



Complete Summary

GUIDELINE TITLE

Breast cancer in limited-resource countries: diagnosis and pathology.

BIBLIOGRAPHIC SOURCE(S)

Shyyan R, Masood S, Badwe RA, Errico KM, Liberman L, Ozmen V, Stalsberg H, Vargas H, Vass L. Breast cancer in limited-resource countries: diagnosis and pathology. *Breast J* 2006 Jan-Feb;12 Suppl 1:S27-37. [45 references] [PubMed](#)

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE
METHODOLOGY - including Rating Scheme and Cost Analysis
RECOMMENDATIONS
EVIDENCE SUPPORTING THE RECOMMENDATIONS
BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS
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INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES
IDENTIFYING INFORMATION AND AVAILABILITY
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SCOPE

DISEASE/CONDITION(S)

Breast cancer

GUIDELINE CATEGORY

Diagnosis

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Nursing
Obstetrics and Gynecology
Oncology

Pathology
Radiation Oncology
Radiology
Surgery

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Health Care Providers
Hospitals
Nurses
Physician Assistants
Physicians
Public Health Departments

GUIDELINE OBJECTIVE(S)

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 diagnosis and pathology

TARGET POPULATION

Women with breast cancer in limited-resource countries

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

1. Medical history
2. Clinical breast examination
3. Physical examination
4. Assessment of metastatic disease, including judicious use of chest radiograph, liver ultrasound, and bone scan
5. Breast imaging, including diagnostic mammography and diagnostic ultrasound
6. Pathology diagnosis performed by trained staff using sterile technique
 - Minimally invasive biopsy guided by palpation or imaging
 - Fine-needle aspiration biopsy
 - Core needle biopsy
 - Limited image-guided sampling
 - Surgical biopsy
 - Onsite cytologist/cytopathologist
7. Hormone receptor testing
8. HER-2/*neu* testing*
9. Advanced imaging studies*
10. Stereotactic biopsy*
11. Sentinel node biopsy*
12. Immunohistochemical staining to detect micrometastases*

Note: *Interventions requiring maximal resources

Record Keeping

1. Permanent, quality medical records
2. Documentation of follow-up
3. Pathology report
4. Local, regional, and national registries

Quality Assurance and Standardization

1. Formal quality assurance procedures
2. Standardized pathology procedures and reports

MAJOR OUTCOMES CONSIDERED

- Level of breast cancer awareness
- Timeliness and accuracy of breast cancer diagnosis, including diagnosis of benign, malignant, invasive, or non-invasive breast lesions
- Tumor stage at diagnosis
- Tumor size at diagnosis
- Aggressiveness of therapy required
- Breast cancer morbidity and mortality rates
- Cost effectiveness

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The Breast Health Global Initiative (BHGI) 2005 Guideline panel for early detection and access to care relied on the literature review performed for the 2002 BHGI report and conducted a new MEDLINE search under the subject headings "breast awareness," "clinical breast examination," "breast self-examination," and "mammography," limited to the English language, from 2000 to 2005. They also performed an additional PubMed search under the subject headings "breast cancer," "low-resource countries," and "developing countries," also limited to the English language, from 1990 to 2005.

NUMBER OF SOURCE DOCUMENTS

219

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Source documents were circulated among expert consensus panelists prior to Global Summit review; commentary and review collected and collated in conjunction with preparation of consensus documents.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Consensus Statement Preparation

The observations from the 2002 Breast Health Global Initiative (BHGI) Global Summit (see companion document, "Breast Cancer in Limited-Resource Countries: An Overview of the Breast Health Global Initiative 2005 Guidelines" in the "Availability of Companion Documents" field) served as the basis of the 2005 BHGI Global Summit, where specific recommendations were addressed.

The BHGI guidelines were reexamined, revised, and extended at the 2005 BHGI Global Summit. Twelve national and international groups joined the BHGI as collaborating organizations (See Appendix A of the companion document, Breast Cancer in Limited-Resource Countries: An Overview of the Breast Health Global Initiative 2005 Guidelines" in the "Availability of Companion Documents" field). In addition, to obtain input on international guideline development, the BHGI established affiliations with three World Health Organizations 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 diagnosis and pathology panel was charged with reviewing, updating, and extending the previously published guidelines on this topic and were asked to prepare a consensus statement summarizing the outcome of their work.

