

# Canadian Cancer Research Survey (CCRS): Data Sources, Methods and Definitions

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## Data Sources

The CCRS initiated in 2005 as an environmental scan of the cancer research funded by the then-members of the Canadian Cancer Research Alliance (CCRA). It was the first joint activity undertaken by CCRA members. Over the years, the number of contributors and organizations tracked has extended beyond the CCRA members.

At present, the database contains seventeen years of data, with over 30,000 projects funded by more than 40 organizations/programs within the federal government, provincial government, and voluntary sectors (charities, associations, and other non-governmental agencies). It includes organizations that fund only cancer research (e.g., Canadian Cancer Society (CCS)), organizations that fund all types of health research (e.g., Saskatchewan Health Research Foundation), and general research/technology research funders (e.g., Natural Sciences and Engineering Research Council (NSERC)).

Details of organizations tracked by the CCRS are provided in Appendix A. Organizational changes due to terminations, mergers, or changes in mandate/organization name are reflected in the survey on an ongoing way. In general, the most recent name of an organization is used.

Most organizations submit data on an annual basis. The minimal dataset contains:

- Funder name
- Funding program
- Nominated principal investigator (PI)
- Host institution/organization
- Project title
- Project description (lay and scientific abstracts are requested)
- Start date
- Duration
- Total amount (\$) (plus partner funding/contributions, where applicable and annual amounts if project exceeds 12 months)
- Other personnel (co-PIs, co-investigators, supervisors)

Extractions of public data sources is done for other organizations in order to complete the national picture of funding. Where data are incomplete, information is imputed based on available data, additional sources of information, and historic information.

### *Project Inclusion*

Projects are based on the researchers' intentions as described in their research proposals, which are submitted for funding decisions. Projects are included in the CCRS if:

- they are funded by funding organizations that support only cancer research
- they are funded by non-cancer specific funders but are relevant to cancer research in whole or in part – this means that they contain references to cancer in the available descriptive information

- they concern tobacco usage, smoking cessation, environmental tobacco smoke, and/or e-cigarettes and are not focused on cardiovascular and/or chronic obstructive pulmonary disease prevention
- they are related to end-of-life care, either cancer-related or without a specific disease focus
- they focus on chronic disease with a specific mention of cancer (if not cancer mention, the project is not included)

### *Scope and Limitations*

All major Canadian cancer research funders from the governmental and voluntary sectors are included in the CCRS.

We have been unsuccessful in getting project-level research funding from the BC Cancer Foundation, institution-specific foundations (e.g., hospital foundations), federal and provincial government programs for which health research is only a small component of their funding, and industry (i.e., industry-sponsored R&D). It should be noted that a portion of this investment is reflected under partnered/leveraged funding, where the investment and partner has been specified by a data contributor.

Canadian research administered by organizations outside Canada is not within the scope of the survey.

Coverage of the CCRS is estimated to be about 50% of all cancer research funding in Canada. This is based on estimates from publicly available information sources. These estimates have varying levels of accuracy.

## Methods and Definitions

### *Project Classification*

Using the available descriptive information, all projects within the CCRA database are classified by area of cancer research, cancer site, and research pillar.

### **Area of Cancer Research**

The [Common Scientific Outline \(CSO\)](#) is the typology used for coding area of cancer research. The CSO is the principal classification framework used by the International Cancer Research Partnership (ICRP). The 34 CSO codes are organized into six broad categories of scientific interest:

- 1-Biology: the biology of how cancer starts and progresses as well as normal biology relevant to these processes
- 2-Etiology: the causes or origins of cancer - genetic, environmental, and lifestyle, and the interactions between these factors
- 3-Prevention: individual and population-based primary prevention interventions, which reduce cancer risk by reducing exposure to cancer risks and increasing protective factors

- 4-Early Detection, Diagnosis and Prognosis: identifying and testing cancer markers, imaging and other methods that are helpful in detecting and/or diagnosing cancer as well as predicting the outcome or chance of recurrence or to support treatment decision making in stratified/personalized medicine
- 5-Treatment: identifying and testing treatments administered locally (such as radiotherapy and surgery) and systemically (treatments like chemotherapy which are administered throughout the body) as well as non-traditional (complementary/alternative) treatments (such as supplements, herbs). The prevention of recurrence and treatment of metastases are also included here.
- 6-Cancer Control, Survivorship and Outcomes Research: includes a broad range of areas: patient care and pain management; tracking cancer cases in the population; beliefs and attitudes that affect behavior regarding cancer control; ethics; education and communication approaches for patients, family/caregivers, and health care professionals; supportive and end-of-life care; and health care delivery in terms of quality and cost effectiveness.

Each project within the CCRA database is assigned at least one relevant CSO code. Where more than one CSO code is assigned to a given project, the project budget is distributed equally among the codes.

### **Cancer Site**

Projects are also classified according to cancer site using the 2019 version of the [International Classification of Diseases \(ICD\)](#).<sup>1</sup> The ICD is the international standard for reporting diseases and health conditions. It is the diagnostic classification standard for all clinical and research purposes and is also used in the national reporting of new cancer cases.

Like the CSO coding, some projects are assigned more than one cancer site. In these cases, the project budget is allocated accordingly to each code so that it sums to 100% of the total. ICD codes are rolled up to 23 cancer sites:

- Bladder
- Bone and connective tissue
- Brain
- Breast
- Cervix
- Colorectal
- Esophagus
- Gallbladder
- Head and neck
- Hodgkin lymphoma

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<sup>1</sup>Of note, on May 25, 2019, member states of the World Health Assembly agreed to adopt ICD-11 (International Classification of Diseases 11<sup>th</sup> Revision), to come into effect on January 1, 2022. Our coding conventions may thus evolve in the future.

- Kidney
- Leukemia
- Liver
- Lung
- Multiple myeloma
- Non-Hodgkin lymphoma
- Ovary
- Pancreas
- Prostate
- Skin (Melanoma)
- Stomach
- Thyroid
- Uterus

Collectively, these cancer sites represent ~90% of all new cancer cases and deaths per year. And represent most of the cancer sites typically reported in statistics generated annually on incidence and mortality in the Canadian Cancer Statistics. When a project does not focus on one or more specific cancer sites, such as research on the basic mechanisms of cell biology or, alternatively, a study of an intervention to improve end-of-life care which applies broadly to cancer patients, the project will be coded “not site specific/applicable to all cancers.”

When a project is focused on a specific risk factor such as smoking and no mention is made of cancer sites in the project description, predetermined site allocations based on expert input are used. As an example, the site allocations for projects focused on smoking are: lung 50%, esophagus 15%, larynx 15%, pharynx 15%, and all other sites 5%. For more on the site algorithms, see Appendix B. These algorithms may be modified as the science advances.

## Research Pillar

Projects are also assigned a single research pillar based on the four research pillars defined by CIHR (see table below) using the assignment decisions identified.

PILLAR	DESCRIPTION	ASSIGNMENT DECISIONS
I - Biomedical research	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. Examples of disciplines that conduct this kind of research: Microbiology, Genetics, Pharmacology, Medicine (including specialties such as Oncology and Cardiology).	Coded to Pillar I if the project is entirely biomedical and/or involves model systems
II - Clinical research	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	Coded to Pillar II if any component of a project is clinical and/or involves humans. Includes companion clinical trials and correlative

PILLAR	DESCRIPTION	ASSIGNMENT DECISIONS
	protocol. Clinical research studies often have specific criteria to define who can be recruited or enrolled in a particular study. Examples of disciplines that conduct this kind of research: Kinesiology, Medicine, Psychology, Social Work, Nursing, Biostatistics, Clinical Epidemiology.	studies as well as psychosocial oncology research.
III - Health systems and health services research	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. Examples of disciplines that conduct this kind of research Health Economics, Public and Health Administration, Political Sciences, Sociology, Geography, Anthropology.	Coded to Pillar III if research focuses on barriers to care, treatment adherence, care utilization, overtreatment, health care transitions, national strategies/frameworks, clinical pathways/guidelines, ethics, patient decision aids, adverse drug reactions, treatment delays/wait times, access/equity, and/or health literacy.
IV - Social, cultural, environmental, and population health research	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. Population health researchers often use case studies, cohort studies (studying similar groups of people), or observation methods to do their research. Examples of disciplines that conduct this kind of research: Performing Arts, Visual Arts, Sociology, Psychology, Law, Philosophy, Nutrition, Public and Population Health, Epidemiology.	Coded to Pillar IV if the research is population-level and unrelated to the health system. Includes research using population-based surveillance surveys (e.g., the International Tobacco Control (ITC) survey, British Columbia Adolescent Substance Use Survey).

