

What do we mean when we ask for more metastatic breast cancer research?

Heather Douglas,¹ Kimberly Badovinac,² and Nancy A. Nixon³

¹MBC Patient Advocate, ²Canadian Cancer Research Survey, CCRA, ³MD, Tom Baker Cancer Centre and University of Calgary

Background

Breast cancer is incurable and deadly once it metastasizes. While approximately 5% of breast cancer patients in Canada are diagnosed with Stage IV disease initially,¹ 20-30% of Stage I-III patients later develop metastatic recurrences.² Although recurrences are not tracked by the provincial cancer registries in Canada, there is evidence to suggest that many metastatic recurrences continue beyond the five-year mark.³ Extrapolating from U.S. sources, an estimated 15,000 to 18,000 people are living with metastatic breast cancer (MBC) in Canada.⁴ Each year, over 5,000 die of metastatic breast cancer.⁵

Each year, MBC teams across Canada join the CIBC Run for the Cure to raise awareness of MBC in the wider breast cancer community and to raise funds for metastatic research at the Canadian Cancer Society (CCS). These teams, formed of people living with MBC and their friends and family members, are strongly committed to research. Their personal fundraising messages refer to seeking more effective treatments and a hope for a cure. But is actual cancer research spending aligned with their hopes?

The purposes of this poster are:

- to provide updated data on how cancer research is being invested in MBC in Canada; and
- to examine how this investment aligns with patient-identified priorities.

Two past studies assisted with our analysis. First, the MBC Alliance, a U.S.-based alliance of patient advocates, non-profit breast cancer organizations, and industry representatives, produced a comprehensive landscape analysis of MBC research in 2014. The MBC Alliance's analysis of the International Cancer Research Partnership (ICRP) and the Health Research Alliance (HRA) grant databases revealed that, of the \$15-billion invested in breast cancer from 2000 to 2013 by major governmental and non-profit funders from North America and the United Kingdom, 7.1% was for MBC research.⁶

Second, the MBC Priorities Setting Partnership (PSP) convened in Canada in 2018 to identify urgent research priorities for MBC using the James Lind Alliance (JLA) methodology.⁷ The initiative was led by the MBC PSP Steering Group, which included four medical oncologists, one nurse, three patients, one caregiver and representatives from the Canadian Breast Cancer Network and Rethink Breast Cancer. MBC patients, caregivers, and health care professionals were surveyed to elicit their questions regarding MBC. Representative research questions were generated from survey responses, which were then distributed via an interim prioritization survey. A shortlist of research questions was taken to a final consensus meeting. The resulting top 10 research priorities are identified in Table 1.

Table 1. Top 10 MBC Research 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?

Nixon NA et al. (2019). Research priorities in metastatic breast cancer: A James Lind Alliance Priority Setting Partnership. *Breast J* (online version) <https://doi.org/10.1111/tbj.13525>

Methodology

MBC research projects were identified in the Canadian Cancer Research Survey, which is a compilation of research grants from 42 organizations initiated and maintained by the Canadian Cancer Research Alliance (CCRA). CCRA estimates that its database covers approximately 60-80% of overall cancer funding in Canada. It does not include institution-specific funding from hospital foundations, research supported by private foundations or industry R&D unless part of research projects included in the database.

All research projects are coded according to the Common Scientific Outline (CSO), which is the classification system used by the International Cancer Research Partnership, of which CCRA is a member. Table 2 summarizes the broad CSO categories, but the coding guidelines are significantly more detailed. The breakdown for 1.0 Biology is included given its relevance to MBC research.

To identify breast cancer metastasis projects, the database (N=22,788) was filtered for research projects coded to breast cancer that were weighted as at least 50% relevant to breast cancer (N=4,076). This sample of projects were then analyzed to see if they were relevant to breast cancer metastasis. All projects coded to CSO 1.4 were examined. Keyword searches (metast*, invasion/invasive, migration, stage 4, cancer spread, etc.) were used to narrow the list. The resulting 905 projects were coded to the MBC PSP priorities identified by Nixon et al. (2019).

Findings

The distribution of the investment by CSO category was examined for the most recent four-year period (2013-2016) for which data are available. Over this period, the MBC research investment of \$38.5 million was 15.5% of the overall breast cancer research investment (\$248.8 million).