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 the panel's conference day and for organizing and executing the writing of the panel's consensus statement. The panels held one full-day meeting. In the morning, summit participants gave plenary presentations on topics related to the diagnosis and pathology of the disease, and current approaches and barriers to delivery of these services in parts of the world where resources are

markedly constrained (see Appendix F of the companion document, Breast Cancer in Limited-Resource Countries: An Overview of the Breast Health Global Initiative 2005 Guidelines" in the "Availability of Companion Documents" field). In the afternoon, the panel reviewed the available evidence, the Breast Health Global Initiative (BHGI) 2003 guidelines on diagnosis, and current international guidelines on breast cancer diagnosis; debated approaches to diagnosis and pathology under the constraints of limited resources; and drafted preliminary recommendations. 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.

The panel was 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 area of diagnosis and pathology. Finally, the panel was asked to identify areas where evidence is lacking and research is needed to better inform future iterations of the guidelines.

The panel's discussion and debate was recorded and transcribed, and the transcript was used as the basis for writing each consensus statement. Panel discussion was directed at creating stratification tables, which list how resources should be allocated based on the definitions of basic, limited, enhanced, and maximal. Panel coauthors coordinated the writing of the statement, sections of which were coauthored by participating panelists.

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.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

Published cost analyses were reviewed in the preparation of this guideline.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Consensus Statement Review

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 coauthors.

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 coauthors and language was adopted to minimize the level of perceived inconsistencies. 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 the companion document, *Breast Cancer in Limited-Resource Countries: An Overview of the Breast Health Global Initiative 2005 Guidelines*.

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 and goals of the Breast Health Global Initiative (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. The combination of consensus and individual statements represents a complete BHGI guideline compendium, which is the final work product of the 2005 Global Summit.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

To encourage a consistent approach to the discussion and the guidelines, the panel was asked to stratify health care resources relevant to their assigned areas into one of four levels (Basic, Limited, Enhanced, and Maximal). Definitions for the levels are provided at the end of the "Major Recommendations" field.

Issues Related to Diagnosis and Pathology

Goal of Diagnosis

The primary goal of diagnosis in countries with limited resources, just as in countries with abundant resources, is to accurately distinguish benign from malignant breast lesions and invasive from noninvasive breast lesions, thereby

permitting delivery of timely and appropriate care. The panel reaffirmed three main themes of the first summit: 1) that improving breast cancer awareness and education facilitates diagnosis of the disease at an early stage; 2) that early diagnosis is advantageous because it is lifesaving and cost effective, and requires less aggressive therapy; and 3) that collecting accurate national statistics about breast cancer (type, tumor size, stage, treatment, and outcome), available resources (personnel, equipment, and facilities), and competing priorities (health or other issues) will help to tailor these guidelines for breast cancer diagnosis and pathology to the needs of an individual country.

Definitions

The panel also reaffirmed the key distinction between a clinical diagnosis and a pathology diagnosis. Clinical diagnosis refers to a diagnosis based on a combination of the history, findings on a clinical breast examination (CBE), and results of breast imaging studies (mammography and ultrasound). These findings may suggest a benign or malignant diagnosis.

Pathology diagnosis, also called tissue diagnosis, refers to a diagnosis based on the microscopic features of cells or tissues, which allow a lesion to be properly categorized pathologically. The interpretation of these microscopic findings is the definitive diagnosis (i.e., the final word).

Simplicity of the Process

Simplicity in the diagnostic process is critical in limited-resource settings because patients may face numerous barriers that prevent repeated visits. To address such barriers and increase compliance, diagnostic tests and tissue sampling techniques should be used in a combination that allows establishing the pathology diagnosis and assessing the extent of the disease in one visit.

Quality of the Process

Panelists emphasized that it is important not only that a diagnostic test is available but also that it is done competently so that a correct diagnosis is made and the treatment providers can be confident about the results. Specific recommendations on quality assurance and standardization of practices are provided in a later section.

