Section 2
Environmental Landscape
Introduction

In reviewing the status of the metastatic breast cancer (mBC) landscape, through a truly holistic lens, consideration of the environmental factors impacting patient care is vital to understanding the complete picture.

Section 1: Patient Care Perspectives focused on discussing patient care and support needs along the care continuum, highlighting the extent to which they are currently being addressed globally and key emerging recommendations that could progress mBC patient care.

While direct clinical management and support for patients with mBC is crucial, it is not the sole aspect of how patients manage and live with their disease. The patient experience is also largely shaped by the surrounding environment, that both directly and indirectly affects patients with mBC. This section explores the breadth of environmental factors that influence the mBC landscape.

As outlined in the introduction to this report, research into the environmental landscape has been designed to broadly assess the current status of mBC. Three core areas have been researched (or are part of ongoing work); Policy Perspectives & Economic Burden, Societal Experience & Public Understanding and the Impact of Patient Support and Advocacy Organizations in mBC.

While this Interim Report captures some of these areas, efforts continue to assess additional factors not captured in this report such as the societal experience of patients with mBC. This additional analysis will be included in subsequent update to this report.

This section of the report shares key findings from new primary research surveys (methodologies are outlined in each chapter), it includes:

- Health Policy of mBC
- Economic Burden of mBC
- Public Understanding of mBC
- The Impact of Patient Support and Advocacy Organizations (PSOs)

One of the most important factors affecting public understanding of mBC is the stigma associated with the disease. This is explored further within the Public Understanding of mBC chapter. In addition, as a key information source for the general population, traditional and online media are discussed and analyzed to provide an overview of their influence. It is of note, however, that an in-depth review of the impact of and information available via social media, and its impact, is required.

The role of PSOs in meeting support needs of mBC patients is also discussed in the Impact of Patient Support and Advocacy Organizations chapter, with a call for further secondary research to identify more ways in which these are and can be addressed by PSOs.
Chapter 1: Health Policy for mBC

- Health policy has a far reaching impact on mBC care; development is shaped by numerous factors and many different perspectives

- There are important differences in cancer care performance between countries which can be attributed to differences in the health policy approach

- A national cancer plan (NCP) sets out a country's ambition to face the demands of cancer
  - Many countries do not yet have a published NCP. In these countries, much needs to be done to incorporate cancer control as a national priority, before a focus on improving the care of those with breast cancer can be implemented
  - Published plans tend to focus on prevention and screening; this will not address the needs of patients already diagnosed with mBC

- Government, professional societies and patient support organizations have all played a critical role in developing health policy that has started to contribute to the better care of breast cancer, including mBC, over the last decade

- Policy decision makers are going to need to find ways to meet the rising burden of cancer as a whole and breast cancer in particular

The influence of health policy on the outcomes and experiences of patients with breast cancer, including mBC, is far reaching; most notably on access to the care and treatment that patients need. Priorities set by governments are shaped by numerous influences and can change the way that breast cancer care is delivered; in fact, public policy touches every aspect of breast cancer.

"Health policy refers to decisions, plans, and actions that are undertaken to achieve specific health care goals within a society. An explicit health policy can achieve several things: it defines a vision for the future which in turn helps to establish targets and points of reference for the short and medium term." (WHO, Health Policy, 2015)
Before discussing health policy specifically in the context of breast cancer, it is helpful to understand the breadth of factors that influence decision-making at a population health level and how this impacts wider cancer health policy. As shown in Figure 2.1, numerous inter-related elements influence and shape the political and health policy environment which makes the healthcare landscape complicated for patients, practitioners and decision makers around the world to navigate.

### Figure 2.1
**Factors Influencing Health Policy**
Stevens, 1994; Remak, 2004; Broekx, 2011; Lidgren, 2007

<table>
<thead>
<tr>
<th>Population Healthcare Need</th>
<th>Demand for Services</th>
<th>Supply of Healthcare Services</th>
</tr>
</thead>
<tbody>
<tr>
<td>Determinants of health</td>
<td>Media and publicity</td>
<td>Historical pattern</td>
</tr>
<tr>
<td>Effective technologies</td>
<td>Available technologies</td>
<td>Public and political pressure</td>
</tr>
<tr>
<td>Evidence</td>
<td>Health professionals</td>
<td>Evidence</td>
</tr>
<tr>
<td>Financial support</td>
<td>Social and educational influence</td>
<td>Cancer registries</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Resource limitations</td>
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</tbody>
</table>

The relevant perspectives that inform health policy creation are diverse and include; patients, healthcare professionals, budget holders, national and international organizations such as professional groups, society itself, and the government. To optimize management of a specific disease area for any patient the factors influencing, driving and shaping health policy must be explored at both a global and an individual country level.

### A Health policy has a critical role in improving cancer outcomes

It has been shown that successful health policy approaches lead to changes in the observed incidence, mortality and survival rates for individual cancers and, as a result, different policy approaches can be compared to identify those that create the greatest cancer health gains for any population of cancer patient. (OECD, 2013a) In an effort to answer the question “Do certain care policies lead to fewer deaths?” the Secretary General of the Organization for Economic Co-operation and Development (OECD) reported the results of a study carried out in 35 countries to explore the policy trends in cancer care over a decade (2000 – 2009). (OECD, 2013a) The study found that there are important differences in cancer care performance between OECD countries which can be attributed to differences in the health policy approach in three main aspects of care:

- Access to resources including infrastructure, personnel and medicines
- Patient care practices including access to evidence based care
- Governance including the development of national cancer plans

Of particular note, the report highlighted that breast cancer mortality declined across all OECD countries over the time period covered by the study. While the changes in outcomes are covered in detail in Section 3: *Scientific Landscape*, from a policy perspective, facilitation of early detection and access to treatments contributed to the observed decrease in breast cancer related deaths. (OECD 2013a)
Methodology: New secondary research was undertaken; examining national cancer plans (NCPs) included on the European Partnership Action Against Cancer (EPPAC) website (http://www.epaac.eu/national-cancer-plans) and the World Health Organization (WHO) website (http://www.who.int/cancer/nccp/en/). While these sites are not comprehensive of all countries, this allowed for a high-level assessment of cancer plans around the world. Included in this review was an evaluation of the most recent NCPs for 25 countries in the European Union (EU) and 4 additional ex-EU countries (Austria, Belgium, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Netherlands, Norway, Poland, Portugal, Slovenia, Spain, Sweden, United Kingdom, Colombia, India, South Korea, and South Australia (a southern state in Australia, as the health system divided by regions). All are accessible via http://www.iccp-portal.org/cancer-plans.

Increasingly, countries have set out their broad ambition to face the demands of cancer through a national cancer plan (NCP). The NCP is a public health program designed to reduce cancer incidence, morbidity, and mortality through “the systematic and equitable implementation of evidence-based strategies for prevention, early detection, diagnosis, treatment, rehabilitation, palliation and research to search for innovative solutions and evaluate outcomes.” (EPAAC) The plan’s design aims to make the best use of available resources, promoting the most cost-effective measures that create the greatest benefit to the majority of the population. (EPAAC) The first plan was published in Germany in 1979 and, since then, NCPs have become increasingly prominent in many countries around the world. (OECD, 2013a) Even in high income countries, national targets captured within NCPs have traditionally focused more heavily on prevention and screening. However trends show that NCP targets are now maturing to include a broader focus on treatment, patient education and aftercare. (OECD, 2013a)

Across the 29 cancer plans reviewed in detail, the United Kingdom referred to mBC specifically. This NCP explicitly noted that a data gap existed regarding the proportion of breast cancer patients who had mBC. This in turn negatively impacted the national health systems ability to effectively plan for services. The cancer plan set out clear targets on a new approach to data collection in order to capture this information; with a stated aim to inform the collection of information on other types of metastatic cancer. (Department of Health, 2011) Despite this positive influence, outcomes for people diagnosed with breast cancer in the UK are lagging behind other countries in Europe. (Allemani, 2015; Macmillan, 2015) This suggests that in reality there can be a disparity between what is recommended in the NCP and what is implemented.

The allocation of financial resource is also an important component considered in the development of national health policy. Decisions about achieving greatest benefit for the greatest number of the population can be quantified by methods including cost effectiveness analysis. A cost effectiveness comparison highlighted the impact of early vs. late mBC diagnosis in Africa/Asia vs. North America. The disability-adjusted life year (DALYs) recorded in this analysis included accounting for societal perspectives, and clearly underscores the economic drivers in the current climate of encouraging early detection and prompt treatment of breast cancer (Figure 2.2). (Groot, 2006) However, there will always be a population of patients who either progress to, or present with mBC, for which there is no cure currently identified. Irrespective of geography, this analysis also shows that the costs associated with treating mBC effectively are far greater than those incurred whilst managing early stages of breast cancer. (Groot, 2006)
Over the last decade, global organizations and initiatives have been formed to shape breast cancer policy development and support national level implementation. In 2013 the World Health Organisation (WHO) published its Global Action Plan for the prevention and control of non-communicable diseases (NCDs) which identified cancer control as one of the major priorities. (WHO, 2013) In some low and middle-income countries, prominent public health threats such as communicable diseases (e.g. HIV, malaria) have caused the greatest pressure on governments. (Anderson, 2006) However, all signatories to the global plan have committed to achieve: (WHO, 2013)

- A 25% relative reduction in premature mortality from NCDs
- An 80% availability of affordable basic technologies and essential medicines

Moreover, the European Parliament, backed by EUROPA DONNA – The European Breast Cancer Coalition, adopted a written declaration “On the Fight Against Breast Cancer in the EU” in 2015. This statement followed previous Resolutions on Breast Cancer, (European Parliament, 2003; European Parliament, 2006) and committed that “those with mBC should have access to, and be treated in, a specialist breast unit (SBU), and their ongoing needs for care and psychosocial services should be coordinated and supported by the SBU.” (European Parliament, 2015) This builds on preliminary steps taken following the European Parliamentary declaration in 2010, which called for the European Commission to develop a framework for accreditation for SBUs by 2011. Debate amongst the medical profession about the need for specialist rather than generalist services for women with breast cancer, has been implicated in delays in implementation in some countries. (Knox, 2015) However, the 2015 declaration has reiterated the call to implement multidisciplinary SBU’s by 2016. (European Parliament, 2015)

The costs associated with treating mBC effectively are far greater than those incurred whilst managing early stages of breast cancer. (Groot, 2006)

Figure 2.2
Cost Effectiveness Comparison of Treating Breast Cancer: Intervention cost-effectiveness by breast cancer stage
Groot, 2006

<table>
<thead>
<tr>
<th>Disease Stage</th>
<th>Disability-adjusted life year (DALY) averted</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Africa/Asia</td>
</tr>
<tr>
<td>Stage I,II or III</td>
<td>&lt;$390</td>
</tr>
<tr>
<td>Stage IV</td>
<td>&gt;$3,500</td>
</tr>
</tbody>
</table>

The incremental cost-effective ratios (ICERs) suggest that the priorities for national breast cancer control programs in these countries should be prevention or treatment of early stage breast cancer whenever possible. Results also indicate the high costs of treating mBC effectively.

(B) Over the last decade, global organizations and initiatives have been formed to shape breast cancer policy development and support national level implementation.

In 2013 the World Health Organisation (WHO) published its Global Action Plan for the prevention and control of non-communicable diseases...
In recognition of the need to drive policy development in breast cancer around the world, organisations such as the Breast Health Global Initiative (BHGI), Union for International Cancer Control (UICC), Pan American Health Organization (PAHO) and WHO have developed knowledge summaries and ‘calls-to-action’ that make economically and structurally feasible recommendations for the care of patients with breast cancer. (UICC, Planning comprehensive breast cancer programs; UICC, Improving access to breast cancer care) By considering these resource-stratified, structured recommendations, countries can plan for cancer care as a whole and, ultimately, improve their provision of care for those with breast cancer including for those with mBC.

These guidelines stress the need for identifying needs and barriers, setting goals for outcomes and quantifying resources. Critical success factors include following a resource-stratified pathway that addresses:

- Structural barriers
- Sociocultural barriers
- Personal barriers
- Financial barriers

Such recommendations are helpful where the quality of cancer care as a whole requires improvement. In the majority of cases, however, recommendations focus on strategies to increase early detection of breast cancer. This is critically important but will not necessarily address the healthcare needs of patients who have already been diagnosed with mBC. (UICC, Improving access to breast cancer care)

Over the last decade, many organizations have worked proactively to create progress in a number of key areas that influence health policy and which will result in better outcomes for patients with cancer, including breast cancer. Organizations include professional clinical bodies, non-governmental organizations and patient support organizations and some of the numerous examples of their work are described here.

"Organizations working in breast health can, and should, learn from one another. It’s important that we share promising practices, exchange information and insight, and promote knowledge sharing about systematic, evidence-based approaches to improve the lives of women living with MBC. Komen engages with 1000s of national and international partner organizations and alliances to leverage resources to make the biggest impact."

