



## Review



## EBCC-14 manifesto: Addressing disparities in access to innovation for patients with metastatic breast cancer across Europe

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## ABSTRACT

The European Breast Cancer Council (EBCC) traditionally identifies controversies or major deficiencies in the management of patients with breast cancer and selects a multidisciplinary expert team to collaborate in setting crucial principles and recommendations to improve breast cancer care. The 2024 EBCC manifesto focuses on disparities in the care of patients with metastatic breast cancer. There are several reasons for existing disparities both between and within countries. Our recommendations aim to address the stigma of metastatic disease, which has led to significant disparities in access to innovative care regardless of the gross national income of a country. These recommendations are for different stakeholders to promote the care of patients with metastatic breast cancer across Europe and worldwide.

## 1. Introduction

The European Breast Cancer Council (EBCC) aims to promote the high-quality evidence-based care of all patients with breast cancer. Each year, the EBCC manifesto identifies crucial topics that need to be

addressed, taking into account differences across European countries. [1–4] The EBCC-14 manifesto focuses on disparities in the care of patients with metastatic breast cancer (mBC).

Inequitable access to healthcare for breast cancer has long been recognised [5–11]. In 2024, disparities in access to healthcare persist

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and continue to widen in some countries, due in large part to challenges in accessing new effective therapies and cancer services and a lack of political will to implement effective public health policies [12–14]. Gross national income is a major factor that drives these disparities [15, 16], and the inadequate care of patients with cancer may result in financial toxicity, creating a vicious cycle for national economics. One-third of people with a cancer diagnosis will permanently give up work and about half will experience income loss; the diagnosis results in financial distress in up to two-thirds of patients [17]. Financial toxicity varies significantly between countries, but demographic and individual socioeconomic factors within a country play a role and younger, unemployed and divorced patients with children are particularly vulnerable to financial toxicity.

While economic disparities and a country's gross national income are frequently cited as barriers to innovative therapies, they represent only two of several factors contributing to unequal access [18,19]. Among the underserved populations are those with lower socioeconomic status, those with a lower education level, people living in rural areas and migrants [20]. Lower socioeconomic status is associated with a lower incidence but higher lethality of breast cancer in Europe [21]. Furthermore, disparities in care are not limited to access to innovative therapies: a recent EUROPA DONNA survey revealed variable and limited access to psycho-oncology, physiotherapy, nutritional services and coordinated care [11], which are basic needs for patients diagnosed with cancer or any chronic disease.

We must be less fatalistic and more optimistic about the trajectory of mBC while remaining realistic about what we can do to improve the care, support and dignity of people living with mBC and to ensure continued investment in their wellbeing. In this article, we identify those innovations that bring the greatest benefit but are not equally accessible, highlight barriers to accessing innovation and propose steps towards improved access to innovation. Our goal is to improve outcomes for patients with mBC by levelling up major disparities between and within countries in Europe, and between mBC and early breast cancer (eBC). Several initiatives are already ongoing but much more can be achieved. Although the EBCC, which comprises clinicians and patients living with or after breast cancer, has neither the mandate nor the powers to implement actionable steps, this manifesto aims to reinforce and complement existing efforts. It may be used to support advocacy for policies at both national and European levels and is divided into five broad categories: stigma, registries and real-world data, multidisciplinary care, clinical research and quality indicators.

## 2. Living with the stigma of mBC

mBC is a diverse disease encompassing a spectrum ranging from potentially curative oligometastatic disease to a dismal prognosis with no effective treatments and very short life expectancy [22]. Consequently, the needs of patients with mBC are heterogeneous and often differ substantially from those of patients with eBC [23]. Many people living with mBC face long-term incurable disease and chronic treatment, which may include multiple lines of therapy, all with different side effects.