Correlation of Findings

Regardless of the type of tissue sampling that is performed for diagnosis, the pathology results must be correlated with all other information, including clinical findings and the findings of imaging studies (if available), to assess for concordance. The panel reaffirmed that this so-called triple test is key for ensuring accurate diagnosis. If the clinical findings, imaging findings, or both are highly suggestive of breast cancer, but the biopsy yields benign findings, the biopsy result is considered discordant; it may be necessary to repeat the biopsy to ensure an accurate diagnosis.

Importance of the System

Implementation of a breast pathology program requires more than the resources needed to perform and interpret the biopsy. This program must be integrated in a comprehensive system that addresses other facets of care. For example, there must be mechanisms in place for specimen labeling and transportation, documentation of pathology results in the patient's medical record, and communication of the results to other health care providers and the patient. Follow-up is also essential after biopsy and enables evaluation of diagnostic performance; this practice is discussed in greater detail in the section on record keeping.

Diagnostic Process

The diagnostic process entails both initial diagnosis (to establish the presence or absence of breast cancer) and, when cancer is present, staging (to determine the extent of disease); the latter may include an examination to ascertain whether a patient has metastases. Knowledge of the stage of the disease is important for estimating prognosis and making choices between curative and palliative therapy. The panel again noted the importance of using the triple test for accurate initial diagnosis and agreed on the need for a judicious approach for the use of tests after diagnosis for staging.

Clinical Assessment

The methods used in clinical assessment for breast cancer include a history, CBE, physical examination, and when appropriate, assessment for metastatic disease.

History

Taking a medical history is the initial step in evaluating a breast complaint. Providers should obtain baseline information regarding symptoms, menopausal status, and breast cancer risk factors, and should document the findings in the patient's record. In addition to obtaining the history relevant to breast health, the panel endorsed obtaining an overall medical history to appropriately document the presence or absence of other illnesses that might affect treatment decisions.

Clinical Breast Examination (CBE)

CBE is a procedure whereby a health care provider examines a woman's breasts, chest wall, and axillae; it can be used as either a screening test or a diagnostic test. When used as a diagnostic test (i.e., in a patient with signs or symptoms of a breast problem), CBE plays a fundamental role in providing information about breast changes that may signal the presence of cancer. A breast mass, nipple discharge, or other changes in the skin, nipple, or both are frequent initial symptoms of breast cancer that require prompt attention. The panel agreed that CBE is important for confirming the presence of a dominant mass and other breast abnormalities, for documenting tumor size, and for determining the local extent of disease.

Physical Examination

In patients with findings suggestive of early breast cancer, physical examination is unlikely to provide diagnostic information beyond that provided by history and CBE, although it may reveal evidence of other illnesses that may have potential implications for treatment decisions, such as malnutrition or acquired immune deficiency syndrome (AIDS). In patients with findings suggestive of advanced breast cancer, physical examination may provide information about the presence of metastases in the lymph nodes and distant sites, as discussed below.

Assessment of Metastatic Disease

Assessment of metastatic disease in patients with primary breast cancer is a component of cancer staging. Patients with metastatic breast cancer uniformly succumb to their disease; however, survival may range from a few months to several years. In countries with limited resources, patients often present with disease that has already metastasized, and proper staging is valuable in planning cancer treatment.

Obtaining a medical history is the first step in the assessment of metastatic disease. Pulmonary, musculoskeletal, and abdominal symptoms may raise clinical suspicion for metastatic disease and prompt a diagnostic examination. Physical examination may reveal lymphadenopathy, hepatomegaly, or bone tenderness that likewise suggests metastatic disease.

Laboratory measurement of the serum alkaline phosphatase level as a method of screening for bone and liver metastases has been suggested. However, elevated alkaline phosphatase levels have high false-positive and false-negative rates. Thus, this test is not a good predictor of bone or liver metastases in patients with breast cancer and cannot be recommended.

