



Review

Supportive and palliative care for metastatic breast cancer: Resource allocations in low- and middle-income countries. A Breast Health Global Initiative 2013 consensus statement[☆]



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ABSTRACT

Many women diagnosed with breast cancer in low- and middle-income countries (LMICs) present with advanced-stage disease. While cure is not a realistic outcome, site-specific interventions, supportive care, and palliative care can achieve meaningful outcomes and improve quality of life.

As part of the 5th Breast Health Global Initiative (BHGI) Global Summit, an expert international panel identified thirteen key resource recommendations for supportive and palliative care for metastatic breast cancer. The recommendations are presented in three resource-stratified tables: health system resource allocations, resource allocations for organ-based metastatic breast cancer, and resource allocations for palliative care. These tables illustrate how health systems can provide supportive and palliative care services for patients at a basic level of available resources, and incrementally add services as more resources become available.

The health systems table includes health professional education, patient and family education, palliative care models, and diagnostic testing. The metastatic disease management table provides recommendations for supportive care for bone, brain, liver, lung, and skin metastases as well as bowel obstruction. The third table includes the palliative care recommendations: pain management, and psychosocial and spiritual aspects of care.

The panel considered pain management a priority at a basic level of resource allocation and emphasized the need for morphine to be easily available in LMICs. Regular pain assessments and the proper use of pharmacologic and non-pharmacologic interventions are recommended. Basic-level resources for psychosocial and spiritual aspects of care include health professional and patient and family education, as well as patient support, including community-based peer support.

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Supportive and palliative care for metastatic breast cancer

Many women diagnosed with breast cancer in low- and middle-income countries (LMICs) present with advanced metastatic disease, or they may present with locally advanced disease and undergo treatment with curative intent but nonetheless develop metastases. Common sites for breast cancer metastases are bone, brain, liver, and lung; less common sites are intra-abdominal and skin. Cure is not usually a realistic treatment outcome for metastatic disease[1], but site-specific interventions (aimed at prolonging life), supportive care measures (treatment of side-effects of therapy, both physical and psychosocial), and palliative care measures (treatment of advanced disease symptoms, including pain management, psychosocial and spiritual issues), can achieve meaningful outcomes and maintain a reasonable quality of life. Allocation of resources specifically for supportive and palliative care should be part of comprehensive oncology care programs[1,2].

Defining “supportive care” and “palliative care”

The terms “supportive care” and “palliative care” are sometimes used interchangeably[3]. However, supportive care in cancer is the prevention and management of the adverse effects of cancer and its treatment. This includes management of physical and psychological symptoms and side-effects across the continuum of the cancer experience from diagnosis through anticancer treatment to post-treatment care. Enhancing rehabilitation, secondary cancer prevention, survivorship and end-of-life care are integral to supportive care. According to European Association for Palliative Care (EAPC), supportive care is more appropriate for patients still receiving antineoplastic therapies and also extends to survivors, whereas palliative care has its major focus on patients with far advanced disease where antineoplastic therapies have been withdrawn[4].

For the purposes of this Breast Health Global Initiative (BHGI) consensus statement we acknowledge: 1) the broad, expanded definition of “palliative care” introduced by the World Health Organization, which calls for palliative care to be introduced at the time of diagnosis of cancer or the start of treatment[5]; and 2) the practical need to be able to identify and categorize common components of treatment-related, site-specific supportive care interventions for metastatic disease and end-of-life-related palliative care, in order to establish evidence-based criteria for program implementation.

Existing evidence and guidelines

Evidence-based breast cancer clinical guidelines for treatment of metastatic breast cancer from international organizations[6], high-income countries (HICs)[7,8] and LMICs[9,10], all recommend supportive/palliative care as part of metastatic breast cancer care. These guidelines expand the concept of palliative care, previously limited to end-of-life care, to include supportive care offered concurrently with curative or life-prolonging treatments for patients with all stages of cancer. Palliative care in this broader setting may reduce time spent in hospitals[11,12] and may be more effective in meeting patients’ goals than usual approaches to end-of-life care practiced by oncologists[13]. There is increasing agreement that patients should be informed about supportive and palliative care services as soon as a diagnosis of advanced disease is made, or soon after the start of tumor-specific treatment[4,14,15]. Implementing this broader concept of palliative and supportive care is challenging[16], even in HRCs[14,17,18], and requires interdisciplinary approaches[2] and shared understanding of the need for health systems to identify

and provide supportive care resources. This consensus statement is one of three companion reports, developed by the BHGI as part of the 2012 Global Summit that provides resource-stratified recommendations covering the continuum of supportive and palliative care services for breast cancer patients. The other consensus statements cover supportive care during treatment[19], and supportive care after curative treatment[20].

BHGI Global Summit and expert panel consensus process

All three BHGI supportive care consensus statements provide recommendations for breast cancer supportive care program implementation in LMICs. Methods developed by the BHGI for the structured creation of evidence-based, 4-tier resource-stratified guidelines and consensus statements (see Table 1) have been previously described[21,22]. A systematic literature review was performed in preparation for the 5th BHGI Global Summit, which was held in association with the International Atomic Energy Association (IAEA), in Vienna, Austria, on October 2, 2012. Supportive care was chosen as a theme for the global summit, as it emphasizes often-overlooked aspects of medical care, which are not always considered directly related to curative intent. The Metastatic Disease and Palliative Care Consensus Panel presented on key topics and then performed consensus analysis through facilitated expert panel discussions to draft the core resource-stratified table matrices, which are the primary outcome of the panel examination and deliberation. Companion consensus statements, *Supportive Care during Treatment*[19], and *Supportive Care after Curative Treatment*[20], were developed in parallel during this 2012 Global Summit. Supportive care is an under-researched area of medicine, especially in LMICs. Systematic reviews and meta-analyses are often not available for select topics, or include only studies from HICs. When studies from LMICs are available on a topic, they are provided as additional references.