*Kim Sabelko, Managing Director, Strategic Partnerships and Programs, Susan G. Komen*
International professional societies such as the American Society of Clinical Oncology (ASCO), St Gallen breast cancer scientific committee and the European Society of Oncology (ESO) in collaboration with the European Society of Medical Oncology (ESMO) have spent considerable effort in influencing policy related to screening, diagnosis and treatment of breast cancer through publication of guidelines. These guidelines support a call to action for healthcare professionals to provide specific and tailored care to patients with mBC, as discussed in detail in Section 3: Scientific Landscape. (Coates, 2015; Partridge, 2014; Giordano, 2014; Ramakrishna, 2014; Van Poznak, 2011; Cardoso, 2014) This is important because such recommendations standardize approaches to treatment and promote the delivery of evidence based cancer care. (OECD, 2013a)

In 2013, the European Society of Breast Cancer Specialists (EUSOMA) produced an update to their position paper, first published in 2000, (EUSOMA, 2000) identifying the minimum requirements to set up a specialist breast centre. The 2000 iteration of the guidelines was widely acknowledged as best practice and informed the European Parliament Resolutions in Breast Cancer 2003 and 2006. (European Parliament, 2003; European Parliament, 2006) In the 2013 update, which took into account recent advances in breast cancer diagnosis and treatment, EUSOMA recognized that the application of minimum standards and quality indicators would drive improvements in breast cancer care. As such, the position paper requires that specialist breast units must be able to provide continuity of care to patients with mBC through an integrated multidisciplinary team that includes access to a high quality palliative care service. (Wilson, 2013)

Furthermore, initiatives such as European School of Oncology (ESO) Breast Centers Network, and the Europe Against Cancer European Breast Cancer Network are a step forward in ensuring quality care for breast cancer patients through collaboration. (Breast Centres Network, 2014; EBCN) The efforts of both Networks aim to strengthen the evidence-base for cancer care. This will improve outcomes for all including those with mBC, and support policy makers in the development their national plans for breast cancer.

In the US, the National Cancer Plan forum, established by the Institute of Medicine, has brought together representatives from the government, industry, academia and consumers to debate critical policy issues in cancer care and research. (IOM, 2015) The reports created from these debates provide straightforward advice to decision-makers and the public about all aspects of cancer including issues critically relevant to those with mBC. Examples include access to affordable cancer therapies, biomarkers for molecularly targeted therapies and implementing a national clinical trials system for the 21st century. (IOM, 2015)

Additionally, the ASCO Institute for Quality is leading the development of Cancerlinq which will aggregate and analyze real-world cancer data in order to allow practices to benchmark, provide personalized insights into optimal care and uncover patterns that identify improved response to treatments. (cancerlinq.org) Additional funding provided by Komen will support the implementation of breast cancer clinical decision support, a specific breast cancer patient portal and the development of breast cancer specific guidelines and measures within Cancerlinq. This will improve the quality of patient care and drive advances in clinical research.
through greater communication and collaboration between breast care specialists. (ASCO, CCF, 2015) While it isn’t clear how much of CancerLinQ resources will be targeted towards mBC, efforts like these are likely to improve the clinical management of breast across all stages.

Furthermore, Patient Support Organizations (PSOs) have provided opportunities for patients to influence health policy themselves. Organizations such as Breast Cancer Network Australia (BCNA), EuropaDonna and Komen have contributed significantly in capturing the experiences of mBC patients and bringing them to the attention of policymakers. Further detail on the role of PSOs in shaping policy can be found in Chapter 4: The Impact of Patient Support and Advocacy Organizations in mBC.

Country level implementation of BC policies has been variable and faces several challenges

Despite the availability of global policies for cancer generally, and breast cancer specifically, adoption has been variable around the world. Based on data collected by WHO in 2013, approximately 40% (79/194) of all countries do not have, or did not report, the existence of an NCP. In Africa, the proportion is higher, with almost three-quarters (39/54) of countries in the continent without a well-defined plan to address cancer. (WHO, Policies, strategies and action plans) In these countries, much needs to be done to incorporate cancer control as a national priority, before a focus on improving the care of those with breast cancer can be implemented.

Where cancer control planning is already more advanced, the focus for breast cancer continues to be limited to early detection and screening. (OECD, 2013a)

While the healthcare needs of a given population are a core contributor to shaping health policy, within or of itself, there are many layers to consider. There is significant variation in health policy for cancer-care between countries, (OECD, 2013a) with health priorities reflecting the most significant healthcare burden to the local population. Where funding is limited, interventions may be directed to areas where the most lives can be improved with the resources available. (Global Health Working Group, 2012)

Based on data collected by WHO in 2013, approximately 40% (79/194) of all countries do not have, or did not report, the existence of an NCP. (WHO, 2013)
physical resources required to implement effective cancer care. Here there is a link between the quality of cancer care and the state of healthcare delivery. Inherent limitations in the health system impede its ability to deliver improved outcomes for patients with mBC. (Anyanwu, 2011; Chalkidou, 2014; de Souza, 2015) Poor cancer outcomes have been linked to insufficient numbers of an appropriately trained health care workforce, limited access to screening and treatment facilities, inadequate supply of necessary drugs and timeliness of treatment after diagnosis. (Harford, 2011)

In realization of these issues, guidelines have been created that account for country-level differences. For example, the BHGI consensus statements provide guidance on resource allocation for supportive and palliative care for patients with breast cancer in low-income and middle-income countries. (Distelhorst, 2015; Anderson, 2006) Moreover, the clinical management recommendations included in the ABC guidelines were developed with consideration to their relevance to all countries around the world. (Cardoso, 2014) Despite these aims, implementation of some recommendations may still be impractical in low resource settings. (UCCI, Planning comprehensive breast cancer programs; Anderson, 2006)

Even among high income countries there are differences in outcomes for cancer including breast cancer. Factors such as socioeconomic status and access to health care services, contribute to disparities in cancer care in the US. (de Souza, 2015) Significant differences have been observed in the incidence rates, and all cause cancer mortality rates for breast cancer by race and ethnicity. (CDC, 2015) Therefore, it remains important for cancer initiatives to be designed to ensure equity of access to cancer care for minority populations. (de Souza, 2015) Moreover, in the UK, where outcomes for breast cancer lag behind that of other European countries, (Allemani, 2015; Macmillan, 2015) a new, independent cancer taskforce has identified six strategic priorities to improve cancer outcomes and transform patient experience. These priorities include a focus on improvements in public health, early diagnosis, patient experience, resource / infrastructure and commissioning. (NHS England, 2015) While these imperatives are a positive step, they continue to focus on early diagnosis and screening, and hence benefit patients with early stage disease to the greatest extent; but targets to ensure better access to end of life care, clinical nurse specialists and improved technology will also begin to address the needs of mBC patients too.

Real-World Spotlight: Malaysia

A recent study from Malaysia described a low-cost program that combined healthcare worker training in cancer detection with measures to increase public awareness. The program improved identification of cancers of the cervix and breast with a reduction in the diagnosis of advanced stage (III and IV) of both by approximately 50%. (Devi, 2007) Opportunities exist to raise public and primary care awareness and improve attitudes towards cancer diagnosis and treatment. (Ermiah, 2012) It is clear that increasing breast cancer awareness in healthcare workers and the general population as a whole is imperative to address late diagnosis.
There is a lack of reliable data on mBC. Localized public health data is critical when decision makers are prioritizing healthcare expenditure. Although there are multiple data sources providing global and national breast cancer figures on prevalence of eBC, there are limited reliable global figures on prevalence of mBC. Some national data sets can be considered though, such as data from Australia estimating mBC prevalence to be 3 to 4 times the number of annual deaths from breast cancer. (Clements, 2012) As mentioned previously, policymakers in the United Kingdom recognised that the lack of data on the number of breast cancer patients with metastatic disease was impacting effective planning of services for these patients. Following an audit of the data available from existing sources, a recommendation was made to expand an existing mandatory data collection tool so that it specifically included information on patients with recurrent and metastatic BC. (NCIN 2012) Low- and middle-income countries often do not have the capacity or tools to collect this type of data in a systematic way across disease states. (UICC, Planning comprehensive breast cancer programs) Although there are exceptions which show that it is possible. In Kenya, for example, data for the single national cancer registry is collected from medical facilities in and around Nairobi. While this is a step in the right direction, information from the rest of the country is still absent. (Muthoni, 2010)

Despite clinical and technological advancements such as electronic health records (EHRs), disease registries and surveillance systems, even policy makers in high-income countries still lack reliable data regarding the burden of mBC. The data sets that are available suggest that the population of patients with mBC is continuing to grow. (Ferlay, 2010; Ferlay, 2015) However, without access to accurate numbers, policy makers cannot make informed policy decisions that will address the burden of disease in their communities. As such, policy makers may not sufficiently recognize the needs of many sub-populations, including those with mBC, which in turn creates challenges to the prioritization of resources.

"Each community, here in the US and across the globe, has unique needs when it comes to breast cancer. It is important to understand these needs, as well as the strengths and assets of the communities we serve, so that we can design evidence-based plans to reduce breast cancer mortality in each of these communities in the US and across the globe. To guide our programming, we work in partnership with local organizations and agencies to conduct health system assessments and community profiles that assess key breast cancer statistics, available infrastructure and quality of public health services, the factors that determine why women enter the breast cancer continuum of care, and the barriers that prevent women from completing the continuum."

Kim Sabelko, Managing Director, Strategic Partnerships and Programs, Susan G. Komen
The rising cancer burden increases pressure on constrained national health budgets. A detailed discussion of the economic aspects of mBC is included separately in Chapter 2: Economic Burden of mBC. However, in the context of health policy, the available health budget can influence policy development and adoption. (OECD, 2013b) Each country has its own priorities when financing healthcare and, as such, budgets vary considerably between nations.

The global burden of cancer continues to increase largely because of the growing and aging world population, alongside an increased uptake of cancer-causing behaviors, particularly smoking, in economically developing countries. (Jemal, 2011) Across the world, there has been a rapid growth in the direct costs of cancer treatment combined with an increasing constraint of healthcare budgets. (Kudrin, 2012) These factors combined show that the growth in healthcare spend has been driven by increasing prevalence of disease and growing costs of technologies and treatments.

Budget holders are increasingly scrutinizing the cost of new therapies. Approaches which focus on a measurement of the cost effectiveness of treatments and interventions have gained greater prominence, even in countries such as France and Japan where Health Technology Appraisal (HTA) has historically focused on clinical efficacy. (Lim, 2014; Massetti, 2015; Kobayashi, 2012; Kudrin, 2012) The acceptable threshold at which new medicines are considered as cost effective differs between countries. (Kudrin, 2012)

Not all countries have established HTA processes. Those without an official, national HTA body may, or may not, complete some review based on cost before a drug is allowed to be used in the country. In this case, reimbursement is dependent on individual budget holders within that country. (Kudrin, 2012) However, this approach can lack transparency. Leading cancer centers and academic institutions in the US have urged for an evaluation and rating process similar to EU and other HTA countries to be applied prior to insurance coverage decisions and price negotiations. (Tefferi, 2015)

As a result of the different approaches employed around the world, the decision to fund any treatment can differ by country or region. One such example is Africa where there is variability in the national reimbursement of cancer treatments across the continent. In South Africa, best-practice cancer treatment is freely available to breast cancer patients within the public health system. (Dickens, 2014) In contrast, in many countries in the sub-Saharan region, patients personally bear the cost of cancer treatment; a formidable task for the majority. (Adisa, 2011) In one study, financial difficulties resulted in nonadherence to chemotherapy schedules in 45% of patients in the sub-Saharan region and also attributed to the infrequent use of new biological agents and subsequent lines of chemotherapy. (Adisa, 2011)
In conclusion, it is increasingly important for policy decision makers to find ways to meet the rising burden of cancer as a whole and breast cancer in particular. The resources required to meet this need are many and include, healthcare infrastructure such as access to hospitals, access to appropriately trained staff, radiotherapy, supportive care and cancer medicines. In breast cancer, while many of the treatments considered as standard-of-care are now available as generic products, (NIH, 2015) patients may still not have access to them as a result of other barriers in the health system.

