment and attitudes, perceptions about food prices and availability, and the influence of the environment on food choices.

Methodological/Measurements Research

- The Modifiable Risk Factors Group indicated that there is a need for: epidemiological population studies of those exposed to workplace carcinogens, and surveillance activities for conducting case-control studies to continue to identify occupational carcinogens (NCIC, 2007a). The Intervention group identified several methodological issues for study: broad participation (including diverse groups) for cohort studies with follow-up longer than one year, understanding of the factors that help and hinder success of an intervention (e.g., contribute to adherence, affect attrition rates, etc), collecting data on community settings using a validated measure (NCIC, 2007b). The Clinical Medicine and Basic Biology group indicated that accurate and validated risk prediction models are an important priority (NCIC, 2007d).
- Key methodological research identified in the environmental and occupational health articles include: increased use of biomarkers in qualitative and quantitative aspects of risk assessment and in the clinical setting, conducting more large epidemiologic studies, development of a national childhood cancer registry, and development of a national database for exposure data (Carroquino, 1998)⁵⁹. As well, Caruso et al. (2006) indicated the importance of better tracking of work schedules, and the importance of examining outcomes over long term. Miller (1995) reported the importance of surveillance of cohorts using linkages to cancer registries and National Death Index for end points, surveys linked to industrial hygiene measurements, methods development for data monitoring, improved efficiency in registration of cancer cases, research on impacts of immunization if products become available, and new tools for exposure assessment.
- In the obesity area, methodological research identified included the broad categories of: improvements in measurement tools, technology and methods (10 priorities listed), tools for bench to bedside translational research (3 priorities listed), Fitness and Functional status (5 priorities listed) and imaging (17 priorities listed) (NIH Strategic Plan for Obesity Research, 2011). McKinnon and colleagues (2009) indicated the importance of the continued development and refinement of valid and reliable (and sensitive and specific) dependent measures (e.g., diet, physical activity, etc.), and measures of policies and related environmental factors. As well, research needs to move past individual-

⁵⁹ It is recognized that in 2007, a major investment of CPAC was the CAREX database.

levels, and incorporate systems/structural changes to be effective. There is a need to further develop methods for natural experiments (i.e., naturally occurring variation in causes, determinants, interventions).

- The Skin Cancer Prevention Working Group (n.d.) indicated the importance of developing sun exposure measures to advance skin cancer prevention.
- Cummings and Orleans (2009) indicated the importance of examining the impact of quitting when taxes are raised in particular subgroups in the population. The Report of the Trans-HHS Cancer Health Disparities Progress Review Group (2004) recommended that there be an increase in funding for community based participatory research, that the impact of cancer is studied by race, ethnicity and SES group.
- Trickett et al., (2011) suggested that important methods research includes moving from intervention-centered models to context-centered interventions in the community, developing measures that are context-centered to examine community impact, clarifying the definition of capacity in diverse communities, identifying new research designs and paradigms to measure community, culture and collaboration, and taking advantage of natural experiments.
- Methods research for physical activity and nutrition areas included a focus on natural experiments, surveillance across clusters, qualitative and participatory methods (Brownson et al., 2008), testing one intervention on different populations, testing more than one intervention on a homogenous population, and using more than 1 marker of cancer risk to test the impact of exercise (McTiernan, 1999). Lytle (2009) recommended the importance of studying the psychometric properties of food environment measurement tools, research that compares different ways to evaluate the same environmental attributes, rigorous designs that limit threats to internal validity, calls for alternative designs to the RCT especially when community is the unit of analysis, advancing the science of measuring the behavioural and health effects of natural experiments, research into the analytical tools of ecological models, and multilevel modelling.
- McBride (2005) recommended methods research in natural experiments for genetic testing, examination of the perceptions of genetic testing in different subgroups, research into public education to improve study recruitment, and the evaluation of different approaches used to recruit and increase minority and the overall population for genetic studies.
- Bowen et al. (2009) recommended research that engages the community, assesses the context, needs, and resources and plans programs in response to those needs.

Knowledge Synthesis

- Research related to knowledge synthesis was not specifically highlighted by articles in any of the selected studies.

Infrastructure and Other Support

- NCIC (2008) recommended that cancer prevention research should be a high priority, that the Cancer Prevention Research Coordinating Committee could provide a vision for research within NCIC and across partners, that there be ongoing funding for the Centre for Epidemiologic Cancer Etiology and Prevention, and that partnerships and collaborations are developed to leverage support. Another recommendation was the importance of dissemination and implementation of cancer risk and prevention knowledge. With respect to funding, targeted funding with rapid response mechanisms was recommended, increased funding for capacity building and a stepwise increase in funding over five years for cancer prevention research.
- The working groups supported the broad recommendations listed in the NCIC report (2008). In addition the Modifiable Risk Factors Group indicated the importance of increasing awareness of ongoing grant competitions, to provide seed funds to bring together experts to prepare grants and networks, to identify appropriate criteria to evaluate the significance of population health research, and the creation of a pan-Canadian cancer cohort study. The Population-Level Group recommended enhancing partnerships with agencies involved in evaluating programs that address healthy lifestyles, the creation of a population level intervention grant (400,000 per year), supporting a data warehouse that pools available datasets to be managed by NCIC, and the fast track of a policy or program evaluation funding stream so that natural experiments can be funded. The Knowledge Exchange, Media and Policy Group indicated that the creation of the Media and Policy Research Network would help to advance the research priorities. The Clinical Medicine and Basic Biology Group indicated that the National Practice-Based Research Network might be a resource for the study of cancer prevention research strategies.
- The NIH Strategic Plan for Obesity (2011) identified the development of public-private partnerships to further research priorities, and priorities for dissemination and implementation research, translational research and training. The importance of partnership development between relevant research organizations was also mentioned in other articles (e.g., Skin Cancer Prevention Group, n.d.). Refining theories of dissemination research was also highlighted by Bowen et al. (2009).
- The Report of the Trans-HHS Cancer Health Disparities Progress Review Group (2004) recommended that partnerships be developed for the support and development of sustainable community-based networks for participatory research in areas of cancer disparities, conducting research in transdisciplinary settings, and

evaluating grants and contracts to identify the steps needed for greater cultural competence and inclusion of representation from subgroups of the population.