### *Funding Program Classification*

All funding programs are grouped in terms of five types of funding mechanism as follows:

- **Operating grants** support all the direct costs involved in conducting specific research projects including salaries for laboratory staff and research assistants, costs of supplies and samples, and other specific research-related expenses. Multi-component projects (program projects), feasibility grants, proof-of-principle grants, regional development grants, innovation grants, and knowledge translation grants are all included in this category. The funding programs supporting these grants may be:
  - open (investigator-initiated), or
  - focused on specific cancer sites and/or research areas (priority-driven).
- **Equipment/infrastructure grants** cover the costs of construction or major remodeling of new research facilities, and/or the purchase, housing, and installation of equipment, scientific collections, computer software, information databases, and communication linkages used primarily for conducting research. It also includes funding for cohort establishment.

- **Career awards** (also known as salary awards) provide protected time for research on either a long- or short-term basis to outstanding researchers who have demonstrated high levels of productivity and research accomplishments. These awards are given to only a small percentage of all researchers. Research chairs are also included under this funding mechanism.
- **Trainee awards** recognize outstanding trainees and support them during their undergraduate, graduate, or postgraduate training. Trainees from Canada who are studying at institutions outside Canada may also be eligible for some types of trainee awards. Block training grants given to institutions that in turn distribute the monies to trainees through a competitive process are also included under this funding mechanism. These awards are in addition to trainee salaries covered in operating grants.
- **Related support grants** support travel, workshops/symposia, and researcher time for proposal development, including letters of intent. These grants involve small sums of money.

### *Data Quality*

Two coders assign the CSO coding to projects on an independent basis. Where there are discrepancies, the coders discuss the projects and determine final agreed-upon codes. Observed agreement between coders exceeds 80%.

Cancer site classification is completed by one coder, unless the project is difficult to code in which case a specific opinion is sought. A check of cancer site classifications by an automated algorithm conducted on the first five years of data identified needed changes in 4% of the projects. No subsequent checks of this kind have been undertaken.

All data is subject to change where inaccuracies are discovered, or new information is supplied. The most current reports and interactive tools reflect the latest version of the database.

### *Reporting Conventions*

The term "cancer research investment" represents the direct funding of cancer research that receives some form of peer review and is administered by organizations participating in the survey. "Peer review" is defined as the process of subjecting a research proposal to the scrutiny of others who are experts in the same or similar fields. The formats for peer review vary among organizations and funding mechanisms and range from formalized reviews to more ad hoc arrangements to the use of in-house expertise as is commonly used for related support grants.

### *Budget Weighting*

Project budgets are weighted in terms of the extent to which they are focused on cancer. Budgets for projects determined to have the study of cancer as their primary focus are weighted at 100%. This includes projects funded by cancer research funding organizations. Budgets for all other research projects that are not entirely focused on cancer are weighted based the available project descriptions.

The table below provides some examples of how project budgets are allocated based on the cancer weighting, CSO coding, and site coding.

ISSUE	PROJECT	WEIGHTING
Project is not entirely focused on cancer	<i>Quality of end-of-life care: The perspectives of bereaved family members of lung cancer and COPD patients, health care providers and policy makers in rural and urban areas</i>	Budget is weighted at 50% as the research is looking at cancer and chronic obstructive pulmonary disease (COPD).
Project spans more than one category of the CSO	<i>Functional genomic classification and selected therapies of breast cancer using genome-wide pooled lentiviral shRNA library screens</i>	Budget is allocated to CSO codes 2.2 – Endogenous factors in the origin and cause of cancer and 5.3 - Systemic therapies - discovery and development.
Project involves more than one cancer site	<i>Molecular Characterization of Circulating Tumour Cells in Breast and Prostate Cancer</i>	Budget is allocated 50-50 to two cancer sites (i.e., breast and prostate).

When the term “number of projects” is specified, it refers to a count of projects without the weightings applied. When the term “project equivalents” is used, it refers to a count of projects with the weightings applied.

In some analyses, the number of researchers is examined and compared at various time periods. To be counted, the researcher must have at least one operating grant, career award, or equipment/infrastructure grant weighted at 80% cancer-relevant or higher (nominated PIs) or have at least one trainee award weighted at 80% cancer-relevant or higher (trainees).

Given that many organizations have different grant cycles and fiscal years, the selection of calendar year is intended to standardize data collection. Unless additional data is provided by the funding organization, annual investment is calculated on a prorated basis and assumes that the project dollars were paid out in equal monthly instalments based on project start and end dates. Investment figures are not adjusted for inflation, unless otherwise noted. Year ranges are also used to reporting to simplify the presentation of the data.

Investment for projects funded by two or more organizations is reflected in the investment amounts of the organizations (and corresponding sector) that provided the funding. For example, the four projects funded through the \$11.7M CIHR Childhood Cancer – Late Effects of Treatment Team Grant funding program leveraged an additional \$1.5M from six other research funders and these dollars are shown for these organizations.

The institutional affiliation of the nominated principal investigator (PI) or project leader is used for analyses based on geography (province). There is only one nominated PI per project. However, components of multi-component projects are considered individual projects if the funding organization provides details (i.e., description, researchers, budget, etc.) on the component parts. The CCS, NRC, Ontario Institute for Cancer Research (OICR), and The Terry Fox Research Institute provide this level of detail for some projects. In these instances, the institutional affiliation of the nominated PI for each component project is used for the geographic analyses.



For clinical trials supported by the CCS through the Canadian Cancer Trials Group (CCTG), each site involved in the trial is treated as a separate project with its own nominated PI and budget (based on per case and site administration funding).

The [Research Support Fund](#) (RSF) provides annual grants to Canadian postsecondary institutions to help offset some of the expenses associated with managing the research funded by the three federal research granting agencies: CIHR, NSERC, and SSHRC. An estimate of the cancer-relevant component of the RSF is computed (see sidebar) annually to complement the project-specific research investment in the CCRS. The RSF helps support and strengthen the research programs and research capacity of smaller institutions by reimbursing a higher proportion of their federal research granting dollars.

#### **Estimate of the “Cancer” Component of the RSF**

1. All projects within the CCRS for CIHR, NSERC and SSHRC are identified.
2. The funding programs for each federal granting agency are included/excluded/weighted according to the RSF program guidelines, and host organizations that are not universities are mapped to affiliated universities, where applicable.
3. The proportion of RSF paid to institutions in the most recent fiscal period is based on the averaged funding received by researchers at that institution over the past three fiscal years by all three funding agencies (data supplied by the RSF program). This is then applied to the CCRS data for the corresponding calendar periods. The assumption is that all projects at an institution receive the same level of support.