In one study, financial difficulties resulted in nonadherence to chemotherapy schedules in 45% of patients in the sub-Saharan region and also attributed to the infrequent use of new biological agents and subsequent lines of chemotherapy. (Adisa, 2011)

Every opportunity to understand both the experience and needs of patients as well as the effective management of mBC through scientific research are invaluable. Such findings must be publicized and promoted to national level health planners and policy makers to best inform health decision-making and could be applied in other countries around the world. Initiatives such as the ABC Patient Advocacy Committee, Metavivor, UICC and Susan G Komen provide a forum to aggregate learnings to maximize steps-forward in mBC care. More in-depth research is needed to understand why current policy approaches haven't improved mBC survival and to identify the critical steps that need to be taken to create this step change.
Chapter 2: Economic Burden of mBC

Economic burden of mBC comprises direct and indirect costs.
The economic burden of cancer is significant, and continues to rise around the world. As our current review is focused on the economic burden of mBC, particular consideration must be drawn to the prevalence of this disease primarily in women, which exhibits additional unique societal challenges compared to other, less gender-defined, metastatic diseases. With women playing important roles both within and outside of the home, the impact of an mBC diagnosis is far-reaching. In addition, as women can often live for several years with mBC, they not only face the unpredictability of the ongoing and cumulative financial burden of living with the disease, but also the impact of the disease on their quality of life and ability to be productive members of society.

Methodology: In order to present a comprehensive overview of the economic burden of mBC from a patient, health care system and societal perspective, a literature review was conducted on the economic burden and cost of illness of mBC, reported over the last 10 years. See Appendix 2.2 for more details on literature search methodology. Within this report, the direct costs associated with treatment of metastatic disease are discussed at a population level, rather than at an individual level.

In considering the economic burden of any disease state, there are two main components 1) the direct costs of the treatment and management approach and 2) the indirect costs associated with the impact of the disease on the patient, caregivers and society. Figure 2.3 further defines what could be classified within each of the cost components and who bears these costs.
Figure 2.3

Classification of Direct and Indirect Cost Components

<table>
<thead>
<tr>
<th>Cost Components</th>
<th>Direct Costs: Direct medical costs are those directly associated with disease treatment and resources used for medical care, e.g.</th>
<th>Indirect Costs: Indirect costs are the monetary losses associated with time lost due to disease or time spent receiving medical care</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Hospitalizations</td>
<td>• Work departure (early retirement/temporary work absence) or time lost from other usual activities</td>
</tr>
<tr>
<td></td>
<td>• Surgery</td>
<td>• Lost productivity due to premature death</td>
</tr>
<tr>
<td></td>
<td>• Physician visits</td>
<td>• Additional childcare needed while receiving medical care</td>
</tr>
<tr>
<td></td>
<td>• Radiation therapy</td>
<td>• Transport to and from medical care</td>
</tr>
<tr>
<td></td>
<td>• Chemotherapy/immunotherapy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Oral Drugs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Emergency care</td>
<td></td>
</tr>
</tbody>
</table>

Who bears the cost

|                               | Direct Costs: • Health systems – governments, insurers, employers (insurance coverage for employees)          | Indirect Costs: • Patients, caregivers, families and more broadly, society                                      |
|                               | • Patients and families (through individual/private insurance, and contributions such as copays)           |                                                                                                               |
While the literature review provided some published evidence describing the economic burden of mBC on individual patients and their families or caregivers, there were limitations in the depth and breadth of the data available. In addition, there were challenges in comparing data between sources, as summarized below:

- Most of the data regarding costs of mBC examines the direct costs relating to medical resource utilization at a healthcare system, rather than individual patient level. This is because most studies have been in countries where a national health system or system of health insurance pays for health care costs and not in countries where individuals bear these costs.

- The majority of data available for patients with mBC is from higher income countries and is likely to underestimate the economic burden, since cancer registries are not always designed to provide complete information and disease progression is not always documented (Remak, 2004).

- There is a lack of data from middle-low income countries where extremely diverse socio-political and economic realities hinder prospective data collection and analysis, making extrapolation unreliable (World Breast Cancer Report, 2012).

- Comparative costs between high income countries have been difficult to make due to variations in health care systems and the definition of cost components examined.

- Drug costs may vary depending on the year of analysis. For example, aromatase inhibitors which are the standard of care for HR+/HER2-mBC, the largest subtype comprising more than 60% of mBC, became generic in the US in 2010/2011. (Orange Book) Hence drug costs in this breast cancer subtype would likely be much lower after Loss of Exclusivity. Furthermore, trastuzumab, an innovative treatment for HER 2+ mBC, was approved in 1998 in the US, and significantly improved outcomes but also contributed to the increase in costs (CenterWatch; Eiermann, 2001).

### There is increased economic burden of mBC on health care systems and society

The direct cost of BC has increased and metastatic disease is a significant contributor to the costs. In Belgium, the average annual healthcare costs for women with breast cancer across all stages of disease, measured over a period of six years, was compared with those of the general population. Results from this study showed that the excess annual healthcare costs for patients with mBC were €23,280; greater than for patients with less advanced disease. (Broekx, 2011) (See Figure 2.4)

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**Figure 2.4**

*Excess Health Care Costs per Breast Cancer Patient over Six Years According to Breast Cancer Stage from 1997-2004*

Broekx, 2011

<table>
<thead>
<tr>
<th>Disease Stage (n=4,975)</th>
<th>Average Healthcare Costs per Breast Care Patient in the Sample (€)</th>
<th>Average health care costs of general population (€)</th>
<th>Difference (Discounted difference at 4%)* (€)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>19,827</td>
<td>10,610</td>
<td>9,217 (8,799)</td>
</tr>
<tr>
<td>II</td>
<td>24,927</td>
<td>10,610</td>
<td>14,318 (13,461)</td>
</tr>
<tr>
<td>III</td>
<td>32,606</td>
<td>10,610</td>
<td>21,996 (20,597)</td>
</tr>
<tr>
<td>IV (mBC)</td>
<td>35,201</td>
<td>10,610</td>
<td>24,591 (23,280)</td>
</tr>
</tbody>
</table>

*Given the 6 year time period, the net present value of costs in 1998 was calculated using an annual discounted rate of 4%*
Cost comparisons between high income countries have been difficult to make due to variations in patient cohorts and health care system funding. As an example, direct costs which calculate the total medical and resource costs, measured by hospital use per patient, (both mBC and relapsed BC) range from €36,000 to €48,000 in Belgium, the Netherlands, France and the U.K. (Frederix, 2014; Bonastre, 2012; Thomas, 2009).

In the US, the cost per patient of mBC treatment to the healthcare economy is increasing. Medicare coverage is provided to people age 65 or older, people under the age of 65 with certain disabilities, and people of all ages with End-Stage Renal Disease. (CMS, Medicare Program) Estimates in 1997-99, which included costs associated with; inpatient hospital visits, skilled nursing facilities, physician/professional services, outpatient hospital clinics, diagnostic testing, home health, hospice care payments as well as payments for covered drugs, durable medical equipment, transport and supplies, show that the mean cost of treating a Medicare mBC patient in the US over an average of 16.2 months was $35,164. (Rao, 2004) Using Bureau of Labor Statistics (BLS) published medical inflation data, this is equivalent to approximately $52,700 in 2009. Davis et al analyzed the Medicare–SEER linked data to estimate costs, including

![Average Adjusted Cost by Breast Cancer Stage and Category for Patients Diagnosed between 2000 and 2005](image)

**Figure 2.5**

**Average Adjusted Cost by Breast Cancer Stage and Category for Patients Diagnosed between 2000 and 2005**

Davis, 2010
breast cancer-related surgery, radiotherapy, chemotherapy, and other medical encounters carrying a breast cancer diagnosis, and predictors of costs in elderly (≥ 65 years) patients diagnosed with breast cancer between Jan 2000 and Dec 2005 (see Figure 2.5). Cancer-related adjusted costs (2009 US $) per mBC patient were reported to be $153,421 over a median follow up period of 26 months (median time between diagnosis and death). Metastatic diagnosis, amongst other factors, was found to be a significant (p<0.001) predictor of higher costs. (Davis, 2010) Of note, based on an analysis including laboratory tests and diagnostics, surgeries and procedures, treatments, outpatient visits, hospitalizations including emergency department (ED) visits, and prescription fills factoring in the amount paid by the insurance plan, patient co-pays, deductibles, coinsurance amounts and out of pocket expenses, the cost of mBC per privately insured patient was on average, $250,000 for an average life expectancy of 2.2 years in 2009. (Montero, 2012)

Cost of BC is the greatest in the final year of life. Mariotto et al (2011) published a projection of the costs of BC care in the United States, using SEER-Medicare linkage data, considered according to phase of care which they defined as initial (within the first 12 months from diagnosis), continuing (the period between initial and final phases) and final (last 12 months of life). This analysis of the direct medical cost estimates by phase of care, found that the average cost of treating breast cancer is greatest in the patients final year of life (See Figure 2.6).

Similar results were reported in a study from a Brazilian public health care system perspective. The analysis found that, even in the metastatic setting, progression of disease was associated with rising healthcare costs, with an increase from Brazilian Real (BRL) 308 in the pre-progression phase to BRL 701 post progression over one year. Furthermore, end-of-life costs were in excess of 5 times greater than in the post progression phase of mBC BRL 4,164 vs BRL 731 respectively (over the same time period). (Haas, 2013) These examples show how effective management at the end of life could have a substantial impact on the direct cost of cancer care in mBC patients.

Indirect costs for mBC are significant to society. Indirect costs of mBC arise from lost wages for time off work (for the patient and their caregiver), unpaid caregiver time, and productivity losses for society. Ignoring these costs could lead to suboptimal policy decision making from a societal perspective and prevent women from comprehending the true financial burden of their disease. (Lidgren, 2007) There may also be an intangible cost arising from the loss of skilled and experienced workers from the labor market. (Fu, 2011)

A large percentage of breast cancer patients leave employment due to their disease, and for breast cancer survivors, returning to work full-time can be a major challenge. (Fu, 2011; Meadows, 2010; de Boer, 2009) A recent retrospective US study demonstrated that breast cancer disease progression is associated with greater work hour loss in the work place. Results show that on average, non-metastatic breast cancer survivors
miss 77 hours of work per quarter. In contrast, mBC patients during the end of life period, lose on average, 128 work hours per quarter (a 66% increase compared to non-metastatic patients). The same study also confirmed that breast cancer progression contributed directly to an increased dropout rate from employment. (Yin, 2015) A separate study found that mBC imposes a significant financial burden on patients through short-term disability costs (approximately $10,000 USD in total vs. matched controls). (Wan, 2013)

Unfortunately the economic burden to caregivers is often overlooked and poorly understood. (Wan, 2013) A Canadian survey of 89 caregivers of patients with mBC found that approximately two-thirds reported some form of adverse impact on work. This included work-absence or the need to take annual or special leave as a result of caregiving responsibilities. In a small number of cases, caregivers had to give up work or decline opportunities for promotion. In addition to the occupational burdens, caregivers also experienced psychological and economic adverse events. (Grunfeld, 2004)

Sorensen estimated the annual U.S. societal costs associated with treatment of mBC patients using an incidence-based cost-of-illness (COI) model framework. An incident cohort of mBC patients were followed over five years, from diagnosis of metastatic disease, through active treatment (for eligible patients) and subsequently to terminal care and death. The incident cohort included both de novo patients and patients who had progressed to mBC from earlier stages of breast cancer and captured both direct and indirect costs. (Sorensen, 2012)

The model estimated additional economic burden of mBC in the U.S. associated with loss of productivity of patients and caregivers to total nearly $3 billion over a five-year span, with the total discounted cost (i.e. adjusted for inflation) to society being over $12 billion (Figure 2.7). This represents a three-fold increase in the cost of mBC to the healthcare system compared with data from the 1990s. The analysis included both direct and indirect cost estimates: utilization of cancer therapies and other medical care resources, treatment-related adverse events, diagnostic costs, lost income and caregiver costs. (Sorensen, 2012)

**Figure 2.7**

**The Estimated U.S. Economic Burden of mBC***

**Sorensen, 2012**

<table>
<thead>
<tr>
<th>Group</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lost productivity of mBC patients and caregivers</td>
<td>$2.9 billion indirect costs over 5 years</td>
</tr>
<tr>
<td></td>
<td>$23,157 per patient-year</td>
</tr>
<tr>
<td></td>
<td>= 23.5% of total direct and indirect mBC costs</td>
</tr>
<tr>
<td>Discounted cost (direct and indirect) to society of mBC (i.e. adjusted for inflation)</td>
<td>$12.2 billion accrued over 5 years</td>
</tr>
<tr>
<td></td>
<td>= $2.4 billion per year</td>
</tr>
<tr>
<td></td>
<td>= $98,571 per patient-year</td>
</tr>
</tbody>
</table>

* An incidence based cost-of-illness model was developed in which an incident cohort of mBC patients are followed over 5 years, from diagnosis of metastatic disease and assessment of management course, through active treatment (for eligible patients) and subsequently to terminal care and death.
**mBC imposes an increasing financial burden on families and caregivers**

When evaluating the financial burden directly to the patient, their families and caregivers, there can be variation in how this impact is qualified and measured. As detailed previously in Figure 2.16, financial burden can constitute both direct costs, such as out of pocket payments related to the care that patients receive or cost of transportation to receive medical care, and indirect costs, such as the cost of childcare or home help needed to support family while receiving medical care.

