



Seizing the moment: The time for harnessing electronic patient-reported outcome measures for enhanced and sustainable metastatic breast cancer care is now

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ABSTRACT

The sustainability of healthcare systems is under pressure. Unlike care for many other chronic diseases, cancer care has yet to empower patients in effectively self-managing both the medical and emotional consequences of their condition, including adapting to changes in lifestyle and work, which is essential to achieve optimal health and recovery. Although proposed as a potential solution for sustainable healthcare and support for optimal health and recovery already decades ago, practical implementation of digital care lags behind.

We believe electronic patient reported outcome measures (ePROMs) could play an important role in creating sustainable healthcare, both to guide complex treatment pathways and to empower survivors to self-manage consequences of diagnosis and treatment. That is, ePROMs can be used for screening and monitoring of symptoms, but also for treatment decision-making and to facilitate communication about quality of life. We therefore see opportunities for improvements in quality of care, quality of life, and survival of cancer patients, as well as research opportunities, as ePROMs collection can lead to better understanding of care needs. The '10 Actions for Change report' of the Advanced Breast Cancer Global Alliance stresses a critical need for improvement of care for metastatic breast cancer (MBC) patients. We therefore in this paper focus on MBC care and research.

Cancer care needs reorganization to secure future sustainability and accessibility. The worldwide incidence of cancer is anticipated to rise by 47% from 19.3 million patients in 2020 to a projected 28.4 million in 2040 [1]. While survival rates have increased by improvements in treatment and early detection [2,3], cancer and related treatment often undermine patients' health-related quality of life (HRQoL) [4]. Optimal supportive oncology requires multiple healthcare providers (HCPs) and specialties to be involved for the accurate diagnosis and management of adverse effects of treatments to improve outcomes, but healthcare systems are ill-prepared for this [5]. Meanwhile, an imminent shortage of oncology services and workforce is projected, with staffing issues

already emerging [6]. While workforce costs have traditionally been the single most significant hospital expense, costs of the healthcare workforce have increased dramatically by the use of overtime and agency staff to fill critically needed positions [7]. This increase in labor costs has not necessarily been associated with better quality of care [7]. As the population ages there is a substantial increase in cancer diagnoses but also in chronic diseases, and the combination thereof. Moreover, complex care needs are expected to surge [6]. A more patient-centered approach is required, including patient participation in the management of health, disease, HRQoL, and care [5], which currently lags behind [8–11].

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Patients with metastatic disease, including those with metastatic breast cancer (MBC), have complex supportive care needs that are currently often unmet [5,12]. Among the annual worldwide 2.2 million breast cancer diagnoses, even with access to the best available care in high-income countries (HICs), 20–30% eventually progress to MBC [1, 13,14]. In addition 5–10% of patients is initially diagnosed with MBC [15,16], while this is 60–80% in low and middle income countries (LMICs), where MBC even represents the majority of breast cancer cases [15]. The Advanced Breast Cancer (ABC) Global Alliance outlines ten urgent and actionable goals for 2015–2025 aiming to achieve substantial improvements in better quality of care through: better healthcare access, communication, and information provision, HRQoL, survival, and research for ABC patients [14]. Recent discoveries of new (combinations of) agents have substantially extended the median overall survival for HER2-positive and ER+/HER2-negative MBC from 2 to 3 to 5 years [17,18]. Consequently, the survivorship care agenda should extend its scope beyond curatively treated patients to encompass MBC patients [19]. New treatments are however costly [6,20], complex and continue for longer, putting an unseen pressure on cancer service with the same staff resources. As cost increases are projected for MBC patients [21], along with the issues described above, it is imperative to consider a more efficient organization of healthcare specifically tailored to address the unique needs of MBC patients.

