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## What Do We Mean When We Ask for More Metastatic Breast Cancer Research?

Heather Douglas<sup>a</sup>, Catherine Hays<sup>b</sup>, Kimberly Badovinac<sup>\*c</sup><sup>a</sup> Patient Advocate, Ottawa, Ontario, Canada<sup>b</sup> Patient Advocate, Rocky View County, Alberta, Canada<sup>c</sup> Canadian Partnership Against Cancer, Toronto, Ontario, Canada

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### ABSTRACT

**Background:** Almost all deaths from breast cancer are due to metastasis. People living with metastatic breast cancer (MBC) and their loved ones have been concerned about the lack of research progress. The purposes of this paper were to analyze breast cancer research spending in Canada, and to evaluate whether MBC research was aligned with patient priorities. The results from the MBC Priority Setting Partnership (MBC PSP) were used as an approximation of patient priorities.

**Methods:** The data source was the Canadian Cancer Research Survey. MBC projects were identified and mapped to the patient priorities.

**Results:** This analysis found that 18% of breast cancer research investment was directed to MBC, with a large proportion of this research investment focused on the biology of metastasis. Four of the top 10 MBC PSP priorities had not been addressed: optimal sequence of therapy, role of continuous versus intermittent treatment, benefits of early palliative care, and best methods for patient education.

**Conclusion:** These figures provide a baseline from which any increases in MBC research and improved alignment to patient priorities can be measured. A cooperative effort by funders, researchers, patients, caregivers, and health care providers is needed to address research gaps.

### Introduction

Breast cancer is incurable and deadly once it metastasizes. Extrapolating from US sources, an estimated 15,000 to 18,000 people are living with metastatic breast cancer (MBC) in Canada, from Stage IV de novo diagnoses or from metastatic recurrences after previous Stage 0-3 diagnoses and treatment.<sup>1</sup> Each year, over 5,000 Canadians die from MBC.<sup>2</sup> The genesis of this paper was a concern among MBC research advocates about the lack of research progress that offers potential cures or

quality long-term survival.

The purpose of this paper is three-fold: (1) to provide an analysis of breast cancer research spending in Canada, (2) to provide an analysis of MBC research spending in Canada, and (3) to assess how the MBC research investment aligns with patient priorities, closely approximated by results from the Metastatic Breast Cancer Priority Setting Partnership (MBC PSP). Patients, patient representative groups, and caregivers represented 60% of the contributors to the MBC PSP.<sup>3</sup>

### Methods

The data source for this descriptive analysis was the Canadian Cancer Research Survey (CCRS)<sup>4</sup>, a longitudinal database of cancer research grants and awards funded by 42 Canadian governmental and non-governmental organizations and programs. The

### \*Address for correspondence:

Kimberly Badovinac, MA, MBA  
Address: Canadian Partnership Against Cancer, 145 King Street  
West, Suite 900, Toronto, Ontario, Canada, M5H 1J8  
Tel: +1 (416) 619-6265  
Email: [kimberly.badovinac@partnershipagainstcancer.ca](mailto:kimberly.badovinac@partnershipagainstcancer.ca)



database contains over 26,000 projects from January 1, 2005 to December 31, 2018. It is updated annually and the 2019 data are in progress. The CCRS is estimated to capture about 60 to 80% of the peer-reviewed cancer research funded by Canadian organizations. All projects are coded to cancer site(s) and to the Common Scientific Outline (CSO)<sup>5</sup>, an internationally used typology of cancer science.

The database was first filtered for projects coded to breast cancer where at least 50% of the research was relevant to breast cancer (N=4,469). Next, keyword searches (metast\*, invasion/invasive, migration, stage 4, cancer spread) combined with CSO codes were used to identify MBC projects (N=905). Finally, each MBC project identified through the search was manually reviewed by a single reviewer (and a subset by a second reviewer) and assigned to one (or none) of the top 10 MBC PSP research priorities.

### Results

Across the 14 years examined, 18% of the investment in breast cancer research was related to MBC (range 14 to 22%) (Figure 1). MBC investment accounted for less than 3% of the overall cancer research investment captured in the CCRS.

The results showed that 84% of the MBC research investment for 2014–2018 was aligned with the MBC PSP priorities (Table 1). The causes of breast cancer metastasis (priority 4a + 4b) represented over 65% of investment, but little was related to the brain-blood barrier, the second part of this priority (4b). Notably, there was no investment in four of the priorities, namely: optimal sequence of therapy (priority 5); continuous versus intermitted treatment (priority 7); the benefit of early palliative care (priority 8); and the best practices of patient

education (priority 9).

### Discussion

At 18%, the proportion of MBC research among Canadian funders included in the CCRS varies from the 7% reported by the Metastatic Breast Cancer Alliance for 2000–2013<sup>6</sup>, to the 58% (for the Breast Cancer Research Program of the U.S. Congressionally-directed Medical Research Program to 15% (U.S. National Institutes of Health) for the fiscal year 2016 reported in a poster from the 2019 San Antonio Breast Cancer Symposium prepared by advocates from the U.S.-based National Breast Cancer Coalition.<sup>7</sup> These differences may reflect the emphases of funders' research funding opportunities and/or the areas of expertise of the researchers successful in these grant competitions. Overall, the low proportion of MBC research compared to the breast cancer total may reflect obstacles such as a lack of in-vivo models, barriers to resource sharing and collaboration, and procurement of tissue/samples throughout disease progression.<sup>8</sup>

A limitation to this work is that CCRS database does not include all research spending in Canada. The database 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).

