

BREAST HEALTH GLOBAL INITIATIVE

Breast Cancer in Limited-Resource Countries: An Overview of the Breast Health Global Initiative 2005 Guidelines

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■ **Abstract:** Breast cancer is the most common cause of cancer-related death among women worldwide, with case fatality rates highest in low-resource countries. Despite significant scientific advances in its management, most of the world faces resource constraints that limit the capacity to improve early detection, diagnosis, and treatment of the disease. The Breast Health Global Initiative (BHGI) strives to develop evidence-based, economically feasible, and culturally appropriate guidelines that can be used in nations with limited health care resources to improve breast cancer outcomes. Using an evidence-based consensus panel process, four BHGI expert panels addressed the areas of early detection and access to care, diagnosis and pathology, treatment and resource allocation, and health care systems and public policy as they relate to breast health care in limited-resource settings. To update and expand on the BHGI Guidelines published in 2003, the 2005 BHGI panels outlined a stepwise, systematic approach to health care improvement using a tiered system of resource allotment into four levels—basic, limited, enhanced, and maximal—based on the contribution of each resource toward improving clinical outcomes. Early breast cancer detection improves outcome in a cost-effective fashion assuming treatment is available, but requires public education to foster active patient participation in diagnosis and treatment. Clinical breast examination combined with diagnostic breast imaging (ultrasound ± diagnostic mammography) can facilitate cost-effective tissue sampling techniques for cytologic or histologic diagnosis. Breast-conserving treatment with partial mastectomy and radiation therapy requires more health care resources and infrastructure than mastectomy, but can be provided in a thoughtfully designed limited-resource setting. The availability and administration of systemic therapies are critical to improving breast cancer survival. Estrogen receptor testing allows patient selection for hormonal treatments (tamoxifen, oophorectomy). Chemotherapy, which requires some allocation of resources and infrastructure, is needed to treat node-positive, locally advanced breast cancers, which represent the most common clinical presentation of disease in low-resource countries. When chemotherapy is not available, patients with locally advanced, hormone receptor-negative cancers can only receive palliative therapy. Future research is needed to better determine how these guidelines can best be implemented in limited-resource settings. ■

Key Words: breast cancer, diagnosis, early detection, guideline, health care systems, health planning, international health problems, low-resource countries, pathology, public policy, recommendations, resource allocation, screening, treatment

Breast cancer is the most common cause of cancer-related death among women around the globe (1). Each year, breast cancer is newly diagnosed in more than 1.1 million women, and these cases represent more than 10% of all new cancer cases. With more than 410,000 deaths each year, the disease accounts for more than 1.6%

of all female deaths worldwide (2,3). Breast cancer is an urgent public health problem in high-resource regions and is becoming an increasingly urgent problem in low-resource regions, where incidence rates have been increasing by up to 5% per year (2,4).

Low-resource countries have generally not identified cancer as a priority health care issue because infectious diseases are the predominant public health threat in such settings. Nonetheless, resources are spent on cancer treatment when patients seek medical care for what is typically advanced-stage disease. Cancer becomes an increasing

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problem in such countries as the control of communicable diseases improves and life expectancy increases (5). However, obstacles to improving cancer care arise from multiple sources, including deficits in public knowledge and awareness, social and cultural barriers, challenges in organizing health care, and insufficient resources.

In high-resource countries, evidence-based guidelines outlining optimal approaches to early detection, diagnosis, and treatment of breast cancer have been defined and disseminated (6–9). These guidelines from wealthy countries are resource neutral and thus not only fail to consider variable resource distributions where overall standards of living are high, but also are unworkable in the presence of ubiquitous infrastructure and resource deficits in limited-resource countries. Moreover, they are not designed to consider implementation costs or provide guidance as to how a suboptimal system can be improved incrementally toward an optimal system. As pointed out by the World Health Organization (WHO), guidelines defining optimal breast care and services have limited utility in resource-constrained countries (10). Thus there presently is a lack of resource-based guidance related to strategies to reduce the burden of breast cancer in settings where optimal care is not feasible.

The development of international evidence-based breast health care guidelines oriented toward countries or regions of the world with limited financial resources is a crucial step toward improving breast health care and breast cancer care in these regions. Although existing guidelines generally assume a high level of resources and are therefore of limited use in many areas of the world, current evidence about the value of earlier diagnosis and cost-effective diagnosis and treatment can nonetheless be applied to define evidence-based “best practices with limited resources” for breast health care for use in countries where access to health care is marginal, breast cancer awareness is marginal, and cultural barriers to effective care exist. To outline a systematic, sequential approach to building a breast program, guidelines for such countries may recommend the use of health care strategies that differ from those used in countries with a high level of resources, but still measurably improve breast cancer outcomes by achieving the best standard of care that is practical in that setting.