We believe electronic patient-reported outcome measures (ePROMs) could enhance care for MBC patients in a sustainable way. PROMs are instruments that directly capture patient health status, avoiding third-party interpretation [22]. Originally developed for HRQoL assessment in trials and research mostly completed with pen and paper, patients nowadays increasingly complete PROMs electronically as part of routine care. HCPs are to discuss PROMs feedback with the patient during clinical consultations, or patients can access scores directly via dashboards or tools [23–25]. We explore ePROM applications for MBC and their benefits and potential to bolster oncology care sustainability.

1. Supporting complex treatment pathways: Better symptom control, HRQoL, and survival

Compared to standard care, regular ePROM completion can notably enhance symptom control [26] through screening, monitoring, and self-monitoring of toxicities [25,27]. This is crucial for managing novel therapies like immunotherapies and targeted therapies and home-based oral treatments, as these present new challenges, including impaired patient-HCP communication, adherence issues, and hampered side effect management [19,28], presumably pressuring healthcare resources and staff. For MBC treatment, extending survival is always counterbalanced with managing toxicities and enhancing HRQoL [29]. MBC patients suffer from substantial symptom burden, with 34% reporting severe pain and other uncontrolled symptoms, while their overall well-being remains uniformly low [30]. Regular PROMs completion can improve HRQoL by a clinically relevant difference [31–33] and lengthen time to HRQoL deterioration [34]. HRQoL was found to be associated with increased overall survival in MBC patients [35], further underscoring the importance of measuring HRQoL in MBC care.

ePROMs complement the ongoing development of newer, more effective, and less toxic therapies to improve survival in MBC patients. That is, it is hypothesized that systematic ePROMs symptom monitoring can prolong systemic therapy use [31,36], which can lead to substantial survival improvements [32,33,36,37]. Studies including MBC patients reported an overall survival benefit of 6% and 5.2 months [32,33], and 5.5% at one-year survival [37]. These substantial survival benefits even counterbalance the annual costs of ePROMs, that are higher than usual care costs (incremental cost-effectiveness ratio of €18 107.9/Quality-Adjusted Life Year (QALY) from the French national health insurance perspective and €10,500.9/QALY from the public payer perspective in Canada) [36]. PROMs could create efficiency and relieve pressure on hospital resources and staff by reducing unplanned emergency room

visits and hospital readmissions [36]. While some studies found no evidence for this [31], others reported that these benefits were pronounced for patients younger than 70 [38]. As this aligns with anticipated age distributions for MBC [21], it is reasonable to expect benefits of ePROMs for MBC. Furthermore, studies found a decrease in oncology consultations, palliative care consultations, and psychosocial care consultations [36], suggesting that patients were kept out of the hospital.

2. Improving self-management and supportive care

MBC patients can miss productive days due to the symptoms caused by their disease or treatment. The value of lost work and home productivity days associated with MBC in the USA was \$67 million for younger women, \$246 million for midlife women and \$66 million for older women in 2015 [39]. Besides being a societal economic burden [39], lost productive days at home and work are, above all, a burden for MBC patients [40]. Cancer patients express a desire to play an active role in their care [3,4], but need the knowledge, skills, and confidence to effectively manage their symptoms, disease and health [41]. Unfortunately, MBC patients often lack disease management information and information about the impact of MBC on their daily lives [40]; 35% of advanced solid cancer patients lacked information about ‘things you can do to stay well’ [12]. By delivering informative feedback to patients, PROMs can support self-management [42]: 21 of 38 (55%) ePROM solutions developed before 2020 already offered self-management recommendations for managing symptoms [43]. Furthermore, PROMs data can be integrated into patient education materials and decision aids, further supporting MBC patients’ informational needs [27]. Future platforms could incorporate complementary lifestyle trackers like wearables to monitor activity and eating behavior, further supporting self-management and healthy behaviors [44].

Among patients with advanced solid cancers, 31% of them lacked an appointed HCP to talk about all aspects of their condition, treatment, and follow-up [12]. PROMs can enhance patient-physician communication [25,27,31] and support (shared) treatment decision-making [25, 27]. However, effective use, interpretation, and communication on PROMs requires specialized training for HCPs [25]. Although several training programs have already been developed and tested that could be disseminated to hospital practice [45,46], further attention is needed to ensure its effectiveness [25].