Example: University of Alberta

- a. Three-year fiscal year (2014/15, 2015/16, 2016/17) total paid to all University of Alberta researchers by CIHR, NSERC, and SSHRC: \$277.7M; averaged annual \$95.6M
- b. RSF payment in 2018/19: \$18.1M
- c. Proportion of investment ( $\$18.1\text{M}/\$95.6\text{M}$ ) = 19.6%
- d. Three-year total paid to cancer researchers at University of Alberta by CIHR, NSERC, and SSHRC from CCRS for calendar years 2014, 2015 and 2016: \$13.6M; averaged annual \$4.5M
- e. Calculated RSF for cancer research ( $\$4.5\text{M} \times 19.6\%$ ) = \$0.9M

## Additional Classifications and Reporting Conventions for Special Topic Reports

### Childhood and Adolescent Cancers

Research projects relevant to childhood and adolescent cancers are identified by searching all available descriptive information using a broad range of keywords and cancer types. Included in whole or in part are projects:

- funded by organizations that wholly focus on childhood and adolescent cancers, including C<sup>17</sup>, the Pediatric Oncology Group of Ontario (POGO), or The Cole Foundation
- funded through programs focused on childhood and adolescent cancers (e.g., Pediatric Cancer Outcomes Initiative Grant, CIHR's Childhood cancers—Late effects of treatment Team Grant)
- conducted on the biological/molecular mechanisms of cancer with mention of applicability to childhood and/or adolescent cancer(s)
- focused on child-specific cancers, including germ cell/gonadal tumours, hepatoblastoma, medulloblastoma, neuroblastoma, retinoblastoma, rhabdomyosarcoma, pineoblastoma, Wilms' tumour, and juvenile onset cancers (e.g., childhood ovarian cancer)
- focused on acute lymphoblastic leukemia with mention of childhood onset and/or conducted at a pediatric centre
- focused on osteosarcoma and/or Ewing's sarcoma with mention of child/adolescent onset and/or conducted at a pediatric centre
- focused on familial neoplastic/genetic syndromes associated with childhood cancer (e.g., Beckwith-Wiedemann, Costello, Li-Fraumeni, etc.)
- focused on inherited immunodeficiency/bone marrow failure syndromes associated with childhood cancer (e.g., Fanconi anemia, Diamond-Blackfan anemia, Bloom syndrome, etc.)
- epidemiology studies looking at the relationship between maternal/early life exposures and child/ adolescent cancer onset
- translational, clinical, behavioural/psychosocial studies, which focus on treatment, survivorship, familial issues, and palliation of children/adolescents with cancer and/or adult survivors of childhood/ adolescent cancers
- focused on improving hematological cancer care, including ways to reduce Graft-versus-Host Disease, with specific application to childhood cancers and/or where conducted in a pediatric centre
- equipment grants with some focus on childhood cancers
- funded workshops/conferences with some focus on childhood cancers

Excluded are:

- projects involving child/adolescent subjects but focused on risk factors/health determinants of cancers with an adult onset (e.g., tobacco prevention research)
- projects focused on basic biological mechanisms, which could be applicable to many cancers

and age groups, where the PI has not mentioned a focus on childhood cancers and/or is not using cell lines from children/adolescents or juvenile model systems

- projects focused on adult-onset cancers (e.g., breast, colorectal, pancreas) or cancers common in children/adolescents where the PI specifically identifies adults as the focus
- projects on placental development/choriocarcinoma
- multi-user or multi-facility equipment grants even if they involve a pediatric institution (single equipment grants to pediatric institutions are weighted based on expert opinion)
- Research Hospital Fund – Large Scale Institutional Endeavours (a program of the Canada Foundation for Innovation)

All projects relevant to childhood and/or adolescent cancers are also coded to the [International Classification of Childhood Cancer \(ICCC\)](#). The ICCC is based on tumour morphology (structure) and was developed to reflect the differences in terms of histology, site of origin, and tumour behaviour of childhood cancers from cancers in adults. It classifies childhood cancers into 12 diagnostic groups, with additional subgroups for further refinement:

- I. Leukemias, myeloproliferative diseases, and myelodysplastic diseases
- II. Lymphomas and reticuloendothelial neoplasms
- III. Central Nervous System and miscellaneous intracranial and intraspinal neoplasms
- IV. Neuroblastoma and other peripheral nervous cell tumours
- V. Retinoblastoma
- VI. Renal tumours
- VII. Hepatic tumours
- VIII. Malignant bone tumours
- IX. Soft tissue and other extraosseous sarcomas
- X. Germ cell tumours, trophoblastic tumours, and neoplasms of gonads
- XI. Other malignant epithelial neoplasms and malignant melanomas
- XII. Other and unspecified malignant neoplasms

### *Limitations*

The CCRS does not capture all the research on childhood and adolescent cancers being conducted in Canada. In addition to the limitations noted for the overall CCRS, research relevant to childhood and adolescent cancers not covered includes that undertaken:

- by researchers at pediatric facilities with support from their affiliated institutional foundations or from other charities, including endowed chairs. This may be substantive for some of the large pediatric hospitals.
- by pediatric centres as part of trial participation relating to the Children's Oncology Group (COG). The COG is one of the trials groups supported by the U.S. National Cancer Institute's Clinical Trials Cooperative Group Program. Most pediatric trials conducted in Canada are COG trials.

## Cancer Risk and Prevention

Projects coded to 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 are examined and assessed for inclusion as a cancer risk and prevention project and each project is weighted according to their relevance to cancer risk and prevention.

All tobacco research projects funded by the organizations tracked in the CCRS are included as cancer risk and prevention studies unless the project descriptions specifically indicate that the research is focused solely on another disease (e.g., chronic obstructive pulmonary disease, cardiovascular disease). The rationale for this reverse-onus approach is two-fold: (1) the strong causal link between tobacco and lung/other cancers and (2) a large proportion of tobacco research is funded by cancer research funders (applying the rule that similar projects from other health/general science research funders should be included).

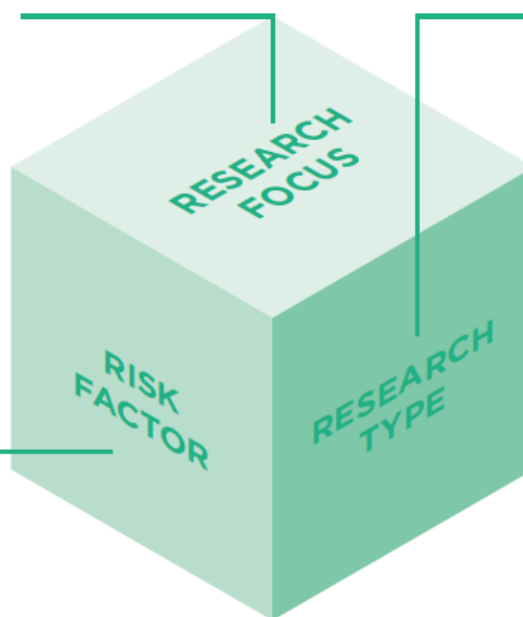
Excluded are projects focused on:

- cancer biology (research on model systems, however, was included if it directly related to specific cancer risk factors)
- tobacco-related projects focused on cardiovascular and/or chronic obstructive pulmonary disease
- genetic studies where the focus was on diagnostic markers and not disease risk
- 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 and removal of precursor lesions is, 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

All projects are coded to the categories of the three dimensions of the cancer risk and prevention cube. See below for full descriptions.

## RESEARCH FOCUS

- Causes
- Determinants that influence causes
- Determinants that influence interventions
- Interventions



## RESEARCH TYPE

- Research involving model systems
- Human research
- Methodological/measurements research
- Knowledge synthesis
- Infrastructure and other support

## RISK FACTOR

- Activity level, body composition and metabolism
- Alcohol
- Contaminants in the air, water and soil
- Diet and nutrition
- Ethnicity, sex and social environment
- Gene-environment interactions
- Genetic susceptibilities
- Hormones
- Infectious agents
- Occupational exposures
- Physiological susceptibilities
- Precursor lesions
- Tobacco
- Treatments/diagnostics
- Multiple/general

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"> <li>• <i>Urinary tract infections and other risk factors for bladder cancer</i></li> <li>• <i>Mechanisms of Kaposi's Sarcoma-associated herpesvirus pathogenesis</i></li> </ul>
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"> <li>• <i>Exploring the psychosocial influences of smoking mothers on daughters' tobacco use</i></li> </ul>
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"> <li>• <i>Assessing the longitudinal patterns and determinants of chronic disease prevention capacity in the Canadian public health system</i></li> </ul>

RESEARCH FOCUS	DEFINITION	EXAMPLE
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"> <li>behavioural change approaches (e.g., smoking cessation, obesity control)</li> <li>social, environmental, and regulatory changes (e.g., mass media campaigns, smoking bylaws)</li> <li>agents/drugs, nutraceuticals, and vaccines</li> <li>prophylactic surgery</li> <li>screening for precursor lesions/causal viruses</li> </ul>	<ul style="list-style-type: none"> <li><i>Molecular mechanisms of drug and dietary interventions for the prevention or reduced progression of prostate cancer</i></li> <li><i>Prophylactic salpingo-oophorectomy in women who carry a BRCA1 or BRCA2 mutation</i></li> <li><i>The impact of a 100% smoke-free bylaw on exposures to environmental tobacco smoke in non-smoking Toronto bar workers</i></li> </ul>