- Both in physical activity and nutrition areas, the importance of streamlining proposal generation and review to be able to study natural experiments were highlighted. As well, recognition of the value of using alternative study designs to the randomized control trial was mentioned (Lytle, 2009; Brownson et al., 2008).

Research Focus

Table 3 describes the number of research priorities identified by CCRA research focus category according to the main focus of each article. As seen in the table, the articles on obesity had the largest number of research priorities categorized using research focus (n=96), followed by occupational/environmental health (n=49), general cancer prevention (n=30), tobacco (n=30), and physical activity (n=23). As well, determinants that influence cause had the largest number of research priorities documented (n=90), followed by determinants that influence interventions (n=67), interventions (n=56) and causes (n=52). Some of the research priorities were not relevant for specific research focus categories and were categorized into an “other” category that is not reflected in Table 3. The main research priorities identified by CCRA research focus are described below. General risk factor themes for each of the groupings of articles by research focus are found in Appendix E.

Causes

- The NCIC article (2008) incorporated broad areas of study for specific research priorities such as biomarkers and intermediate end-points, modifiable risk factors and environmental/occupational factors that affect cancer. The working groups identified specific research priorities related to the causes of cancer such as the impact of Vitamin D on cancer, the role of genetic and environmental factors in cancer risk, recognition of the importance of molecular epidemiology in understanding cancer risk, the impact of pesticides and other environmental toxins on cancer, the impact of workplace carcinogens on cancer, and the importance of examining groups that may be at greatest risk of cancer.
- In the nutrition area, Milner (2003) reported several priorities: the importance of examining critical intake and duration required to bring about a physiological change in cancer incidence and duration, and a need for a better understanding of how bioactive food components may influence processes differently in normal and neoplastic conditions.

Table 3: Number of Research Priorities Identified by CCRA Research Focus

	Causes	Determinants that Influence Causes	Determinants that Influence Interventions	Interventions	Overall
General (n=5)	13	3	9	5	30
Community-based research (n=1)	0	0	0	0	0
Obesity (n=2)	5	52	15	24	96
Nutrition (n=2)	3	5	0	1	9
Genomics (n=1)	0	1	6	3	10
Dissemination Communication (n=2)	0	0	12	0	12
Disparities (n=1)	0	0	0	1	1
Occupational/ Environmental (n=3)	27	11	5	6	49
Tobacco (n=2)	1	11	14	4	30
Physical Activity (n=2)	2	7	6	8	23
Sun Safety (n=1)	1	0	0	4	5
Overall	52	90	67	56	265

- Caruso et al. (2006) indicated the importance of understanding how sleep, work recovery and other factors influence cancer risk. Miller (1995) identified the following priorities: to examine the available monitoring mechanisms to examine the impact aspirin has on cancer, research to understand when information is sufficient to justify reductions in exposure, molecular biology studies to determine people most at risk for various cancers, study of cancer risks on those who have been exposed to particular contaminants. Carroquino (1998) also identified topics of interest with specific research priorities for each of the topics: studying biomarkers to understand cancer impact (and specific questions related to biomarkers were identified), research using animal models to assess toxicological differences between adults and children and how that may influence cancer risk, and examination of developmental changes from gestation through to adulthood, and how these changes may result in susceptibility to cancer.
- McTiernan (1999) identified one research priority to determine cancers associated with physical inactivity from observational data.

Determinants that Influence the Causes

- NCIC (2008) identified the broad category of the social determinants of health including research priorities related to underserved populations. The Population-Level working group further recommended the importance of understanding facilitators and barriers to primary prevention in diverse populations, researching how to study community characteristics to understand behavioural variability at the community level. The Clinical Medicine, Basic Biology and Individual Level Interventions Group indicated the importance of understanding the nature of communication in the clinical encounter in order to reduce cancer risks.
- In the obesity area, research priorities were identified in the broad categories of biological mechanisms regulating energy balance: the specific roles of organs, tissues and molecules in the development of obesity, health disparities and the correlates, determinants and consequences of obesity (NIH Strategic Plan for Obesity Research, 2011). McKinnon and colleagues (2009) identified the following specific priorities: understanding the effects of subsidies for agricultural commodities on supply and prices, and resulting effects on population-level eating patterns, the costs to individuals of making behaviour changes recommended for obesity prevention, food pricing and its influence on food consumption, the effects of taxes or financial incentives to encourage healthy food choices at both the macro and micro levels, in addition to community design and its impact on energy-balance behaviours including zoning policies.
- In the tobacco area, Cummings and Orleans (2009) identified determinants of causes research priorities in broad categories including tax and price policies (n=6), product regulation policies (n=3), policies to assure effective counter-marketing and public education campaigns (n=3) and policies to expand clean indoor air laws and restrictions. Gritz et al. (2007) recommended that research be conducted to characterize nicotine

dependence so that strategies to reduce smoking initiation and prevalence can be developed particularly in high-risk and underserved groups targeted by the tobacco industry.

- In the environmental area, Miller (1995) recommended that the sociological determinants of smoking continue to be studied, that research is conducted to influence the determinants of drinking, the determinants of heavy drinking, factors that impact healthy eating, and cancer risks of particular groups such as risks associated with a particular occupation. Caruso et al (2006) recommended that long work hours and outcomes be examined in greater detail to understand the impact of other variables.
- Brownson et al (2008) recommended that population subgroups be studied to understand barriers and facilitators to doing physical activity be explored (in community design, urban settings, etc.), and the impact perceptions of safety have on physical activity.
- Lytle (2009) recommended the following priorities: the importance of conducting pilot or effectiveness studies where the environment is manipulated to see the impact of the change; examine food purchasing behaviours, along with the physical environment and attitudes, perceptions about food prices and availability, and the influence of the environment on food choices.

Determinants that Influence Interventions

- The Population-Level Group recommended that factors that result in intervention success/adherence or attrition be studied particularly in underserved populations (NCIC, 2007).
- McKinnon et al. (2009) recommended research into effective methods of communicating diet and physical activity information to the general population to reduce obesity. The Strategic Plan for NIH Obesity Research (2011) identified 13 research priorities related to determinants of interventions such as exploring how values, motives, and behaviours from non-health areas may change obesity related behaviours (e.g., how concerns about the environment may increase active transportation), and ways to enhance adherence to behaviours recommended in weight-control programs, such as self-monitoring behaviours, increased physical activity, and reduction in caloric intake.
- Bowen et al. (2009) recommended the following determinants that influence interventions: understanding characteristics of the innovation/intervention, questions related to timing such as motivations tailored to the adopter characteristics at different stages over time, and understanding the process of adapting an intervention such as scalability and sustainability of interventions.
- Kreuter et al. (2007) recommended the following research priorities: understanding whether narrative communication is more effective than non-narrative communication

for overcoming resistance and facilitating information processing, determine how narrative communication can be more effectively used, understanding how the perception of the message is affected by the person/organization delivering it, the impact of various characteristics of the sender and receiver of the message.