Table 1
Resource allocation levels: basic, limited, enhanced, and maximal.

Resource allocation level	Description
Basic	Core resources or fundamental services absolutely necessary for any breast health care system to function; basic-level services are typically applied in a single clinical interaction.
Limited	Second-tier resources or services that are intended to produce major improvements in outcome, and are attainable with limited financial means and modest infrastructure; limited-level services may involve single or multiple clinical interactions.
Enhanced	Third-tier resources or services that are optional but important; enhanced-level resources should produce further improvements in outcome and increase the number and quality of therapeutic options and patient choice.
Maximal	High-level resources or services that may be used in some high-income countries, and/or may be recommended by breast care guidelines that do not adapt to resource constraints. They should be considered lower priority than those resources or services listed in the basic, limited, or enhanced categories on the basis of extreme cost and/or impracticality for broad use in resource-limited environments; to be useful, maximal-level resources typically depend on the existence and functionality of all lower-level resources.

Stratification scheme: The table stratification scheme implies incrementally increasing resource allocation at the basic, limited, and enhanced levels. Maximal-level resources should not be targeted for implementation in LMICs, even though they may be used in some higher-resource settings.

Key resources needed for supportive care with metastatic disease

The expert international panel identified thirteen key resource recommendations for supportive and palliative care for metastatic breast cancer. The recommendations are presented in three sections 1) health systems resource allocations; 2) resource allocation for organ-based metastatic disease management; and 3) resource allocations palliative care. In each section, a description of a resource category is followed by resource-stratified consensus panel recommendations. Recommendations are also presented in resource-stratified tables. These resource-stratified tables illustrate how a health system can provide supportive care services to patients with metastatic breast cancer, starting at a basic level of resource allocation and incrementally adding program resources. The section *Special Concerns and Emerging Issues in LMICs* highlights key issues from the panel deliberations. If a topic is covered in more detail in another companion consensus statement, a link and reference is provided.

Health systems (Table 2)

Health professional education/training (Table 2, row 1)

Description: The term “health professional” was chosen by the consensus panel to acknowledge the range in medical and other professionals who provide supportive and palliative care services in LMICs. When specialists are identified as a required resource, it is assumed that a specialist has a certification for their area of expertise.

Health professional education for supportive care for metastatic disease and palliative end-of-life care should focus on training

multidisciplinary and interdisciplinary teams, and coordination of care. Even in the lowest resource settings, breast cancer patients should have multiple care providers, with coordination of care as a key component of supportive and palliative care program implementation. Efforts are underway in high-resource settings to create interdisciplinary teams and educate primary-care physicians, nurses, and other specialists, such as oncologists and surgeons, in palliative care. Including nursing staff in palliative care training is important, as nurses report a lack of skills training, as well as confidence and tools needed to provide adequate palliative care[23].

Health professionals working with breast cancer patients should be trained to recognize and manage site-specific metastases using clinical practice guidelines adapted to available resources. (See the companion BHGI consensus statement, *Supportive Care during Treatment*[19], for a list of guidelines that address cancer symptom management, including pain management.) Pain management for cancer patients should be part of standard medical and nursing school training programs[24–27], as well as part of continuing education efforts. Pain management education should include the distinction between nociceptive and neuropathic pain, and the importance of adequate pain medication [28]. The method of training may vary based on available resources [29]. Although diploma and certificate courses are the most comprehensive, less costly short courses and distance learning can also provide important pain management training by focusing on improving skills or overcoming barriers to adequate pain management[28]. Barriers identified included regulatory hindrances to opioid access, and fear of opioids among the public, professionals and administrators. Other barriers identified include insufficient capacity for non-pharmacological interventions, lack of coordination between services, and limited provider interaction time with

Table 2

Health systems resource allocations: health education, care models, and diagnostic testing for metastatic breast cancer.

	Basic	Limited	Enhanced	Maximal
Health Professional Education ^a	Appropriate use of CPG Awareness of CAM used by patients PC pain assessment and management; side-effects of pain drugs Skin complications Psychosocial (end-of-life) Spiritual (end-of-life) Health literacy, cultural literacy, communication skills	Appropriate referral to specialists Pain syndromes; referral strategies Emotional/spiritual aspects of death and dying	Palliative care training for nursing staff In-service PC updates	
Patient and Family Education	Late-disease risks, complications of advanced disease, PC TX Pain self-management Skin care Psychosocial (end-of-life) issues Spiritual (end-of-life) issues	Emotional and spiritual aspects of death and dying Advanced care planning		
Care Models	Patient-centered decision-making Clinician communication with patient and family (eg, conferences) Trained PC volunteers Home-based PC with community and family support Hospital-based PC with community and family support	Home-based PC with trained PC nursing support Hospital-based PC with trained PC nursing support Outpatient PC with trained health professional support PC consulting services (referrals) Multidisciplinary ^b team approach	Home-based PC with clinic and hospital back up Outpatient PC clinics with trained PC physicians PC in-patient unit PC training center Quality assurance system Interdisciplinary ^b team approach	PC specialist services
Diagnostic Testing	Confirmation tests for metastasis in symptomatic patients			

Note: The table stratification scheme implies incrementally increasing resource allocation at the basic, limited, and enhanced levels. Maximal-level resources should not be targeted for implementation in LMICs, even though they may be used in some higher-resource settings.