THE BREAST HEALTH GLOBAL INITIATIVE

Cosponsored by the Fred Hutchinson Cancer Research Center and the Susan G. Komen Breast Cancer Foundation, the Breast Health Global Initiative (BHGI) is a program that strives to develop evidence-based, economically

feasible, and culturally appropriate guidelines that can be used in nations with substantial resource constraints to improve breast health outcomes. In October 2002, the BHGI held the first Global Summit Consensus Conference on International Breast Health Care (hereafter referred to as the 2002 Global Summit) in Seattle, Washington. The aim of the 2002 Global Summit was to establish breast health guidelines that address how care may best be provided in countries where health care resources are significantly limited (11). The BHGI guidelines were developed using a panel consensus approach with analysis of evidence-based breast cancer research. Based on definitions created by the WHO for national cancer programs (10), panels of breast cancer experts representing 17 countries and 9 world regions created guidelines to address early detection, diagnosis, and treatment of breast cancer in countries with limited health care resources (i.e., those with either low- or medium-level resources according to WHO criteria).

The resulting 2002 BHGI guidelines were published and have been made available in an unrestricted fashion on the Internet for worldwide access (12–15). To date, they have been the only comprehensive consensus guidelines that specifically address issues surrounding the implementation of breast care in limited-resource countries.

2002 BHGI GLOBAL SUMMIT: SUMMARY OF RESULTS

To be applicable and effective, practice guidelines must go beyond summarization of available evidence-based research to consider and sometimes challenge the values that are implicit in the way practice questions have been framed and outcomes have been chosen (16). Gender inequalities in health are a consequence of the basic inequality between men and women in many societies. Despite the importance of socioeconomic factors, women’s health is also greatly affected by the extent and quality of health services available to them (17). At the 2002 Global Summit, two axioms were adopted as principles for guideline development:

- All women have the right to access to health care, although considerable challenges exist in implementing breast health care programs when resources are limited.
- All women have the right to education about breast cancer, but it must be culturally appropriate and targeted and tailored to the specific population.

A review of the published and presented data confirmed that in countries with limited resources, most women have

advanced or metastatic breast cancer at the time of diagnosis (5). Based on an evidence-based review and consensus discussion, four observations were made:

- Because advanced breast cancer has the poorest survival and is the most resource intensive to treat, efforts aimed at early detection can reduce the stage at diagnosis, potentially improving the odds of survival and cure, and enabling simpler and more cost-effective treatment. These efforts are likely to have the greatest overall benefit in terms of both survival and costs.
- There is a need to build programs that are specific to each country's unique situation.
- The development of cancer centers can be a cost-effective way to deliver breast cancer care to some women when it is not yet possible to deliver such care to women nationwide.
- Collecting data on breast cancer is imperative for deciding how best to apply resources and for measuring progress.

These observations from the first Global Summit served as the basis of the 2005 BHGI Global Summit Consensus Conference on International Breast Health Care (hereafter referred to as the 2005 Global Summit), where specific recommendations were addressed.

METHODS: 2005 BHGI GLOBAL SUMMIT

With extended sponsorship of national and international collaborating organizations, the BHGI guidelines were reexamined, revised, and extended at the second Global Summit, held January 12–15, 2005, and hosted by the Office of International Affairs of the National Cancer Institute in Bethesda, Maryland. Twelve national and international groups joined the BHGI as collaborating organizations (Appendix A). In addition, to obtain input on international guideline development, the BHGI established affiliations with three WHO programs: the Cancer Control Programme, Health System Policies and Operations, and the Alliance for Health Policy and Systems Research. The 2005 Global Summit brought together more than 60 international experts from 33 countries of all resource levels. The experts had diverse specialties related to breast care and breast cancer: screening, pathology and cytology, surgery, oncology, radiation therapy, health economics, medical ethics, sociology, and advocacy. The experts were charged with reviewing, updating, and extending the previously published guidelines, and were organized into four panels: early detection and access to care, diagnosis and pathology, cancer treat-

ment and allocation of resources, and health care systems and public policy. Each panel was asked to prepare a consensus statement summarizing the outcome of their work (18–21).

PANEL SELECTION

Drawing from the experts who participated in the 2002 Global Summit, the BHGI formed an international Scientific Advisory Committee (Appendix C). For each 2005 Global Summit panel, this committee selected two cochairs—one from a country with limited resources and the other from a country with adequate resources (Appendix D). In addition, the Scientific Advisory Committee developed a comprehensive list of more than 100 international experts from which the panel cochairs selected their panelists and speakers for the summit. The committee reviewed and approved the final panel and speaker selections.

PANEL ORGANIZATION AND CONFERENCE PREPARATION

Panel cochairs were asked to create a program whereby their expert panel could produce consensus guidelines. The cochairs were responsible for drafting the agenda for their panel's conference day and for organizing and executing the writing of their panel's consensus statement. Each panel held one full-day meeting, with a morning session consisting of plenary presentations on topics selected by the cochairs (Appendixes E–H) and an afternoon session consisting of discussion and debate among panelists regarding the content of their consensus statement. In addition, to reinforce the aim of the guidelines and to describe the diverse settings in which they might be used, each day began with a presentation by a breast cancer advocate from a limited-resource country to summarize the personal experience of women facing breast cancer in her country.

RESOURCE STRATIFICATION DEFINITIONS

To encourage a consistent approach to the discussion and the guidelines, each panel was asked to stratify health care resources relevant to their assigned areas into one of four levels, defined as follows:

- Basic level—Core resources or fundamental services absolutely necessary for any breast health care system to function. By definition, a health care system lacking any basic-level resource would be unable to provide breast

cancer care to its patient population. Basic-level services are typically applied in a single clinical interaction.