RISK FACTOR	DEFINITION	EXAMPLE
1. 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 included under this factor.	<ul style="list-style-type: none"> <li><i>Immune mechanisms in physical activity and cancer</i></li> </ul>
2. 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"> <li><i>The health effects of patterns of alcohol consumption</i></li> </ul>
3. 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 like cell phones), non-ionizing, and solar radiation). In utero exposures and second-hand smoke exposures (non-household) are included under this risk factor. Radiation exposure resulting from the work environment, however, is included in Occupational Exposures and radiation exposure from diagnostic tests in Treatments/Diagnostics. Projects on endocrine disruptors are located under Hormones.	<ul style="list-style-type: none"> <li><i>Exposure to air pollutants and the incidence of lung cancer</i></li> <li><i>Molecular mechanisms of solar mutagenesis</i></li> <li><i>• Risk of brain cancer from exposure to radiofrequency fields from wireless telecommunications devices in childhood and adolescence</i></li> </ul>
4. 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. Also included is research on contaminants in breast milk transmitted to children. This research can be distinguished from Activity Level, Body Composition & Metabolism by its emphasis on food/nutrients.	<ul style="list-style-type: none"> <li><i>Fruits and vegetables and ovarian cancer risk: a pooled analysis</i></li> <li><i>Influences on rural adolescents' eating habits</i></li> <li><i>Mechanisms for the anti-cancer effects of docosahexaenoic acid and eicosapentaenoic acid</i></li> </ul>

<b>RISK FACTOR</b>	<b>DEFINITION</b>	<b>EXAMPLE</b>
5. 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"> <li>• <i>Health risk behaviours and socio-economic status: explaining the social gradient in health</i></li> </ul>
6. 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"> <li>• <i>Gene-environment interactions in post-menopausal breast cancer: a case-control study</i></li> </ul>
7. Genetic Susceptibilities	Research whose intent is to define the role of genes (familial mutations and polymorphisms) on cancer risk. Research on genetic testing/counselling is also included under this factor.	<ul style="list-style-type: none"> <li>• <i>Contribution of known and suspected cancer susceptibility genes in high-risk breast and/or ovarian cancer families of French-Canadian descent</i></li> </ul>
8. 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 disruptors 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"> <li>• <i>Reducing breast cancer risk factors by molecular engineering: The redesign of hormonal supplements</i></li> <li>• <i>High androgen/low progesterone exposures and ovarian cancer</i></li> <li>• <i>Endocrine disrupting chemicals (EDCs), pituitary hormones, and estrogen metabolizing enzymes as modifiers of breast cancer susceptibility</i></li> </ul>
9. 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"> <li>• <i>Inuit women's understanding of human papillomavirus: implications for health education and prevention in Nunavik, Québec</i></li> </ul>
10. Occupational Exposures	Research that endeavours to identify the cancer risks associated with exposures in the workplace.	<ul style="list-style-type: none"> <li>• <i>Occupational histories of breast cancer patients</i></li> </ul>
11. Physiological Susceptibilities	Research on health conditions or physical attributes that may be associated with cancer risk. Studies on breast density as a risk factor for breast cancer are included here.	<ul style="list-style-type: none"> <li>• <i>Does Systemic Lupus Erythematosus increase the risk of malignancy? An international multi-site retrospective cohort study</i></li> </ul>
12. Precursor Lesions	Research that focuses on premalignancies and precursor stages of invasive cancer (such as polyps, DCIS).	<ul style="list-style-type: none"> <li>• <i>Community screening of and intervention in high-risk oral premalignant lesions</i></li> </ul>
13. 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. Child exposures in the family home or vehicle are included here.	<ul style="list-style-type: none"> <li>• <i>The neurobiological substrates of the motivational effects of nicotine in dependent and withdrawn mice</i></li> <li>• <i>Revealing tobacco industry secret science and using it to improve public health</i></li> </ul>
14. 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	<ul style="list-style-type: none"> <li>• <i>Effects of warfarin on the risk of urogenital cancer</i></li> <li>• <i>Cancer risk following radiation exposure from computed</i></li> </ul>

<b>RISK FACTOR</b>	<b>DEFINITION</b>	<b>EXAMPLE</b>
	on the risks associated with radiation treatment of cancer patients are excluded.	<i>tomography in children and adolescents</i>
15. Multiple/General	Studies that consider a broad range of factors and their relationship to cancer. Also included is research on cancer prevention not aimed at specific risk factors.	<ul style="list-style-type: none"> <li>• <i>Measuring cancer prevention knowledge and behaviours in a Nova Scotia university population</i></li> <li>• <i>CIHR Team in microsimulation modeling of the impact of health interventions and policies</i></li> </ul>

<b>RESEARCH TYPE</b>	<b>DEFINITION</b>	<b>EXAMPLE</b>
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"> <li>• <i>Investigating the genotoxic effects of in utero benzene exposure on bone marrow cells of young mice</i></li> </ul>
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"> <li>• <i>Case study observations of consumption of antioxidants and risk of lung cancer among Montrealers</i></li> <li>• <i>Effect of vaginal self-sampling on cervical cancer screening rates: a community-based study</i></li> </ul>
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"> <li>• methods development, research on statistical approaches and methods to enhance the measurement of outcomes, endpoints, and variables of interest</li> <li>• exposures measurement, research on the physical measurement of one or more substances/exposures within a specified environment</li> <li>• surveillance, research on identifying the frequency/incidence of risk behaviour(s) in a specified population</li> <li>• economic evaluations, research that examines the costs and health effects of an intervention in order to assess the extent to which it can be regarded as providing value</li> </ul>	<ul style="list-style-type: none"> <li>• <i>Development and validation of new statistical methods for modelling intermediate events in survival analysis</i></li> <li>• <i>Comparing methods of obtaining exposure data in epidemiological studies involving children and pregnant women</i></li> <li>• <i>The British Columbia Adolescent Substance Use Survey</i></li> <li>• <i>Economic evaluation of population screening for cervical cancer using HPV testing in Canada</i></li> </ul>
Knowledge Synthesis	Literature reviews, and policy, ethics and legal analyses, meta-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"> <li>• <i>A knowledge synthesis of tobacco cessation continuing education programs for dental hygienists</i></li> </ul>
Infrastructure & Other Support	Funding for:	<ul style="list-style-type: none"> <li>• <i>Infrastructure to support a research program on the early</i></li> </ul>



RESEARCH TYPE	DEFINITION	EXAMPLE
	<ul style="list-style-type: none"> <li>equipment/infrastructure needed to conduct cancer risk and prevention research</li> <li>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</li> <li>knowledge dissemination—support for workshops, conferences, symposia, and travel awards for trainees and researchers to attend these events</li> <li>letters of intent, which offset researchers' time to develop proposals of prospective research projects</li> </ul>	<i>determinants of adult chronic disease</i> <ul style="list-style-type: none"> <li><i>Tobacco use in special populations research training program</i></li> <li><i>2nd International Francophone Conference on Tobacco Control – Paris, France: "Lessons learned in Canada about health warnings on cigarette packages" (travel award)</i></li> </ul>

This very large platform investment, the Canadian Partnership for Tomorrow's Health (CanPath),<sup>2</sup> by the Canadian Partnership Against Cancer and regional partners at more than \$150M forms a large portion of the overall cancer risk and prevention research investment. It is coded as follows:

RESEARCH FOCUS	RISK FACTOR	RESEARCH TYPE
Causes 100%	6. Gene-environment interactions 33% 15. Multiple/general 67%	Infrastructure & Other Support 100%

### Limitations

There are no additional limitations other than what has been already described.

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<sup>2</sup>Formerly known as the Canadian Partnership for Tomorrow Project (CPTP). Scientific leadership transitioned to the University of Toronto in April 2018.