Although public perception has advanced, cancer is still surrounded by stigma, taboo and euphemism, which affects ethnic minorities disproportionately [24]. One in 10 respondents to a UK survey indicated they would find it difficult being around someone with cancer and a similar proportion said they would find it difficult to talk to someone with cancer [24]. The stigma and fatalistic view of mBC may prevent some individuals from seeking advice, information or medical care. Many patients and their families cope with stigma through non-disclosure, exacerbating difficulties in accessing support [25]. Family worries bring an additional emotional burden and most young adults with cancer are worried about their family's financial situation [26]. Following a diagnosis of advanced cancer, a reduced ability to work and lower income are coupled with increased treatment-related

expenses (direct and indirect), combining to place a substantial financial burden on patients [17,27].

Compared with individuals diagnosed with eBC, patients with mBC have reported a sense of abandonment and neglect [25,28,29]. Psychological and emotional support provision are often tailored towards eBC rather than mBC [28]. People with mBC are frequently undervalued, under-recognised and under-represented [30] but want to be counted, seen, supported and treated. In some countries, politicians may neglect the benefit of prolonging the lives of people with mBC, preferring to invest in eBC [11,31].

To overcome such stigma, the public, policy makers and healthcare providers need to recognise that mBC is not synonymous with imminent death and that people with mBC deserve the same opportunities and rights as everyone else. We should ensure that individuals with mBC can continue with their important contributions to society, including family, community, science, the arts, journalism and activism. The prognosis for people with mBC has improved dramatically in recent years, and it is not uncommon for people to live with mBC for 10 years [32,33]. Society needs to know this, accept this and be able to fully support patients and their caregivers. Furthermore, as breast cancer is so prevalent and treatments are improving, the number of people living with mBC is likely to continue growing and all should be well cared for and encouraged to continue to be a productive part of society.

Several powerful campaigns are raising public awareness of mBC, including those by EUROPA DONNA [34] and the Advanced Breast Cancer (ABC) Global Alliance [35]. Investment in public education is critical to disseminate information to the broadest possible audience, raise awareness of the important contribution of people with mBC, and recognise the impact on those surrounding and supporting people living with mBC, particularly when resources are limited. Ongoing initiatives to ensure that the specific needs of patients with mBC receive the attention they deserve include the Lancet Breast Cancer Commission [29,36], Europe's Beating Cancer Plan [37] and the ABC Global Alliance [28]. These initiatives strive to change the collective mentality towards mBC to be more optimistic, and to recognise the very different challenges experienced and care provision needed by people living with mBC compared with eBC.

Receiving healthcare for mBC can become a full-time job [35,38,39]. Nevertheless, many people with mBC need or want to continue working, perhaps because the workplace provides them with a sense of normality and purpose. The challenges associated with the emotional, physical and cognitive changes brought about by mBC are often poorly understood and should be addressed [28]. Changing labour laws to allow people with mBC to continue working in a more flexible way according to their altered physical and psychological capacity, with compensation to the individuals and the employers, would bring cost savings benefitting both governments and society, as well as reducing the stigma of mBC and improving individuals' self-esteem [40].

The stigma associated with a diagnosis of mBC extends beyond the general public to the healthcare profession [25]. Denying intensive care units to people with advanced cancer during the COVID-19 pandemic is an example of the discrimination against people living with advanced cancer [41,42].

The stigma of metastatic disease should not guide social-clinical management. Patients with mBC deserve the best possible care, regardless of their prognosis, to enhance survival outcomes and quality of life (QoL). All patients should have access to appropriate support (medical, social, psychological, workplace) and supportive care throughout their mBC [19]. Future policies should focus on survivorship (including mental, psychosocial and nutritional support) across healthcare systems [43–46]. As disease progresses, patients deserve optimal end-of-life care and their caregivers deserve psychosocial support.

**Recommendation 1.** Increase the visibility of mBC to society and facilitate the involvement of people with mBC in trials, the workplace and everyday life as much as they want and are able.