Interventions

- NCIC (2008) indicated that interventions related to obesity, physical activity and diet were priority areas for consideration, in addition to interventions of underserved populations.
- The Strategic Plan for NIH Obesity Research (2011) recommended the following interventions for research: bariatric surgery compared to behavioural or pharmacological approaches among adolescents and adults, the use of medications and weight management interventions. McKinnon et al. (2009) recommended the importance of evaluating the impact of school policies and environments on outcomes of interest.
- McTiernan (1999) recommended conducting a series of clinical trials to measure exercise change effects on biomarkers to learn about exercise behaviour change in individuals at high risk for cancer.
- The Skin Cancer Prevention Working Group (n.d.) identified the importance of skin cancer prevention and evaluation programs such as the impact of an internet portal for skin cancer prevention information.
- Brownson et al. (2008) recommended intervention research into assessing the impact of walk to school programs on physical activity among youth, impact of having schools open to community outside of regular school hours on physical activity, impact of daily physical education or activity on attendance and academic achievement, and determining if mixed-use development increases walking and biking. McTiernan (1999) recommended that intervention studies should be designed to test exercise effects on more than one marker for cancer risk, and to test various exercise interventions on similar populations and single interventions on diverse populations.

IMPLICATIONS FOR A PREVENTION RESEARCH AGENDA

This synthesis is one source to inform a cancer prevention research agenda for Canada. How the synthesis is used will depend on some parameters for the overall research agenda (e.g., strategic goals, accountability, criteria for selecting research priorities). The reciprocal is also possible; that the synthesis may help to inform some of these parameters.

In this section, we list a few parameters that may be considered in the overall framing and positioning of the CCRA research strategy. While these possible parameters go beyond the specific scope of this synthesis, they will influence how the results of the synthesis are used.

Parameters to Consider for the CCRA Prevention Research Agenda

With very few exceptions, parameters or a framework guiding the development of research priorities was not included in the articles included in the synthesis. Parameters might include:

- Audience for the research priorities – whose activities are to be informed by the research priorities?
- Positioning in relation to other research priorities – will CCRA reinforce research priorities identified by other leading organizations? Or will members establish a niche for CCRA that is complementary to other research priorities?
- Criteria for selecting research priorities – what criteria will be included and what emphasis will be given to each criterion?
- Perspectives included in the priority setting process – to what extent will policy and program leaders be involved in setting research priorities? What will be the role of researchers? What emphasis will be given to different perspectives?
- Scope of the research priorities – what will be the breadth and depth of topic areas and types of research?
- Time period for the research priorities and any planned renewal of priorities over time – at what intervals will research priorities be reviewed and updated? Who will have responsibility for this review and renewal process?
- Indicators of success for the prevention research agenda – what will demonstrate the CCRA prevention research agenda has been a success in the short- and the long-term?

Little guidance was offered by this synthesis on the above elements of a research priority-setting framework. For example, only three of the articles identified criteria that were used in developing research priorities. And although several articles described membership on working groups tasked with setting research priorities, none of the descriptions mentioned the relative emphasis given to different perspectives.

Articles were also silent on plans for updating research priorities. In the rapidly evolving area of cancer prevention, this is particularly important. For example, in the next six months the U.S. National Cancer Institute is releasing a series of papers referred to as research gaps in policy measures of the framework convention on tobacco control (D. Hammond, personal communication, September 22, 2011). Given that research priorities are constantly evolving and moving ahead, updating the research agenda on a regular basis might be an important consideration.

Research Priorities

The synthesis revealed a very wide-range of cancer prevention research priorities, including areas that are well-established and others that are in their infancy. The detailed results appear in the previous section (3.0) and in the data extraction spreadsheet. In this section, we provide a few observations that examine similarities and differences across research focus, research type and risk factor.

- From the selected articles, the number of obesity research priorities far exceeded other research topics. Research priorities for general cancer prevention research, and environmental/occupational health were a distant second according to the number of research priorities in research type and research focus respectively. This may reflect varying degrees of momentum in different research areas. It might also mostly be a result of the types of articles in the synthesis. For example, both the NIH Strategic Plan and the NCIC Cancer Prevention Initiative Strategy and Working Group Reports were not peer reviewed journal articles and were not limited by space constraints. In developing the research agenda, caution should be taken in comparing the number of research priorities identified in one article to the number identified in another.
- Most research priorities were determinants that influence causes. Fewest priorities were related to causes of cancer. This may also be partially a reflection of the articles included in the knowledge synthesis. The research priorities in the obesity articles often used obesity as an outcome and not cancer which was required to be considered a cause according to CCRA's definition of cause.
- Research priorities for knowledge synthesis, dissemination / communication, and community-based research appear under-developed. Fewer research priorities in these areas may also be a reflection that research priorities in these topic areas are not easily classified into CCRA's analytical framework of risk factors, research type and focus. For example, research priorities identified by Trickett et al. (2011) could not be classified into the research focus categories and were all categorized as "other". Furthermore, priorities for knowledge syntheses may emerge once specific research initiatives are underway.
- Reviewed articles included Canadian content to the extent possible (CCRA, 2010, NCIC, 2008, NCIC, 2007a, NCIC 2007b, NCIC, 2007c, NCIC, 2007d, Miller, 1995). In most cases, research priorities are applicable in a variety of settings (e.g., in both the United States and in Canada). However, caution should be taken in applying research priorities to the Canadian setting in some cases. For example, the article by Cummings and Orleans (2009) was focused on tobacco policy research priorities. While many of the specific research priorities are likely applicable in both the United States and Canada, some may not be relevant in the Canadian policy context.
- *Natural experiments*: These were recommended across research areas, focus and type. Funding mechanisms may need to be flexible with fairly quick turnaround in order to be responsive to the opportunities afforded by naturally occurring variation in environments or other conditions.
- *Cancer disparities*: Examining cancer disparities in different subgroups was identified in many articles and seen as a cross-cutting theme for consideration in the research agenda.
- *Methodologies*: A common emphasis was on ensuring measures are psychometrically sound (reliable, valid, specific and sensitive to change), particularly those used for surveillance purposes. The importance of surveillance of risk factors using these valid and reliable measures was also recommended. With respect to researcher controlled interventions, the importance of internal validity, and cohort studies was mentioned across research type and in the interventions section. Another theme that was highlighted across research type and research focus was encouraging alternatives to

randomized trials that focus on a plurality of methods and developing a context-sensitive science of prevention.