Abbreviations: CAM, complementary and alternative medicine; CPG, clinical practice guideline; PC, palliative care; TX, treatment.

^a Patient, family and/or partner education may be the primary intervention for some supportive care services.

^b “Multidisciplinary team approach” refers to a patient care model that includes experts from different disciplines, whereas an “interdisciplinary team approach” requires a more integrated and coordinated approach to patient care, where experts from different disciplines establish shared patient care goals.

patients[25]. Health professional training efforts should include home-based care management for terminally ill patients[30], and include community health nurses who visit patients in their homes.

Note: “Multidisciplinary team approach” refers to a patient care model that includes experts from different disciplines, whereas an “interdisciplinary team approach” requires a more integrated and coordinated approach to patient care, where experts from different disciplines establish shared patient care goals for a more holistic approach to patient care.

#1. Panel recommendations: At **basic levels** of resource allocation, health professional education should include the appropriate use of clinical practice guidelines and awareness of alternative and complementary medicine use in the community. Pain management education should include simple pain assessment strategies, the appropriate use of available pain and psychotropic medications, including morphine, and knowledge of the side-effects of such medications. Awareness of skin complications should be included. The psychosocial and spiritual aspects of end-of-life should be included. Health literacy, cultural literacy and communication skills should be part of health professional supportive care training. At **limited levels**, health professional education should include the importance of referrals to available specialists, awareness of complex breast cancer pain syndromes, and the need to refer select patients to pain specialists/programs. It should also include the emotional and spiritual aspects of death and dying. At **enhanced levels**, health professional education should include palliative care training of nursing staff, and regular in-service interdisciplinary palliative care discussions (updates).

Patient, family and caregiver education (Table 2, row 2)

Description: Communication with patients and families about treatments and side-effects can affect patient responses[31,32]. Patients should be encouraged to report new, persistent symptoms to their healthcare team, outside of scheduled appointments. For patients with good health literacy, written instructions on pain management plans and symptom control should be provided. Skilled questioning by health professionals during patient interactions can help elicit patient preferences[33]. Educating family members is a critical component of supportive care: they are often involved in patient care, yet they may not accurately interpret, communicate or act on patient preferences, and family perception of patient wishes may differ from the physician’s perception[32]. Physicians were found in one study to be more responsive to family preferences for place of discharge, and more responsive to patient preference for discontinuation of late treatment[32]. Advanced directives are important tools to convey patient preferences in order to help patients, families and health providers communicate more effectively about end-of-life choices, and to document patient decisions. Cultural or family traditions regarding the sharing of end-of-life information should be respected. Patient education should be tailored to the health literacy of the patient and their preferred method of receiving information, and their social and cultural values[34]. Patient-family-physician conferences should be part of routine patient care, with a focus on patient-centered decision-making. (See the *Care Model* section in this manuscript.)

#2. Panel recommendations: At **basic levels** of resource allocation, patient education should focus on late-disease risks, complications of advanced disease, and palliative care treatments and their side-effects. Patients and their families should be provided with information on pain management, skin care, and psychosocial and spiritual aspects of end-of-life care. At **limited levels**, patient and family education should include emotional and spiritual aspects of death and dying, and be culturally appropriate. Advanced care planning information should be available.

Care models (Table 2, row 3)

Description: Training health professionals and educating patients provides the foundation for supportive and palliative care, but establishing effective care models for delivery, especially at the end-of-life, is equally important. The location of end-of-life care is a primary concern for patients and their families. A recent review of end-of-life care in 34 countries found that most patients wished to die at home (although this varied from 18 to 100%, based on country, income levels and disease status of those surveyed)[35]. However, the accessibility of pain relief, the availability of affordable care, and the amount of assistance in coping with the burden of care, influenced the choice of location for end-of-life care[35]. Other research suggests that patient preference for the place of death may change over time due to a variety of factors[36]. Understanding and meeting patient preferences as they evolve over time should be a measured outcome for palliative care services[37].

#3. Panel recommendations: At **basic levels** of resource allocation, patient-centered decision-making should be a key component of end-of-life care and should include patient-family-health professional conferences. Trained volunteer support and home- and hospital-based palliative care that includes community and family support should be available. At **limited levels**, trained palliative care nursing support should be available, including home-based and hospital-based support. Outpatient services and referrals for consulting should be available. Palliative care should include a multidisciplinary team approach. At **enhanced levels**, home-based palliative care should include back-up clinic and hospital support. Trained palliative care physicians should be available at outpatient clinics. In-patient palliative care units and interdisciplinary patient care should be available. Palliative care training centers and quality assurance systems should be in place. At **maximal levels**, palliative care specialist services should be considered.

Diagnostic testing (Table 2, row 4)

Description: Although extensive metastatic work-ups in asymptomatic patients are not recommended, confirmation testing for metastasis and monitoring for late-disease complications, such as spinal cord compression, should be available. Confirmation testing includes X-ray imaging and basic laboratory tests (eg, serum calcium, creatinine, and magnesium levels)[8], and can help distinguish symptoms of site-specific metastases from comorbidities or treatment-related toxicities. (See the companion BHGI consensus statement, *Supportive Care during Treatment*[19], for recommendations for treatment-related toxicities.)