### 3. Registries and real-world data

One of the first challenges when trying to redress inequity in mBC is the unknown prevalence of mBC in many countries [47]. Few countries have registries of patients living with mBC: some record breast cancer diagnoses but do not differentiate between eBC and mBC [29,48] and others have no registries [11]. This lack of information limits our ability to identify unequal access to innovation for mBC and allocate resources appropriately. Furthermore, the content structure of existing databases makes comparison between countries difficult [49], and lack of information on social factors and demographics, including ethnicity, hampers attempts to identify and address disparities [50]. Therefore, collection of a defined set of data, with minimal requirements aligned internationally, is critical. Analyses by the International Cancer Benchmarking Partnership illustrate the value of such efforts in identifying and understanding disparities [51]. Recently updated recommendations for standardised data collection in European registries aim to facilitate comparison and integration of databases [49]; sharing national registries globally is critical to obtaining reliable data [52]. Furthermore, policies and legal frameworks need to allow interconnection and data sharing between registries. There is a balance between data protection and patients' wishes to be heard and recognised; therefore, legal exceptions to data protection should be considered openly and proactively [52]. Cross-referencing between registries of chemotherapy administration and cancer would require policy makers to respond to calls for a waiver to data protection laws.

**Recommendation 2.** Implement a national cancer registry recording stage at diagnosis and relapses in every European country and share with the International Agency for Research on Cancer (IARC) to understand how many people are living with mBC.

Some countries have registries that provide a rich resource for analysing access and outcomes, including The Netherlands Cancer Registry [53–57], the SONABRE registry (also in The Netherlands) [32,58–60], the French Epidemiological Strategy and Medical Economics (ESME) programme [61–65], the German Centre for Cancer Registry Data [66], the Belgian Cancer Registry [67], the Swedish Cancer Registry [68] and the Association of Nordic Cancer Registries (NORDCAN) database [69]. The power of such registries is exemplified by the experience in New Zealand. Analysis of mBC registry data demonstrated that the life expectancy of people with mBC in New Zealand was half that of patients in Australia; that patients received a median of only one treatment line for mBC; and that empirical (or no) treatment was offered to many patients. There was very little investment in treatment for mBC, no treatment guidelines and a perception that access to treatment was less important because patients were incurable. These findings provided the impetus for dramatic changes within the entire oncology community to improve access and outcomes and new investments [31].

As well as identifying disparities in care, real-world data can demonstrate the benefit of best-quality care, potentially supporting reimbursement decisions and filling evidence gaps that cannot be addressed through clinical trials. As many reimbursement decisions are taken nationally, the generalisability of data from one country may not be acceptable to decision makers and policy drivers in another; however, the impact of differences in the availability and access to best possible care can be compared between countries if real-world data are collected nationwide. Standardising real-world data reporting is encouraged, for both registries and hospitals [70,71], and efforts are underway for Europe-wide coordination [72–74].

**Recommendation 3.** Harmonise, monitor and use routinely collected real-world and registry data (including but not limited to details of biomarker/genetic testing, treatment and quality of life) to support reimbursement policies and improve access to treatment, trials and services and to evaluate outcomes.

### 4. Multidisciplinary care

#### 4.1. Ensure equal access to high-quality multidisciplinary care

There are several reasons why high-quality multidisciplinary care is denied, including: financial/insurance and reimbursement policies [3, 11,28,29,75], indirect costs, geographical variations (with less access in rural or underserved areas [11,29,76]), socioeconomic inequities [29], limited healthcare resources/bottlenecks, frailty and geriatric assessment and disparity in regulatory approval. These inequalities exist at all stages of mBC care.

#### 4.2. Ensure timely referral to a multidisciplinary specialist care pathway

Detection and treatment of breast cancer at an early stage reduce inequalities in breast cancer outcomes [77]. Improved screening and earlier detection also result in a change in the profile of patients presenting with de novo mBC [78]. In Europe, the proportion of patients with a first diagnosis of mBC has decreased in the past two decades but, in most European countries, older patients and those with the lowest socioeconomic status are more likely to present with de novo mBC [79]. Globally, women in rural areas are more likely to be diagnosed at a later stage than those in urban areas [80–82].