- *Study of biomarkers*: The development, study, validation and use of biomarkers for examining intermediate end-points and outcomes was recommended for use in qualitative and quantitative risk assessments, across research type, research focus, and as a focus for methodological research, in particular.
- *Molecular epidemiology*: This theme emerged particularly in the area of research involving model systems, infrastructure and the research focus of causes.

These observations are a modest start to what may be gleaned from the detailed data extraction spreadsheet. Some decisions about the parameters or framework for the CCRA prevention research agenda will help to discern which findings are most relevant and at what time.

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Report of the Trans-HHS Cancer Health Disparities Progress Review Group (2004). Making Cancer Health Disparities History. Submitted to the Secretary, U.S. Department of Health and Human Services. Retrieved from: <http://www.hhs.gov/chdprg/pdf/chdprg.pdf>. Accessed August 2011.

Skin Cancer Prevention Working Group. (2007). *Under the Queensland Sun*, the Queensland Skin Cancer Prevention Strategic Plan 2008 – 2013.

Strategic Plan for NIH Obesity Research. A Report of the NIH Obesity Research Task Force. 2011. U.S. Department of Health and Human Services. National Institutes of Health. Report no. 11-5493.

Trickett, E. J., Beehler, S., Deutsch, C., Green, L.W., Hawe, P., McLeroy, K., Miller, R.L., Rapkin, B.D., Schensul, J.J., Schulz, A.J., and Trimble, J.E. (2011). Advancing the Science of CommunityLevel Interventions. *American Journal of Public Health*, 101, 1410–1419.

Appendix A: Initial Searches Conducted

<p>Strategy #1:</p> <p>1) cancer OR Neoplasms[MeSH] OR “chronic disease” OR “chronic diseases” OR Chronic Disease[MeSH] AND</p> <p>2) prevent OR prevention OR prevents AND</p> <p>3) research OR Research[MeSH] AND</p> <p>4) framework OR frameworks OR strategy OR strategies OR recommend*</p> <p>Total: 10,989</p>	<p>Strategy #2</p> <p>1) cancer AND prevention AND 3 AND 4</p> <p>OR</p> <p>2) Neoplasms/prevention and control [MeSH] AND 3 AND 4</p> <p>OR</p> <p>3) chronic disease prevention AND 3 AND 4</p> <p>Total: 10,596</p>
<p>Strategy #3</p> <p>1 AND prevention research AND 4</p> <p>Total: 9,466</p>	<p>Strategy #4</p> <p>(cancer OR “chronic disease”) AND prevention research framework = 578 OR</p> <p>(cancer OR “chronic disease”) AND prevention strategy = 4,515 OR</p> <p>(cancer OR “chronic disease”) AND prevention recommendations =2,796</p> <p>Total: 6,997</p>

The searches completed in the tables listed show the initial searches conducted with high yields.

Appendix B: Search Terms Used for Article Selection

<p>Scopus Search:</p> <p>cancer OR “chronic disease”</p> <p>AND prevention AND research</p> <p>AND framework* OR strategy OR recommendation*</p> <p>Total : 997</p>	<p>PubMed Search:</p> <p>1) cancer prevention research framework</p> <p>Total : 444</p> <p>2) Related articles search of those determined to be most relevant</p> <p>Total: 407</p>
<p>Searches for specific risk factors:</p> <ul style="list-style-type: none"> - completed in PubMed (yield in Scopus not as promising) - included the following key terms: alcohol, tobacco, smoking, physical activity, nutrition, diet, healthy eating, obesity, healthy weights, unhealthy weights, clinical prevention, viral HPV, viral HBV, sun safety, sun exposure, occupational exposure, environmental exposure <p>Total: 281</p>	

Appendix C: Additional Articles for Consideration in Developing the Research Agenda

High level research frameworks

A report of an Expert Group. (2004). Research in the behavioural and social sciences to improve cancer control and care: a strategy for development. *European Journal of Cancer*, 40, 316–325.

Best, A., Hiatt, R.A., Cameron, R., Rimer, B.K., and Abrams, D.B. (2003). The Evolution of Cancer Control Research: An International Perspective from Canada and the United States. *Cancer Epidemiology, Biomarkers & Prevention*, 12, 705–712.

Emmons, K.M. (2000). A research agenda for tobacco control. *Cancer Causes and Control*, 11, 193-194.

Engstrom, P.F. (1999). A New Era for Cancer Prevention and Control Research. *Cancer Epidemiology, Biomarkers & Prevention*, 8, 955–956.

Hiatt and Rimer. (1999). A new strategy for Cancer Control Research. *Cancer, Epidemiology, Biomarkers and Prevention*, 8: 957-964.

Related to process rather than research priorities

Hawk, E.T., Greenwood, A., Gritz, E.R., McTiernan, A., Sellers, T., Hursting, S.D., Leishow, S and Grad, O. for the Translational Research Working Group. (2008). The Translational Research Working Group Developmental Pathway for Lifestyle Alterations. *Clinical Cancer Research*, 14(18), 5707-5713.

O’Fallon, L.R., Wolfe, G.M., Brown, D. Dearry, A. and Olden, K. (2003). Strategies for Setting a National Research Agenda That Is Responsive to Community Needs. *Environmental Health Perspectives*, 111, 1855–1860.

Editorial article focused on research designs more than research priorities

Prentice, R.L. (2004). Chronic disease prevention: public health potential and research needs. *Statistics in Medicine*, 23, 3409–3420.

More specific agenda referred to in this article that was selected

Krieger, N., Emmons, K.M., Burns White, K. (2005). Cancer disparities: developing a multidisciplinary research agenda – preface. *Cancer Causes and Control*, 16, 1–3.

McKinnon, R.A., Reedy, J., Handy, S.L., Brown Rodgers, A. (2009). Measuring the Food and Physical Activity Environments Shaping the Research Agenda. *American Journal of Preventive Medicine*, 36(4S), S81-S85.