The CSO investment for all breast cancer research is shown in Figure 1 for comparative purposes. Much of the MBC research investment (76.7%) was in CSO 1 - Biology (Figure 1). This investment represented nearly one-third of the overall breast cancer research investment in this CSO category. CSO 5- Treatment represented 15% of the MBC investment. CSO categories, 2 - Etiology, 4 - Early

Figure 1. Breast Cancer Research Investment by CSO, 2013-2016 (%)

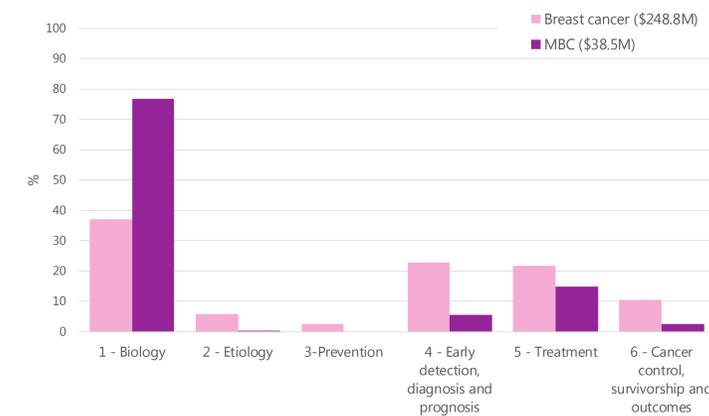


Figure 2. Research Investment, 2005-2016 - Breast Cancer (\$M)

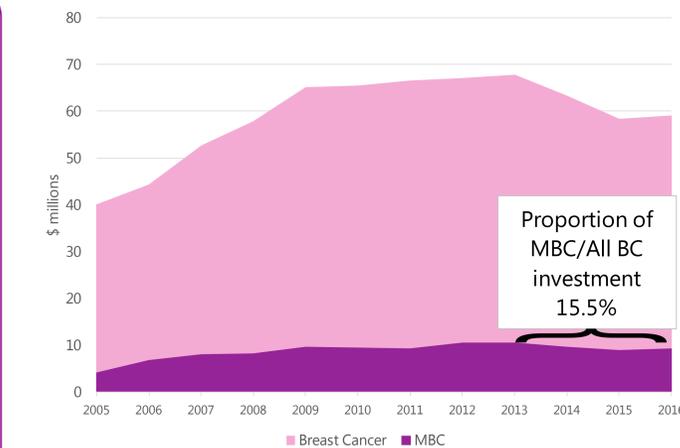
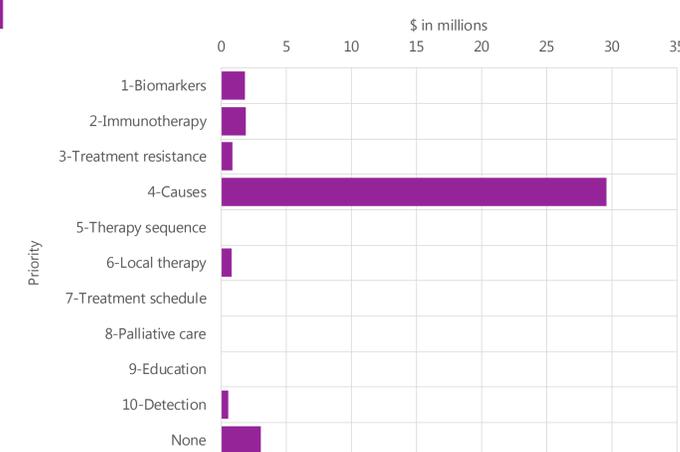


Figure 3. MBC Research Investment by Priority, 2013-2016 (\$M)



Detection, Diagnosis & Prognosis, and 6 - Cancer Control, Survivorship & Outcomes, had low levels of investment, and obviously, CSO 3 - Prevention with its focus on primary prevention had no investment. Much of the research in CSO 4 was focused on imaging methods to detect metastases, while the research in CSO 6 tended to focus on palliative approaches to pain management.

MBC research represented 1.8% of the overall cancer research investment made by Canadian funders from 2005 to 2016. The annual MBC research investment varied from \$4.2M (2005) to \$10.6M (2012) (Figure 2).

The top four funders of MBC research over the 2013-2016 period (data not shown) were the Canadian Institutes of Health Research (\$11.9M), Canadian Breast Cancer Foundation (CBCF) (\$11.3M), The Terry Fox Research Institute (TFRI) (\$3.6M), and CCS (\$2.3M). As of February 1, 2017, CCS and CBCF merged operations. Over half of the 2013-2016 MBC research investment went to principal investigators located in Montréal (24%), Toronto (23%) and London (11%).