Once diagnosed, all patients with mBC should be managed at a specialist centre by a multidisciplinary team (MDT) of experts relevant to their individual situation [2]. Multidisciplinary care improves outcomes in breast cancer [2,83,84], whereas treatment in non-specialist centres has a detrimental effect [2,85]. MDT implementation must be optimised to ensure that all patients are reviewed and discussed [2,86, 87]. MDTs were the focus of a previous EBCC manifesto [2] and are not discussed in detail here; however, it is worth highlighting that MDT discussion increases the likelihood of a patient participating in a clinical trial (discussed in Section 4). In addition, molecular tumour boards are increasingly important, with more personalised treatment options requiring molecular testing as well as pathology [88,89]. Although more complex and expensive than conventional MDTs, the ability of molecular tumour boards to improve patient selection for targeted therapies may provide more cost-effective care and improved access to clinical trials [90,91]. Importantly, MDT care via a specialist centre does not preclude delivery of (systemic) treatment closer to home, which can lessen the burden of treatment on patients' quality of life. This can often be achieved through virtual meetings, networks and satellite centres, allowing optimal discussion and involvement of all specialists.

Most recent innovations in systemic therapy for mBC involve targeted treatments, many of which have demonstrated efficacy in biomarker- or molecularly selected subtypes of mBC. A comprehensive workup to determine the most appropriate management of an individual with mBC is therefore critical and requires high-quality timely imaging and biomarker testing backed by adequate reimbursement and up-to-date guidance to clinicians [8,89,92–94]. Diagnostic tests have been reported to account for less than 2 % of total healthcare spending but to influence 60 % of clinical decision making [89,95].

The diagnosis of mBC requires the demonstration or confirmation that metastatic tissue is present in a specific organ by means of imaging. Besides considerations of diagnostic effectiveness, the choice of imaging modality may vary according to local availability, adherence to guidelines or consideration of innovative therapeutic approaches. Although still often recommended in guidelines, standard imaging modalities (bone scintigraphy, computed tomography), may not be sufficient for an early diagnosis of metastasis. Modern ("next-generation") imaging modalities (18-fluoro-deoxyglucose positron emission tomography [FDG-PET]/computed tomography and whole-body magnetic resonance imaging) allow reliable diagnosis of oligometastasis, consideration of metastasis-directed treatments and subsequent evaluation of the response to treatment [96]. The potential to offer patients the most innovative therapeutic approaches and/or enrolment in trials assumes

the availability of these modern imaging modalities [97]. These modern imaging methods should be available for all patients in whom they are recommended according to guidelines.

At mBC diagnosis, a metastatic site should be biopsied under imaging guidance to exclude a benign lesion or metastasis from a different cancer and to lessen the risk of treating the ‘wrong’ phenotype [93,98–101]. Biomarkers (hormonal, molecular and gene expression) in primary versus metastatic samples are often discordant, affecting therapeutic targets and treatment selection [102–105].

Despite existing guidelines for biomarker testing to select patients for evidence-based therapeutic options [93,106,107], disparities in essential pathology/biomarker testing remain [108]. Access to genetic testing is variable [89,109], and some patients are required to pay through out-of-pocket funding or private insurance [11,108]. In some cases patients have to request genomic tests, which requires patient awareness and education on testing [11]. A recent study demonstrated that at least one genomic drug target with high-level evidence can be identified with next-generation sequencing in more than half of patients with mBC [105].

Barriers to the use of essential and innovative diagnostic tests include outdated regulations, inadequate infrastructure for data collection and laboratory analysis, insufficient training and fragmented approval and funding systems [89]. Uptake of genomic testing may depend on the likelihood of identifying an actionable target and the availability of a treatment targeting the identified biomarker, as well as turnaround times and cost [110,111]. Tackling access to biomolecular technologies is a critical step in reducing inequalities with respect to precision medicine for cancer [111]. Digital pathways to overcome resource shortages and bottlenecks for appointment-based genetic testing and counselling have shown high patient and healthcare professional acceptability and may broaden access [112].