#4. Panel recommendations: At **basic levels** of resource allocation, confirmation tests for metastatic disease in symptomatic patients are recommended.

Supportive care: organ-based (site-specific) metastatic disease management

Bone metastases (Table 3, row 1)

Description: Approximately 70–80% of advanced breast cancer patients develop bone metastases during the course of their disease[38]. Accelerated bone loss and associated complications, such as fractures, may also be a consequence of adjuvant treatment[39]. Although patients with bone-only metastases have a longer survival than those with visceral metastases, their symptom burden is high, and includes bone pain, hypercalcemia, pathologic fractures, and spinal cord compression[38]. Spinal cord compression can be a severely disabling and potentially life-threatening complication, requiring radiological studies, radiotherapy, or surgery[6]. Bone metastatic complications can severely affect quality of life, and significantly impact healthcare system costs[40]. Clinical practice

Table 3
Supportive care resource allocations: organ-based (site-specific) metastatic disease management.

	Basic	Limited	Enhanced	Maximal
Bone Metastases	Drug therapy: steroids, NSAIDs, opioids (eg, oral and parenteral morphine), co-analgesics Consider spinal cord compression and fractures	Radiotherapy Surgery Routine evaluation for spinal cord compression and fractures	Radioisotopes Bone-modifying agents	Radiofrequency ablation/ cryoablation
Bowel Obstruction	Drug therapy: morphine (oral or parenteral), steroids, laxatives, antiemetics, anticholinergics NG-tube	Non-morphine opioids	Venting G-tube	Somatostatin analogues
Brain Metastases	Drug therapy: analgesics, steroids, anti-emetics, anticonvulsants	Whole brain radiotherapy	Stereotactic radiotherapy Surgery	
Liver Metastases	Drug therapy: analgesics, steroids, anti-emetics, antihistamines		Biliary stents Percutaneous drainage Embolization	Liver resection
Lung Metastases	Drug therapy for breathlessness: opioids, anxiolytics and antipsychotics, steroids Thoracocentesis Oxygen therapy for hypoxemic patients	Pleurodesis: Thoracotomy, VATS Radiotherapy		
Skin Metastases/ Complications	Wound and skin assessment Drug therapy: Analgesics; Broad spectrum antibiotics Simple dressings and skin barriers Activated charcoal; metronidazole Teaching wound dressing to patients and family	Silver nitrate Radiotherapy Debridement surgery	More sophisticated dressing material Calcium alginate for hemostasis Stoma/wound therapy Air mattress, egg crate mattress	Plastic surgery Vacuum (negative pressure) wound therapy Mechanical bed

Note: The table stratification scheme implies incrementally increasing resource allocation at the basic, limited, and enhanced levels. Maximal-level resources should not be targeted for implementation in LMICs, even though they may be used in some higher-resource settings.
Abbreviations: G-tube, gastric tube; NSAIDs, non-steroidal anti-inflammatory drugs; NG, nasogastric; VATS, video-assisted thoracic surgery.

guidelines provide detailed recommendations regarding treatment of bone metastases, including specific therapies such as radiotherapy[41–43], bone-modifying agents such as bisphosphonates and denosumab[44], and the prevention and treatment of side-effects of treatment, including osteonecrosis of the jaw [45,46]. Pain is a major symptom of bone metastasis and bone pain management is often inadequate, even in patients referred for palliative radiotherapy[47]. When symptom control is the main goal, radiotherapy may be given as single fractions. Surgery can alleviate spinal cord compression and pain, and ensure bone continuity and functionality, whereas radiotherapy and dexamethasone can help control bone pain and assist with recalcification and stabilization, thus reducing spinal cord compression and minimizing risks of paraplegia[48]. Bisphosphonates should also be considered to prevent or delay onset of skeletal-related disease or treatment side-effects[44], to treat malignancy-associated hypercalcaemia[49], and to reduce pain intensity. Overall, bisphosphonates are well-tolerated; adverse effects include influenza-like symptoms, arthralgia, and gastrointestinal symptoms[50]. Whereas radioisotopes have a high cost and require experienced nuclear medicine services.

#5. Panel recommendations: At **basic levels** of resource allocation, bone pain management should include steroids, non-steroidal anti-inflammatory drugs (NSAIDs), opioids (eg, oral and parenteral morphine), and co-analgesics (following WHO pain ladder recommendations). Patients should be assessed for fractures and early spinal cord compression by enquiring about back pain, and with plain X-ray of the spine, as appropriate. At **limited levels**, radiotherapy (with dexamethasone) and surgery should be available. Patient follow-up should include routine evaluation for spinal cord compression or fractures for high-risk patients. At **enhanced levels**, radioisotopes, bone-modifying agents (eg, bisphosphonates, denosumab) should be available. At **maximal levels**, radiofrequency ablation or cryoablation could be considered.