Studies have highlighted a greater financial burden for patients with mBC than those with non-metastatic disease; this likely reflects increased disease severity, co-morbidities and side-effects associated with increasingly complex treatment strategies. (Zafar, 2013; Wan, 2013; Davidoff, 2013) Several surveys and publications describe the financial need and related concerns of mBC on the individual from an Australian, European and U.S. perspective. For example, in a primary research survey, with Breast Cancer Center healthcare professionals, 31% of respondents identified financial support as a top 5 unmet need for patients with mBC. (Breast Cancer Center Survey, Pfizer, 2015)

In an Australian survey of 579 women and 3 men with mBC, one-fifth of respondents identified financial assistance as an unmet need. (BCNA Survey, 2015) 49% of respondents were treated in the private health system and 44% treated in the public health system (7% of individuals asked did not respond). The survey found that 60% of respondents reported acute financial difficulty. For women in the public system, loss of income (37%) and out-of-pocket expenses (28%) were most frequently reported as the reason for these financial difficulties. (BCNA Survey, 2015) Women in the Australian survey were asked to provide estimates of their mBC related out-of-pocket costs incurred in the previous month. The values given ranged from $0 - $25,000 for women treated in the private health setting and $0 - $10,500 for women treated in the public health system; with an average total monthly out-of-pocket cost of $687.17 for all women. Figure 2.8 demonstrates the breakdown of cost drivers contributing towards these out-of-pocket expenses. (BCNA Survey, 2015)

“The cost of treatment meant I used all my life savings ... this is tough and has resulted in uncertainty ... Am I going to have enough money to see me out? How does all of this affect my standard of living and therefore my relationships with family and friends?”

*BCNA Survey Respondent, 2015*
Respondents also identified, other-out-of-pocket costs; including, travelling for treatment (e.g. petrol, flights, accommodation and parking), associated treatment and care, such as second opinion appointments; complementary and alternative treatments, including vitamins, massage, naturopathy, Chinese medicine and practical assistance such as employing home help. (BCNA Survey, 2015)

In the U.S., greater out of pocket expenses reflect a shift of some of the cost burden of cancer treatment from insurers to patients. Out of pocket expenses could include direct payments to providers, prescription drugs, as well as unpaid liabilities such as travel costs and lost wages. There is evidence that the related out-of-pocket expenses are particularly high for cancer care, (Zafar, 2013; Davidoff, 2013) and the associated financial hardship has negative consequences on care choices, quality of life, and disease outcomes. (Irwin, 2014)

“**We are not on the poverty line, but I have lost half my wage and we relied on that to live.**”

*BCNA Survey Respondent, 2015*

In an Australian survey, 60% of respondents reported they had experienced financial difficulty (within the previous week). (BCNA Survey, 2015)

**Figure 2.8**

Aspects of Treatment that Have Incurred the Most Significant Total Out-of-Pocket Cost, Based on Data Collected from August-September 2014

BCNA Survey, 2015

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Out-of-Pocket Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scans</td>
<td>$1000</td>
</tr>
<tr>
<td>Surgery</td>
<td>$2000</td>
</tr>
<tr>
<td>PBS Drugs</td>
<td>$3000</td>
</tr>
<tr>
<td>Non-PBS Drugs</td>
<td>$4000</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>$5000</td>
</tr>
</tbody>
</table>

PBS = Pharmaceutical Benefit Scheme

Based on an Australian survey of women with secondary (metastatic) BC (n=420)

Q: Which parts of your secondary breast cancer treatment have the most significant out-of-pocket costs, and how much has this cost you?

Patients with mBC face greater financial burden and have higher per patient costs than for those with non-metastatic disease.

(Zafar, 2013; Wan, 2013; Davidoff, 2013)
European patients describe experiencing financial burden arising from increased living costs and an adverse change in their financial situation. (Here and Now, Novartis, 2013) Additional living costs occur from travel expenses or check-ups, supplementary treatments, help around the house or for a special diet. As a result, many women with mBC reported reducing expenditures on non-healthcare related items. Patients report that they are struggling to manage expenses (38% of women surveyed) including the mortgage (15% of women surveyed). In a European survey, the majority of women living with advanced breast cancer report a decline in household income as a direct result of their cancer, with 87% reporting an increase in living costs. The majority of women recognize a need for financial support. (Here & Now, Novartis, 2013)

Reductions in income can be significant, with one in ten women describing a 50% fall in household earnings in one study across 11 European countries (Austria, Denmark, France, Germany, Greece, Italy, Netherlands, Poland, Spain, Sweden, U.K.). 62% of study respondents stated that they need improved financial support. Approximately 40% experience psychological and physical problems as a direct result of the change to financial circumstances. (Here & Now, Novartis, 2013)

In a US survey of 134 breast cancer patients, nearly one-third of which had mBC, financial distress was detrimental to patient well-being and response to medical care. Financial hardship included difficulty in paying for basic necessities (16%) and exhausting a patient’s savings (19%). (Irwin, 2014)

Approximately 40% of women with mBC experience psychological and physical problems as a direct result of the change to financial circumstances. (Here & Now, Novartis, 2013)

A diagnosis of mBC brings with it a high degree of uncertainty about the future and the consequences of diagnosis on patient lifestyle, family, work and friends. In addition to the emotional and physical impact of diagnosis, there are financial considerations that patients must manage throughout the course of their disease. U.S. data shows the families of patients with mBC incurred nearly 40% higher indirect costs compared with those families of patients with eBC. (Wan, 2013)

Clear acknowledgement and communication of the economic burden of mBC and related financial concerns is required to inform policy decision-making and allow patients to have a clear picture of the potential financial burden to themselves and their families in order to adequately plan for the future. (Lidgren, 2007; Hunink, 2014)
Chapter 3: Public Understanding of mBC

- Public awareness and understanding of mBC is still limited even though public understanding of eBC has risen
- Global misperceptions about mBC prognosis exist, such as ‘mBC is curable’ or ‘mBC has no hope’
- Patients with mBC may feel isolated and helpless due to a lack of understanding and stigma associated with the disease
  - Limited progress has been made to address these issues over the last decade
- Globally, variations in cultural bias impact public understanding and perceptions of mBC
- Perceptions and health-related behaviors around mBC can be altered through wider, more accurate communication of information on experiences with the disease
- Public exposure to messages regarding mBC has been increasing steadily over time
- Media communication has the potential to elevate the patient voice, reverse stigma and create a supportive environment for patients with the disease

Stigmatization of mBC increases women’s health risks, isolates them from relevant resources, and prevents patients from accessing the medical and social support that are key to survival and maintaining quality of life. Often this can lead to women delaying presentation to a clinician until they are exhibiting symptoms of the disease. (LIVESTRONG report, Beckjord, 2012; Tfayli, 2010)

While public understanding of early breast cancer (eBC) has risen in recent years, it is generally thought that understanding of mBC specifically is inadequate. (MBC Alliance, 2014, Executive Summary) Although public understanding may not directly impact how a patient with mBC is treated, inaccurate perception from others in society, matters greatly to a patient or caregiver. Inaccurate perception of disease implications, stigmatization, and cultural attitudes, influence the social and emotional experience for all affected by an mBC diagnosis, whether they are patients, caregivers or families. There is much work to be done to improve societal understanding of mBC, with media likely to play a role given the positive effect seen in educating the general public on eBC.
Methodology: To better understand the general public’s awareness, understanding, and perceptions of ABC/mBC globally, a general population survey was conducted during June 3 - July 30, 2015. In this survey, commissioned by Pfizer, a total of 14,315 adults aged 18+ from the general population (mBC patients and non-patients) participated. The 14 participating countries were: UK, France, Germany, Poland, Turkey, India, Taiwan, Japan, South Africa, Brazil, Mexico Argentina, Chile and Colombia. In all countries, respondents were sampled from internet consumer research panels and invited to complete a 15-minute self-administered questionnaire in local languages; in Argentina, Chile, and Colombia; internet panel samples were combined with face-to-face interviews. In some countries (Poland, Turkey, India, Taiwan, South Africa, Brazil, Mexico), samples may not be fully representative of the population segment without online access, due to lower Internet penetration among the general public and/or less developed Internet panels in those countries. A similar (but not identical) survey was conducted in the US in 2014; n=2090 and formed the basis of the report: Breast Cancer: A Story Half Told, findings and recommendations, 2014.

Together, these studies represent the first, wide-reaching, global effort to assess public understanding and comprehension of both eBC and mBC. Results from these surveys provide a strong foundation for the findings within this chapter.

A Public awareness and understanding of mBC is lacking in the context of global breast cancer awareness

Global awareness of breast cancer amongst the general public is high. In a recent international survey of over 14,000 members of the general public across 14 countries, on average 54% of respondents knew someone with breast cancer. It is also the cancer with which adults are most familiar in the majority of countries surveyed across the globe. (mBC General Population Survey, Pfizer, 2015) These results echo findings of a similar survey conducted with 2,000 members of the general public in North America in 2014. (A Story Half Told, Pfizer, 2014)

National and international breast health awareness and promotional campaigns have been fundamental in increasing awareness of breast cancer over the decades. In turn, the building of support communities, an increase in the availability of information, and a movement for patients encouraged to take ownership of the detection, diagnosis, and treatment of their disease has been observed. Such activity has mainly been in the context of eBC and its survivorship, with limited focus on patients with recurrent, advanced or metastatic BC. (mBC Alliance, 2014) This is reflected in a global lack of familiarity with the terms ‘advanced breast cancer’ or ‘metastatic breast cancer’ compared with ‘breast cancer’ by the general population across a range of countries. (mBC General Population Survey, Pfizer, 2015; A Story Half Told, Pfizer, 2014)

For more than 160,000 women living in the U.S. with advanced, stage IV breast cancer, the situation is not one they can turn off on their TV sets, or avoid by skipping out from pink-decorated malls: they’re living and coping with the metastatic form of the disease, active treatments, side effects and, still, no known cure. Their outlook is tempered, maybe best portrayed in a spectrum of gray.

Huffington Post, 2010
In October 2009, the US Senate and House voted to support the designation of October 13 as a National MBC Awareness Day, as a result of the efforts of the Metastatic Breast Cancer Network. (Huffington Post, 2010; Metastatic Breast Cancer Awareness Day, 2012) Since 2010, this day has drawn attention to the unique needs and challenges of patients with mBC, across Europe and North America. (Metastatic Breast Cancer Network, 2010) While this is a positive step, the impact of this dedicated day has not been widespread and public knowledge remains limited, particularly regarding the distinction between early and mBC and the implications of these diagnoses.

The focus on early detection combined with significant advances in treatments for eBC, resulted in a perception that breast cancer has been largely “cured”. The “breast cancer survivor” identity obscures the reality that approximately 20%-30% of women diagnosed with eBC will eventually progress to metastatic disease, (O’Shaughnessy, 2015; EBCTCG, 2015) which is incurable.

Perceptions about mBC in society can be seen as two extremes: those who are optimistic about prognosis of the disease, and those who think of it as hopeless. In most countries surveyed, 74–87% of respondents believed that early detection and/or treatment will prevent disease progression and 48–76% believed that advanced breast cancer is curable, suggesting that there is a lack of public knowledge of the prognosis for patients with mBC (Figure 2.9). (mBC General Population Survey, Pfizer, 2015) The public perception of a breast cancer “cure” may impact patients’ ability, both newly diagnosed with mBC or recurring from eBC, to adjust perception away from “curing” their breast cancer to “living” with metastatic disease.

Despite those who hold expectations of cure, globally, the terms ‘aBC/mBC’ and ‘breast cancer’ are associated with negative words by the general public. (mBC General Population Survey, Pfizer, 2015) There are also some perceptions of mBC as a hopeless disease and that the time and effort in treating and supporting mBC patients would be wasted, compared with eBC patients. (mBC Patient Support Organization Survey, Pfizer, 2015) These extremities in perspective highlight a lack of awareness and understanding about the disease and how it differs from early-stage breast cancer.

Breast cancer in this area [certain countries in Africa], is almost synonymous with stage IV, there are very little survivors. For these women a breast cancer diagnosis is a death sentence with little hope.

Dr. Olufunmilayo Olopade, Director of the Center for Clinical Cancer Genetics, University of Chicago, 2015
Figure 2.9

Percentage of the General Public Surveyed that Believe Advanced or mBC can be Cured
mBC General Population Survey, Pfizer, 2015; A Story Half Told, 2014, Pfizer

For all countries except the US, the percentage of respondents who either somewhat agree or agree strongly with the following question: “How much do you agree or disagree with the following statement about advanced or metastatic breast cancer? “Advanced or metastatic breast cancer is curable” (mBC General Population Survey, Pfizer, 2015). This research was not powered to draw comparisons between countries.

*US respondents totaled 2090. Responses were obtained via a separate survey asking whether respondents strongly agreed/agreed that patients with breast cancer can be cured if caught early with the right treatment.