A recent survey of biomarker testing in Europe indicated that access to single biomarker tests was lower in countries that lacked diagnostic laboratory infrastructure (including several Eastern and Central European countries), had inefficient organisation of diagnostic laboratory infrastructure and/or inadequate public reimbursement of testing, and where pharmaceutical companies and patients pay for testing [94]. In Central and Eastern European countries, limited reimbursement is a significant barrier to molecular testing [113]. Uptake of multigene testing (e.g. next-generation sequencing) is even more variable, and advanced biomolecular technologies are inaccessible in many countries [111]. Furthermore, the problem of access to diagnostic tests varies within as well as between countries. In Western and Northern Europe more than 90 % of laboratories participate in quality assurance schemes, but the percentage is lower elsewhere [94]. If quality assurance is lacking, test results are less reliable and physicians and patients may have little confidence in using them to make treatment decisions. Without action, the problem of access to biomarker testing is likely to worsen with the increasing number of tumour-agnostic therapies relying solely on molecular markers to define eligibility [114].

Increasingly, liquid biopsy is playing an important role in diagnostics and workup [115] but there are several barriers to its uptake, not least the expense and complexity of implementation [88,116]. Equal access to high-quality and timely biomarker testing of mBC, backed by adequate reimbursement and up-to-date guidance to clinicians, is a priority.

#### *4.3. Ensure the availability of best standard-of-care management, including innovative treatments and long-term support*

If enrolment in a clinical trial is not an option or is not in an individual’s best interests, all Europeans with mBC should have timely access to best standard-of-care management. Numerous treatment advances have improved outcomes for patients with mBC [19,93]; however, disparities in timely access to these developments result in inequitable outcomes. Geographical variations are seen in access to standard care, even within countries, and specific patient groups, such

as older patients, may be less likely to receive innovative care [117]. Significant improvements in radiation therapy techniques (e.g. hypofractionation and stereotactic radiation therapy) reduce toxicity and treatment burden and may improve QoL [118–120]. Optimal modern personalised radiation therapy options should be offered to all patients with mBC, across the spectrum of disease.

Delaying palliative radiation therapy adversely affects QoL and overall survival. Early integration of specialist palliative (or supportive) care to manage symptoms, pain and QoL improves outcomes for patients with advanced cancer [121–124]. Supervised physical exercise appears to improve mental wellbeing and physical fitness and reduce fatigue and pain in patients with mBC, highlighting the importance of holistic care [125]. Specialist palliative care can improve patient and caregiver satisfaction and reduce the amount of time spent in acute hospital settings [126]. However, inpatient palliative care is often provided only in the final month of life, and (outside large cancer centres) is delivered less frequently to older than younger patients [127].

#### *4.4. Equitable access and sustainable funding for the best available treatments and support*

The high and increasing costs of innovative cancer medicines are well recognised [128–131]. Regulatory and reimbursement policies have an important impact on access to these medicines [132–134]. If reimbursement is well aligned with guidelines and optimal clinical practice, healthcare provision is more cost effective and limited resources can be distributed more equitably [3]. This topic was covered extensively in the EBCC-12 manifesto [3] and will not be rediscussed here. However, it is worth highlighting that for many patients with mBC, new and effective drugs may not be available if they are not routinely reimbursed in a country.

A unified regulatory approval process for the European Union means that approval is synchronised within its member countries. Nevertheless, the pace at which medicines reach eligible patients is variable and there are opportunities to improve access [135]. Patients can sometimes access new treatments through early-access programmes or off-label use, but even these show disparities between and within countries [136]. Improving pricing and reimbursement timelines, fostering collaboration between national health authorities and market authorisation holders, and implementing nationally harmonised data-generating early-access programmes can enhance timely and equitable access to innovative cancer treatments [135].