- Limited level—Second-tier resources or services that produce major improvements in outcome, such as increased survival, but which are attainable with limited financial means and modest infrastructure. Limited-level services may involve single or multiple clinical interactions.
- Enhanced level—Third-tier resources or services that are optional but important. Enhanced-level resources may produce minor improvements in outcome but increase the number and quality of therapeutic options and patient choice.
- Maximal level—High-level resources or services that may be used in some high-resource countries, but nonetheless should be considered lower priority than those in the basic, limited, or enhanced categories on the basis of cost or impracticality for limited-resource environments. In order to be useful, maximal-level resources typically depend on the existence and functionality of all lower-level resources.

This stratification scheme assumes incremental resource allocation and implementation. For example, the limited level assumes that a setting already has all of the resources recommended for the basic level. Using this scheme, the short-term goal is to move to the next level. Although the long-term goal may be to move to the maximal level in certain areas (e.g., the implementation of population-based mammographic screening), overall, most limited-resource countries must address more fundamental needs before these maximal-level resources or services can be realistically applied.

It should be noted that multiple resource levels often coexist within a country, region, or even an individual health care facility. A country may have community clinics that provide care at the basic level, regional hospitals

that provide care at the limited level, and a national cancer center that provides care at the enhanced or maximal level. Because circumstances vary so widely around the world, decisions about how to plan the overall structure of a national breast program must be made on a country-by-country, region-by-region, or facility-by-facility basis.

The panels were also asked to develop checklists for the various interventions. For each intervention, these checklists would describe the strengths, limitations, and necessary resources needed to apply that intervention in the areas of early detection, diagnosis, treatment, or health care systems and public policies. Finally, the panels were asked to identify areas where evidence is lacking and research is needed to better inform future iterations of the guidelines.

STATEMENT PREPARATION AND REVIEW PROCESS

Consensus Statement Preparation and Review

Each panel's discussion and debate were recorded and transcribed, and the transcripts were used as the basis for writing the four consensus statements. Panel discussion was directed at creating the stratification tables (Tables 1–7), which list how resources should be allocated based on the definitions of basic, limited, enhanced, and maximal. Panel cochairs coordinated the writing of statements, sections of which were coauthored by participating panelists. Consensus statement drafts were reviewed and edited by all coauthors of each statement. The final draft, including resolution of disagreements among coauthors, was the responsibility of the panel cochairs.

The consensus statements were then compared centrally for internal consistency in stratification by a subset of coauthors. Differences among panel recommendations were reviewed with panel cochairs and language was adopted to minimize the level of perceived inconsistencies.

Table 1. Early Detection and Access to Care

Level of resources	Detection method(s)	Evaluation goal
Basic	Breast health awareness (education ± self-examination) Clinical breast examination (clinician education)	Baseline assessment and repeated survey
Limited	Targeted outreach/education encouraging CBE for at-risk groups Diagnostic ultrasound ± diagnostic mammography	Downstaging of symptomatic disease
Enhanced	Diagnostic mammography Opportunistic mammographic screening	Opportunistic screening of asymptomatic patients
Maximal	Population-based mammographic screening Other imaging technologies as appropriate: high-risk groups, unique imaging challenges	Population-based screening of asymptomatic patients

Table 2. Diagnosis and Pathology

Level of resources	Clinical	Pathology	Imaging and laboratory tests
Basic	History Physical examination Clinical breast examination Surgical biopsy Fine-needle aspiration biopsy	Interpretation of biopsies Cytology or pathology report describing tumor size, lymph node status, histologic type, tumor grade	
Limited	Core needle biopsy Image-guided sampling (ultrasonographic ± mammographic)	Determination and reporting of ER and PR status Determination and reporting of margin status	Diagnostic breast ultrasound ± diagnostic mammography Plain chest radiography Liver ultrasound Blood chemistry profile/CBC
Enhanced	Preoperative needle localization under mammographic or ultrasound guidance	On-site cytopathologist	Diagnostic mammography Bone scan
Maximal	Stereotactic biopsy Sentinel node biopsy	HER-2/ <i>neu</i> status IHC staining of sentinel nodes for cytokeratin to detect micrometastases	CT scanning, PET scan, MIBI scan, breast MRI

CBC, complete blood count; CT, computed tomography; ER, estrogen receptor; IHC, immunohistochemistry; MIBI, 99mTc-sestamibi; MRI, magnetic resonance imaging; PET, positron emission tomography; PR, progesterone receptor.

In cases where resources were definitively stratified differently by the consensus panels, the panel recommendations were maintained in the tables, and instead, the nature of the differences are summarized, explained, and discussed in this overview.

Individual Statement Preparation

Morning plenary speakers were invited to submit individual statements for publication on their topics along with the consensus statements. In many cases, individual

statements were needed to develop and analyze specific topics that were too detailed and focused for inclusion in the consensus statements as a whole, but nonetheless were vital to an understanding of the overall guideline recommendations for limited-resource countries.