Bowel obstruction (Table 3, row 2)

Description: Breast cancer metastasis to the bowel is rare, but can cause significant symptoms related to malignant bowel obstruction[51,52], which is an indicator of poor prognosis[53,54]. Bowel obstruction can also be caused by adhesions, post-irradiation bowel damage, inflammatory bowel disease, and hernias[54]. Symptoms of bowel obstruction include bowel pain, nausea and vomiting, and constipation. Opioids are the most effective drug for managing pain associated with bowel obstruction; steroids may help to reduce inflammation at the site of obstruction[55]. Partial obstruction due to constipation may require laxatives[56]. Anti-emetics and anti-cholinergics are used to treat nausea and vomiting[52,53]. Nasogastric tubes should be available as a short-term intervention to drain stomach contents in order to reduce nausea. Gastric venting with percutaneous endoscopic gastrostomy (PEG) tube placement can help reduce nausea and vomiting due to malignant gastrointestinal obstruction. PEG provides a rapid, safe method of achieving symptomatic relief without the risks of surgical procedures or the discomfort of a nasogastric tube[57,58]. Somatostatin analogues can reduce gastrointestinal secretions[59–61].

#6. Panel recommendations: At **basic levels** of resource allocation, morphine (oral and parenteral) should be available. Steroids (to treat inflammation), laxatives (to treat partial bowel obstructions), and antiemetics and anticholinergics should be available, and used according to clinical practice guidelines. Nasogastric tube (NG-tube) should be available. At **limited levels**, expanded non-morphine opioids should be available for pain. At **enhanced levels**, gastric venting (venting G-tube) should be available to reduce nausea and vomiting due to malignant gastrointestinal obstruction. At **maximal levels**, somatostatin analogues could be considered.

Note: Drug therapy and procedures should be administered according to clinical practice guidelines for management of bowel obstruction, based on the degree of obstruction and the condition of the patient. Some therapies are contraindicated for fully

Table 4
Palliative care resource allocations: pain management and end-of-life care with metastatic disease.

	Basic	Limited	Enhanced	Maximal
Pain Management ^a	Pain consideration ^b (simple assessment) Pain drugs ^a , including morphine (basic) Management of pain-related physical symptoms CAM and non-drug pain management	Other pain drugs ^a Radiotherapy (single and multi-fraction) PT and OT for functional limitations or pain management	Pain screening Pain care plan Opioid pumps, methadone, fentanyl patch Consultation with specialist in pain therapy Surgery (cord compression, fracture, obstruction)	Locoregional anesthesia, spinal analgesia
Psychosocial (End-of-life)	Psychosocial (end-of-life) consideration ^b Patient, family, and caregiver education ^c Psychosocial support: community-based Bereavement support: community based	Patient, family, and caregiver education ^c : emotional aspects of death Advanced care planning	Screening and referrals for depression/distress by mental health specialist Psychosocial counseling by mental health specialist Antidepressants Social services for financial, legal and family matters	Psychiatrist, psychologist, or social worker coordinated mental health care
Spiritual (End-of-life)	Spiritual consideration ^b Spiritual support: community based		Clinic or hospital associated spiritual support Hospital or hospice spiritual reflection and meditation space	

Note: The table stratification scheme implies incrementally increasing resource allocation at the basic, limited, and enhanced levels. Maximal-level resources should not be targeted for implementation in LMICs, even though they may be used in some higher-income settings.

^a Pain management should follow the WHO pain ladder. Morphine should be available and easily accessible at a basic level of resources.

^b "Consideration" is a term used in this table to refer to basic patient evaluation through patient-provider interactions, including dialogue, observations, and other appropriate means of evaluation.

^c Patient, family and caregiver education may be the primary intervention for some supportive care services.

obstructed bowels, and may require surgical interventions or more conservative management[56]. If early bowel obstruction is suspected, the use of motility agents may help overcome obstruction.

Brain (Table 3, row 3)

Description: Brain metastases are becoming increasingly prevalent as survival rates increase, with a reported incidence of brain metastases of 10–17% in clinical populations[62,63], and 30% based on autopsy findings[64]. Brain metastases indicate a poor prognosis. Symptoms of brain metastasis include headache, neurological disturbances, or seizures, all of which can significantly reduce quality of life[42]. Drug therapies can reduce brain swelling and edema and manage symptoms such as headaches, nausea and vomiting, and seizures, although there is limited evidence for anticonvulsants as seizure prophylaxis[65]. More advanced treatments include stereotactic radiotherapy and surgical resection for small operable solitary metastases, or for decompression of tumor mass. Radiosurgery may be an option for some unresectable brain metastases, but should include a risk-benefit analysis that balances the potential survival benefit against the adverse neurocognitive effects[6].

#7. Panel recommendations: At **basic levels** of resource allocation, symptom management of brain swelling and edema should include the use of analgesics and steroids (dexamethasone is the drug of choice); nausea and vomiting can be managed with corticosteroids[66] and other anti-emetics. Anticonvulsants may be considered[65]. At **limited levels**, whole brain radiotherapy should be available[42,67]. At **enhanced levels**, stereotactic radiotherapy based on lesion size or accessibility[68], and surgical resection, should be available.

Liver metastases (Table 3, row 4)

Description: About half of breast cancer patients with advanced disease develop liver metastases[69]. Symptoms include jaundice, pain (from capsular swelling, distension, and irritation), abdominal fullness, pruritus and bilious obstruction. Nausea and vomiting may occur due to gastric compression; anorexia, fever and liver failure may occur. Drug therapy can help manage some symptoms; more

aggressive interventions (biliary stents, percutaneous drainage, or tumor embolization) may be needed to relieve bilious obstruction. Tumor embolization has been reported to give good results in several studies[70,71]. Liver resection has been reported to result in a longer survival[69].