Go, V.L.W., Butrum, R.R., Wong, D.A. (2003). Diet, Nutrition, and Cancer Prevention: The Postgenomic Era. *The Journal of Nutrition*, 133, 3830S–3836S.

More recent agenda selected from/instead of this article

Katzmarzyk PT, Baur LA, Blair SN, Lambert EV, Oppert JM, Riddoch C. (2008). Expert panel report from the International Conference on Physical Activity and Obesity in Children, 24-27

June 2007, Toronto, Ontario: summary statement and recommendations. *Applied Physiology, Nutrition, and Metabolism*, 33(2), 371-388.

National Cancer Institute. (1998). Tobacco research implementation plan: priorities for tobacco research beyond the year 2000. Tobacco Research Implementation Group, National Cancer Institute, National Institutes of Health.

Owen, N., Humpel, N., Leslie, E., Bauman, A., and Sallis, J.S. (2004). Understanding Environmental Influences on Walking Review and Research Agenda. *American Journal of Preventive Medicine*, 27(1), 67–76.

Prentice RL, Willett WC, Greenwald P, Alberts D, Bernstein L, Boyd NF, Byers T, Clinton SK, Fraser G, Freedman L, Hunter D, Kipnis V, Kolonel LN, Kristal BS, Kristal A, Lampe JW, McTiernan A, Milner J, Patterson RE, Potter JD, Riboli E, Schatzkin A, Yates A, Yetley E. (2004). Nutrition and physical activity and chronic disease prevention: research strategies and recommendations. *Journal of the National Cancer Institute*, 96, 1276–87.

Spiegel, A.M. and Alving, B.M. (2005). Executive summary of the Strategic Plan for National Institutes of Health Obesity Research. *American Journal of Clinical Nutrition*, 82(2), 211S-214S.

Did not identify prevention research priorities (specific)

Herberman, R.B., Pearce, H.L., Lippman, S.M., Pyenson, B.S., and Alberts, D.S. (2006). Cancer chemoprevention and cancer preventive vaccines--a call to action: leaders of diverse stakeholder groups present strategies for overcoming multiple barriers to meet an urgent need. *Cancer Research*, 66, 11540-11549.

Khoury, M.J. and Mensah, G.A. (2005). Genomics and the prevention and control of common chronic diseases: emerging priorities for public health action. *Preventing Chronic Disease Public Health Research, Practice and Policy*, 2(2), 1-8.

Lioy, P.J. (2010). Exposure Science: A View of the Past and Milestones for the Future. *Environmental Health Perspectives*, 118, 1081–1090.

National Coordination Component of the Canadian Diabetes Strategy (2003). Draft Blueprint for Action for the National Diabetes Strategy.

National Lung Health Framework (2008). Retrieved from: www.lunghealthframework.ca.

O’Callaghan, T. (2011). The prevention agenda. *Nature*, 471, S2-S4.

Articles related to conducting research in low to middle income countries

Baris, E., Brigden, L.W., Prindiville, J., Silva, V.L.e.S., Chitanondh, H., and Chandiwana, S. (2000). Research priorities for tobacco control in developing countries: a regional approach to a global consultative process. *Tobacco Control* 9:217–223

Bousquet, J., Kiley, J., Bateman, E. D., Viegi, G., Cruz, A. A., Khaltaev, N. et al. (2010). Prioritised research agenda for prevention and control of chronic respiratory diseases *The European*

Respiratory Journal : Official Journal of the European Society for Clinical Respiratory Physiology, 36(5), 995-1001.

Mendis S, Alwan A, eds. (2011) Prioritized research agenda for prevention and control of noncommunicable diseases. Geneva, World Health Organization.

Appendix D: Dimensions and Categories of the Cancer Risk and Prevention Cube

RESEARCH FOCUS	Definition	Example
Causes	Research that attempts to identify causes of cancer, factors associated with cancer risks, and possible mechanisms/modulators involved in carcinogenesis	<ul style="list-style-type: none"> • <i>Urinary tract infections and other risk factors for bladder cancer</i> • <i>Mechanisms of Kaposi's Sarcoma-associated herpes virus pathogenesis</i>
Determinants that Influence Causes	Research on attitudes, behaviours, and genetic and societal factors that may influence adoption and maintenance of behaviours involved in cancer causation and risk reduction.	<ul style="list-style-type: none"> • <i>Exploring the psychosocial influences of smoking mothers on daughters' tobacco use</i>
Determinants that Influence Interventions	Research on factors that may influence the efficacy of risk reduction and cancer prevention strategies	<ul style="list-style-type: none"> • <i>Assessing the longitudinal patterns and determinants of chronic disease prevention capacity in the Canadian public health system</i>
Interventions	<p>Research that seeks to identify, develop, and test/evaluate interventions that may prevent cancer. Interventions include:</p> <ul style="list-style-type: none"> • behavioural change approaches (e.g., smoking cessation, obesity control) • social, environmental, and regulatory changes (e.g., mass media campaigns, smoking bylaws) • agents/drugs, nutraceuticals, and vaccines • prophylactic surgery • screening for precursor lesions/causal viruses 	<ul style="list-style-type: none"> • <i>Effects of exercise and caloric restriction on biomarkers of cancer risk: a randomized controlled trial</i> • <i>Prophylactic salpingo-oophorectomy in women who carry a BRCA1 or BRCA2 mutation</i> • <i>The impact of a 100% smoke-free bylaw on exposures to environmental tobacco smoke in non-smoking Toronto bar workers</i>