Individual Statement Selection and Review

In lieu of the standard external peer-review process, submitted individual statements underwent a special internal review process, reflecting the unique structure

Table 3. Treatment and Allocation of Resources: Stage I Breast Cancer

Level of resources	Local-regional treatment		Systemic treatment (adjuvant)	
	Surgery	Radiation therapy	Chemotherapy	Endocrine therapy
Basic	Modified radical mastectomy			Ovarian ablation Tamoxifen
Limited	Breast-conserving therapy ^a	Breast-conserving whole-breast irradiation as part of breast-conserving therapy Postmastectomy irradiation of the chest wall and regional nodes for high-risk cases	Classical CMF ^b AC, EC, or FAC ^b	
Enhanced			Taxanes	Aromatase inhibitors LH-RH agonists
Maximal	Sentinel node biopsy Reconstructive surgery		Growth factors Dose-dense chemotherapy	

^aBreast-conserving therapy requires mammography and reporting of margin status.

^bRequires blood chemistry profile and complete blood count (CBC) testing.

AC, doxorubicin and cyclophosphamide; CMF, cyclophosphamide, methotrexate, and 5-fluorouracil; EC, epirubicin and cyclophosphamide; FAC, 5-fluorouracil, doxorubicin, and cyclophosphamide; LH-RH, luteinizing hormone–releasing hormone.

Table 4. Treatment and Allocation of Resources: Stage II Breast Cancer

Level of resources	Local-regional treatment		Systemic treatment (adjuvant)	
	Surgery	Radiation therapy	Chemotherapy	Endocrine therapy
Basic	Modified radical mastectomy	— ^a	Classical CMF ^b AC, EC, or FAC ^b	Ovarian ablation Tamoxifen
Limited	Breast-conserving therapy ^c	Breast-conserving whole-breast irradiation as part of breast-conserving therapy Postmastectomy irradiation of the chest wall and regional nodes for high-risk cases		
Enhanced			Taxanes	Aromatase inhibitors LH-RH agonists
Maximal	Sentinel node biopsy Reconstructive surgery		Growth factors Dose-dense chemotherapy	

^aChest wall and regional lymph node irradiation substantially decrease the risk of postmastectomy local recurrence. If available, it should be used as a basic-level resource.

^bRequires blood chemistry profile and complete blood count (CBC) testing.

^cBreast-conserving therapy requires mammography and reporting of margin status.

AC, doxorubicin and cyclophosphamide; CMF, cyclophosphamide, methotrexate, and 5-fluorouracil; EC, epirubicin and cyclophosphamide; FAC, 5-fluorouracil, doxorubicin, and cyclophosphamide; LH-RH, luteinizing hormone–releasing hormone.

and goals of the BHGI program. All individual statement submissions were reviewed by panel coauthors and selected internal BHGI nonauthor reviewers. Individual statements that did not address issues specific to limited-resource countries were referred for journal submission outside of the BHGI guidelines. Some individual statements that developed individual topics of a more limited scope relevant to limited-resource countries were incorporated into guideline consensus articles. Individual statements that were accepted for publication were determined by the coauthors, internal BHGI reviewers, and the BHGI director to have specific merit in support of the consensus guidelines.

After final acceptance, all individual statements were coordinated with the consensus guideline statements for internal referencing as data in one or multiple consensus

statements. As such, the combination of consensus and individual statements represents a complete BHGI guideline compendium, which is the final work product of the 2005 Global Summit and is published as a complete unit in this *Breast Journal* supplement.

2005 GLOBAL SUMMIT GUIDELINE OUTCOME SUMMARY

The four consensus panels each generated resource stratification tables (Tables 1–7). Detailed background material and organizing discussions are provided in individual consensus statements published together with this overview document (18–21). In most areas there was good agreement between consensus panels in the

Table 5. Treatment and Allocation of Resources: Locally Advanced Breast Cancer

Level of resources	Local-regional treatment		Systemic treatment (adjuvant)	
	Surgery	Radiation therapy	Chemotherapy	Endocrine therapy
Basic	Modified radical mastectomy		Neoadjuvant AC, FAC, or classical CMF ^a	Ovarian ablation Tamoxifen
Limited		Postmastectomy irradiation of the chest wall and regional nodes		
Enhanced	Breast-conserving therapy ^b	Breast-conserving whole-breast irradiation	Taxanes	Aromatase inhibitors LH-RH agonists
Maximal	Reconstructive surgery		Growth factors Dose-dense chemotherapy	

^aRequires blood chemistry profile and complete blood count (CBC) testing.

^bBreast-conserving therapy requires mammography and reporting of margin status.

AC, doxorubicin and cyclophosphamide; CMF, cyclophosphamide, methotrexate, and 5-fluorouracil; EC, epirubicin and cyclophosphamide; FAC, 5-fluorouracil, doxorubicin, and cyclophosphamide; LH-RH, luteinizing hormone–releasing hormone.