MBC patients are currently unaware of, or do not receive, the supportive care they need [12,47,48]. In patients with solid advanced tumors, unmet care needs were associated with anxiety, stress, depression, and decreased HRQoL [12]. By ensuring that all involved HCPs have access to patients’ PROMs, a more multidisciplinary and holistic perspective can be fostered in patient care, crucial for addressing the complex needs of patients with advanced cancer [12,40].

Currently, the burden and unmet needs of MBC patients are difficult to measure due to lack of accurate, high-quality, population-based data [12,14,49]. This data would provide information to support alignment of care with supportive care needs, and is therefore crucial to improve quality of care and policymaking [19,27,40]. An MBC-specific core outcome set (COS) was recently developed to standardize disease and treatment measurement, including an MBC-specific PROM that captures MBC patients’ most relevant symptoms and effects on HRQoL [50,51]. This is vital in measuring MBC patients’ needs and preferences without bias [52].

Overcoming challenges for successful ePROM implementation

Digitalization of care, proposed as a possible solution for sustainable care already decades ago, faces hindrances due to regulatory, technological, and organizational questions [53]. The full potential of digitalized care such as ePROMs is only reached by high degrees of pervasiveness, interoperability, and embedment into broader information systems [53]. Integrating PROMs in care demands time, efforts, and

resources, but was found feasible beyond research settings [25,54,55] if sufficiently supported by technical briefings, technical telephone support, and on-site support services [56]. Even very sick patients with limited digital experience have shown to regularly complete PROMs [26, 57], although older MBC patients, patients with lower HRQoL, and less technically skilled patients encounter more barriers [56], potentially widening the 'digital divide' [58]. However, with assistance from, for instance relatives, older patients were able to complete home-based assessments, although hospital-based assessment might align even better with their needs and capabilities [59]. Efforts should be made to include all patients, regardless of literacy, health literacy, digital literacy, and access to technology and care [60], by clearly explaining the purpose and benefits of PROMs, involving representative populations in PROM development, using accessible formats and alternative administrative modes, and allowing completion from home, with help from a professional, or by a proxy [60].

Another barrier for digitalized care such as ePROMs is the lack of validation of its use in clinical practice [61]. As current studies about PROMs display a considerable variation in participants, settings, interventions, and measures used to quantify outcomes [31], large cluster-randomized trials remain necessary. Specifically, more research is needed to determine clinical efficacy and safety of PROMs in clinical practice [53], cost-effectiveness [36], and the mechanisms through which PROMs work in diverse contexts [27,31].

Metastatic cancer care suffers from global inequality challenges [19], and PROMs in clinical practice may exacerbate this disparity. Studies about ePROMs were generally conducted in HICs [25,31], limiting their applicability to developing regions where electronic systems may be unfeasible. Consequently, the reported benefits are inclined to favor developed nations, creating an even larger lead over developing countries. However, promising structural digital healthcare applications for mobile phones have already been demonstrated in LMICs as well [62]. Besides, some of the statistically significant described effects, for instance the increases in survival [32,33,36,37] may appear small in isolation, but can collectively have a substantial impact on MBC care [63]. This underscores the importance of shaping a more efficient and thereby sustainable approach for both overall cancer care and individual patients' future by supporting complex treatment pathways and empowering survivors to self-manage consequences of disease and treatment.

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K.M. de Lig: Conceptualization, Writing – original draft. **L.B. Koppert:** Conceptualization, Writing – review & editing. **B.H. de Rooij:** Conceptualization, Writing – review & editing. **L.V. van de Poll-Franse:** Conceptualization, Writing – review & editing. **G. Velikova:** Conceptualization, Writing – review & editing. **F. Cardoso:** Conceptualization, Writing – review & editing.

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