Since 2018, several promising competitions have been announced and are not yet reflected in the CCRS. Stand up to Cancer Canada, CIHR, and Canadian Cancer Society announced the SU2C MBC Dream Team winner in 2019, with funding up to \$6 million.<sup>9</sup> The Cancer Research Society and the Quebec Breast Cancer Foundation announced a \$1 million competition in late 2020. The call was

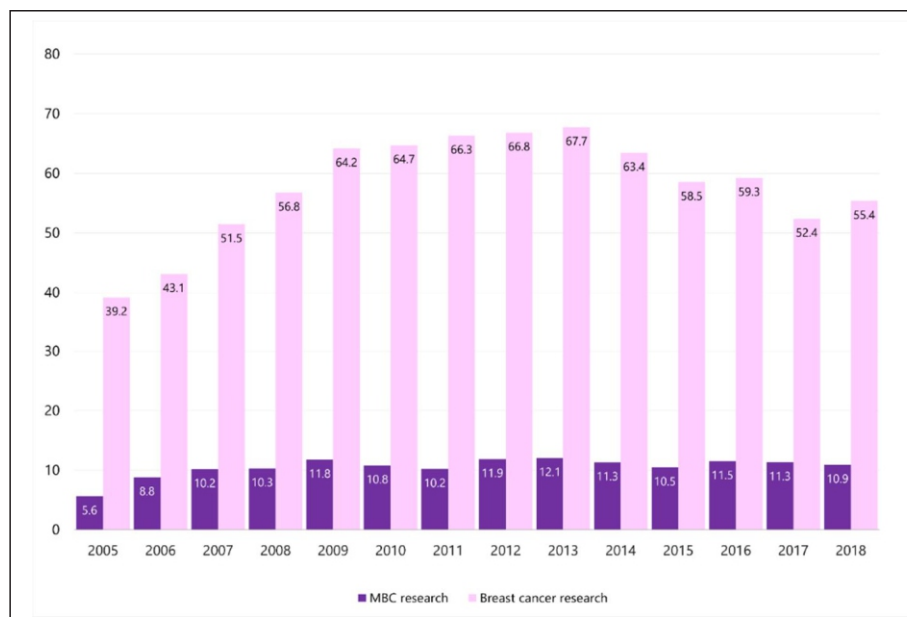


Figure 1. Breast cancer research investment in Canada included in the CCRS, 2005–2018 (CAD million)



influenced by the MBC PSP priorities and projects must focus on personalized medicine, immunotherapeutic approaches, or overcoming drug resistance.<sup>10</sup> In March 2021, Rethink Breast Cancer and Pfizer Canada announced a \$200,000 competition for strategies to improve the quality of care of MBC patients, which has the potential to address two of the unfunded MBC PSP research priorities (early palliative care and patient education).<sup>11</sup>

In summary, this analysis provides a baseline from which any increase in MBC research spending and progress on the alignment of research with patient priorities can be measured and targeted funding opportunities may be needed to address obstacles and identified gaps, those priorities which are not currently funded. Including all stakeholders – patients, caregivers, health care providers, researchers, and funders – appears to be critical to ensure these and evolving priorities are promoted and pursued.

**Table 1.** Research investment by MBC PSP Priority

Priority	CAD		%	
	2014-2018	2018 only	2014-2018	2018 only
1. Identification of biomarkers, or intrinsic features of the tumor that can be used to guide treatment decisions	2,531,140	578,916	4.55	5.30
2. Role of immunotherapy in treatment for MBC	2,399,899	332,571	4.32	3.05
3. Delaying and overcoming treatment resistance	2,094,554	538,428	3.77	4.93
4a. Identifying what causes (i.e., cellular, genomic changes) breast cancer cells to metastasize	37,286,204	6,511,822	67.09	59.62
4b. Identifying what changes in breast cancer cells allow them to penetrate the blood-brain barrier	408,263	31,292	0.73	0.29
5. Optimal sequence of therapy in MBC	0	0	0.00	0.00
6. Role for local therapy (radiation or surgery to sites of metastatic disease) in MBC	1,260,597	101,648	2.27	0.93
7. Role for continuous treatment with systemic therapy vs intermittent treatment	0	0	0.00	0.00
8. Early palliative care for MBC patients	0	0	0.00	0.00
9. Best methods of education for MBC patients around treatment options and decision making	0	0	0.00	0.00
10. Role for non-invasive, more accurate methods for detecting spread of disease (including following curative-intent treatment)	525,075	100,700	0.94	0.92
Total	46,505,732	8,195,377		
\$ invested not in top 10	9,068,901	2,725,927	16.32	24.96
Total MBC Research Investment	55,574,633	10,921,303	100.00	100.00

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### Conflict of Interest

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