## Translational Cancer Research

Translational cancer research, often referred to as “bench-to-bedside”, bridges fundamental scientific research and clinical research. The penultimate goal of translational research is the application of precision medicine—preventive approaches, diagnostics, monitoring, and treatments that consider individual variability in genes, environment, and lifestyle. For the purposes of the CCRS, translational research is restricted to research that confirms and advances discoveries into tangible modalities (pre-clinical) and tests modalities in the clinic (clinical). Implementation research, which is designed to transfer clinical findings to practice settings and communities, is excluded.

Projects coded to the CSO categories 4-Early Detection, Diagnosis, and Prognosis and 5-Treatment are examined and weighted according to their relevance to translational research.

Excluded projects are those that focus on:

- basic discovery (biomolecular or epidemiological)
- model systems where the research did not have immediate translational research goals
- surveillance, survivorship, and outcomes research
- treatment of cancer-causing infectious diseases
- provision of general/multi-faceted infrastructure
- training/capacity building, creation/maintenance of tumour banks/tissue repositories, and large research platforms not directly linked to specific translational research activities/modalities. It is recognized, however, that these funded resources are essential for the conduct of translational research, although they are not translational research projects themselves.

The selected projects are coded to modality and phase as shown in the diagram below and further described in the following table.

		Modality			
Phase	<b>Risk Assessment (RA)</b> Research intended to characterize the cancer-related health status of an individual		<b>Interventive (INT)</b> Research intended to change the cancer-related health status of an individual via prevention or treatment		
	Pre-clinical <sup>2</sup>	I. Biospecimen-based (biomarkers)	II. Image-based (imaging)	I. Agents (drugs & biologics)	II. Immune Response Modifiers (immunotherapies)
	Clinical <sup>3</sup>				III. Interventive Devices (devices)
Major initiative	Centres, networks, and platforms that support risk assessment research – e.g., Ontario Cancer Biomarkers Network, BC Clinical Genomics		Centres, networks, and platforms that support interventive research – e.g., BioCanRx, Canadian Cancer Clinical Trials Network (3CTN)		

1 Adopted from E.T. Hawk et al. (2009). The Translational Research Working Group Developmental Pathways: Introduction and Overview. *Clinical Cancer Research*, 14(18), 5664–5671.

2 Includes all research from post-discovery to pre-clinical, where new modalities are created and tested using model systems.

3 Includes phases I, II, and III clinical trials.

MODALITY CATEGORY	MODALITY	DESCRIPTION
<b>Risk Assessment (RA)</b> projects: characterize the cancer-related health status of an individual and consist of biospecimens (biological molecules found in blood, other body fluids, or tissues) and image-based devices (e.g., computed tomography, contrast agents, and imaging enhancers)	RA-I. Biospecimen-based	Protocols, reagents, or devices/instruments that reveal cancer risk from analysis of blood and/or tissues, the presence of a specific cancer or recurrent cancer, the stage or severity of a specific cancer, and how well the body responds to therapeutic intervention(s).
	RA-II. Image-based	Devices like magnetic resonance imaging, computed tomography, and positron emission tomography scanners that identify the presence of a specific cancer, the stage or severity of a specific cancer, how well the body responds to treatment(s), and how to plan the most efficacious treatment based on anatomical, functional, or molecular parameters. Also includes research on imaging agents, contrast agents, imaging enhancers, and therapeutic agents with secondary imaging attributes.
<b>Interventive (INT)</b> projects: change the cancer-related health status of an individual by either prevention or treatment and consist of agents (drugs or biological compounds), immune response modifiers (agents that mimic, augment, or require participation of a person's immune cells for optimal effectiveness), and interventive devices (e.g., radiation	INT-I. Agents	Small molecules, biological compounds and radiosensitizers.
	INT-II. Immune response modifiers	Therapies that either stimulate an individual's immune system so that it will recognize and destroy cancerous cells (also known as "active" immunotherapy, which includes vaccines, oncolytic viruses, cytokine therapy), or provide the immune response to the patient (also known as "passive" immunotherapy like monoclonal antibody drugs, adoptive T-cell therapy).

<b>MODALITY CATEGORY</b>	<b>MODALITY</b>	<b>DESCRIPTION</b>
therapy, cryoablation, high-intensity focused ultrasound).	INT-III. Interventional devices	May target local-regional sites of cancers or precancerous lesions or be delivered in systemic ways (i.e., for treatment of hematological malignancies or metastases). Examples include radiation therapy, cryoablation, radiofrequency or microwave ablation, interstitial laser thermal therapy, photodynamic therapy, high-intensity focused ultrasound, and minimally invasive surgery tools. May be delivered noninvasively, percutaneously, endoscopically, laparoscopically, transvascularly, or by open surgery. Research focused on the mechanism for guiding/monitoring the device and its effects is also included under this modality, as is research focused on radiobiological modelling and dosimetry.

### *Limitations*

The CCRS has modified its approach to the coding of translational research over time. Industry is a major investor in translational research, but industry-initiated/sponsored research is not part of the CCRS. A new coding system may be introduced in the future to reflect advances in the field.

## Cancer Survivorship and Palliative and End-of-life Cancer Care

Projects coded to the CSO category, 6 – Cancer Control, Survivorship, and Outcomes Research are reviewed for their relevance to cancer survivorship and/or palliative and end-of-life cancer care. Projects focused on end-of-life care that do not specifically mention a cancer patient population are weighted at 80%, based on Canadian experts' estimates of the proportion of the palliative and hospice care patients with a cancer diagnosis.

Cancer survivorship research focuses on post-primary cancer treatment care, including:

- post-cancer treatment rehabilitation
- long-term or late complications of cancer and its treatments
- other physical and psychological impacts experienced by cancer survivors and their family/caregivers
- social support needs of cancer survivors and their family/caregivers
- economic sequelae of cancer for survivors and their family/caregivers
- interventions to improve quality of life
- the delivery of care, access to care, and quality of care received by survivors after their primary cancer treatment

Model systems research relevant to cancer survivors, like the effects of chemotherapy on the cognitive function in an animal model, is also included.

The palliative and end-of-life phase focuses on both the care given to and issues relevant to cancer patients at the end of life. Palliative and end-of-life care research included studies on:

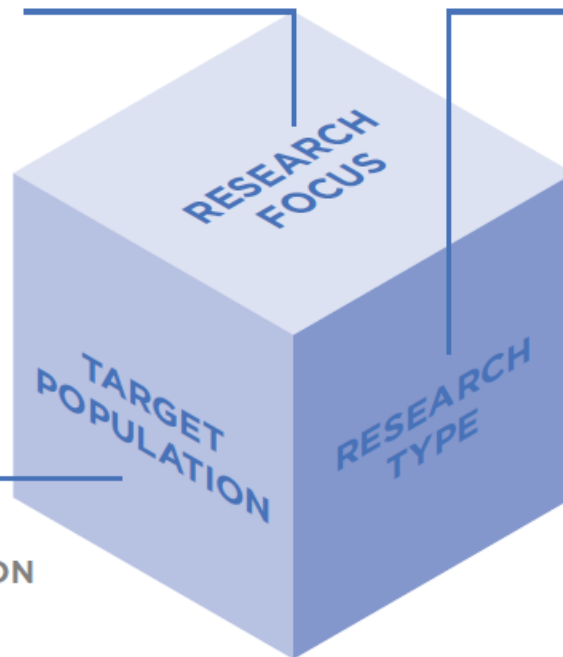
- pain, cachexia, delirium, respiratory issues, and other physical symptoms associated with advanced and metastatic cancer
- the spiritual, emotional, and social support needs of patients with advanced disease and their families, and issues of bereavement and grieving
- end-of-life care and how best to deliver quality care for patients with advanced disease
- the quality of death
- ethical issues associated with death and dying

Model systems research relevant to palliative and end-of-life care, such as testing of palliative therapies for pain management using mouse models, is also included.

In addition to allocating projects to either survivorship and/or palliative and end-of-life, projects are coded to three other dimensions described in detail below.