A number of studies have evaluated the role of bone scanning, chest radiography, and liver ultrasonography in breast cancer staging at the time of diagnosis. Overall the yield for these imaging studies is low and stage dependent. The prevalence of metastases detected by imaging techniques is near zero in patients with stage I or II breast cancer (0.5%), but dramatically increases in patients with stage III disease (8–40%). In a study of patients with stage III disease, the findings of bone scan, chest radiograph, and liver ultrasound were positive for metastases in 14%, 7%, and 6% of cases, respectively. An additional important consideration is the occurrence of false-positive results in tests with a low yield. Such results cause additional testing at a significantly increased cost and unnecessarily subject patients to anxiety, discomfort, and less frequently, morbidity.

Therefore, the panel recommends a judicious approach to laboratory and imaging studies to assess metastatic disease, regardless of the level of resources available. Extensive, routine laboratory and imaging studies are not justifiable in patients with early breast cancer in the absence of symptoms or physical findings. In contrast, in patients with T4 or N1–2 breast cancer, bone scanning, chest radiography, and liver ultrasonography have a higher yield and are indicated when resources permit. The panel recommends their introduction at the limited resource level (chest radiograph and liver ultrasound) and enhanced-resource level (bone scan).

Breast Imaging

The breast imaging modalities used in diagnosing breast lesions include diagnostic mammography and diagnostic ultrasound.

Diagnostic Mammography

Diagnostic mammography is complementary to physical examination in evaluating women with signs and symptoms of breast cancer, and provides a more accurate assessment of the extent of disease in women known to have cancer. It also provides additional information about the contralateral breast because a small but significant percentage (3–5%) of women with breast cancer will have synchronous or metachronous cancer in the other breast.

Diagnostic mammography requires trained personnel, equipment, facilities, reporting, and follow-up systems, and establishing and maintaining a high-quality diagnostic mammography program is relatively costly. Moreover, this imaging cannot replace the need for a pathology diagnosis in women with signs or symptoms of breast cancer. The panel identified the following factors influencing the decision to introduce diagnostic mammography: 1) the availability of the equipment and skilled personnel, 2) the cost of film for mammography, 3) the predominant size of lesions at presentation (e.g., palpable versus nonpalpable disease), 4) the patient population being assessed (e.g., younger women, who have dense breasts and who may be more likely to have cysts, versus older women), and 5) alternatives for establishing the diagnosis (e.g., aspiration to establish that a mass is a cyst). In addition, in countries with limited resources, few women are able to undergo breast-conserving therapy because of the typically advanced stage of cancer at presentation and because this therapy is resource intensive. In this context, the benefit of determining the extent of cancer within the breast seems low when compared with the cost of a diagnostic mammography program.

The panel concluded that the introduction of diagnostic mammography can be recommended at the limited level of resources. If mastectomy is the only available surgical treatment for breast cancer, diagnostic mammography is not essential; however, if breast conservation is offered, diagnostic mammography is necessary to determine if there is cancer elsewhere in the same quadrant (multifocal disease) or in different quadrants (multicentric disease).

Approaches to treating breast cancer hinge on the stage at the time of diagnosis because treatment for locally advanced breast cancer differs from that for early stage breast cancer. Mammography can help distinguish early stage from late-stage cancer, although this benefit varies depending on the patient and the cancer.

Diagnostic Ultrasound

Breast ultrasound can be used as a screening test (when performed in asymptomatic women, with the goal of identifying otherwise occult breast cancer) or as a diagnostic test (when performed in women with abnormalities on physical examination, mammography, or both). For women who have a palpable breast lump or a focal symptom, ultrasound can play an important role in further

evaluation of the clinical findings. In this group of women, ultrasound has three important contributions: distinguishing simple cysts from solid masses, providing an estimation of the likelihood of malignancy in a solid mass, and guiding tissue sampling for a pathology diagnosis.

Ultrasound, like mammography, can help determine the extent of cancer within the breast, which again is important when breast-conserving therapy can be offered to women. Ultrasound is more widely available than mammography in countries with limited resources and is particularly useful in women with palpable lesions, as noted above. In addition, this modality can also help assess the status of the axilla, can guide a minimally invasive (needle) biopsy in the axilla, and can allow examination of the liver to detect metastatic disease. The panel therefore recommends introduction of diagnostic ultrasound at the limited-resource level.