RISK FACTOR	Definition	Example
Activity Level, Body Composition & Metabolism	Research that focuses on elucidating the role of adiposity, activity level, and metabolism on cancer risk. Research on metabolic syndrome/insulin resistance is incorporated under this factor.	<ul style="list-style-type: none"> • <i>Immune mechanisms in physical activity and cancer</i>
Alcohol	Research that undertakes to clarify the role of alcohol consumption on cancer risk. Research on factors that may influence alcohol use and alcohol dependence is also included under this factor.	<ul style="list-style-type: none"> • <i>Alcohol as an apoptotic trigger in head and neck cancers</i>
Contaminants in the Air, Water & Soil	Research that attempts to identify the cancer risks and mechanisms of carcinogenesis associated with contaminants found in the general environment, such as radiation (ionizing (both natural and man-made sources), non-ionizing, and solar radiation). Radiation exposure resulting from the work environment, however, can be found under Occupational Exposures and radiation exposure from diagnostic tests is included Treatments/Diagnostics. Projects on endocrine disrupters are located under Hormones.	<ul style="list-style-type: none"> • <i>Exposure to air pollutants and the incidence of lung cancer</i> • <i>Molecular mechanisms of solar mutagenesis</i>
Diet & Nutrition	Research that explores the relationship between dietary patterns and cancer, the effects of specific dietary nutrients on reducing/increasing cancer incidence, determinants of dietary behaviour, and the relationship between food preparation methods and cancer risk. This research can be distinguished from Activity Level, Body Composition & Metabolism by its emphasis on food/ nutrients.	<ul style="list-style-type: none"> • <i>Fruits and vegetables and ovarian cancer risk: a pooled analysis</i>
Ethnicity, Sex & Social Environment	Research that focuses on elucidating the role of demographic, cultural, and socio-economic factors on cancer risk.	<ul style="list-style-type: none"> • <i>Health risk behaviours and socio-economic status: explaining the social gradient in health</i>
Gene-environment Interactions	Research that aims to identify what and how genetic factors and lifestyle and/ or environmental factors interact to influence cancer risk.	<ul style="list-style-type: none"> • <i>Gene-environment interactions in post-menopausal breast cancer: a case-control study</i>
Genetic Susceptibilities	Research whose intent is to define the role of genes (familial and polymorphisms/sporadic mutations) on cancer risk. Research on genetic testing/ counselling is also included under this factor.	<ul style="list-style-type: none"> • <i>Contribution of known and suspected cancer susceptibility genes in high-risk breast and/or ovarian cancer families of French Canadian descent</i>
Hormones	Research that explores the role of exogenous and endogenous hormones on cancer causation and cancer prevention. Exogenous hormones include hormone replacement therapies, oral contraceptives, phytoestrogens (from dietary sources), and endocrine disrupters from environmental sources. Endogenous hormones refer to a person's own levels of sex steroid hormones and corticosteroid hormones. Research on insulin and the insulin-like growth factor can be found under Activity Level, Body Composition & Metabolism.	<ul style="list-style-type: none"> • <i>Reducing breast cancer risk factors by molecular engineering: The redesign of hormonal supplements • High androgen/low progesterone exposures and ovarian cancer • Endocrine disrupting chemicals (EDCs), pituitary hormones, and estrogen metabolizing enzymes as modifiers of breast cancer susceptibility</i>

Infectious Agents	Research that examines viral and bacterial infections and their role in cancer risk. Research on the prevention and treatment of viruses and infections that cause cancer is also included under this factor.	<ul style="list-style-type: none"> • <i>Inuit women's understanding of human papillomavirus: implications for health education and prevention in Nunavik, Québec</i>
Occupational Exposures	Research that endeavours to identify the cancer risks associated with exposures in the workplace.	<ul style="list-style-type: none"> • <i>Occupational histories of breast cancer patients</i>
Physiological Susceptibilities	Research on health conditions or physical attributes that may be associated with cancer risk.	<ul style="list-style-type: none"> • <i>Does Systemic Lupus Erythematosus increase the risk of malignancy? An international multi-site retrospective cohort study</i>
Precursor Lesions	Research that focuses on precursor stages of invasive cancer (such as polyps, DCIS). Projects on the treatment of DCIS that are intended to inform breast cancer treatment are excluded.	<ul style="list-style-type: none"> • <i>Community screening of and intervention in high-risk oral premalignant lesions</i>
Tobacco	Research that examines the carcinogenic effects of tobacco, determinants of tobacco use, pharmacokinetics of nicotine/nicotine dependence, industry strategies, and tobacco reduction/control strategies.	<ul style="list-style-type: none"> • <i>The neurobiological substrates of the motivational effects of nicotine in dependent and withdrawn mice</i> • <i>Revealing tobacco industry secret science and using it to improve public health</i>
Treatments/Diagnostics	Research that explores the cancer risk associated with drugs and other medical treatments and diagnostic tests (including tests involving radiation exposure). Research studies on the risks associated with radiation treatment of cancer patients are excluded.	<ul style="list-style-type: none"> • <i>Effects of warfarin on the risk of urogenital cancer</i> • <i>Cancer risk following radiation exposure from computed tomography in children and adolescents</i>
Multiple/General	Studies that consider a broad range of factors and their relationship to cancer. Research on cancer prevention not aimed at specific risk factors is also included under this factor.	<ul style="list-style-type: none"> • <i>Multiple chronic disease behavioural risk factors in Canadian children and adolescents: An investigation of individual level and environmental level determinants</i> • <i>Survey of physician attitude toward cancer prevention</i>

RESEARCH TYPE	Definition	Example
Research Involving Model Systems	Research directed at elucidating mechanisms of known risk factors used to corroborate observational research. It encompasses in vitro studies, animal model research, other laboratory studies, and nutritional science studies. This research is often used as a precursor to interventional studies in humans to provide evidence of biological plausibility.	<ul style="list-style-type: none"> • <i>Investigating the genotoxic effects of in utero benzene exposure on bone marrow cells of young mice</i>
Human Research	Research on humans (in vivo), that includes descriptive research, ecological and migrant studies, case-control and cohort studies, and intervention studies and trials. Human research with a laboratory component that involves analysis of blood, saliva, and/or tissue samples is also included under this research type.	<ul style="list-style-type: none"> • <i>Case study observations of consumption of antioxidants and risk of lung cancer among Montrealers</i>
Methodological/Measurements Research	Research studies that focus on improving data capture and analysis in future laboratory and human research studies. Included are: <ul style="list-style-type: none"> • methods development, research on statistical approaches and methods to enhance the measurement of outcomes, endpoints, and variables of interest • exposures measurement, research on the physical measurement of one or more substances/exposures within a specified environment • surveillance, research on identifying the frequency/incidence of risk behaviour(s) in a specified population 	<ul style="list-style-type: none"> • <i>Development and validation of new statistical methods for modelling intermediate events in survival analysis</i> • <i>Comparing methods of obtaining exposure data in epidemiological studies involving children and pregnant women</i> • <i>The British Columbia Adolescent Substance Use Survey</i>
Knowledge Synthesis	Literature reviews, and policy, ethics and legal analyses, and other qualitative research studies that are intended to identify research gaps, inform decision makers, and/or influence the adoption of interventions.	<ul style="list-style-type: none"> • <i>A knowledge synthesis of tobacco cessation continuing education programs for dental hygienists</i>
Infrastructure & Other Support	Funding for: <ul style="list-style-type: none"> • equipment/infrastructure needed to conduct cancer risk and prevention research • capacity building–training programs and/or network support, the intent of which is to impart and build on knowledge and skills within a specified area or community • knowledge dissemination–support for workshops, conferences, symposia, and travel awards for trainees and researchers to attend these events • letters of intent, which offset researchers' time to develop proposals of prospective research projects 	<ul style="list-style-type: none"> • <i>Infrastructure to support a research program on the early determinants of adult chronic disease</i> • <i>A pan-Canadian resource network for tobacco research policy and practice</i> • <i>2nd International Francophone Conference on Tobacco Control– Paris, France: "Lessons learned in Canada about health warnings on cigarette packages"</i>