## RESEARCH FOCUS

- Physiological effects
- Psychological effects
- Quality of life
- Social needs/social support
- Economic sequelae
- Care delivery, access and quality
- Thanatological issues



## RESEARCH TYPE

- Model systems
- Descriptive
- Intervention
- Prediction/assessment
- Knowledge synthesis
- Other support

## TARGET POPULATION

- Patients
- Family/caregivers

TARGET POPULATION	DEFINITION	EXAMPLE
Patients	Projects where the focus or study population is patients.	<ul style="list-style-type: none"> <li>• <i>Examination of the impact of a physical activity intervention on adolescent cancer survivors: determinants of health-related quality of life</i></li> </ul>
Family/Caregivers	Projects where the focus or study population is family members and/or caregivers.	<ul style="list-style-type: none"> <li>• <i>Psychological distress of informal caregivers who support patients suffering from advanced cancer</i></li> </ul>

RESEARCH FOCUS	DEFINITION	EXAMPLE
Physiological effects	Studies identifying and managing specific late/long-term physical effects of cancer/cancer treatment (e.g., cardiovascular, respiratory, digestive, neurological, reproductive) on patients and symptoms such as pain, cachexia/anorexia, dyspnea, etc., associated with end of life. Includes physiological effects experienced by family/caregivers.	<ul style="list-style-type: none"> <li>• <i>Charting the course of arm morbidity in breast cancer: A prospective, longitudinal follow-up</i></li> <li>• <i>Development and Feasibility Testing of a Home-Based Physical Activity Intervention for Family Caregivers of People with Advanced Cancer</i></li> </ul>
Psychological effects	Research identifying and managing specific psychological effects (for example, depression, anxiety, distress, fear of recurrence, intimacy issues) of survivorship/end of life for patients and family/caregivers.	<ul style="list-style-type: none"> <li>• <i>Screening for depression in breast cancer patients: Acute distress versus persistent distress</i></li> </ul>
Quality of life	Research focused on a broad range of symptoms/outcomes rather than specific effects as identified under other foci. Includes projects focused on survivors and/or family/	<ul style="list-style-type: none"> <li>• <i>Exploring the impact of thyroid cancer on young women's quality of life</i></li> </ul>

RESEARCH FOCUS	DEFINITION	EXAMPLE
	caregivers from post-treatment to end of life.	
Social needs/social support	Studies on the social support needs of survivors and family/caregivers.	<ul style="list-style-type: none"> <li><i>The role of prostate cancer support groups in health promotion</i></li> </ul>
Economic sequelae	Studies of the economic effects of cancer for survivors and their families/caregivers. Research dealing with work/employment and vocational/educational issues are also included.	<ul style="list-style-type: none"> <li><i>The impact of out-of-pocket costs, provincial/territorial medical travel and drug policies on breast and prostate cancer patients</i></li> </ul>
Care delivery, access and quality	Research on the ways that post-treatment and end-of-life care are delivered/organized and effects on individuals and systems. Includes evaluative studies, research on optimal care models, studies on gaps/inequities in access, costs/cost-effectiveness of care, and quality of care.	<ul style="list-style-type: none"> <li><i>Different profiles of care received by patients dying of cancer during the last six months of life: A study based on administrative datasets</i></li> </ul>
Thanatological issues	Research on death/dying and the psychological mechanisms of dealing with death/dying. Includes attitudes toward death, meaning and behaviours of bereavement and grief, and moral/ethical issues.	<ul style="list-style-type: none"> <li><i>Engaging existential suffering in end-of-life: a grounded theory inquiry</i></li> </ul>

RESEARCH TYPE	DEFINITION	EXAMPLE
Model systems	Research conducted in animals, human or animal cells, or other test systems or theoretical models.	<ul style="list-style-type: none"> <li><i>Role of neurotensin receptors in a mouse model of chronic cancer pain</i></li> </ul>
Descriptive	Studies that observe/describe human behaviour, interaction, or systems prospectively or retrospectively. Covers the range of studies from small, single-centre, non-randomized studies to cohort or population-based studies. Administrative data sources or registries may be involved.	<ul style="list-style-type: none"> <li><i>Prevalence of neuropathic pain symptoms in patients with cancer bone pain referred for palliative radiotherapy</i></li> </ul>
Intervention	Research on treatments/programs designed to prevent/control adverse treatment-related and late effects of cancer and/or optimize health/quality of life. The intervention may be directed at survivors, family/caregivers, or formal care providers. It may be pharmaceutical, surgical, psychotherapeutic, behavioural, supportive, informational, etc. Includes retrospective observational studies.	<ul style="list-style-type: none"> <li><i>A Phase III international randomized trial of single versus multiple fractions for re-irradiation of painful bone metastases</i></li> </ul>
Prediction/assessment	Studies focused on systematically assessing/measuring and predicting symptoms, outcomes, and late effects. Includes research on instrument development, validation, and refinement as well as statistical approaches to improve measurement.	<ul style="list-style-type: none"> <li><i>Identifying factors associated with functional decline in older women living with breast cancer: Development and validation of a self-reported risk profile</i></li> </ul>
Knowledge synthesis	Projects that aggregate/summarize the existing body of knowledge by applying specific methods of research identification and appraisal	<ul style="list-style-type: none"> <li><i>Systematic review: Measures of sexual quality of life for female cancer survivors</i></li> </ul>

RESEARCH TYPE	DEFINITION	EXAMPLE
	(for example, systematic reviews, meta-analyses).	
Other support	Funding for projects that support the conduct of research (for example, capacity building grants, support for research networks and workshops, equipment and infrastructure grants).	<ul style="list-style-type: none"> <li>• <i>The Electronic Living Laboratory for Interdisciplinary Cancer Survivorship Research: Bridging the gap for chronic cancer care</i></li> </ul>

### *Limitations*

The general limitations apply, but it is worth repeating that the CCRS does not include all intramural cancer research supported by federal and provincial governments/agencies or by universities, hospitals, or cancer centres and that there may be research conducted in the areas of cancer survivorship and palliative and end-of-life cancer care under the auspices of these programs.



## Metastatic Breast Cancer

The impetus for and development of this report was provided by two patient partners with metastatic breast cancer (MBC) who were interested in tracking the MBC investment as it relates to the overall breast cancer research investment and to research priorities identified through a James Lind Alliance process conducted in 2018. To identify research projects for inclusion, the following steps are employed:

- Include projects coded to breast cancer where at least 50% of the research is relevant to breast cancer
- Apply keyword searches (metast\*, invasion/invasive, migration, stage 4, cancer spread, etc.) combined with CSO code (1.4) to identify prospective projects
- Manually review prospective projects - single coder reviews all projects and a subset is reviewed by a second coder
- Assign, where relevant, to the top 10 MBC PSP research priorities (see below)

### Metastatic Breast Cancer (Canada) Top 10 Priorities

1. What biomarkers or intrinsic features of the tumour can be used to identify response to specific treatments and dosing schedules?
2. What is the role of immunotherapy for metastatic breast cancer?
3. How can treatment resistance be delayed, and minimized?
4. What causes (i.e., cellular, genomic changes) breast cancer cells to metastasize, and what changes allow them to penetrate the blood-brain barrier?
5. What is the right sequence of therapy in metastatic breast cancer?
6. Does local therapy (radiation or surgery to sites of metastatic disease) improve survival outcomes in metastatic breast cancer?
7. Is continuous treatment with systemic therapy (including HER2-targeted therapy and chemotherapy) better than intermittent treatment?
8. Does early palliative care improve outcomes for metastatic breast cancer patients?
9. What are the best methods of education for patients around treatment options and decision making that can lead to improved patient outcomes?
10. Can safer, more accurate methods, including blood tests of detecting spread of disease (including following curative intent treatment) be developed?

(Source: <https://www.jla.nihr.ac.uk/priority-setting-partnerships/metastatic-breast-cancer-canada#tab-27631>)

### *Limitations*

The general limitations apply, but it is worth repeating that the CCRS does not include industry-supported clinical trials, BC Cancer (not a contributor to CCRS), and sources from outside Canada (in particular, the U.S. Department of Defense's Congressionally Directed Medical Research Programs and Susan G. Komen).