“I think the minute you say metastatic or secondary [breast cancer], people just think they’re on their way out, why should we bother putting research money to it…and that makes it really difficult to research this group of patients separately.”

European Respondent, mBC PSO Survey, Pfizer, 2015
The lack of broader understanding of mBC negatively impacts mBC patients’ experience while living with their disease and adds to stigma, distress, and isolation.

Sadly, a significant proportion of the public believe that breast cancer progresses or recurs because patients do not take preventative measures, such as correctly taking medicine and attending appointments. (mBC General Population Survey, Pfizer, 2015; MBC Alliance Report, 2014) These findings were echoed in a similar survey of the public in the US. (A Story Half Told, Pfizer, 2014) Negative public perceptions of mBC impact the association that mBC patients have with the disease.

“People don’t understand the word metastatic to begin with... And when I’d tell them I was stage 4, they’d give me pity or stay away or see me a year later and think I was a ghost. They couldn’t believe I was alive.”

US mBC patient, fredhutch.org, 2014

Half of patients with mBC report feeling social rejection in the form of isolation, shame and feeling like outcasts, particularly within the breast cancer community. (MBC Alliance, 2014) These elements are characteristic of the mBC experience in the overall population as well, and influence patient behaviors such as their willingness to seek support or make treatment and quality of life decisions. It is notable that the feeling of isolation identified in mBC patient surveys from 2008-2009 are still present in later studies, highlighting the limited progress over time in changing perceptions of mBC. (Else-Quest, 2009; Faces of mBC, 2010; MBC Alliance, 2014)

“Positive messages about early detection and lifestyle choices that might reduce breast cancer risk may in a subtle way reinforce the misperception that these things will be effective for everyone – and that if someone develops breast cancer or metastatic breast cancer, it must have been their fault.”

Kimberly Sabelko, Managing Director, Strategic Partnerships and Programs, Susan G. Komen, 2015
"But dealing with an incurable illness and the side effects of its treatment aren’t the only burden MBC patients have to bear. Many also have to educate others about their disease, explaining over and over that no, the scans and blood tests and treatments will never come to end. No, the metastasized breast cancer in their lungs is neither lung cancer nor linked to smoking. No, staying positive and ‘just fighting hard’ isn’t going to beat back their late-stage disease."

fredhutch.org, 2014

Results from a 2013 global survey of 1,273 women with mBC in 12 countries demonstrated that, regardless of country income level, most women with mBC felt that others do not empathize with their experience. Nearly two-thirds (63%) of women said they “often feel like no one understands what they are going through” while two in five women said they “feel isolated from the non-advanced breast cancer community” (see Figure 2.10). (Count Us, Know Us, Join Us, Novartis, 2013) This sense of isolation from the larger breast cancer community can be attributed to a lack of available resources to address their needs, appropriate messaging and the negative perceptions associated with a terminal diagnosis. This isolation is mirrored, globally, by the general public where 18-49% of people indicated that patients with mBC should keep it a secret and not discuss it with anyone other than their physician (Figure 2.11). This was most pronounced in India and Turkey, where almost half of people surveyed agreed with this statement (49% and 42%, respectively) (mBC General Population Survey, Pfizer, 2015).

Figure 2.10

Percentage of Women with mBC by Country that Feel their Experience is not Understood by Others and Feel Isolated from the Breast Cancer Community

Count Us, Know Us, Join Us, Novartis, 2013

- Percentage that do not feel understood by others
- Percentage who do feel isolated from the breast cancer community
While the majority of breast cancer patients are female, men also are diagnosed with both early and advanced disease; globally, an average of 69% of people are aware that breast cancer occurs in men as well as women. (mBC General Population Survey, Pfizer, 2015) Literature shows little information regarding men, and specific research is needed to understand how men's needs differ from those of women.

The overwhelming focus on eBC in messages conveyed by the media, breast cancer awareness campaigns and the association between early disease and survival, generates the perception of two distinct breast cancer patient groups: those who survive and those who die as a result of their disease. The treatable, yet incurable nature of mBC means patients with advanced disease do not fall distinctly into either of these groups. This “gray area” impacts patients with metastatic disease with respect to their quality of life and their level of distress along disease continuum. These patients are considered to be “without a voice” in the general breast cancer community. (Count Us, Know Us, Join Us, 2013; Inside Vandy: Vanderbilt University, 2013; Metastatic Breast Cancer Network, 2015; History of Metastatic Breast Cancer Awareness Day, 2013)

On average, 28% of the general population indicated that patients with mBC should keep it a secret and not discuss it with anyone other than their physician. (mBC General Population Survey, Pfizer, 2015)

While the majority of breast cancer patients are female, men also are diagnosed with both early and advanced disease; globally, an average of 69% of people are aware that breast cancer occurs in men as well as women. (mBC General Population Survey, Pfizer, 2015) Literature shows little information regarding men, and specific research is needed to understand how men's needs differ from those of women.
“The way we [in the US] talk about breast cancer has fundamentally changed over the past four decades. Prior to the 1970s, breast cancer was a taboo subject -- many did not dare to say the words “breast cancer” aloud. We’ve overcome that stigma, and now, across the globe, we need to do the same for mBC.”

Kimberly Sabelko, Managing Director, Strategic Partnerships and Programs, Susan G. Komen

The journey to change perceptions of eBC has taken many years and the level of success differs geographically. In the 1970’s the journalist Rose Kushner shared with the public, not only her experience but also the science behind her breast cancer. She successfully combined her own story with the basics of cell biology, using everyday language to reach her audience (LA Times, 2014). Over the years, public figures willing to take a similar plunge and share their experiences have helped make conversations about breast cancer more acceptable. (LA Times, 2014)

In some developing countries, there still remains a need to overcome a stigma associated with breast cancer, overall, before strategies to change the perception of mBC, specifically, can take effect. Local culture and beliefs that can discourage patients from seeking care early-on, include the physical implications of treatment (especially mastectomy), lack of access to knowledge about breast health, and family/community rejection following a breast cancer diagnosis. The lack of options for early detection due to limited access to routine care and examinations, as well as lack of access to affordable, high-quality treatment options contribute to the poor outcomes for patients with breast cancer and perpetuate the negative image of breast cancer in these communities. (Shulman, 2010)

“Because it is such a devastating diagnosis, women (in some sub-Saharan African countries) feel that they cannot let anyone know that they have cancer, isolating them from help and support from friends and family. The stigma is so high that women stay under the radar. By the time they come out, the breast is fungating and smelling, leading to them being ostracized from society furthering hindering them from getting help at the time they need it the most.”

Dr. Olufunmilayo Olopade, Director of the Center for Clinical Cancer Genetics, University of Chicago, 2015
Enhanced media attention (traditional and online) towards mBC has the potential to shape public perceptions and create a supportive environment for mBC patients

The availability of accurate, relevant information on mBC is essential to create a uniform cultural understanding of the disease, that will in turn help stimulate a sense of community and provide a supportive environment for mBC patients. Currently, there is a lack of specific, robust public information from sources felt to be trusted. Globally, less than half of the general population feels that reliable information on advanced or metastatic BC is easy to access (Figure 2.12). (mBC General Population Survey, Pfizer, 2015) Perhaps reflective of this lack of available information, a US survey highlighted that 61% of the general population knew little to nothing about mBC. (A Story Half Told, Pfizer, 2014)

When considering specific information sources, those surveyed receive information on breast cancer through traditional media (TV, radio, newspapers etc.) as well as the internet; and approximately a third of participants rely on charitable organizations to provide relevant information. (mBC General Population Survey, Pfizer, 2015)

Given the reliance on media as a source of mBC information, a deeper analysis of media coverage on mBC was conducted. The analysis began with assessment of two core articles reporting on the role of media (The BRIDGE survey, 2009 and Cancer and the Media Report, Fishman, 2010). The BRIDGE survey results revealed that over 50% of patients felt that BC received too little public attention; 73% of those surveyed wanted increased public awareness of mBC, including a greater level of media attention for people living with the disease (60%) and more recognition of public figures with the disease (55%). (BRIDGE Metastatic Breast Cancer Patient Survey, 2010)

Figure 2.12
Access to reliable information on aBC/mBC
mBC General Population Survey, Pfizer, 2015

(% Easy/Very Easy)
A 2010 analysis of news reports from the US highlight the limited focus on mBC; only 13.1% of 436 articles reported that aggressive cancer treatments can fail to cure or extend life, or that certain cancers are incurable (Fishman, 2010). Reports on cancer treatments and outcomes have included information on aggressive treatment options and patient survival, with seemingly little focus or discussion on the prognosis and treatment outcomes for late-stage cancers or terminal diagnoses, such as mBC. (Fishman, 2010) This may have portrayed a view of treatment for advanced disease that is inappropriately optimistic, leading to an unrealistic perception of the mBC patient experience. Furthermore, articles rarely discussed treatment side effects, such as neuropathy, pain, hair loss and nausea, which are common to cancer treatments. (Fishman, 2010).

Since these findings were reported in 2010, some progress has been made in increasing public exposure to mBC. To compliment these surveys, an analysis of yearly distribution of collected newspaper articles and newswires between 2006 and 2014 was conducted (see Appendix 2.3).

**Methodology:** In order to gain an understanding of public exposure to information on mBC, a qualitative literature review was conducted using secondary source data restricted between the years of 2005 to 2015 from LexisNexis®. Key word searches were conducted in LexisNexis® and were restricted to the years of 2005-2015 resulting in 998 abstracts. A standard TF-IDF text mining method was used to assign weight to the word stems identified in each article. Initial text mining analyses rendered 13,824 word stems covering a broad range of subject areas. For the year 2005, data gaps existed within LexisNexis® and only limited results were found, therefore data from 2005 was omitted from the analysis. In addition, the time of analysis (June 2015) resulted in only 6 months of data for 2015, this year was therefore also omitted from the analysis as it was not representative of a complete year. Please see Appendix 2.3 for detailed methodology.

This analysis indicates that public exposure to messages regarding mBC has been increasing steadily over time (Figure 2.13).

**Figure 2.13**

**Yearly Distribution of Newspaper Articles and Newswires on mBC Collected from 2006 through 2014**

Research from Appendix 2.3
Further analysis of the media coverage on mBC (See Appendix 2.3) shows that the majority of mBC media content focusses on treatments, safety, efficacy and clinical studies (Figure 2.14); the volume of such content has increased slowly with time. Treatment guidelines and quality standards receive less media coverage compared with articles on specific therapies; however, since 2009, there has been an increase in media reports focusing on pain and suffering in the context of mBC (Figure 2.15) - this is a small but important step forwards in raising awareness.

In the time period of the media analysis conducted for mBC, several milestones have occurred that could have contributed to the increase in media coverage and built a positive momentum (Figure 2.16). These efforts have focused on the unique challenges that mBC patients face.

**Figure 2.14**
Frequency of the Terms Approvals, Trials, Safety and Efficacy in mBC Media Coverage 2006 through 2014
Research from Appendix 2.3

**Figure 2.15**
mBC Media Coverage of Palliative Care, Pain, Suffering, Fear and Job Loss from 2006 to 2014
Research from Appendix 2.3
Contrary to what we often hear, death from breast cancer strikes all ages... from teens upward... This disease deserves strong public attention. It is not a disease of the elderly. It takes too many lives in their prime.

“CJ” (Dian) Corneliussen-James, Co-Founder, President, and Director of Advocacy, METAvivor Research & Support, 2015

<table>
<thead>
<tr>
<th>ADVANCEMENT</th>
<th>MILESTONE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recognition of mBC as distinct from early BC</td>
<td>Creation of metastatic breast cancer day on Oct 13 (Huffington Post, 2009)</td>
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<td></td>
<td>First International Consensus Conference for Advanced Breast Cancer in 2011 (Cardoso, 2012)</td>
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<td>Formation of the mBC Alliance in US (MBC Alliance, 2013)</td>
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<td>Launch of the mBC Alliance Landscape report (mBC Alliance Press Release, 2014)</td>
</tr>
<tr>
<td>Launch of several high profile initiatives to educate the public and breast cancer community, and spur action on behalf of patients</td>
<td>“Count Us, Know Us, Join Us” (Count Us, Know Us, Join Us, Novartis, 2013)</td>
</tr>
<tr>
<td></td>
<td>“Here and Now” in Europe (The Here and Now Campaign Report, Novartis, 2013)</td>
</tr>
<tr>
<td>High profile mBC patient perspectives and personal stories in the media</td>
<td>As an example, Laurie Becklund, the late Pulitzer-Prize winning journalist, reported her frustrations at the lack of mBC attention, in particular from breast cancer awareness groups themselves. (LA Times 2014) She wrote of the inability to ‘count’ this patient group or access new treatments in a timely fashion, finally calling for a database to record as much data as possible about this group.</td>
</tr>
<tr>
<td>Advances in science with positive phase 3 data or approval of new drugs for mBC patients</td>
<td>New approvals (FDA Hematology/Oncology Approvals)</td>
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<tr>
<td></td>
<td>Pertuzimab (NCI, 2012)</td>
</tr>
<tr>
<td></td>
<td>Ado-trastuzumab emtansine (NCI, 2013)</td>
</tr>
<tr>
<td></td>
<td>Everolimus (NCI, 2012)</td>
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</table>
Although these milestones represent a step forward for mBC, further efforts are required. Most of these activities have been restricted to North America and Europe. Public understanding of mBC remains limited (mBC General Population Survey, Pfizer, 2015, A Story Half Told, Pfizer, 2014); many mBC patients still experience isolation and stigma (MBC Alliance, 2014). Though mBC Awareness Day has brought more focus on mBC, it is one day in an entire month devoted to breast cancer where the emphasis remains on early-stage breast cancer and the need for self-examination and early detection. (National Breast Cancer Foundation, 2015) Further analysis is needed to understand the proportion of media coverage on mBC relative to overall breast cancer media coverage. Even if mBC coverage increases in absolute terms the impact of this difference may be limited if it remains a small fraction of the total media coverage for BC.

