PIP Digest

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

Patient Involvement in Cancer Research Program
Programme de Participation des Patients à la recherche sur le cancer

In this PIP Digest, we describe major types of cancer research and current priorities in cancer research.

CANCER RESEARCH: Types of Research

Key Concepts

- Major types of cancer research
- Research priorities, national and international

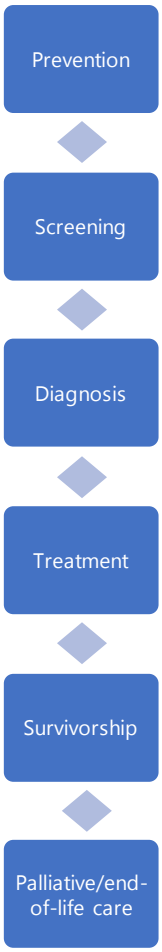
Related PIP Digest

- Cancer Research: Cancer Research Funding

"Cancer research has always been among the most interdisciplinary of fields, mirroring the complexity of the many diseases it addresses."[1]

Many classifications are used to describe different types of research. In this PIP Digest, we use the definitions of the four major research pillars used by the Canadian Institutes of Health Research. Every aspect of cancer research, from prevention through to end-of-life care, is captured under these research pillars. Each pillar of research involves many different disciplines and provides important opportunities to engage patients.

[1]From: National Academy of Sciences, National Academy of Engineering, and Institute of Medicine. (2005). *Facilitating Interdisciplinary Research*. Washington, DC: The National Academies Press. https://doi.org/10.17226/11153.



BIOMEDICAL	CLINICAL	HEALTH SYSTEMS AND HEALTH SERVICES	SOCIAL, CULTURAL, ENVIRONMENTAL, AND POPULATION HEALTH
This type of research studies normal and abnormal human function from the level of cells and molecules all the way up to the whole body. Basic biomedical researchers do their work in a laboratory using test tubes, cell samples, microscopes, chemical analysis, and other applicable tools or methods.	Clinical research is health research on people, typically to evaluate the effectiveness of drugs, medical devices and practices. It may involve researchers asking questions, administering drugs, taking blood or tissue samples, or checking the progress of patients as they take a treatment according to a study's protocol. Clinical research studies often have specific criteria to define who can be recruited or enrolled in a particular study.	This is a type of research that seeks to improve the efficiency and effectiveness of health professionals, such as doctors, nurses, or physiotherapists, or the health care system itself through changes to practice and policy. Health services researchers often use surveys, focus groups, randomized controlled trials, and comparisons of data from health records and other sources in their studies.	This research works to enhance the health of Canadian populations (or subpopulations, such as those from a particular region or ethnic group) by understanding how social, cultural, environmental, work-related, and economic factors affect people's health. It also involves the evaluation of certain health interventions such as the effect of tobacco control programs on populations.
Disciplines: Biology, Computer Science, Genetics, Mathematics, Microbiology, Oncology, Pharmacology, Physiology, Zoology	Disciplines: Biostatistics, Clinical Epidemiology, Kinesiology, Medical Biophysics, Nursing, Oncology, Psychology, Social Work	Disciplines: Anthropology, Bioethics, Geography, Health Economics, Political Sciences, Public and Health Administration, Sociology	Disciplines: Epidemiology, Nutrition, Law, Performing Arts, Philosophy, Psychology, Public and Population Health, Sociology, Visual Arts

Adapted from: CIHR's *Health Research in Canada and You* (2014) available at http://www.cihr-irsc.gc.ca/e/documents/Health_Research_in_Canada_and_You_e.pdf

The example below shows how research on cancer metastases can involve all four pillars:

BIOMEDICAL	CLINICAL	HEALTH SYSTEMS AND HEALTH SERVICES	SOCIAL, CULTURAL, ENVIRONMENTAL, AND POPULATION HEALTH
A study looking at the biological mechanisms that cause cancer cells to invade nearby tissue and migrate to other areas of the body	A clinical trial on a new combination therapeutic designed to reduce metastatic disease	Research on the benefits of a telemedicine approach designed to support patients with metastatic disease	A population-based study to determine the prevalence of metastatic disease among different ethnic groups

Research Prioritization

Many cancer research funding organizations identify priority areas for research funding. These priorities relate to the organization's mandate — that is, if the organization funds only biomedical research, its research priorities will fall in that area; if the organization supports research on a specific type of cancer (for example, ovarian), the research priorities will relate to that type of cancer.