**Recommendation 4.** Ensure that all patients with mBC in Europe have access to high-quality multidisciplinary information and care (imaging, molecular biology, pathology, radiation, systemic therapy, surgery, side-effect management, palliative and supportive care, physical exercise, trials, etc).

## **5. Clinical research**

### *5.1. Broaden access and include patient-centred goals in research to improve patient outcomes*

Clinical research represents an important means of improving patient outcomes in mBC. Clinical trials offer the opportunity for innovative treatments and improved survival, irrespective of the intervention’s efficacy [137–139]. Indeed, simply being treated in a research-active hospital seems to improve outcomes irrespective of whether the individual enrolls in a trial. However, access to clinical trials varies according to country, geographical location (urban versus rural), race and other factors [5,11,140–142]. Trials are typically conducted in high-income countries [13,143,144], even though the largest gains in cancer control may be achieved in areas with the poorest cancer outcomes [13]. Some patients cross borders to participate in clinical trials that give access to treatments not available in their home country [144]. Patients

older than 70 years, those of a lower socioeconomic status and minority groups are often under-represented in clinical trials [145–150], and there is typically limited ethnic and racial diversity [143]. This in turn leads to less generalisable results and uncertainty about benefits in minority or under-represented populations [13].

Barriers to clinical trial participation include complex informed consent processes [151], physical distance from participating centres [90], financial barriers such as transport costs, lack of childcare support or time off work or caring duties, language or cultural barriers, lack of trust and misinformation [143]. In addition, patients with brain metastases or those with very aggressive, early relapsing disease are often excluded from clinical trials, even though further research is needed for these patients.

Precision medicine and a deeper understanding of cancer biology has led to increased complexity in clinical trial designs, often involving central assessment of tumour samples with the associated practical and logistical demands, high screen failure rates and recruitment challenges. In addition, EU legal and regulatory requirements, such as for in vitro diagnostic medical devices, can be difficult to meet. Biospecimens donated from patients who participate in clinical trials and their associated biomarker reports should be open access (i.e. available to all researchers in the field), broadening the potential to generate new hypotheses and new clinical trials.

While sophisticated drug development and regulatory clinical trials remain a priority, multidisciplinary, pragmatic and independent clinical trials with practice-changing potential should be facilitated in Europe [13,152]. Trials answering clinically relevant questions about therapeutic strategies based on medically meaningful endpoints should be open to as many patients from as diverse backgrounds as possible. Modifying site management practices and using shorter, more focused case report forms could reverse the spiralling costs of clinical trials without a detrimental impact on quality [153]. Pragmatic trials representative of real-life populations ensure robust methodology for decision making and minimise uncertainty about a drug's effectiveness [151].

In parallel with broadening access to clinical trials, more should be done to improve the way in which research is conducted. Trials should aim higher and be more ambitious, striving to improve the endpoints of greatest importance to patients [152,154]. The Common Sense Oncology movement strives to ensure that cancer care focuses on outcomes that matter to patients [154]. Initiatives of the EU Mission for Cancer aim to increase access to optimised affordable treatment interventions, with a particular focus on simple practical trials in oncology [152]. Unfortunately, some healthcare and funding systems may result in the overuse of treatments that offer very modest improvements in outcomes, while in other systems people cannot access cost-effective treatments that bring substantial and meaningful benefits [154]. To enhance research in underserved populations, where the greatest strides in cancer care may be made, funding from international research initiatives should be more equitable, supporting neglected research priorities and strengthening research capacity and infrastructure in low- and middle-income countries [13].