Table 6. Treatment and Allocation of Resources: Metastatic (Stage IV) and Recurrent Breast Cancer

Level of resources	Local-regional treatment		Systemic treatment		
	Surgery	Radiation therapy	Chemotherapy	Endocrine therapy	Supportive and palliative therapy
Basic	Total mastectomy for ipsilateral breast tumor recurrence ^a			Ovarian ablation Tamoxifen	Nonopioid and opioid analgesics
Limited		Palliative radiation therapy	Classical CMF ^b Anthracycline monotherapy or in combination ^b		
Enhanced			Taxanes Capecitabine Trastuzumab	Aromatase inhibitors	Bisphosphonates
Maximal			Growth factors Vinorelbine Gemcitabine Carboplatin	Fulvestrant	

^aRequired resources are the same as those for modified radical mastectomy.
^bRequires blood chemistry profile and complete blood count (CBC) testing.
 CMF, cyclophosphamide, methotrexate, and 5-fluorouracil.

assigned stratification levels. However, review of the tables demonstrated certain points where some resources did not appear to have complete alignment. These points are described below.

Introduction of Breast Ultrasound and Diagnostic Mammography in Low-Resource Countries

In high-resource countries, diagnostic mammography is a fundamental resource for examination of lesions with any clinical presentation. Women age 30 years and older with a palpable lump undergo diagnostic mammography as the initial diagnostic study of choice (22). In high-resource countries, breast ultrasound is used to

augment diagnostic mammography to specifically examine localized findings from the diagnostic mammogram or clinical breast examination (CBE). Screening breast ultrasound (general survey of the whole breast in clinically asymptomatic women) is generally discouraged because of the insufficient evidence base to determine if it is efficacious and cost-effective in the screening setting (23). A multicenter trial is now under way in the United States to evaluate the efficacy of screening whole breast ultrasound (24).

On the other hand, it was noted by multiple BHGI panelists that diagnostic breast ultrasound generally becomes available in low-resource countries before

Table 7. Health Care Systems and Public Policy

Level of resources	Services	Facilities	Record keeping
Basic	Primary care services Surgical services Pathology services Oncology services Nursing services Palliative services	Health facility Operating facility Pathology laboratory Pharmacy Outpatient care facility	Individual medical records and service-based patient registration
Limited	Imaging services Radiation oncology services Peer support services Early detection programs	Imaging facility Radiation therapy Clinical information systems Health system network	Facility-based medical records and centralized patient registration Local cancer registry
Enhanced	Opportunistic screening programs Cancer follow-up Rehabilitation services Group support	Centralized referral cancer center(s) Population-based cancer registry	Facility-based follow-up systems Regional cancer registry
Maximal	Population-based screening program Individual psychosocial care	Satellite (noncentralized or regional) cancer centers	National cancer registry

diagnostic mammography is commonly used. Mammography is a highly specialized imaging tool that is considerably more expensive than ultrasound. Until the recent application of digital technology, which is itself quite expensive, mammographic imaging required the use of x-ray film, for which the cost and the quality control requirements can be an insurmountable barrier to widespread use in a low-resource country (25). Many health facilities will not purchase mammographic equipment because it is dedicated to the single use of breast imaging without any other radiographic applications. In contrast, ultrasound is commonly available in all resource settings because it can be used for imaging many parts of the body and it requires no film other than that which is desired for record keeping. Ultrasound equipment can use multiple different transducers, making it useful for many different applications. Thus there is an impetus for use of breast ultrasound in settings where mammography is unavailable, simply because the tool exists.

Breast ultrasound as an initial diagnostic test may have more utility in low-resource countries. Breast ultrasound is particularly useful for imaging masses in the breast, can be used to distinguish solid masses from fluid-filled cysts, and can characterize the shape and morphology of solid masses, all of which are very useful in determining which patients with palpable masses are more likely to have disease requiring a tissue biopsy (22). Because patients in low-resource settings most commonly present with locally advanced, palpable invasive cancers, ultrasound can provide considerable supplemental information after a positive CBE for evaluation of the extent of disease in the breast (26). Furthermore, premenopausal breast cancer appears to be relatively more common in low-resource countries, based on the younger average age at diagnosis. Younger, premenopausal women more commonly have dense breasts that are less amenable to mammographic imaging and more amenable to ultrasound imaging (27).

Based on these findings, the BHGI Diagnosis and Pathology Panel advocates that both diagnostic mammography and breast ultrasound be implemented for breast imaging whenever possible. However, if forced to pick between these two breast imaging studies as the “next step,” the panel recommends that diagnostic ultrasound be implemented first (Table 2), despite the fact that this is the reverse order of implementation usually seen in high-resource countries.

Nonetheless, diagnostic mammography is a key component of breast imaging, and of particular importance for breast-conserving therapy. In preparation for breast-

preserving radiation therapy, cancers should be removed with negative surgical margins (6). Although breast ultrasound is useful for assessing the extent of the invasive component of a breast cancer, ductal carcinoma in situ (DCIS) is not well imaged on breast ultrasound, but can be seen on mammography when the disease forms microcalcifications. Surgical margins should be clear of both invasive and noninvasive cancer, which is best predicted by the combined use of diagnostic mammography and breast ultrasound before surgery. Thus the BHGI Treatment and Allocation of Resources Panel members consider the availability of diagnostic mammography to be necessary in order to offer breast-conserving therapy (Tables 3–5).