#8. Panel recommendations: At **basic levels** of resource allocation, symptom management of liver metastases includes pain control with analgesics and steroids, and anti-emetics and anti-histamines for nausea or pruritus. At **enhanced levels**, biliary stents, percutaneous drainage, and tumor embolization should be available. At **maximal levels**, liver resection (selective metastasectomy) could be considered.

Lung metastases (Table 3, row 5)

Description: Lung metastasis is common in recurrent breast cancer. One study found that 71% of advanced breast cancer patients had metastatic lung cancer at autopsy[72]. Lung metastases can cause respiratory compromise by direct effect of the metastases on lung tissue, airway obstruction, or from pleural effusion. Symptoms include shortness of breath, exertional dyspnea, pleuritic pain and cough. Although surgical resection may prolong survival in a subset of patients[73,74], it is not recommended as routine care. The use of oxygen therapy for hypoxemic patients should be discussed with patients and families[75].

#9. Panel recommendations: At **basic levels** of resource allocation, treatment of breathlessness includes opioids, anxiolytics, antipsychotics, steroids, and fluid drainage by thoracocentesis. Oxygen therapy for hypoxemic patients should be available, to be continued if a preliminary trial improves breathlessness. At **limited levels**, pleurodesis, by pleural drain, open thoracotomy or video-assisted thoracoscopic surgery (VATS) should be available. Radiotherapy should be available for management of metastases causing dyspnea or hemoptysis.

Skin metastases and complications (Table 3, row 6)

Description: Breast cancer is the most common cancer to metastasize to the skin[76]. Site-specific skin presentations include

fungating wounds and chronic skin ulcers, which require regular wound management due to strong odor, exudate, and pain, which can cause psychosocial distress. Locally advanced breast cancer may also cause fungating wounds, and surgery can be complicated by impaired wound healing. Radiation dermatitis is a common complication of radiotherapy (both primary and adjuvant). Immediate attention to developing skin complications may prevent more serious complications. Best practice for skin care should be followed, including preventive measures to avoid skin breakdown and relieve symptoms (burning, itching or pain), with special attention to skin folds, moist areas and skin surfaces where rubbing/friction could occur. Aqueous cream to maintain skin moisture level and integrity, and short-term corticosteroid use to manage itching and burning, may be helpful[77]. Simple measures, such as washing skin with mild soap and water, are essential for the prevention and treatment of acute radiation dermatitis. Moist desquamation should be treated according to best practice for moist wound healing, with special attention to type of dressing based on amount of exudate, and with antibiotics as needed. Surgery may be considered, if needed[7]. Education for health professionals in assessing and dressing wounds using sterile techniques and good hygiene practice is important.

#10. Panel recommendations: At **basic levels** of resource allocation, management of skin complications includes wound and skin assessment, analgesics, broad-spectrum antibiotics, and simple dressings and skin barriers (for fragile skin and trauma prevention). Activated charcoal and topical metronidazole powder should be available. Patient and families should be taught wound dressing techniques. At **limited levels**, topical hemostasis agents (eg, silver nitrate) to treat bleeding, and radiotherapy and surgical debridement to manage necrotic skin complications and fungating wounds, should be available. At **enhanced levels**, more sophisticated dressing material should be available, as well as calcium alginate for hemostasis, and stoma/wound therapy. For patients with limited mobility, air or egg crate mattresses should be available. At **maximal levels**, plastic surgery, vacuum (negative pressure) wound therapy and mechanical beds may be considered.

Note: Because there are no clear, universally accepted guidelines for wound management, it is important that healthcare systems with limited resources focus on wound management strategies known to be effective, and ensure that health professionals are well educated about evidence-based recommendations.

Palliative care: pain management and end-of-life care

Pain management (Table 4, row 1)

Description: Breast cancer patients report pain as a major symptom of disease and treatment. A systematic review[78] found that pain prevalence in patients ranged from 33% after treatment to 59% during treatment and 64% in patients with metastatic disease. Metastatic-disease-related pain can include local and diffuse bone pain, pain from spinal cord compression, bowel obstruction, or brain swelling, or from skin complications such as ulcers and fungating wounds[79]. Pain management should include regular pain assessments, and proper use of pharmacologic and non-pharmacologic interventions. Health professional pain management education should be a primary focus of supportive care and palliative end-of-life medical training, and should include the universal principles of pain management: safe and effective use of strong opioids for cancer pain relief; understanding the relative differences in analgesic effects of various drugs; close and accurate clinical monitoring of patients' pain levels and well-being; and identifying pain-related emergencies (eg, bone fracture, spinal cord compression, infection, or bowel obstruction)[79,80].

Pain assessment tools should be simple and consider patient health literacy. Simple one-dimensional pain intensity tools, such as a body chart with a Numeric Pain Rating (NRS), Visual Analogue Scale (VAS), or verbal descriptor scale[81], can be utilized. In patients with cognitive impairments and limited ability to communicate, behavioral observation of the patient's facial expressions, movement patterns and non-verbal sounds, and reports from family, may be used to make judgments of pain intensity[82].

Other assessment tools that measure pain or treatment-outcome satisfaction include the Brief Pain Inventory (BPI), which is available in over a dozen languages[83–87], the Palliative Outcome Scale[88], the ESAS[89–91], the Pain Management Index [92], the Memorial Pain Assessment Card[84,93], and the McGill Pain questionnaire[94–96].