## Appendix A. Organizations Tracked in the CCRS

SECTOR	RELATIONSHIP TO CCRA	ORGANIZATION	ABBREVIATION	DATA SOURCE	IMPORTANT ISSUES
Federal government	Member	BioCanRx		Submits data	Originally funded under through the Networks of Centres of Excellence. Since 2024, funded through the Strategic Science Fund.
Federal government	Member	Canadian Institutes of Health Research	CIHR	Submits data	
Federal government	Member	Canadian Partnership Against Cancer	CPAC	Submits data	
Federal government	Member	Genome Canada		Submits data	
Federal government	Member	National Research Council Canada	NRC	Submits data	Did not provide data for years 2011 to 2016, but resumed reporting in 2016/17
Federal government	Member	Public Health Agency of Canada	PHAC	Data obtained through CIHR	Although Health Canada funds the Canadian Partnership Against Cancer, the Partnership is shown as a separate organization in the CCRS.
Federal government	Non-member	Canada Excellence Research Chairs	CECR	Website extract	
Federal government	Non-member	Canada Foundation for Innovation	CFI	Website extract	Reported directly for years 2005, 2006 and 2007. Partner contributions are estimated from the CFI maximum contribution, unless available from other sources.
Federal government	Non-member	Canada Research Chairs Program		Website extract	Submitted data up to 2020.
Federal government	Non-member	Networks of Centres of Excellence	NCE	Website extract	

SECTOR	RELATIONSHIP TO CCRA	ORGANIZATION	ABBREVIATION	DATA SOURCE	IMPORTANT ISSUES
Federal government	Non-member	Social Sciences and Humanities Research Council	SSHRC	Website extract	
Federal government	Non-member (former member)	Natural Sciences and Engineering Research Council	NSERC	Website extract	Reported directly for years 2005 to 2018.
Federal government	Non-member	Canadian Research Coordinating Committee – New Frontiers in Research Fund		Website extract	
Provincial government	Member	Alberta Innovates		Submits data	No data provided for years 2020, 2021, 2022
Provincial government	Member	CancerCare Manitoba	CCMB	Submits data	
Provincial government	Member	Fonds de recherche du Québec – secteur de santé	FRQS	Submits data	
Provincial government	Member	Michael Smith Health Research BC		Submits data	
Provincial government	Member	Nova Scotia Cancer Care Program – Nova Scotia Health Authority		Submitted data	No longer funds research.
Provincial government	Member	Ontario Health - Cancer Care Ontario	CCO	Submitted data	Currently not funding research.
Provincial government	Member	Ontario Institute for Cancer Research	OICR	Submits data	
Provincial government	Member	Research Manitoba		Submits data	
Provincial government	Member	Saskatchewan Cancer Agency	SCA	Submits data	
Provincial government	Member	Saskatchewan Health Research Council	SHRF	Submits data	
Provincial government	Non-member	ResearchNB		Website extract	Provided data for years 2006 to 2018.
Provincial government	Non-member	Newfoundland and Labrador Centre for Applied Health Research	NLCAHR	Submits data	Currently not funding projects.
Provincial government	Non-member	Ontario Ministry of Colleges and Universities		Website extract	Submitted data up to 2021.
Provincial government	Non-member	Research Nova Scotia		Submits data	Precursor organization, Nova Scotia Health Research Foundation, was a member.

SECTOR	RELATIONSHIP TO CCRA	ORGANIZATION	ABBREVIATION	DATA SOURCE	IMPORTANT ISSUES
Charity/Voluntary	Member	Alberta Cancer Foundation	ACF	Submits data	
Charity/Voluntary	Member	Beatrice Hunter Cancer Research Institute	BHCRI	Submits data	
Charity/Voluntary	Member	Bladder Cancer Canada		Submits data	
Charity/Voluntary	Member	Brain Tumour Foundation of Canada	BTFC	Submits data	
Charity/Voluntary	Member	Breast Cancer Canada	BCSC	Submits data	
Charity/Voluntary	Member	C <sup>17</sup> Research Network		Submits data	
Charity/Voluntary	Member	Canadian Association of Radiation Oncology	CARO	Website extract	Submitted data prior to 2016
Charity/Voluntary	Member	Canadian Cancer Society	CCS	Submits data	Canadian Cancer Trials Group (CCS-funded trials) submits directly
Charity/Voluntary	Member	Cancer Research Society	CRS	Submits data	
Charity/Voluntary	Member	Kidney Foundation of Canada	KFOC	Submits data	
Charity/Voluntary	Member	Leukemia and Lymphoma Society of Canada	LLSC	Submits data	
Charity/Voluntary	Member	Movember Canada		Submits data	Includes research projects were funded through Prostate Cancer Canada for years 2009 to 2019. Prostate Cancer Canada amalgamated with CCS in 2020.
Charity/Voluntary	Member	Myeloma Canada		Submits data	
Charity/Voluntary	Member	Ovarian Cancer Canada		Submits data	
Charity/Voluntary	Member	Pancreatic Cancer Canada		Submits data	
Charity/Voluntary	Member	PROCURE		Submits data	
Charity/Voluntary	Member	Quebec Breast Cancer Foundation	QBCF	Submits data	
Charity/Voluntary	Member	Terry Fox Research Institute	TFRI	Submits data	

<b>SECTOR</b>	<b>RELATIONSHIP TO CCRA</b>	<b>ORGANIZATION</b>	<b>ABBREVIATION</b>	<b>DATA SOURCE</b>	<b>IMPORTANT ISSUES</b>
Charity/Voluntary	Non-member	Pediatric Oncology Group of Ontario	POGO	Website extract	
Charity/Voluntary	Non-member	Cole Foundation		Website extract	

## Appendix B. Cancer Site Algorithms

TOPIC	ICD CODE/ CCRS CODE	DESCRIPTION	ALLOCATION	NOTES
Alcohol-related cancers/alcohol as risk factor	C06.9	Mouth, unspecified/Oral cavity NOS	15.00	
	C10.9	Oropharynx, unspecified	15.00	
	C15	Esophagus	35.00	
	C22.9	Liver, unspecified	25.00	
	C50	Breast	10.00	
Arsenic exposure (risk factor)	A000	Non-specific/All sites	25.00	
	C34	Bronchus and lung	25.00	
	C43	Skin [melanoma]	25.00	
	C67	Bladder	25.00	
Brachytherapy (without specific application identified)	C34	Bronchus and lung	25.00	
	C50	Breast	25.00	
	C61	Prostate	25.00	
	C69.9	Eye, unspecified	25.00	
BRCA1/2	C50	Breast	70.00	Used when it is not obvious that the project is focused on one site versus the other. When both sites are indicated in the title, a 50/50 allocation is used.
	C56	Ovary	30.00	
Childhood cancers (non-specified)	A000	Non-specific/All sites	20.00	
	C40	Bone and articular cartilage of limbs	6.00	
	C49	Other connective and soft tissue	6.00	
	C64	Kidney	4.00	
	C71	Brain	16.00	
	C74.9	Adrenal gland, unspecified	5.00	
	C85.9	Non-Hodgkin lymphoma, unspecified type	17.00	
	C95.9	Leukemia, unspecified	26.00	
Childhood cancers (hereditary)	C64	Kidney	14.00	
	C69.2	Retinoblastoma	74.00	
	C71	Brain	5.00	
	C91.0	Acute lymphoblastic leukemia, acute lymphocytic leukemia	7.00	