Honest, realistic and accurate representation in the media of the experience and outcomes of patients with mBC may enable the wider community to better support both patients and their caregivers. The communication of accurate information is essential in building a shared sense of empathy between patients with breast cancer, regardless of disease stage, as well as with the general public, and is especially important in destigmatizing metastatic disease. Charitable organizations and patient groups provide mBC patients with a global ‘voice’ through the sharing of personal stories and educational materials, which can contribute to enhanced public understanding of the disease and help reduce the isolation experienced by these patients.

In October 2015, the US based Metastatic Breast Cancer Alliance launched a social media campaign featuring real patients, #MetastaticSayIt, to educate the public about mBC. (MBC Alliance, 2015) More such efforts are needed across the world to highlight the mBC patient experience, within the appropriate cultural and social context.

Increased media coverage may mobilize public engagement and in turn help spur action amidst policymakers to advance the priorities for mBC. As an example, global research indicates that the extensive media coverage of AIDS and the gaping unmet need for treatments garnered the FDA to seek improved approval processes for these drugs, indicating that public engagement was a driving force to place AIDS treatments on the FDA priority list. (Carpenter, 2002)

Information presented in traditional and social media does influence public perception. However, not all available sources of information are evidence based and misinterpretation is possible. As such, information must be robustly supported by credible data, and communicated in a clear and consistent tone, to effect change in the perception of mBC.
Cultural perspectives impact the public understanding of mBC and associated health related behaviors

“People would rather have AIDS than cancer, they know that they can survive AIDS but do not think they can survive cancer... in Zambia, cancer equals death.”

_Udie Soko, Co-founder and Executive Director at the Zambian Cancer Society, Zambia, 2015_

Regional and local cultural norms drive variations in the public perception of breast cancer and the creation of tailored resources can in part, shape the public’s perception towards mBC, positively affecting patient lives by reducing social stigma and enhancing community support networks. For example, Chinese women are not routinely inclined to check for breast cancer due the cultural belief that cancer is a punishment and is contagious, and due to the desire to keep personal health matters private. (LIVESTRONG Report, Beckjord, 2012) A focus group study evaluating attitudes among Chinese women demonstrated that women’s attitudes towards breast cancer screening were significantly improved after watching a short video about the process that includes a soap opera and a segment with a physician. The authors argued that creating a culturally tailored video helped in increasing mammography use among Chinese women. (Wang, 2008)

Similarly, in South Africa, there is a reluctance to present with breast cancer symptoms and undergo physical examinations. There is a perceived invasion of privacy associated with the examination, due in part to the social opinion that private areas of the body should not be discussed. (LIVESTRONG Report, Beckjord, 2012)

In Pakistan, women with mBC often delayed telling their family that they had found a breast lump until it caused them significant pain and anxiety. (Banning, 2009) In Pakistan and Nepal, there is a widely held belief that breast cancer is a communicable disease that can be contracted by touch or contamination. This results in women concealing their diagnosis from their families and spouses, with some opting not to seek care at all. (Banning, 2012; Bhatt, 2011) This level of stigma associated with the disease not only has a negative impact on diagnosis and treatment, but also creates a heavy psychosocial burden on these women.

There is a division between those countries where discussion of the breast is permissible and those where it is not. Those countries, where communication around breast health and breast cancer is more acceptable, demonstrate an evolution in societal norms and culture over time. This evolution reflects ‘normalization’ of breast cancer through repeated communications. However, it is still necessary to minimize ongoing reluctance to communicate and educate about mBC. It is important to use sustainable community-based avenues, such as community health workers, women’s groups, churches, and health facilities to successfully reach women outside of urban areas where women have greater access to education. (Multhoni, 2010; Ford, 2003; Fernandez, 2009) Charities, such as the Uganda Women’s Cancer Support Organization (UWOCASO) aim to raise breast cancer awareness to give such a voice to Ugandan cancer survivors. (UWOCASO, 2015)
The use of fear-based messages is unlikely to motivate women to undertake early detection, and instead may intensify their anxiety about the disease (Cancer World, 2013). However, a recognition of the severity of breast cancer could be beneficial if it brings about a reduction in stigma and reluctance to communicate about advanced-stage disease (Cancer World, 2013).

Irrespective of socio-economic status, stigma unfortunately still exists for patients with mBC. More work must be done to help alleviate the burden of stigma on patients and ensure broader, community-wide support for patients with mBC to live with their disease.

“[In some African countries], people did not even have a word for breast cancer. They did not know what breast cancer was...physicians would always diagnose infectious diseases first before they said the word cancer because it was not in their [vocabulary]. Since then, there has been increased awareness.”

Dr. Olufunmilayo Olopade, Director of the Center for Clinical Cancer Genetics, University of Chicago, 2015

Marie Pandeloglou, mBC patient, with her mother. Marie is living with the disease.
Chapter 4: The Impact of Patient Support and Advocacy Organizations in mBC

- A number of Patient Support Organizations (PSOs) have begun to focus more attention on supporting patients with mBC in recent years.
- PSOs consider the hierarchical order of needs to be similar between eBC and mBC patients; however, they acknowledge the greater level of support needed for mBC patients.
- PSOs spend a lower proportion of efforts on mBC due to several factors including limited resources, perception of relative size of mBC patient population, local needs, logistical and cultural barriers in accessing mBC patients.
- Patient advocacy efforts in influencing health policy for breast cancer vary by region.
- Peer support networks offered by PSOs are particularly important to mBC patients, but often challenging to implement.

In this report the term Patient Support Organization (PSO) is used to describe organizations that offer a range of services to support patients directly (e.g. peer support groups, education, information), and/or advocate on their behalf to advance patient care, including policy changes, public education and raising research funding. PSOs are typically charitable or non-profit organizations and may differ widely in scope of operations. PSOs operate in many countries and strive to meet the needs they consider to be the highest priority to the patients and caregivers in their communities. (mBC Patient Support Organization Survey, Pfizer, 2015)

Patient Support Organizations (PSOs) play a vital role in supporting breast cancer patients and their families, providing a wide range of services to meet their evolving needs. (A Story Half Told, Pfizer, 2014) Collaborations developed by PSOs have helped to drive common agendas and initiatives to support the mBC community. Such collaborations include the Metastatic Breast Cancer Alliance in the US and the pan-European organization, Europa Donna, which offers specialist 'sub-groups' to address the unique needs of women with mBC. (mBC Alliance, 2014; europadonna.org; Metastatic Breast Cancer: Focus for Advocacy, Europa Donna, 2014)

Based on new primary research encouraging trends can be seen in the levels of support and advocacy for patients with mBC, however global variation exists. Although it is recognized that there continue to be issues surrounding appropriate and effective support for patients with mBC, some PSOs have employed concerted efforts in driving change and improvements have been made. In a 2014 survey conducted by a PSO with 17 of its mBC patient members, 11 said that they felt their local breast cancer support or advocacy group adequately met their needs for information and support. Despite a small representation of patients, this was recognized as an improvement on past surveys where a majority had not felt appropriately supported. (Metastatic Breast Cancer: Focus for Advocacy, Europa Donna, 2014)
**Methodology:** To improve understanding of the needs of mBC patients, and the activities and contribution by PSOs in meeting these needs, a qualitative primary research project was commissioned by Pfizer, that included 50 in-depth telephone interviews, each 45-60 minutes in length (some were face-to-face interviews) with key members of PSOs. The countries included were Canada, US, Belgium, France, Germany, Greece, Ireland, Italy, Poland, Spain, Turkey, UK, Australia, China, Japan, South Korea, Argentina, Brazil, Colombia, Costa Rica, Dominican Republic, Mexico, Egypt, Kenya, Rwanda, Saudi Arabia, Uganda, and Zambia.

Respondents were PSO leaders (CEOs, Presidents, Directors, etc.) of charitable and non-profit organizations that focus on mBC, breast cancer, and/or cancer on a local, national, and global level. They were selected to participate in the survey on the basis of their strategic and/or program responsibilities and their involvement in directing, developing, and/or managing health education, outreach, evaluation, and/or outcomes for their organization. On average, the tenure of respondents within a specific PSO is 8 years, with a range of 1 to 20+ years.

The surveyed PSOs vary greatly in size, with the number of employees and volunteers ranging from 2 to 1500+; the average staff size was under 20. The number of years surveyed PSOs have been supporting the needs of the breast cancer community also vary, ranging from 1 to 50+ years with an average of 11.5 years. (mBC Patient Support Organization Survey, Pfizer, 2015)

Research was conducted from June 15, 2015–August 3, 2015.

**A PSOs acknowledge the greater support needs of mBC patients, but prioritize them differently depending on available resources and local needs**

The PSOs surveyed (mBC Patient Support Organization Survey, Pfizer, 2015) highlight a hierarchy of patient needs that exist for patients with breast cancer or mBC, and that more basic needs (awareness of breast cancer, self-examination, detection, access to treatment and availability of physicians to provide treatment) must be met before “higher-level” needs can be addressed (psychological support, aids to decision making, aids for improving self-image) (Figure 2.17).

*In some countries, such as the US, reconstruction is considered as a basic treatment

**The hierarchy does not suggest relative importance, provision of services, nor utilization of services, but instead provides an overlay that applies in context where needs are met as well as where they are not.*
Generally, PSOs consider that relative to one another, eBC and mBC patient needs are similar. This is reflected by consistency in the hierarchical order of needs for both eBC and mBC patients. However, the extent of those needs does differ between early and metastatic disease. PSOs report that patients with mBC have much greater need in terms of psychological support, financial support and access to services, compared with those patients who have earlier stage disease. While stage (especially eBC vs. mBC) is an important driver of needs, other factors also shape this; one crucial differentiator highlighted was de novo vs recurrent diagnosis of mBC. Others include diversity of patients in terms of personality, desire for information, and course of illness. (mBC Patient Organization Survey, Pfizer, 2015).

While acknowledging the needs of mBC patients, PSOs report that a lower proportion of their efforts are directed towards mBC within BC overall. A range of barriers impact PSOs ability to meet patient needs, especially in mBC; these include; limited resources, perspective on mBC needs, cultural factors, and logistics.

PSOs report that the proportion of funding between eBC and mBC is often dictated by the size of the patient population. PSOs perceive mBC as a smaller patient population and it therefore receives a proportionately smaller share of support. This perception of PSOs is challenged by the reality that in some parts of the world, such as developing countries, 50-80% of patients are being diagnosed with advanced disease. (Unger-Saldana, 2014)

PSOs report that patients with mBC have much greater needs in terms of psychological support, financial support and access to services, compared with those patients with earlier stage disease.

(mBC Patient Support Organization Survey, Pfizer, 2015)

PSO services specifically focused on mBC patients are not only dependent on the available funding, but also on local need and therefore regional variation in provision of support services can be seen (Figure 2.18). Awareness and education is frequently offered to both general BC and mBC patient populations, however awareness, though among the top services provided, is relatively less frequently offered for mBC (92-98% vs. 70-79%). Most PSOs surveyed reported that they offer peer support for mBC patients. In North America, peer support is offered to the general BC population by approximately 50-75% of PSOs; however, this is not a frequently offered support service for mBC patients. (mBC Patient Support Organization Survey, Pfizer, 2015)

One way for PSOs to effectively support the mBC population is in the specialization of services; a “complete, don’t compete” approach is taken, that yields complementary services rather than those that

“\n
The women who are living with metastatic breast cancer are getting 100% of our programs, but the numbers are smaller. If we have 4500 callers and peer supporters, maybe we are talking about 70 women [who are mBC patients]. \n
”

North American Respondent, mBC PSO Survey, Pfizer, 2015
compete against other organizations. Each organization can vary in size, scope, reach, and mission, and as such the goal of overcoming barriers to meeting mBC needs should not be pursued at the expense of making PSOs homogeneous. (mBC Patient Support Organization Survey, Pfizer, 2015)

"If there are other organizations doing [something], we’re not going to recreate the wheel. We’d rather just direct them to other organizations that are… the best fit for their needs."