Hormone Therapy and Hormone Receptor Testing

Hormone therapy is among the simplest methods of providing systemic therapy for estrogen receptor (ER)-positive breast cancers. As an oral medication, tamoxifen can be provided with minimal infrastructure other than an outpatient pharmacy. If tamoxifen is too expensive, surgical or radiation-induced oophorectomy has proven efficacy and can be performed in premenopausal women. For this reason, the Treatment and Allocation of Resources Panel categorized ovarian ablation and tamoxifen as basic-level resources for all stages of invasive cancer (Tables 3–6).

This recommendation for basic-level stratification by the Treatment and Allocation of Resources Panel contrasts with the recommendations of the Diagnosis and Pathology Panel that described ER and progesterone receptor (PR) testing as being a limited-level resource. Indeed, the use of ER and PR testing is of significant value because tamoxifen or oophorectomy is unlikely to be efficacious when the cancer fails to express ER and PR. Nonetheless, patients can be given these hormonal therapies, even if ER and PR testing is unavailable. However, if this algorithm is followed, a large fraction of patients will receive treatment that, were testing available, could be predicted not to have therapeutic utility.

The rate of ER-positive cancers may vary among different racial groups. In one study, the incidence of ER- and PR-positive cancers was found to be similar in Japanese and American women (28). By comparison, another study analyzing more than 1000 tumors of Chinese women found the ER positivity rate to be 54%, which is significantly lower than for Caucasian women, even when considering the potential confounding variable of menopausal status (29). Thus ER and PR testing, while considered to be a limited-level rather than basic-level resource, has

obvious importance for better guiding the use of therapy. Indeed, the savings in selective use of hormonal treatments should offset if not completely pay for the cost of hormone receptor testing.

Cytotoxic Chemotherapy and Related Infrastructure

With stage I breast cancer (≤ 2 cm tumor, node negative), chemotherapy can be used, and in high-level resource countries is generally recommended for those cancers between 1 and 2 cm in size (30). However, because the prognosis for stage I cancer is already good, chemotherapy only marginally increases survival in node-negative disease, particularly for smaller cancers (20). In contrast, as breast cancer becomes more advanced, and particularly with node-positive disease, chemotherapy becomes a mainstay of systemic therapy. To properly reflect this difference in the utility of chemotherapy between early stage and later stage disease, the Treatment and Allocation of Resources Panel determined that cytotoxic chemotherapy is a limited-level resource therapy for stage I cancer (Table 3) and for metastatic cancer (Table 6), but it is a basic-level resource for patients with stage II or locally advanced cancer (Tables 4 and 5).

Cytotoxic chemotherapy is a more resource intensive therapy to provide because of the need to give ongoing systemic therapy infusions, monitor blood counts, and treat potential complications. Because there are some breast cancers that do not absolutely require cytotoxic chemotherapy, such as stage I cancer, the infrastructure to support cytotoxic chemotherapy is not considered a basic-level resource at all levels. Thus there is a paradox that in a health care system that lacks the infrastructure for providing systemic chemotherapy, stage I, ER-positive cancers can be effectively treated and stage IV ER-positive cancer can be palliated, but stage II and locally advanced disease can only be palliated at best. Ironically these more advanced, but treatable cancers are the most common presentations in low-resource countries. The conclusion, then, for a hospital administrator or health care minister is that if they choose to seriously undertake breast cancer treatment in their environment, they need to establish the infrastructure early on for cytotoxic chemotherapy, even though this resource is considered higher than a basic-level resource for some stages of breast cancer.

CONCLUSION

As the most common cause of cancer-related death among women, breast cancer warrants attention within health care systems. Efforts toward the early detection,

diagnosis, and treatment of breast cancer can be guided by evidence-based principles using a stratified approach to the introduction of needed resources. The BHGI guidelines provide a framework by which health care systems can adapt existing resources, or sequentially introduce new resources using cost-effective strategies, in ways that will optimize outcome. Future directions should include research to determine how these guidelines can best be implemented in order to help women around the globe stricken by this disease.

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Appendix A. Breast Health Global Initiative Collaborating Organizations

Alliance for Health Policy and Systems Research (AHPSR)
American Society for Breast Disease (ASBD)
Breast Surgery International (BSI)
Centers for Disease Control and Prevention (CDC)
International Atomic Energy Agency (IAEA)
International Network for Cancer Treatment and Research (INCTR)
International Society for Nurses in Cancer Care (ISNCC)
International Society of Breast Pathology (ISBP)
Middle East Cancer Consortium (MECC)
Pan American Health Organization (PAHO)
International Union Against Cancer (UICC)
World Society for Breast Health (WSBH)

Appendix B. Membership of the BHGI Steering Committee

Gabriel N. Hortobágyi, MD, FACP
Chairman, BHGI Steering Committee
Professor and Chairman of the Department of Breast Medical Oncology, Nellie B. Connally Chair in Breast Cancer, Director of the Breast Cancer Research Program,
University of Texas MD Anderson Cancer Center, Houston, Texas