General pain management often requires multimodal approaches[97]. Resources often determine the availability and type of analgesics and adjuvant pain treatments. The WHO pain ladder has been used as a resource for developing pain management strategies in LMICs[98]. Non-pharmacologic pain management should also follow the WHO recommendations[99]. There are a number of comprehensive guidelines on cancer pain management available[15,79,99]. Side-effects of analgesics also need to be managed, and include fatigue, cognitive dysfunction, dry mouth, constipation, nausea, sweating and weight gain[100].

#11. Panel recommendations: At **basic levels** of resource allocation, pain consideration is often a dialogue between the patient and health professional that elucidates the nature, location and extent of pain and its impact on daily life. A simple one-dimensional pain intensity tool can be used. Immediate-release oral morphine and parenteral morphine should be readily available, as should clinicians who are able to prescribe opioids. Pain-control remedies should follow the WHO ladder and include Step One analgesics and adjuvants (such as dexamethasone and tricyclic antidepressants) administered according to clinical practice guidelines. Basic non-pharmacologic pain management interventions should also be available and include management of pain-related physical symptoms. Patients' preference for alternative and complementary pain medication should be explored. At **limited levels**, additional pain-control remedies should include expanded access to drugs on the WHO ladder: Step 2 analgesics (such as codeine and tramadol), and slow-release oral morphine, and Step 3 opioid options (such as oxycodone or hydromorphone). Radiotherapy should be available (single fractions may be as effective as multiple fractions for pain relief). Non-pharmacological methods should include physical therapy and occupational therapy for functional loss and pain management. At **enhanced levels**, the use of multidimensional pain screening tools and pain care plans should be considered. Pain-control remedies should include opioid pumps, and other strong opioids such as methadone and transdermal fentanyl. Consultation for pain therapy with a pain specialist should be available, and include management of complex pain syndromes. Surgery for spinal cord compression, fracture, or obstruction should be available. At **maximal levels**, locoregional anesthesia and spinal analgesia, such as neuraxial infusion of opioids, spinal cord stimulation and nerve blocks, could be considered.

Psychosocial aspects of end-of-life care (Table 4, row 2)

Description: The diagnosis of metastatic disease can generate profound anxiety and fears of death and dying and raise spiritual concerns[101]. These fears may be heightened when there are few resources to support individuals and their families, and when there is social and cultural stigma associated with cancer. All health professionals working with cancer patients should have training in the psychosocial and spiritual aspects of cancer, as well as breast-cancer-specific complications related to body image and sexual

health. (See the companion BHGI consensus statement, *Supportive Care during Treatment*[19], for discussions on spirituality.) In addition, supportive and palliative care training should include specialists treating cancer patients.

Training in psychosocial components of end-of-life care should include awareness that depression can be a cumulative response to progression of metastatic cancer and proximity to death[102]. Severity of physical suffering, past history of depression/psychiatric illness, and a lack of social support can all increase the likelihood of depressive symptoms[103]. Assessment tools for depression and other psychosocial problems have been developed or adapted for use in LMICs[104–108]. A simplified distress thermometer (DT) and depressed mood thermometer (MT) have been used in a number of LMIC studies[109]. However, formal screening for psychosocial issues should be implemented only when resources for formal referral and treatment are available. Breast cancer patients with advanced disease, and their families, often require additional emotional support, which can be provided by breast cancer or general cancer community organizations and support groups. Clear and empathic communication between health professionals, patients and families is a critical aspect of psychosocial care required in any palliative care setting, and training in these skills is useful. Bereavement support should be available to families, including spiritual support in the community. (See the *Spiritual Aspects* section.)

#12. Panel recommendations: At **basic levels** of resource allocation, patient education is a primary intervention. Consideration of a patient's pain (through patient-provider dialogue, observations, and other appropriate means) should be provided. Community-based psychosocial support and bereavement support should be available. At **limited levels**, education of patients, their family, community, and health professionals should include emotional aspects of advanced breast cancer and death. Advance care planning should be offered. At **enhanced levels**, screening and referrals for depression and distress should be available. Referral to professional counseling for psychological, financial, legal and family matters should be available. Antidepressants should be available. At **maximal levels**, other psychosocial resources that require psychiatrist or psychologist, or social worker coordinated care, such as formal psychosocial treatment programs, could be considered.

Spiritual aspects of end-of-life care (Table 4, row 3)

Description: Spirituality is emerging as a distinct area of supportive care in HICs[110–112] and LMICs[114–116] and greater spiritual well-being has been associated with higher perceived quality of life and satisfaction with doctor–patient relationships in HICs[111,112]. The traditional role for health professionals has been to recognize the importance of religious/spiritual beliefs in seriously ill patients, and to refer patients to their own religious leader or community[110]. For many patients, the provision of spiritual care by a religious counselor is most desirable. A more active model for health professionals in assessing spiritual well-being of cancer patients is now recognized, and has been incorporated into many supportive cancer care programs[110]. Attention to spiritual well-being, which includes faith, a sense of meaning, and inner peace [108], should be considered part of supportive breast cancer care [117,118]. Spiritual counseling either within or outside of religious practice may be helpful for breast cancer patients[113]. General assessment of spiritual health should be part of patient evaluations; health professionals should be aware of available support services within their community and health care system. (See the companion BHGI consensus statement, *Supportive Care during Treatment*[19], for further recommendations and discussion on spirituality.)