Academic- and government-led trials that assess less resource-intensive schedules or strategies may also alleviate disparity, for example with lower doses, less frequent dosing or shorter treatment durations [155]. Dose optimisation may improve tolerability while maintaining efficacy, but is often overlooked in clinical trials [156,157]. In mBC, efficiency research, exemplified by trials such as SONIA [158], provides an opportunity to limit the impact of expensive drugs on healthcare budgets by using them more efficiently [129]. Furthermore, if cost savings generated from less intensive regimens are reinvested, such trials may be self-funding.

There is currently no mechanism to fund and organise Europe-wide trials answering critical questions in mBC that are outside the regulatory interests of pharmaceutical companies. National organisations exist in some countries, but for specific questions or in rare settings, a coordinated overarching European collaboration would provide answers

faster. The HORIZON programme demonstrates that a Europe-wide strategy is feasible [159], but current HORIZON trials do not specifically address mBC. The Cancer Medicines Forum, coordinated by the European Medicines Agency and the European Organisation for the Research and Treatment of Cancer (EORTC), although not breast cancer-specific, is currently the most advanced policy mechanism for treatment optimisation in Europe [160].

**Recommendation 5.** Ensure there is a mechanism to fund Europe-wide pragmatic optimisation trials to address questions of public interest.

## 6. Quality indicators to measure access and quality of care

Quality indicators (QIs) are measurable parameters for performance monitoring. Without registries to document predefined guidelines and goals, QIs cannot be monitored or used to implement or adapt policies to ensure equitable access. In 2023, QIs for mBC were published by the European Society of Breast Cancer Specialists (EUSOMA) and the ABC Global Alliance [161]. QIs for evaluating cancer care in low- and middle-income countries have also been developed, understanding that health system infrastructure/availability differs among countries [16]. Therefore, QIs are an important tool to identify inequality.

The task now is to determine adherence to QIs. European accreditation for breast units is voluntary, but most countries have certification bodies and systems to determine quality of care. Some countries, including Germany, Austria and Italy, have mandatory certification systems. QI data can be used as an advocacy tool to mobilise resources and provide accountability and transparency to the public and funders [162].

Adherence to quality assurance protocols for radiation therapy planning has been shown to minimise toxicity and improve survival. A recent consensus document from the European Society for Radiotherapy and Oncology (ESTRO) recommended implementing a culture of quality assurance and treatment recording according to predefined guidelines in both clinical trials and daily practice. The aim is to ensure the generation of high-quality data, especially as novel systemic therapies are constantly being introduced into practice, and their safety in combination with radiation therapy is unknown [163].

**Recommendation 6.** Ensure the implementation of newly established quality indicators across Europe.

The European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS) is well established and helps healthcare providers to prioritise finite resources [164]. However, no similar tool is available for non-pharmaceutical interventions. Such a tool would bring value and reduce inequity by avoiding the use of treatments that lack high-level evidence (sometimes the incurable nature of disease leads to more empiric, less evidence-based treatment), and improve accessibility by helping payers prioritise those strategies bringing the greatest clinical benefit, allowing wiser spending and more equitable access. Work is already underway to develop such an instrument to assess value in radiation therapy [165].

**Recommendation 7.** Consider developing and introducing a tool to rate the importance of interventions beyond anticancer drugs (similar to the ESMO-MCBS for drugs).

## 7. Conclusion

Several recurring themes emerge when exploring inequalities in access to care for people living with mBC: the elderly, those living in rural areas, those with lower educational or socioeconomic status, certain cultural and racial groups, and those with reduced financial means are more likely to be affected by inequalities and have inferior care, especially in healthcare systems with minimal or no national social support for health, where affordability governs access. This manifesto urges

action to overcome these disparities (Table 1).