Diana Rowden
Director, International
The Susan G. Komen Breast Cancer Foundation, Dallas, Texas

Sherif Omar, MD, FACS
Past President, National Cancer Institute, Cairo University, International Network for Cancer Treatment & Research (INCTR), Breast Cancer Strategy Group, Cairo,
Egypt

Hélène Sancho-Garnier, MD
International Union Against Cancer (UICC), Strategic Leader for Prevention and Early Diagnosis, Val d'Aurelle, France

László Vass, MD, PhD, FIAC
President, World Society for Breast Health (WSBH), Budapest, Hungary

Joseph D. Purvis, MD
Industry/Corporate Partner Representative
Executive Director, Clinical Research, Oncology, AstraZeneca Pharmaceuticals, Wilmington, Delaware

Bhadrasain Vikram, MD
Head, Radiotherapy & Applied Radiation, Biology Section, International Atomic Energy Agency (IAEA) of the United Nations (UN), Vienna, Austria

Benjamin O. Anderson, MD
Chair and Director, BHGI
Joint Associate Member, Public Health Sciences Division, Fred Hutchinson Cancer Research Center, and Professor and Director, Breast Health Center, Department
of Surgery, University of Washington, Seattle, Washington

Joe Harford, PhD
Director, Office of International Affairs, NIH/National Cancer Institute (NCI), Bethesda, Maryland

Raimund Jakesz, MD
Professor and Head, Department of General Surgery, Vienna General Hospital, Clinical Department of General Surgery, Vienna University Surgical Clinic, President,
Breast Surgery International, Vienna, Austria

Michael Silbermann, DMD, PhD
Executive Director, Middle East Cancer Consortium (MECC), Haifa, Israel

Shahla Masood, MD
Editor, *The Breast Journal*
Professor and Associate Chair, Department of Pathology, University of Florida, Jacksonville, Florida

Sylvia C. Robles, MD, MSc
Senior Public Health Specialist, Health, Nutrition and Population, Human Development Network, The World Bank, Washington, DC

Appendix C. Membership of the BHGI Scientific Advisory Committee

Member	Organization
Ute-Susann Albert, MD, MIAC Benjamin O. Anderson, MD	Department of Gynecology, Endocrinology and Oncology, Philipps-University Marburg, Marburg, Germany Chair and Director, Breast Health Global Initiative; Joint Associate Member, Public Health Sciences Division, Fred Hutchinson Cancer Research Center, and Professor and Director, Breast Health Center, Department of Surgery, University of Washington, Seattle, Washington
Rakesh Chopra, MD Raimund Jakesz, MD	Senior Consultant, Indraprastha Apollo Hospital, New Delhi, India Professor and Head, Department of General Surgery, Vienna General Hospital; Clinical Department of General Surgery, Vienna University Surgical Clinic, Vienna, Austria
Susan Lim, MD, PhD Riccardo Masetti, MD	Consultant and General Surgeon, Susan Lim Surgery Pte. Ltd., Gleneagles Medical Centre, Singapore Director of the Breast Surgical Unit, Associate Professor of Surgery, Professor of Surgical Oncology, Department of Surgery, Catholic University of Rome, Italy
Gilberto Schwartzmann, MD	SA Office, Anti-Cancer Drug Development, Academic Hospital (HCPA), Federal University of Rio Grande do Sul, Porto Alegre, Brazil
Joseph Stines, MD László Vass, MD, PhD Zhenzhou Shen, MD	Chief, Department Radiology, Centre Alexis Vautrin, Vandoeuvre Les Nancy Cedex, France Head, Department of Pathology/Cytopathology, University Teaching Hospital F.FLÓR of Pest County, Budapest, Hungary Department of Surgery, Cancer Hospital, Fu Dan Medical University, Shanghai, People's Republic of China

Appendix D. Panel Cochairs for the 2005 Global Summit

Panel 2005	Cochair	Cochair
Early Detection and Access to Care	Maira Caleffi, MD, PhD, Surgeon and President, Breast Institute of Rio Grande do Sul, Porto Alegre, RS, Brazil	Robert A. Smith, PhD, Director of Cancer Screening, American Cancer Society, Atlanta, Georgia
Diagnosis and Pathology	Roman Shyyan, MD, MSc, Surgeon, Lviv Cancer Center, Lviv, Ukraine	Shahla Masood, MD, Professor and Associate Chair Department of Pathology, University of Florida, Jacksonville, Florida
Treatment and Allocation of Resources	Alexandru Eniu, MD, Department of Breast Tumors, Cancer Institute I. Chiricuta, Cluj-Napoca, Romania	Robert W. Carlson, MD, Professor of Medicine, Division of Oncology, Stanford University, Stanford, California
Health Care Systems and Public Policy	Cheng-Har Yip, MD, Professor and Head of Surgery, Department of Surgery, University Malaya Medical Centre, Kuala Lumpur, Malaysia Benjamin O. Anderson, MD, Joint Associate Member, Epidemiology, Fred Hutchinson Cancer Research Center, Professor of Surgery, Director, Breast Health Center, University of Washington Medical Center, Seattle, Washington	Scott D. Ramsey, MD, PhD, Associate Member, Cancer Prevention Program, Fred Hutchinson Cancer Research Center, Seattle, Washington