The MBC research investment when grouped according to the 10 MBC PSP priorities revealed no investment in four of the largely clinical priorities and very low investment in all but priority 4 (Figure 3). For the purposes of this study, all biomedical research on mechanisms of metastases were coded to priority 4. These data show that, except for priority 4, the priorities have received scant to no funding. Within the Canadian Cancer Research Survey, investments in research on immunotherapies and precision medicine - i.e., biomarkers and imaging tools to support precision medicine and drug development - have increased, so we may expect to see increases in the investment in MBC research in priorities 1, 2, 3, and 10. Priorities 5, 6, 7, 8, and 9, however, may require directed funding in order to be addressed.

Table 2. Common Scientific Outline (CSO)

- 1-Biology: Research on how cancer starts and progresses as well as normal biology relevant to these processes.
 - 1.1 Normal Functioning
 - 1.2 Cancer Initiation: Alterations in Chromosomes
 - 1.3 Cancer Initiation: Oncogene and Tumour Suppressor Genes
 - 1.4 Cancer Progression and Metastasis
 - 1.5 Resources and Infrastructure
- 2-Etiology: Research to identify the causes or origins of cancer—genetic, environmental and lifestyle, and the interactions between these factors.
- 3-Prevention: Research on identifying 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 & Prognosis: Research on identifying and testing cancer markers, imaging and other methods that are helpful in detecting and/or diagnosing cancer and cancer spread as well as predicting the outcome or chance of recurrence.
- 5-Treatment: Research on identifying and testing treatments administered locally and systemically as well as complementary/alternative approaches. Also includes research into the prevention of recurrence and the treatment of metastases.
- 6-Cancer Control, Survivorship & Outcomes: Research on a broad range of areas: patient care and pain management; tracking cancer cases in the population; beliefs and attitudes that affect behaviour regarding cancer control; education and communication approaches for patients and health care professionals; supportive and end-of-life care; and health care delivery in terms of quality and cost-effectiveness.

Source: <https://www.icrpartnership.org/cso>

Discussion

With metastasis causing essentially all deaths from breast cancer, it remains surprising to observe that MBC accounts for only a minority portion of breast cancer research in Canada. This proportion was 15.5% in the most recent time period (2013-2016) available in the CCRS, but remains higher than figures estimated by the MBC Alliance in the U.S.

Our analysis of the CCRS grant database identified gaps and a mismatch of actual spending versus the patient-identified priorities in Canada. It thus highlights the importance of increasing the involvement of MBC patient representatives in research grant priority setting and decision making.

Updated tracking is obviously needed to gauge the progress being made in terms of the 10 MBC research priorities, especially given significant recent research announcements - e.g., the SU2C Canada Metastatic Breast Cancer Dream Team and the Terry Fox New Frontiers Program Project Grant, "Targeting Metabolic Vulnerabilities in Cancer." To this end, we are committed to updating this analysis to better reflect the current funding landscape.

Acknowledgements

The authors would like to thank the people living with MBC and their families and friends who form the Metastatic Breast Cancer teams at the CIBC Run for the Cure, whose support and advocacy for metastatic breast cancer research helped inspire this poster.

We would like to thank the Canadian Institute of Health Research and other CCRA members for their support of the Patient Involvement in Cancer Research Program (PIP), and specifically the Cancer Research Society for its sponsorship of first author Heather Douglas.

We are grateful to Dr. James (Jim) Hudson, who advised on the methodology and priority coding conventions, and reviewed an earlier draft of this poster. A thank you to Cathie Hays and Patricia Stoop, who also provided feedback on this work.

References

- ¹Canadian Cancer Statistics Advisory Committee. (2018) *Canadian Cancer Statistics 2018*. Toronto, ON: Canadian Cancer Society.
- ²O'Shaughnessy J. (2005). Extending survival with chemotherapy in metastatic breast cancer. *Oncologist*, 10 (Suppl 3):20-9.
- ³Pan H et al. (2017). 20-Year risks of breast-cancer recurrence after stopping endocrine therapy at 5 years. *N Engl J Med*, 377(19):1836-46.
- ⁴Mariotto AB et al. (2017). Estimation of the number of women living with metastatic breast cancer in the United States. *Cancer Epidemiol Biomarkers Prev*, 26(6):809-15.
- ⁵Statistics Canada. Table 13-10-0142-01 Deaths, by cause, Chapter II: Neoplasms (C00 to D48).
- ⁶Metastatic Breast Cancer Alliance. (2014). *Changing the Landscape for People Living with Metastatic Breast Cancer*. <https://www.mbcalliance.org/research/landscape-analysis> (accessed 2019-10-02).
- ⁷Nixon NA et al. (2019). Research priorities in metastatic breast cancer: A James Lind Alliance Priority Setting Partnership. *Breast J* (online version) <https://doi.org/10.1111/tbj.13525>



Walker at the 2019 CIBC Run for the Cure. Source: T. James-Wong