Appendix E: Risk Factor Theme Identified for Research Type and Research Focus Research Priorities

Table 4: Research Priorities Identified by CCRA Research Type with Risk Factor Themes Listed

	Research Involving Model Systems	Human Research	Methodological/ Measurements Research	Knowledge Synthesis	Infrastructure	Dissemination	Funding	Overall
General (n=5)	4 Activity Level, Body Composition & Metabolism; Diet & Nutrition; Gene-environment Interactions; Infectious Agents; Precursor Lesions; Multiple/General	18 Activity Level, Body Composition & Metabolism; Contaminants in the Air, Water & Soil; Ethnicity, Sex & Social Environment; Occupational Exposures; Precursor Lesions; Tobacco; Multiple/General	16 Contaminants in the Air, Water & Soil; Ethnicity, Sex & Social Environment; Occupational Exposures; Multiple/General	0	15 Activity Level, Body Composition & Metabolism; Diet & Nutrition; Multiple/General	2 Multiple/General	10 Multiple/General	65
Community-based research (n=1)	0	0	3 Multiple/General	0	0	0	0	3
Obesity (n=2)	25 Activity Level, Body Composition & Metabolism; Diet & Nutrition	65 Activity Level, Body Composition & Metabolism; Diet & Nutrition	41 Activity Level, Body Composition & Metabolism; Diet & Nutrition; Ethnicity, Sex & Social Environment	0	2 Activity Level, Body Composition & Metabolism; Diet & Nutrition	15 Activity Level, Body Composition & Metabolism; Diet & Nutrition	0	148
Nutrition (n=2)	6 Gene-environment Interactions	3 Diet & Nutrition	5 Diet & Nutrition; Gene-environment Interactions	0	0	0	1 Multiple/General	15
Genomics (n=1)	1 Ethnicity, Sex & Social Environment; Genetic Susceptibilities	8 Genetic Susceptibilities	4 Ethnicity, Sex & Social Environment; Genetic Susceptibilities	0	0	0	0	13
Dissemination Communication (n=2)	0	8 Multiple/General	2 Multiple/General	0	0	5 Multiple/General	0	15

	Research Involving Model Systems	Human Research	Methodological/Measurements Research	Knowledge Synthesis	Infrastructure	Dissemination	Funding	Overall
Disparities (n=1)	0	0	3 Ethnicity, Sex & Social Environment	0	3 Ethnicity, Sex & Social Environment	0	1 Ethnicity, Sex & Social Environment	7
Occupational/Environment (n=3)	17 Contaminants in the Air, Water & Soil; Infectious Agents; Occupational Exposures; Treatments/Diagnostics; Multiple/General	23 Alcohol; Contaminants in the Air, Water & Soil; Ethnicity, Sex & Social Environment; Hormones; Occupational Exposures; Tobacco; Multiple/General	17 Contaminants in the Air, Water & Soil; Infectious Agents; Occupational Exposures; Multiple/General	0	2 Multiple/General	0	0	59
Tobacco (n=2)	1 Tobacco	16 Ethnicity, Sex & Social Environment; Tobacco	0	0	0	0	0	17
Physical Activity (n=2)	3 Activity Level, Body Composition & Metabolism	15 Activity Level, Body Composition & Metabolism; Ethnicity, Sex & Social Environment	6 Activity Level, Body Composition & Metabolism	0	2 Activity Level, Body Composition & Metabolism	0	1 Activity Level, Body Composition & Metabolism; Multiple/General	27
Sun Safety (n=1)	0	4 Contaminants in the Air, Water & Soil	1 Contaminants in the Air, Water & Soil	0	1 Contaminants in the Air, Water & Soil	1 Contaminants in the Air, Water & Soil	0	7
Overall	57	160	98	0	25	23	13	376

Table 5: Number of Research Priorities Identified by CCRA Research Focus with Risk Factor Themes Listed

	Causes	Determinants that Influence Causes	Determinants that Influence Interventions	Interventions	Overall
General (n=5)	13 Activity Level, Body Composition & Metabolism; Contaminants in the Air, Water & Soil; Diet & Nutrition; Gene-environment Interactions; Hormones; Infectious Agents; Occupational Exposures; Precursor Lesions; Tobacco; Multiple/General	3 Ethnicity, Sex & Social Environment; Multiple/General	9 Ethnicity, Sex & Social Environment; Multiple/General	5 Activity Level, Body Composition & Metabolism; Diet & Nutrition; Infectious Agents; Precursor Lesions; Multiple/General	30
Community-based research (n=1)	0	0	0	0	0
Obesity (n=2)	5 Activity Level, Body Composition & Metabolism; Diet & Nutrition; Ethnicity, Sex & Social Environment	52 Activity Level, Body Composition & Metabolism; Diet & Nutrition; Ethnicity, Sex & Social Environment	15 Activity Level, Body Composition & Metabolism; Diet & Nutrition	24 Activity Level, Body Composition & Metabolism; Diet & Nutrition	96
Nutrition (n=2)	3 Diet & Nutrition; Gene-environment Interactions	5 Diet & Nutrition; Gene-environment Interactions	0	1 Diet & Nutrition	9
Genomics (n=1)	0	1 Ethnicity, Sex & Social Environment; Genetic Susceptibilities	6 Genetic Susceptibilities	3 Genetic Susceptibilities	10
Dissemination Communication (n=2)	0	0	12 Multiple/General	0	12
Disparities (n=1)	0	0	0	1 Multiple/General	1
Occupational/ Environmental (n=3)	27 Contaminants in the Air, Water & Soil; Diet & Nutrition; Gene-environment Interactions; Infectious Agents; Occupational Exposures	11 Alcohol; Contaminants in the Air, Water & Soil; Diet & Nutrition; Ethnicity, Sex & Social Environment; Occupational Exposures; Tobacco	5 Diet & Nutrition; Ethnicity, Sex & Social Environment; Hormones; Tobacco	6 Contaminants in the Air, Water & Soil; Diet & Nutrition; Infectious Agents; Occupational Exposures; Treatments/Diagnostics; Multiple/General	49