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## Declaration of Competing Interest

MI reports speaker fees/honoraria from Novartis, Seattle Genetics, Daichi, Menarini/Stemline and Gilead, research grants (to institution) from Pfizer, Roche, Inivata Inc, Natera Inc and Gilead, and meeting/travel grants from Roche, AstraZeneca and Gilead (all outside the submitted work). TS reports personal fees for advisory board participation from MSD and Roche and for invited speaker engagements at regional conferences from Roche and Pfizer (outside the submitted work). EB reports honoraria from Pfizer, Lilly and Incyte, consulting/advisory roles for Pfizer, Sandoz-Novartis, Daiichi Sankyo/AstraZeneca and Menarini, and travel/accommodation/expenses from Pfizer and Novartis. DL reports payment (to institution) from the European Medicines Agency for board participation and payment (to institution) from the ESMO Sarcoma and Rare Cancers meeting for participation as a guest speaker. GSS reports institutional research support from Agendia, AstraZeneca, Merck, Novartis, Roche and Seagen. He is a board member of the Dutch Medicines Evaluation Board. AV-S reports speaker honoraria from Ibex Medical Analytics, Myriad, AstraZeneca, Roche and MSD, advisory board participation for Ibex Medical Analytics and Prima, travel support from Ibex Medical Analytics and AstraZeneca, research grants from Ibex Medical Analytics, Owkin, Prima, AstraZeneca and MSD Avenir, and stock options for Ibex Medical Analytics. IM declares small fees as honoraria for advisory boards supported by Eli Lilly, Novartis, Pfizer, SeaGen, Daiichi Sankyo, AstraZeneca, Gilead, and Menarini Stemline. PA reports honoraria from Synthon, Roche and Gilead, consulting or advisory roles for MacroGenics, Boehringer Ingelheim, Novartis, amcure, Roche, Novartis, Amgen, Servier, G1 Therapeutics, Radius Health, Deloitte, Menarini, Gilead Sciences, Incyte and Lilly, research funding from Roche (to institution) and travel/accommodation/expenses from Amgen, MSD Oncology, Roche Belgium, Pfizer, Daiichi Sankyo/AstraZeneca and Gilead Sciences. FC reports consultancy roles for Amgen, Astellas/Medivation, AstraZeneca, Celgene, Daiichi Sankyo, Eisai, GE Oncology, Genentech, Gilead, GlaxoSmithKline, IQVIA, MacroGenics, Medscape, Merck-Sharp, Merus BV, Mylan, Mundipharma, Novartis, Pfizer, Pierre-Fabre, prIME Oncology, Roche, Sanofi, Samsung Bioepis, Seagen, Teva and TouchIME. VPR reports no conflict of interest related to the current article and reports grants from Agendia BV more than 5 years ago. DC reports non-personal relationships (any fees go to employer) with AstraZeneca, Eisai, Seagen, Roche, Pfizer, Lilly, Novartis, Synthon, GSK, Gilead, Daichi and Menarini/Stemline; he is Chair of the Board of the non-profit “Make

**Table 1**  
Summary of recommendations.

Theme	Recommendation
Living with the stigma of mBC	Increase the visibility of mBC to society and facilitate the involvement of people with mBC in trials, the workplace and everyday life as much as they want and are able
Registries and real-world data	Implement a national cancer registry recording stage at diagnosis and relapses in every European country and share with the International Agency for Research on Cancer (IARC) to understand how many people are living with mBC Harmonise, monitor and use routinely collected real-world and registry data (including but not limited to details of biomarker/genetic testing, treatment and quality of life) to support reimbursement policies and improve access to treatment, trials and services and to evaluate outcomes
Multidisciplinary care	Ensure that all patients with mBC in Europe have access to high-quality multidisciplinary information and care (imaging, molecular biology, pathology, radiation, systemic therapy, surgery, side-effect management, palliative and supportive care, physical exercise, trials, etc.)
Clinical research	Ensure there is a mechanism to fund Europe-wide pragmatic optimisation trials to address questions of public interest
Quality indicators to measure access and quality of care	Ensure the implementation of newly established quality indicators across Europe Consider developing and introducing a tool to rate the importance of interventions beyond anticancer drugs (similar to the ESMO-MCBS for drugs)

2nds Count” charity and the Breast International Group. FP, FVD, OK-P and FL report no conflicts of interest.

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