Appendix E. Plenary Session Agenda of the Early Detection and Access to Care Panel

Advocate Presentation
Augustine Quashigah, President, Breast Cancer Support Group of Ghana, West Africa
"Impact of Accessibility on Effectiveness of Early Detection of Breast Cancer"
Tony Hsiu-His Chen, MSc, PhD (epidemiologist, preventative medicine, Taiwan)
"Tumor Size and Breast Cancer Detection"
Stephen W. Duffy, BSc, MSc (cancer screening, England)
"Is Earlier Detection of Symptomatic Breast Cancers Still Early?"
Dido Franceschi, MD (surgeon, Panama/Miami, Florida)
"Breast Cancer Detection without Mammography: The Role of Breast Self-Awareness (BSA)"
Robert M. Chamberlain, PhD (epidemiology, Houston, Texas)
"Breast Cancer Detection in Romania"
Gheorghe Peltecu, MD (gynecologist, Romania)
"Outcome of Screening by Clinical Breast Examination in Manila, Philippines"
Paola Pisani, PhD (epidemiology, International Agency on Research in Cancer/WHO, France)

Appendix F. Plenary Session Agenda of the Diagnosis and Pathology Panel

Advocate Presentation

Alicia Gimeno, Director, Educational Coordinator, Corporacion Yo Mujer (advocate group) Santiago, Chile

"Practice of Breast Pathology"

Helge Stalsberg, MD (pathologist, Norway)

"Overview of Tissue Sampling Techniques"

Riccardo Masetti, MD (surgeon, Italy)

"Breast Cancer Diagnostic Procedures in India: Consideration of Cost-Effectiveness and Availability of Resources"

Rajendra Badwe, MD (surgical oncologist, India)

"Fine Needle Aspiration Biopsy (FNAB) as a Diagnostic Procedure for Patient Triage"

László Vass, MD, PhD, FIAC (pathologist, Hungary)

"Optimal Pathology Report: Its Most Relevant Diagnostic and Prognostic Information"

Hernan Vargas, MD, FACS (surgeon, Peru/Torrance, California)

"Linkage of Epidemiological Studies and Clinical Practices in Diagnosis of Women's Cancers"

Rengaswamy Sankaranarayanan, MBBS, MD (Screening Group, International Agency for Research on Cancer/WHO, France)

Appendix G. Plenary Session Agenda of the Treatment and Allocation of Resources Panel

Advocate Presentation

Tatiana Soldak, MD, Medical Director, CitiHope, International; Director, Belarusian Breast Cancer Screening and Early Diagnosis Project (New York, New York)

"Mastectomy vs. Breast Conservation: Influence of Limited Resources on Decision Making"

Raimund Jakesz, MD (surgeon, Austria)

"Situation Analysis in Ghana, West Africa"

Benjamin O. Anderson, MD (breast surgeon, BHGI Chair and Director, Seattle, Washington)

"Combined Modality Management of Locally Advanced Breast Cancer"

Gabriel N. Hortobágyi, MD, FACP (medical oncology, University of Texas MD Anderson Cancer Center, Houston, Texas)

"Metastatic Breast Cancer: Easier to Treat in a Country with Limited Resources?"

Jamie de la Garza-Salazar, MD (medical oncologist, Mexico)

"Ethical and Cultural Considerations for Breast Cancer Treatment in Developing Countries"

Gail Geller, ScD (ethicist, Johns Hopkins University School of Medicine, Bioethics Institute, Baltimore, Maryland)

"Inflammatory Breast Cancer: A Different Disease in the Middle East?"

Sherif Omar, MD (surgical oncologist, Cairo, Egypt)

Appendix H. Plenary Session Agenda of the Health Care Systems and Public Policy Panel

Advocate Presentation

Ranjit Kaur, MS, President, Reach for Recovery/International Union Against Cancer (UICC); President, Breast Cancer Welfare Association; Chairman, Malaysian Breast Cancer Council, Malaysia

"Global Breast Cancer Statistics: The 5 Continents Databases and GLOBOCAN"

D. Maxwell Parkin, PhD (formerly with International Agency on Research in Cancer, WHO, France; currently consultant, Clinical Trials Service Unit and Epidemiological Studies Unit, University of Oxford, United Kingdom)

"Health Care Systems in Developing versus Developed Countries"

Rafael Bengoa, MD (Director, Health System Policies and Operations, World Health Organization, Switzerland)

"Cost-Effectiveness as a Tool for Priority Setting in Developing Countries"

Scott Ramsey, MD, PhD (health economist, Translational and Outcomes Research Group, Fred Hutchinson Cancer Research Center, Seattle, Washington)

"Global and Regional Cost and Effects of Breast Cancer Control"

Rob Baultussen, PhD (health economist, The Netherlands)

"Tackling Early Detection of Breast Cancer in Multicultural Societies"

Larissa Remennick, PhD (medical sociologist, Israel)

"Public Education and Advocacy in Implementing Health Care Change"

Susan Braun, MA (President and CEO, Susan G. Komen Breast Cancer Foundation, Dallas, Texas)