North American Respondent, mBC PSO Survey, Pfizer, 2015

### Table: Most Frequent Activities Provided to Support Patients with mBC

**Activities Engaged in to support mBC**

<table>
<thead>
<tr>
<th>Activities Engaged in to support mBC</th>
<th>US and Canada (n=11)</th>
<th>Europe (n=14)</th>
<th>Asia Pacific (n=7)</th>
<th>Latin America (n=10)</th>
<th>Africa and Middle East (n=8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Awareness</td>
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<tr>
<td>Patient Education</td>
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<tr>
<td>Treatment Education</td>
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<tr>
<td>Access Advocacy</td>
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<td>Peer Support</td>
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<td>Supporting Pts toBecome Adv.</td>
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<tr>
<td>Policy Advocacy</td>
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<tr>
<td>Financial</td>
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<tr>
<td>Data Generation</td>
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<tr>
<td>Clinical Trials/Registries</td>
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<tr>
<td>Regulatory</td>
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<tr>
<td>Legal</td>
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<td></td>
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<tr>
<td>Funding Scientific Research</td>
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</table>

This table represents the most frequently provided services only. Activities not highlighted are still offered across regions based on survey responses with the exception of policy and regulatory support in Asia/Australia and funding for scientific research in the Africa/Middle East region. The criteria for which activities are classified as 'most frequent' varies by region.

*Environmental Landscape*

The Impact of Patient Support and Advocacy Organizations in mBC
Peer support networks offered by PSOs are particularly important to mBC patients, but often challenging to implement.

“There are many women who have to face the disease again as recurrent or with metastases in another part of the body. If they have a recurrence, we just lose them. We don’t know where they are. They feel that they are not the ‘winners’ anymore, so they withdraw from the whole group.”

_European Respondent, mBC PSO Survey, Pfizer, 2015_

One of the key services that PSOs provide BC patients is peer support networks. For mBC patients, peer support is of particular importance in the context of the emotional challenges and social isolation they experience, as outlined in Section 1: Patient Care Perspectives. Evidence demonstrates that online support groups offer women with mBC the feeling of being supported by one another, even though they may not have met face-to-face. Online support groups also served as a place for information exchange, making women more active in their treatment decisions, and reducing ambiguity about new symptoms. Group cohesiveness benefits were seen in the women. Peer support groups directly alleviated their anxiety, helped them gain better medical care, reduced their need for social support, and increased their openness to others. Participation in such peer networks also reduced the sense of isolation that women feel, as they often feel partners, friends, and relatives are not able to completely understand what they are going through. (Vilhauer, 2009)

Studies have shown that stage-specific groups are more helpful to women with mBC than mixed-stage groups (ie those that include both eBC and mBC patients), also seen via online support groups. (Vilhauer, 2009; Vilhauer, 2011) This is often because of the unique experiences a patient with mBC is living through; mBC onset (de novo vs. recurrent), progression (indolent vs aggressive), symptoms experienced, and treatment goals are all individualized to a greater extent vs. eBC patients. Some PSOs also reported that eBC patients were reluctant to be in the same peer groups as mBC patients. (mBC Patient Organization Survey, Pfizer, 2015)

“We are shutting down [our mBC group] after 7 years….because it is too painful when someone dies.”

_North American Respondent, mBC PSO Survey, Pfizer, 2015_

Despite the rationale and clear benefit of providing peer support for mBC patients, PSOs admit that true peer support is difficult to achieve. Barriers include a reluctance by mBC patients to participate, patients do not wish to build their identity primarily on mBC, and they may become less active overall. In addition mBC peer group members may find it traumatizing if their mBC peers progress or pass away. (mBC Patient Organization Survey, Pfizer, 2015)

“Up until now [with the eBC patients] we were trying to break the stereotype or notion that ‘breast cancer means death.’ It took us a lot of time to deal with that. When it comes to metastases, everything is going back to the beginning—patients hear ‘metastases’ and they think it means painful death. That’s the way people here think about metastases.”

_European Respondent, mBC PSO Survey, Pfizer, 2015_

North American Respondent, mBC PSO Survey, Pfizer, 2015
Patient advocacy efforts in influencing health policy for breast cancer vary by region

Patient advocacy can also have a significant influence on policy decision-making. (Lerner, 2002) In high-income countries, improvements in breast cancer care have been achieved as a result of efforts by patients and their supporters, as well as survivors, the healthcare industry and media. (UICC, Planning Comprehensive Breast Cancer Programs) In countries where patient advocacy groups devote attention to breast cancer, these efforts have successfully increased awareness of mBC and contributed to increased access to cancer screening, diagnosis, and treatment. (Here & Now, Novartis, 2013)

PSOs are involved in the development of health policy at both the local and national level. This involvement includes increasing policy-maker awareness of patient and caregiver needs through educational programs, receptions, and one-to-one meetings with specific government officials.

- In the US, the National Breast Cancer Coalition (NBCC) launched ‘Breast Cancer Deadline 2020 - a call to action for policymakers, researchers, breast cancer advocates and other stakeholders to know how to end the disease by 2020’ (Breast Cancer Deadline 2020)

- Komen listed amongst its 2015 advocacy priorities the identification of expanded US federal funding for breast cancer research and policies that improve insurance coverage of breast cancer treatment; including, support for legislation that creates parity in insurance coverage for oral medicines compared with intravenous treatments (Susan G. Komen, National Public Policy)

- In Europe, Europa Donna is actively engaged in advocating for the European Parliament Written Declaration of Breast Cancer and other national parliamentary lobbying projects in EU member countries to raise awareness of the needs of mBC patients in policy and in BC guidelines (EuropaDonna.org)

Patient surveys carried out by the Breast Cancer Network Australia have identified both the support and information needs for patients with mBC and brought existing policy gaps to the attention of health decision-makers around work place issues, access to superannuation, breast care nurses and supportive care (BCNA Survey, 2015)

For more information on PSO involvement with policy initiatives please refer to Chapter 1: Health Policy for mBC.

Figure 2.19
PSO Provision of Policy Advocacy Services by Region
mBC Patient Support Organization Survey, Pfizer, 2015

<table>
<thead>
<tr>
<th>Region</th>
<th>BC general</th>
<th>mBC specific</th>
</tr>
</thead>
<tbody>
<tr>
<td>North America</td>
<td>82%</td>
<td>45%</td>
</tr>
<tr>
<td>EU</td>
<td>86%</td>
<td>57%</td>
</tr>
<tr>
<td>Latin America</td>
<td>70%</td>
<td>70%</td>
</tr>
<tr>
<td>Africa/Middle East</td>
<td>29%</td>
<td>0%</td>
</tr>
<tr>
<td>Asia/Australia</td>
<td>75%</td>
<td>38%</td>
</tr>
</tbody>
</table>

When comparing the PSO’s perceived needs of mBC patients vs. reported activities, policy was identified by PSOs as an area where there is a gap in activity. (mBC Patient Organization Survey, Pfizer, 2015)
Provision of policy advocacy services by PSOs also varies according to region (Figure 2.19). When comparing the perceived needs of mBC patients and the reported PSO activities, policy was identified by PSOs as an area where there is a gap in activity in most regions. (mBC Patient Organization Survey, Pfizer, 2015)

The PSO advocacy efforts to influence health policy are tailored to region-specific or local challenges. In developing countries such as Africa, PSOs need to address basic infrastructural issues, such as access to radiotherapy and pain medications before specific mBC issues are approached.

Many PSOs are actively involved in supporting access to cancer medications and reimbursement coverage for all necessary tests and treatments.

Many PSOs list “making the patient voice heard” as one of their principal goals. (mBC Patient Organization Survey, Pfizer 2015)  Despite being a key area of focus for many PSOs, creating opportunities for the elevation and vocalization of the patient voice to policy makers can be challenging, especially in low- and middle-income countries. Instability in the political infrastructure, a lack of fiscal or human resources available to lead advocacy efforts, socioeconomic or educational status can limit an individual’s ability to effectively advocate for themselves or others. (UICC, Planning Comprehensive Breast Cancer Programs) However, effective mBC advocacy is possible in low- and middle-income countries. For example, in Nigeria, a campaign was conducted to raise awareness at all levels of government, of the need to subsidize cancer treatment as a strategy to reduce the incidence of mBC. (Adisa, 2011)

A multi-stakeholder approach to developing advocacy efforts has demonstrated impact in raising awareness of breast cancer in high income countries. (UICC, Planning Comprehensive Breast Cancer Programs) Learnings can be taken from coordinated approaches to help guide policy makers towards implementing change. (UICC, Planning Comprehensive Breast Cancer Programs)

PSOs play a critical role in defining the mBC patient experience. While it is encouraging that progress has been made, and PSOs recognize the unique needs of mBC patients, barriers to providing optimal support remain. Through achieving a better understanding of the current disease state and the role of PSOs, further progress in the provision of tailored and compassionate support to mBC patients can be made.

“The goal of many PSOs is to make sure that the voices of women living with metastatic BC are heard during Breast Cancer Awareness Month because so much is going on and most of it relates to early-stage: ‘Let’s look for a cure.’ ‘Treatment is better.’ ‘Diagnosis is better.’ But there’s still a large number [of patients] who are becoming metastatic.”

North American Respondent, mBC PSO Survey, Pfizer, 2015
Emerging Recommendations

While negative perception and misunderstanding around mBC exists globally, approaches and strategies to address this will vary depending on each country and its resources. There are opportunities to drive change through improved education and awareness across both the general public and PSOs. These emerging recommendations focus heavily on changing the perception of mBC, prioritizing the unique needs of mBC patients and addressing these with tailored solutions. These recommendations need to be solidified through further dialogue and will require long-term commitment across a broad range of stakeholders to see effective change for mBC patients across the world. In addition, further opportunities for action will emerge based on ongoing analysis of the policy and economic landscape as well as societal perspectives on mBC.

**Increased global access and availability of PSO support services specific to mBC**
- Development of more mBC-specific support services is critical with an increased emphasis on impact to patients and families, especially for younger women
- Increase proactive communication highlighting specific support services, including counseling and online support groups.
- Increase global accessibility to support services for all patients with mBC

**Development of a global mBC alliance for advocacy, replicating some of the successes seen by organizations such as the US mBC Alliance**
- Provide a platform for advocates to educate each other on how to use stories, messages, the media, and social media to transform society’s understanding of mBC
- Collectively drive the need for access to treatments and palliative care, and for research on mBC
- Develop a brief for patient support organizations to drive consistency of communication about mBC

**Advanced widespread global awareness of mBC, with honest and accurate presentation of the realistic experience of patients, enabling the wider community to better support both patients and their caregivers in managing the impact of mBC on their lives**
- Encourage public figures with mBC to share their experiences, similar to what has been seen for eBC
- Provide mBC with a distinct identity separate from eBC - Leverage mBC day globally beyond the current geographies and potential expand to a longer duration than just a day

**Investment in education campaigns and outreach strategies is needed to grow awareness and action around mBC, in the same way that has been done for eBC**
- It is necessary to educate not only patients, caregivers, and healthcare professionals, but the donor community, general public journalists, government officials, and other key stakeholders, in order to harness a successful advocacy movement
- Emphasize with PSOs specifically the great need for long-term and often increasing assistance for mBC patients
- In limited-resource countries, appropriate advocacy and education should focus government attention on the growing burden of breast cancer including the untimely deaths due to mBC, and highlight the need for increasing national focus. (Koon 2013)
Empower media (both traditional and social) to deliver tailored, evidence based approaches to mBC communication and education

• Engage key global experts to directly educate the media about mBC care globally and the need to drive change
• Utilize traditional media to guide the general public to appropriate sources of mBC information
• Develop a reporting brief for the media about best practice in reporting mBC and advanced cancer generally

"CJ" (Dian) Corneliussen-James was diagnosed in 2006. She is living with the disease.
Appendices and References

Section 2: Appendix 2.1
Policy Trends Research Methodology

**Purpose:** The purpose of this search was to understand global political actions on behalf of patients with metastatic breast cancer (mBC).

**Method:** For this search, a literature scan was conducted to better understand policy trends that may impact the mBC space. Although a formal systematic literature review was not conducted, this section was written based on a thorough search of literature around metastatic breast cancer and policy trends.

**Sources:** In order to gain an understanding of policy trends, a qualitative literature scan was conducted using secondary source articles. The search was restricted between the years of 2005 and 2015 using the peer reviewed journal *Health Affairs* to find relevant articles. Other supplemental sources were also obtained using PubMed.