	Causes	Determinants that Influence Causes	Determinants that Influence Interventions	Interventions	Overall
Tobacco (n=2)	1 Tobacco	11 Ethnicity, Sex & Social Environment; Tobacco	14 Tobacco	4 Ethnicity, Sex & Social Environment; Tobacco	30
Physical Activity (n=2)	2 Activity Level, Body Composition & Metabolism	7 Activity Level, Body Composition & Metabolism; Ethnicity, Sex & Social Environment	6 Activity Level, Body Composition & Metabolism	8 Activity Level, Body Composition & Metabolism; Ethnicity, Sex & Social Environment	23
Sun Safety (n=1)	1 Contaminants in the Air, Water & Soil	0	0	4 Contaminants in the Air, Water & Soil	5
Overall	52	90	67	56	265

APPENDIX 3

Peer Reviewed Literature

Bowen DJ, Sorensen G, Weiner BJ, Campbell M, Emmons K, Melvin C (2009). Dissemination research in cancer control: where are we and where should we go? *Cancer Causes Control*, 20, 473-485.

Brownson RC, Kelly CM, Eyster AA, Carnoske C, Grost L, Handy SL, Maddock JE, Pluto D, Ritacco BA, Sallis, JF, Schmid TL (2008). Environmental and Policy Approaches for Promoting Physical Activity in the United States: A Research Agenda. *Journal of Physical Activity and Health*, 5, 488-503.

Carroquino MJ, Galson SK, Licht J, Amler RW, Perera FP, Claxton LD, Landrigan PJ (1998). The U.S. EPA Conference on Preventable Causes of Cancer in Children: A Research Agenda. *Environmental Health Perspectives*, 106(3), 867,873.

Caruso CC, Bushnell T, Eggerth D, Heitmann A, Kojola B, Newman K, Rosa RR, Sauter SL, Vila B (2006). Long Working Hours, Safety, and Health: Toward a National Research Agenda. *American Journal of Industrial Medicine*, 49, 930–942.

Gritz ER, Sarna L, Dresler C et al. (2007). Building a united front: aligning the agendas for tobacco control, lung cancer research and policy. *Cancer Epidemiology and Biomarkers Prevention*, 16, 859-863.

Kreuter MW, Green MC, Cappella JN, Slater MD, Wise ME, Storey D, Clark EM, O’Keefe DJ, Erwin DO, Holmes K, Hinyard LJ, Houston T, Wooley S. (2007). Narrative Communication in Cancer Prevention and Control: A Framework to Guide Research and Application. *Annals of Behavioral Medicine*, 33(3), 221-235.

Lytle LA (2009). Measuring the Food Environment: State of the Science. *American Journal of Preventive Medicine*, 36(4), Supplement, S134-S144.

McBride CM (2005). Blazing a trail: a public health research agenda in genomics and chronic disease. *Preventing Chronic Disease* [serial online]. Retrieved from: http://www.cdc.gov/pcd/issues/2005/apr/05_0008.htm.

McKinnon RA, Orleans CT, Kumanyika SK, Haire-Joshu D, Krebs-Smith SM, Finkelstein EA, Brownell KD, Thompson JW, Ballard-Barbash R (2009). Considerations for an Obesity Policy Research Agenda. *American Journal of Preventive Medicine*, 36(4), 351-357.

McTiernan A, Schwartz RS, Potter J, Bowen J (1999). Exercise Clinical Trials in Cancer Prevention Research: A Call to Action. *Cancer Epidemiology, Biomarkers & Prevention*, 8, 201–207.

Miller AB (1995). Primary Prevention of Cancer: Needs and Opportunities for Research. *Environmental Health Perspectives*, 103(Supplement 8), 313-317.

Milner JA (2003). Incorporating basic nutrition science into health interventions for cancer prevention. *Journal of Nutrition*, 133, 38205-38268.

Trickett EJ, Beehler S, Deutsch C, Green LW, Hawe P, McLeroy K, Miller RL, Rapkin BD, Schensul JJ, Schulz AJ, Trimble JE (2011). Advancing the Science of CommunityLevel Interventions. *American Journal of Public Health*, 101, 1410–1419.

Grey Literature

Canadian Cancer Research Alliance. (2010). Investment in Cancer Risk & Prevention Research, 2005-2007: A Special Report from the Canadian Cancer Research Alliance's Survey of Government and Voluntary Sector Investment in Cancer Research. Toronto: CCRA.

Cummings KM, Orleans CT (2009). Policies to achieve a smoke-free society: a research agenda for 2010-2015. Retrieved from: http://www.saprp.org/research_agenda.cfm.

National Cancer institute of Canada (2008). NCIC Cancer Prevention Initiative Strategy for Cancer Prevention Research in Canada Final Report.

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NCIC Cancer Prevention Initiative Working Group 3: Knowledge Exchange, Media and Policy Group. Response to Request for Applications. Submitted by: Greg Williams (WG Chair), Heather Logan, Kathryn O'Hara, Michael Orsini, Barbara Whylie, George Browman, Erica Di Ruggiero, Sylvia Leonard, Alan Shiell. Submitted: May 22, 2007c.

NCIC Cancer Prevention Initiative Working Group 4: Clinical Medicine and Basic Biology Group. Response to Request for Applications. Submitted by: Denis Grant (WG Co-Chair), Harriet Richardson (WG Co-Chair), Norman Boyd, Eduardo Franco, Pam Goodwin, Ernie Hawk, Barry Kramer, Sandra Krueckl, Jacques Simard, Alexandre Zlotta. Submitted: May 2, 2007d.

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As noted previously, an additional 24 policy documents were reviewed and selected from the Partnership's Prevention Policies Directory⁶⁰ and are listed below:

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