#13. Panel recommendations: At **basic levels** of resource allocation, spiritual consideration (through patient-provider dialogue and other appropriate means) and referral to community-based spiritual support should be available from religion-based or nonreligious sources. At **enhanced levels**, clinic- or hospital-associated spiritual support, and hospital or hospice spiritual reflection and meditation space, should be available.

Special concerns and emerging issues in LMICs

Communication skills for end-of-life care: Effective communication between patients and health professionals has been associated with patient satisfaction with care at end-of-life[119]. However, many health professionals feel that they lack appropriate training to deal with end-of-life issues[120]. In that regard, many oncologists report the communicating of poor prognosis as one of the most challenging and stressful aspects of their profession[121]. Education about effective patient communication should be part of supportive care training programs, should be culturally sensitive and appropriate, and should recognize that patient educational needs may differ based on age, culture, religion and nationality[34]. The majority of patients want full disclosure of information, if it is communicated sensitively, to allow them to participate fully in decision-making[122]. A European Society for Medical Oncology (EMSO) survey of oncologists found that even when patients express a desire for information, many oncologists are unwilling, unable or uncomfortable in disclosing information regarding diagnosis, benefits of treatments, and prognosis[122]. Cultural competency is required in such communication[34], as well as consideration of a patient's right to know and the patient's family dynamics. Talking about death may be considered taboo or bad luck in some cultures, or it may only be considered appropriate to talk to certain family members about death. Enquiring into patient preferences for level and form of communication (eg, health literacy and cultural literacy) can be valuable. Further research is needed in order to better understand longitudinal, interactive, and interdisciplinary processes of decision-making in palliative care[123].

Screening tools: Screening tools can help to identify patients who may benefit from early palliative care. The National Cancer Center Network (NCCN) developed screening criteria, and recommends that all patients be screened for palliative care needs[124]. In LMICs, where a less time-consuming tool may be needed[125], these criteria can be of value to health systems in developing their own criteria and screening tools. Such quality improvement projects have been shown to increase frequency of, and indications for, palliative care referrals[126].

Referrals: Quality palliative care benefits patients, family and caregivers, and in an HIC setting has been shown to reduce inpatient length of stay, admissions and overall costs[127]. Education of health professionals regarding appropriate use of clinical practice guidelines[19] and referral strategies are key to improving palliative care for advanced-stage disease. Lack of adequate physician education in palliative care has been associated with late referrals to palliative care in both HICs[128,129] and LMICs[130]. The under-detection of pain in breast cancer patients contributes to late referrals[129]; a lack of health system criteria for pain referrals also contributes to late or poor referral rates in HICs[131] and LMICs [130]. Barriers to early referrals include oncologists' concerns about "letting go" of patients[132], inaccurate prognosis, logistical factors, and other medical concerns[133], including the concern that referrals to palliative care would alarm patients and their families [134]. Coordinated interdisciplinary approaches, with education of health professionals and patients about palliative care, may improve referral rates for metastatic cancer patients[132], and help transition patients with continuing needs to concurrent palliative

care programs[135]. The broadening scope of palliative care, and its emerging integration into oncology programs, make education regarding the timing of palliative care referrals a high priority. Various models of “automatic” referral have been proposed, including palliative care consultation for all solid tumor patients admitted to hospital[136]. Such models, together with education, can also help to replace the older associations of palliative care exclusively with end-of-life, with a broader supportive care concept that includes early palliative care[137–140].

Discussion

This consensus statement expands on the 2008 BHGI guidelines for resource-stratified treatment of site-specific metastases of breast cancer and palliative care[141]. Palliative care requires interdisciplinary care teams to address physical, psychosocial, and spiritual needs of breast cancer patients and their families. Interdisciplinary teams should include pharmacists, psychologists and psychiatrists, nurses, social workers and spiritual caregivers, with access to the services of nutritionists, physical and respiratory therapists, and other specialists, including nurses trained in wound care. In LMICs, basic palliative care services often include trained volunteers and home- or hospital-based programs.

Pain management should be a priority in supportive care for metastatic breast cancer and end-of-life palliative care. Morphine should be available and easily accessible. Pain is often inadequately treated due to: 1) reluctance of patients to report unrelieved pain; 2) health professionals' inadequate knowledge of pain management techniques; 3) negative attitudes of health professionals toward the use of opioids; and 4) limitations in healthcare systems, including easy access to morphine. Pain assessment, using simple pain intensity tools or pain scales, should be a routine part of patient monitoring in order to assess whether existing treatments are providing adequate pain relief, or if pain medications can be reduced.

Integration of supportive care and palliative treatment into mainstream healthcare service provision has emerged as the “gold standard” in comparative analysis of palliative care development [142]. Introducing supportive care during initial treatment, continuing supportive care after initial curative treatment, and ensuring supportive care and palliative end-of-life care for metastatic breast cancer, will ensure breast cancer programs provide a continuum of care in LMICs.

Although research is scant with regards to identifying and quantifying the most effective components of palliative care programs, some comparative data are emerging[143]. A number of LMICs have reported implementation of palliative care programs [144,145]. A systematic review found a modest contribution to the palliative care literature from LMICs, with the majority of studies being from upper-middle-income countries, and 25% of the data from LMICs being published by HIC institutions[146]. Ongoing efforts and collaborations are required in terms of advocacy, policy making, and service development if global integration of palliative care into oncology programs is to be achieved. Collaborative research efforts are needed for the measurement and improvement of patient outcomes in LMICs.

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