**Search terms:** Search terms were chosen based on their relevance to policy and metastatic breast cancer.

<table>
<thead>
<tr>
<th>Category</th>
<th>Key Terms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease</td>
<td>“metastatic breast cancer” OR “advanced breast cancer”</td>
</tr>
<tr>
<td>Category</td>
<td>“policy”</td>
</tr>
</tbody>
</table>

**Results:** In *Health Affairs*, the search “metastatic breast cancer’ policy” yielded 19 search results. Similarly, “advanced breast cancer’ policy” yielded 13 search results. These articles were reviewed for information on on cost-effectiveness policy, coverage and reimbursement policy, distinct case studies, and general cancer care. Articles from these searches were fully reviewed for content and relevance, those that were most relevant to mBC policy for the purpose of this report were included in this section. In addition, other articles found from other database or general searches were included in this section to enhance understandings of policies around metastatic and advanced breast cancer.

**Limitations:** This search was not a systematic literature review and therefore may not scientifically reflect global political decisions on metastatic breast cancer. However, *Health Affairs*, as well as the other peer-reviewed sources used, are trusted sources for gleaning information about global political views in many therapeutic areas and therefore, we believe that this section accurately portrays general policy trends in mBC.
Section 2: Appendix 2.2
Economic Burden Literature Review Methodology (3/17/2015)

**Purpose:** The purpose of this literature search was to understand the economic challenges mBC patients and their families face from the point of diagnosis until end of life.

**Method:** For this search, we used a systematic search methodology in order to mitigate the risk of missing relevant content by incorporating all perspectives and by including content from trusted and revered sources, particularly that of economic and financial hardships.

**Sources:** In order to gain an understanding of the economic burden of mBC, a literature review was conducted using secondary source data. The search was restricted between the years of 2005 to 2015 from four main databases: Medline, Medline In-Process, EMBASE, and Cochrane Library.

**Search terms:** Search terms were selected with the intent to ascertain all essential articles related to economic and financial experiences of mBC patients, caregivers, and their families. A complete list of search terms is provided in the table below.

<table>
<thead>
<tr>
<th>Category</th>
<th>Key Terms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease</td>
<td>'metastatic breast cancer'</td>
</tr>
<tr>
<td>Category</td>
<td>economic burden' OR 'cost' OR 'cost of illness'</td>
</tr>
</tbody>
</table>

EMBASE search conducted on the 17th March 2015:

<table>
<thead>
<tr>
<th>Searches</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>'breast'/exp OR breast AND ('metastasis'/exp OR metastasis)</td>
<td>89,063</td>
</tr>
<tr>
<td>'breast metastasis'/exp OR 'breast metastasis' AND [2005-2015]/py</td>
<td></td>
</tr>
<tr>
<td>'breast'/exp OR breast AND ('metastasis'/exp OR metastasis) AND [2005-2015]/py</td>
<td></td>
</tr>
<tr>
<td>#1 OR #2 OR #3</td>
<td></td>
</tr>
<tr>
<td>economic AND burden</td>
<td></td>
</tr>
<tr>
<td>'cost'/exp OR cost</td>
<td></td>
</tr>
<tr>
<td>#10 OR #12</td>
<td></td>
</tr>
<tr>
<td>#4 AND #13</td>
<td></td>
</tr>
</tbody>
</table>
### MEDLINE search conducted on the 18th March 2015:

<table>
<thead>
<tr>
<th>Searches</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Search metastatic breast cancer.mp Filters: published in the last 10 years</td>
<td>22639</td>
</tr>
<tr>
<td>Search (metastatic OR metastasis).mp breast (cancer OR tumour OR malignan* OR oncology OR carcinoma* OR neoplas* OR mass OR growth* OR cyst).mp; Filters: published in the last 10 years</td>
<td>29</td>
</tr>
<tr>
<td>#1 OR #2</td>
<td>22665</td>
</tr>
<tr>
<td>Search &quot;Cost of Illness&quot;[Majr] Filters: published in the last 10 years</td>
<td>5021</td>
</tr>
<tr>
<td>#3 AND #4 Published in the last 10 years</td>
<td>9</td>
</tr>
<tr>
<td>Search (&quot;economic burden&quot;) OR &quot;cost&quot; Filters: published in the last 10 years</td>
<td>175154</td>
</tr>
<tr>
<td>#10 OR #12</td>
<td>455</td>
</tr>
<tr>
<td>#5 OR #7 Published in the last 10 years</td>
<td>455</td>
</tr>
</tbody>
</table>

### Cochrane search conducted on the 18th March 2015:

<table>
<thead>
<tr>
<th>Searches</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>MeSH descriptor: [Breast Neoplasms] explode all trees</td>
<td>8904</td>
</tr>
<tr>
<td>metastatic or metastasis).mp</td>
<td>453</td>
</tr>
<tr>
<td>#1 and #2</td>
<td>38</td>
</tr>
<tr>
<td>MeSH descriptor: [Cost of Illness] explode all trees</td>
<td>1167</td>
</tr>
<tr>
<td>#3 and #4 Publication Year from 2005 to 2015</td>
<td>3</td>
</tr>
</tbody>
</table>

### Cochrane search conducted on the 18th March 2015:

<table>
<thead>
<tr>
<th>Searches</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>breast (cancer or tumour or malignan* or oncology or carcinoma* or neoplas* or mass or growth* or cyst).mp</td>
<td>574</td>
</tr>
<tr>
<td>(metastatic or metastasis).mp</td>
<td>453</td>
</tr>
<tr>
<td>#1 and #2</td>
<td>179</td>
</tr>
<tr>
<td>(economic or burden or cost).mp</td>
<td>2207</td>
</tr>
<tr>
<td>#3 and #4 Publication Year from 2005 to 2015</td>
<td>93</td>
</tr>
</tbody>
</table>
**Results:** After the searches were completed and duplicates were removed, a total of 526 abstracts were collected and recorded in an excel document, including relevant sources information and abstract text. Of these abstracts, 37 full text articles and 10 abstracts were assessed for eligibility. Articles were removed from the original collection due to differences in language, being therapy specific, demonstrating burden of skeletal events only, not pertaining to mBC, and not portraying cost data. A total of 26 articles and 3 abstracts were included in the quantitative synthesis.

These articles were then fully reviewed to glean key messages and information about the economic challenges of mBC patients. Thorough examination of all articles and abstracts allowed for the best selection of articles relevant to the economic burden piece; however, the writing does include references to other sources to add appropriate context.

**Limitations:** Despite this systematic approach, limitations to this search methodology exist. Specifically, articles irrelevant for this chapter might have appeared in the search through selected search terms being used in different contexts. For example, if the search term was “metastatic breast cancer,” non-“metastatic breast cancer” could also appear. To account for this challenge, each abstract was reviewed to determine relevance and inclusion criteria. In addition, there is a potential risk of missing articles if the databases failed to capture all relevant articles in the space based on the search terms used. However, based on the credibility and number of databases, this limitation is unlikely to significantly impact the findings. Lastly, to add necessary context to research findings, articles from separate searches are included in this piece and therefore, for those articles, we cannot be certain that the articles represent all possible perspectives in this space.
Section 2: Appendix 2.3
Public Understanding Literature Search (July 2015)

**Purpose:** The purpose of this search was to gain an understanding of the public perception of metastatic breast cancer and its potential impact on the patient experience, a literature review was conducted of media and newswire sources.

**Method:** For this search, we used a systematic search methodology in order to mitigate the risk of missing relevant content by incorporating all perspectives and by including content from trusted and revered sources.

**Search Terms:**

<table>
<thead>
<tr>
<th>Category</th>
<th>Key Terms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease</td>
<td>MBC OR “metastatic breast cancer”, “stage four” OR “stage 4” OR “stage IV”, LABC OR “locally advanced breast cancer”, ABC OR “advanced breast cancer”, HER2+ OR “HER2 positive” OR HER2-positive, HER2- OR “HER2 negative” OR HER2-negative, ER+ OR “estrogen receptor positive”, ER- OR “estrogen receptor negative”, ER OR “estrogen receptor”, “Hormone receptor positive”, “Hormone receptor positive”, ER+/HER2+ OR HER3+/ER+, ER+/HER2- OR HER2/-ER+, ER-/HER2+ OR HER2+/ER-, “pre menopausal” OR pre-menopausal, premenopausal, “post menopausal” OR post-menopausal, postmenopausal, “secondary breast cancer”, TNBC OR “triple negative breast cancer” OR ER-/HER- OR HER2-/ER-</td>
</tr>
</tbody>
</table>
### Search Terms:

<table>
<thead>
<tr>
<th>Category</th>
<th>Key Terms</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Outcome Measure</strong></td>
<td>OS OR “Overall survival”, “survival rate”, PFS OR “Progression free survival”, “TTP” OR time to progression</td>
</tr>
<tr>
<td><strong>Trial</strong></td>
<td>“Phase I” OR “Phase 1” OR P1, “Phase II” OR “Phase 2” OR P2, “Phase III” OR “Phase 3” OR P3, “Phase IV” OR Phase 4” OR P4, “comparative effectiveness” OR “head-to-head” OR “head to head”</td>
</tr>
<tr>
<td><strong>Metastases</strong></td>
<td>“Brain metastases” OR “central nervous system metastases” OR “nervous system metastases” OR “CNS metastases” OR brain, “Liver metastases” OR Liver, “Skin metastases” OR “Epithelial metastases” OR Skin, “bone metastases” OR bone</td>
</tr>
<tr>
<td><strong>Patient Reported Outcome</strong></td>
<td>“Patient reported outcomes” OR PRO OR “patient-reported outcomes”, Efficacy</td>
</tr>
<tr>
<td><strong>Tolerability</strong></td>
<td>Tolerance OR Tolerability</td>
</tr>
<tr>
<td><strong>Side Effects</strong></td>
<td>“adverse effect” OR “adverse effects” OR “adverse reaction” OR “Adverse events” OR AE OR Aes OR PSE OR “Patient safety event” OR “side effects” OR SE OR “adverse reaction” OR “adverse drug reaction” OR “unexpected adverse drug reaction” OR “other adverse event” OR “OAE”, drug-drug interaction OR DDI, toxicity</td>
</tr>
<tr>
<td><strong>Value</strong></td>
<td>“cost effectiveness” OR “Cost effective,” OR “cost-effectiveness,” OR “beneficial value” OR “QALY” OR “economic value”, “value” OR “risk benefit”, Cost, efficiency OR “cost efficiency”</td>
</tr>
<tr>
<td><strong>Social</strong></td>
<td>discrimination OR prejudice, employment OR fired, insurance OR coverage OR reimbursement OR uninsured OR “employer-sponsored insurance” OR “employer sponsored insurance”, “family support” OR support OR family OR burden OR “family impact”, “in-home care” OR “in home care” OR “hospital care” OR hospital OR in-patient OR “in patient” OR “hospice care” OR “hospice”, prescription OR refill OR medication OR drug, “daily routine” OR lifestyle OR “daily activities”, “Caregiver”, “quality of life” OR QoL OR HRQoL OR “health-related quality of life”, Advocacy, Legislation, Awareness, “patient education”, “cancer fund”, “government aide”, “NGO”</td>
</tr>
<tr>
<td><strong>Country</strong></td>
<td>All country members of the United Nations</td>
</tr>
</tbody>
</table>
Results: Standard text mining method, TF-IDF approach, was used to assign weight to the word stems identified in each article. All media extractions are tokenized, non-letters removed, and stemmed to reduce complexity. Initial text mining analyses rendered 13,824 word stems covering a broad range of subject areas ranging from treatment to spiritual terms such as “god”. Key word searches were conducted in Lexus Nexis and were restricted to the years of 2005-2015 resulting in 998 abstracts. To review the trends of the selected terms, an analysis was performed using a modified version of the “bag-of-words” text mining concept. This method searches for binary outputs of absence or presence by disregarding word order and grammar. To perform this analysis abstract content all punctuation except for +, - and / was replaced with a space and content was scanned using the selected key terms. Results were marked with a “1” or “0” respectively if a term was present or absent.

Limitations: Despite this systematic approach, limitations to this search methodology exist. Specifically, articles irrelevant for this chapter might have appeared in the search through selected search terms being used in different contexts. For example, if the search term was “metastatic breast cancer,” non-“metastatic breast cancer” could also appear. To account for this challenge, each abstract was reviewed to determine relevance and inclusion criteria. In addition, there is a potential risk of missing articles due the fact that our research was restricted to newspaper articles only.
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Inside Vandy: Vanderbilt University. 10.2.2013. Newspaper. (Inside Vandy, Vanderbilt University, 2013)


Global Status of mBC Decade Report


Pakseresht S, Ingle GK, Garg S, Sarafraz N. Stage at diagnosis and delay in seeking medical care among women with breast cancer, Delhi, India. Iran Red Crescent Med J. 2014;16(12): e14490. DOI: 10.5812/ircmj.14490. (Pakseresht, 2014)