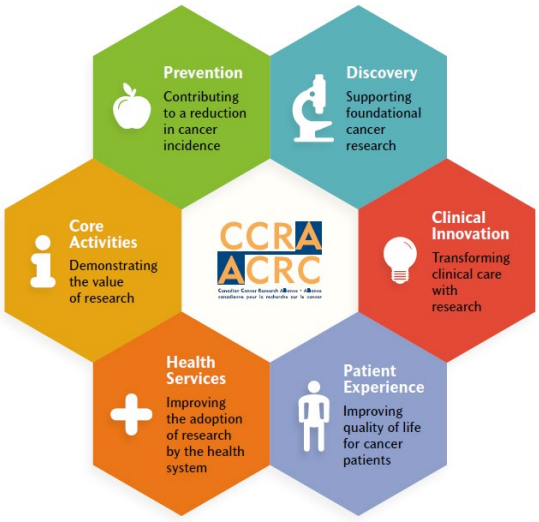
Decisions about priorities often involve assessing the state of existing knowledge and determining where a funding organization thinks it can best make a difference. Funders may come together to support research areas of mutual interest. This is a good way to close gaps in under-supported areas. Patients often identify different priorities than either clinicians or researchers, which makes their involvement in priority setting particularly important.

The CCRA member organizations all have strategic priorities for research funding. The CIHR Institute for Cancer Research, for example, has three priority areas for 2015–2020: high fatality cancers; health economics and health services research in cancer control; and redressing cancer risk factor disparities and prevention service inequities.

In its 2016-2021 strategic plan, the Ontario Institute of Cancer Research, identifies three research priorities: finding new ways to treat difficult cancers; optimizing cancer patient management and treatment decisions; and driving improvements in cancer prevention and care delivery.

Collectively, the CCRA members have also developed a broader pan-Canadian strategy, *Target 2020*,[2] that identifies a series of action items grouped around six themes. They are also developing a new vision and new strategic plan.

Addressing research gaps is critically important in advancing cancer science at the global level. When you attend cancer research conferences in Canada, you will no doubt hear from Canadian researchers about their work in these areas.



Target 2020 Themes

International Perspective

At the international level, research prioritization has taken many forms. In the United States, the National Cancer Institute (NCI) established a Provocative Questions (PQ) Initiative in 2011. The goal of the PQ initiative is "to support research projects designed to use sound and innovative research strategies to solve specific problems and paradoxes in cancer research." The PQs are not intended to represent the full range of NCI's priorities in cancer research but rather to challenge cancer researchers to explore specific problems in key areas of cancer research that are deemed important but have not received sufficient attention.

[2] *Target 2020* can be accessed at the CCRA website: www.ccra-acrc.ca.

PROVOCATIVE QUESTIONS

PQ1: **What are the causes for the rising numbers of cancers in people younger than 50 years of age?** Research here will be designed to improve our understanding of why certain cancers are occurring in younger populations, beyond hereditary factors, and to identify markers for early detection and better screening approaches.

PQ2: **How does intermittent fasting affect cancer incidence, treatment response, or outcome?** Research in animal models has shown that a long-term reduction in food intake as well as intermittent fasting reduces cancer incidence. Research here will be focused on understanding how restricting our food intake to specific hours of the day or days of the week or month affects cancer risk factors, cancer incidence, treatment response, toxicity, and/or other related cancer outcomes.

PQ3: **How can selective pressures – things within or outside of cells - affect how cells compete and cooperate during the start and development of cancer?** Cells interact with each other in response to selective pressures to drive competition and cooperation. This results in the survival of the more "fit" cells at the expense and loss of less fit cells. Understanding this mechanism in relation to cancer initiation is the goal of research addressing this question.

PQ4: **What mechanisms explain sex differences in cancer incidence, tumour location, or response to treatment?** There is a growing literature that suggests that males and females differ in the kinds of cancer they get, the characteristics of those cancers, the progression and response to treatment, and their overall survival. Research here will help us better under the biological mechanisms across sexes that could be used to inform approaches to cancer prevention, diagnosis and treatment.

PQ5: **What strategies can block or reverse changes to tumour cells that are created by cancer treatments and lead to treatment resistance?** Research here will focus on better understanding the fundamental pathways and molecular drivers of the changes in the cancer cell and the drugs and drug combinations that will prevent these changes.

PQ6: **How can cancer cachexia be reversed?** Cancer cachexia - the loss of body weight and muscle mass, and weakness - associated with many types of cancer is often a signal of poor long-term survival. The goal for this research is to understand cancer cachexia at a mechanistic level so that our ability to identify those at risk of cachexia and prevent or halt cachexia will be enhanced.