TOPIC	ICD CODE/ CCRS CODE	DESCRIPTION	ALLOCATION	NOTES
Drinking water contaminants (risk factor)	C22.0	Liver/hepatocellular carcinoma	25.00	
	C64	Kidney	25.00	
	C67	Bladder	25.00	
	C72.9	Central nervous system, unspecified	25.00	
Environmental Tobacco Smoke (ETS)	C34	Bronchus and lung	100.00	If project relates to both smoking and ETS exposure, the tobacco algorithm is used.
Epstein-Barr Virus (EBV) related cancers	C11.9	Nasopharynx, unspecified	17.00	
	C16	Stomach	17.00	
	C83.7	Burkitt lymphoma	17.00	
	C84.9	Mature T/NK-cell lymphoma, unspecified	17.00	
	C85.9	Non-Hodgkin lymphoma, unspecified type	16.00	
	D47.9	Neoplasms of uncertain or unknown behaviour of lymphoid, hematopoietic and related tissue, unspecified	16.00	
Female cancers, unspecified	C50	Breast	70.00	
	C53	Cervix	4.00	
	C55	Uterus	17.00	
	C56	Ovary	9.00	
Gastrointestinal cancers/cancers of the digestive tract (non-specified)	C15	Esophagus	6.00	
	C16	Stomach	12.00	
	C17.9	Small intestine, unspecified	2.00	
	C19	Colorectal	80.00	
Germ cell tumours (non-specified)	A000	Non-specific/All sites	10.00	
	C56.9	Sertoli-Leydig Cell Tumour	45.00	
	C62.9	Testis, unspecified	45.00	
Graft versus Host Disease (GvHD)/Bone marrow transplantation/hematopoietic stem cell transplantation	A000	Non-specific/All sites	8.00	
	C85.9	Non-Hodgkin lymphoma, unspecified type	13.00	
	C90.0	Multiple myeloma	4.00	
	C91.0	Acute lymphoblastic leukemia	12.00	

TOPIC	ICD CODE/ CCRS CODE	DESCRIPTION	ALLOCATION	NOTES
	C92.0	Acute myeloblastic leukemia	28.00	
	C92.1	Chronic myeloid/ myelogenous leukemia, BCR/ABL-positive	23.00	
	D46.9	Myelodysplastic syndrome, unspecified	12.00	
Gynecological cancers (non-specified)	C53	Cervix	18.00	
	C54	Corpus uteri	45.00	
	C56	Ovary	29.00	
	C57.9	Female genital organ, unspecified	8.00	
Head and neck cancers (non-specified)	C01	Base of tongue	14.00	
	C02	Other parts of tongue	14.00	
	C03	Gum	14.00	
	C04	Floor of mouth	14.00	
	C05	Palate	14.00	
	C06	Other parts of mouth	14.00	
	C14.0	Pharynx, unspecified	16.00	
Hematological malignancy (unspecified)	C81.9	Hodgkin lymphoma, unspecified	6.00	
	C85.9	Non-Hodgkin lymphoma, unspecified type	47.00	
	C90.0	Multiple myeloma	15.00	
	C95.9	Leukemia, unspecified	32.00	
Herpes Simplex	C06.9	Mouth, unspecified/Oral cavity NOS	33.00	
	C44	Skin, other	34.00	
	C90.2	Plasmacytoma, extramedullary	33.00	
HHV 6&8	C44	Skin, other	20.00	
	C46	Kaposi's sarcoma	20.00	
	C85.1	B-cell lymphoma, unspecified	20.00	
	C85.9	Non-Hodgkin lymphoma, unspecified type	20.00	
	D36	Benign neoplasm of other and unspecified sites	20.00	
HIV	C46	Kaposi's sarcoma	50.00	



TOPIC	ICD CODE/ CCRS CODE	DESCRIPTION	ALLOCATION	NOTES
	C85.9	Non-Hodgkin lymphoma, unspecified type	50.00	
HPV (both sexes)	C10.9	Oropharynx, unspecified	14.00	Reference: <a href="https://hpcvcentre.net/statistics/reports/CAN_FS.pdf">https://hpcvcentre.net/statistics/reports/CAN_FS.pdf</a>
	C06.9	Oral cavity	34.00	
	C32	Larynx	11.00	
	C21.0	Anus, unspecified	9.00	
	C51	Vulva	11.00	
	C52	Vagina	2.00	
	C53	Cervix	16.00	
	C60	Penis	3.00	
HPV (Females)	C10.9	Oropharynx, unspecified	5.00	Reference: <a href="https://hpcvcentre.net/statistics/reports/CAN_FS.pdf">https://hpcvcentre.net/statistics/reports/CAN_FS.pdf</a>
	C06.9	Oral cavity	21.00	
	C32	Larynx	4.00	
	C21.0	Anus, unspecified	12.00	
	C51	Vulva	21.00	
	C52	Vagina	4.00	
	C53	Cervix	33.00	
HPV (Males)	C10.9	Oropharynx, unspecified	24.00	Reference: <a href="https://hpcvcentre.net/statistics/reports/CAN_FS.pdf">https://hpcvcentre.net/statistics/reports/CAN_FS.pdf</a>
	C06.9	Oral cavity	47.00	
	C32	Larynx	19.00	
	C21.0	Anus, unspecified	5.00	
	C60	Penis	5.00	
Li-Fraumeni syndrome (associated cancers)	A000	Non-specific/All sites	14.00	
	C41.9	Bone and articular cartilage, unspecified	15.00	
	C49.9	Connective and soft tissue, unspecified	15.00	
	C50	Breast	13.00	
	C71	Brain	30.00	
	C74	Adrenal gland	13.00	
Low fruit and vegetable intake/Diet (risk factor)	C15	Esophagus	5.00	
	C16	Stomach	15.00	
	C19	Colorectal	15.00	
	C34	Bronchus and lung	65.00	
Lynch Syndrome	C16	Stomach	12.00	
	C17	Small intestine	1.00	
	C19	Colorectal	80.00	
	C22.0	Liver/hepatocellular carcinoma	2.00	
	C68.9	Urinary organ, unspecified	4.00	

TOPIC	ICD CODE/ CCRS CODE	DESCRIPTION	ALLOCATION	NOTES
	C72.8	Overlapping lesion of brain and other parts of central nervous system	1.00	
Neuroendocrine/ Carcinoid Tumours	A000	Non-specific/All sites	3.00	Based on: Hallet J, Law CH, Cukier M, Saskin R, Liu N, Singh S. Exploring the rising incidence of neuroendocrine tumors: a population-based analysis of epidemiology, metastatic presentation, and outcomes. Cancer. 2015 Feb 15;121(4):589-97.
	C16	Stomach	6.00	
	C17	Small intestine	20.00	
	C18.9	Colon, unspecified	14.00	
	C20	Rectum	19.00	
	C25	Pancreas	12.00	
	C34	Bronchus and lung	26.00	
Obesity (risk factor)	C15	Esophagus	10.00	
	C19	Colorectal	35.00	
	C50	Breast	20.00	
	C55	Uterus	20.00	
	C64	Kidney	15.00	
Peutz-Jeghers Syndrome	A000	Non-specific/All sites	30.00	Based on: Van Lier, MG, Wagner, A, Mathus-Vliegen, EM. (2010). High cancer risk in Peutz-Jeghers syndrome: a systematic review and surveillance recommendations. Am J Gastroenterol, 105(6):1258-64.
	C16	Stomach	10.00	
	C17	Small intestine	15.00	
	C19	Colorectal	20.00	
	C25	Pancreas	10.00	
	C50	Breast	15.00	
Physical inactivity (risk factor), without obesity mention	C19	Colorectal	60.00	
	C50	Breast	40.00	
Physical inactivity (risk factor), with obesity mention	A000	Non-specific/All sites	5.00	
	C19	Colorectal	60.00	
	C50	Breast	25.00	
	C54.1	Endometrium	10.00	
Smokeless tobacco	C06.9	Mouth, unspecified/Oral cavity NOS	34.00	
	C14.0	Pharynx, unspecified	33.00	
	C32	Larynx	33.00	
Tobacco (also used for e-cigarettes)	A000	Non-specific/All sites	5.00	Science on e-cigarettes still emerging, so this is a temporary coding solution.
	C14.0	Pharynx, unspecified	15.00	
	C15	Esophagus	15.00	
	C32	Larynx	15.00	
	C34	Bronchus and lung	50.00	
Upper Aerodigestive Tract (UADT)	C06.9	Mouth, unspecified/Oral cavity NOS	55.00	
	C10.9	Oropharynx, unspecified	5.00	

TOPIC	ICD CODE/ CCRS CODE	DESCRIPTION	ALLOCATION	NOTES
	C11.9	Nasopharynx, unspecified	5.00	
	C13.9	Hypopharynx, unspecified	5.00	
	C32.9	Larynx, unspecified	30.00	
Von Hippel-Lindau Syndrome (VHL)	C64	Kidney	70.00	
	C74.1	Medulla of adrenal gland (pheochromocyto ma)	15.00	
	D18.0	Haemangioma, any site	15.00	