PQ7: **What methods can be developed to integrate patient-generated health data into electronic health records?** Patient-generated health data are health-related data created, recorded by, or gathered directly from patients. These include patient-reported data and passively collected physical measures from mobile and wearable devices. Best practices for using patient-generated health data is limited. Research on new analytic and data science methods to improve the capture and use of patient-generated health data within existing electronic health records will help to predict and monitor cancer-related outcomes, and ultimately, inform a precision medicine approach.

PQ8: **What strategies can be implemented to ensure better care for cancer patients with complex needs?** The research here will develop and test interventions that would improve the coordination of healthcare for people with complex health needs throughout their cancer journey (diagnosis to survivorship). These interventions would be aligned with patient preferences, goals and needs as well as the goals of the broader health system. Determinants of health – the broad range of biological, behavioural, socioeconomic, cultural, and environmental factors that determine an individual's health – are a key component of this research.

PQ9: **What methods can be developed to effectively study rare cancers?** The research here will identify new study designs, statistical approaches or computational tools to describe, analyze and monitor small groups of people with rare cancers and interpret how these groups are affected by certain exposures or treatments.

In the U.K., there is a slightly different emphasis. The United Kingdom's largest cancer charity, Cancer Research UK, conducts workshops with scientists, innovators, and thought leaders, and people affected by cancer to identify the "toughest challenges" in cancer. Most recently, an independent advisory panel determined six "grand challenges" emerging from those workshops. These challenges guide its latest funding competition, aimed at supporting international, multi-disciplinary teams.[3]

1. **Unusual mutation patterns:** Carcinogens (like tobacco smoke) trigger chemical changes inside cells, leading to errors in the reading of the DNA genetic code. The patterns of these DNA changes are different for each carcinogen and scientists identify known carcinogens from their chemical signatures. There are, however, unusual signatures whose origins are not known, and, in cancers caused by factors such as obesity, there are many different signatures and they are difficult to distinguish. Working backwards from these patterns, the goal is to find the cancer-causing events and ultimately, use this information in cancer prevention efforts.
2. **3D tumour mapping:** Cancer cells live in complex communities. Just like houses in a city, each cell in a tumour is different from its neighbor and relies on infrastructure to support its existence. There are different neighbourhoods—some worse than others. Tumours contain blood vessels that deliver nutrients, and act as highways for different cell types to move around. When a tumour spreads, the cancer cells themselves use these blood 'roads' to migrate. If we could make a 3D map of a tumour, similar to a Google map, we could find new targets for treatment and, eventually, use this view to track what is going on in real time, such as how a patient responds to treatment.
3. **Distinguishing lethal versus non-lethal cancers:** One of the biggest challenges in cancer research is being able to identify cancers that deadly from those that are not. This research will help accelerate detection of lethal cancers and prevent the harms associated with the over-diagnosis and treatment of non-lethal cancers.
4. **Understand why mistakes in certain genes only cause cancer in specific parts of the body:** Different mistakes in DNA can cause different types of cancer. Faulty versions of the BRCA1 or BRCA2 genes are well-known for their links to breast cancer, for example. What remains unknown is why these errors cause cancer in specific organs and not others. If scientists can figure out how certain cancer genes cause particular types of cancer, they may be able to find ways to prevent these cancers from developing and, as well, identify new ways to treat them.
5. **Understand how lifestyle factors, such as obesity, cause cancer:** Overweight and obesity are linked to a number cancer types, but how excess bodyweight causes cancer is unknown. Similarly, being physically active can reduce the risk of developing cancer, but the mechanics of why this is are not fully understood. Fully understanding

[3]Adapted from: https://www.cancerresearchuk.org/funding-for-researchers/cancer-grand-challenges/about-grand-challenge.

how obesity and other lifestyle factors cause different types of cancer could help with cancer prevention, diagnosis, and treatment.

6. **Understand how microbes inside our bodies affect cancer treatment.:** Scientists have shown that the microbes inside our bodies can play a role in how cancers develop including by damaging DNA or altering how the immune system responds to cancer cells. The microbiota also affects how patients respond to certain treatments. A better understanding of the mechanisms by which microbiota will ultimately help improve treatments so more patients benefit.

In summary, cancer research takes many forms, and different organizations may prioritize different areas of research given their mandates or the processes they use for identifying priorities. Knowledge sharing, collaborative funding programs, and the involvement of patients are crucial ways to help identify needed research, ultimately, identify successful new approaches to prevention and cure.

Last revised: 2019-Jul-02