Pathology Diagnosis

The diagnosis of breast cancer carries prognostic and therapeutic implications that are life changing for a woman. The panel strongly and uniformly recommends that all women suspected of having breast cancer have an accurate pathology diagnosis that confirms the presence of the disease before beginning definitive treatment. This includes women who have clinical findings strongly suggestive of cancer. A pathology diagnosis should not be bypassed, even when health care resources are very limited, because a misdiagnosis of breast cancer can lead to erroneous treatment of women without breast cancer, which is harmful to the woman and wasteful of treatment resources.

The most basic function of pathology in breast care is the formulation of timely and accurate diagnosis. It can be achieved by the use of appropriate biopsy (tissue sampling) techniques, optimal tissue processing, and competent interpretation of gross and microscopic pathology findings. A successful pathology service requires timely and accurate comprehensive reporting, as well as archiving of slides, tissue blocks, and reports with accurate patient and specimen identification.

A variety of methods are available for sampling a breast lesion to determine if it is cancer, and they have comparable accuracy if properly performed. Two general groups of methods are reliable for obtaining a pathology diagnosis: minimally invasive biopsy, also called percutaneous needle biopsy (i.e., fine-needle aspiration biopsy [FNAB] and core needle biopsy), and surgical biopsy (i.e., incisional biopsy and excisional biopsy).

The panel reaffirmed that the choice among these methods in the limited-resource setting will be influenced by factors such as availability of the necessary equipment and expertise. Regardless of the method used, procedures should be performed by appropriately trained staff and with sterile technique to minimize the risk of infectious complications. In addition, single-use equipment should be disposed of after use, and multiuse equipment should be properly sterilized between uses.

Minimally Invasive Biopsy

Minimally invasive biopsy has advantages over surgical breast biopsy. The former is less invasive, less expensive, does not cause scarring or deformity, and can be performed in a clinic, obviating the need for an operating room. For women with early stage breast cancer, minimally invasive biopsy can convert what would otherwise have been two operations (surgical biopsy for diagnosis, followed by definitive surgery for treatment) into one operation (a single definitive surgery after needle biopsy); for women with locally advanced or metastatic breast cancer, it can provide a pathology diagnosis, enabling initiation of treatment.

Minimally invasive biopsy techniques differ with respect to two parameters: the needle used (fine needle versus core needle) and the method used to guide needle placement (palpation versus imaging). For most palpable lumps, the needle can be placed under the guidance of palpation; for other lesions, the needle may be placed with image guidance (discussed below).

Fine-needle aspiration biopsy involves removal of cellular specimens with a small (22- or 25-gauge) needle. Advantages of FNAB include that it is the least invasive and least expensive breast biopsy method. Disadvantages include the need for personnel trained in obtaining and interpreting breast cytology specimens; small sample size, and difficulty in interpreting atypical and indeterminate lesions, as well as a moderately high frequency of insufficient samples. The frequency of insufficient samples, reported in as many as one-third of palpable and nonpalpable lesions, can be minimized by obtaining multiple (e.g., five or more) specimens and by having a cytologist onsite to review them, when feasible.

Fine-needle aspiration biopsy is the most cost-effective approach to biopsy if properly performed and if a quality cytopathology service is available. Provisions can be made to refer the pathology interpretation of the FNAB samples to other regional consultants in specialized centers. In countries with limited resources, the panel recommends introduction of FNAB at the basic level, provided the accompanying requirement for a quality cytopathology service is also met.

Core needle biopsy is also commonly used to obtain tissue samples from breast lesions, particularly nonpalpable and image-detected abnormalities. In this procedure, tissue specimens are removed with a cutting needle (usually 14-gauge) and automated gun. Obtaining multiple (e.g., three to five) specimens maximizes the chance of definitive diagnosis. However, as for FNAB, the success of this procedure depends on appropriate patient selection, the availability of experienced pathologists, and correlation of the pathology findings with the clinical and imaging information. Core needle biopsy has limitations similar to those of FNAB with respect to small sample size and difficulty in interpreting atypical and indeterminate lesions. Given this modality's higher cost and limited availability in many countries, the panel recommends its introduction at the limited-resource level.

Surgical Biopsy

Surgical biopsy is the traditional method for obtaining a pathology diagnosis of breast lesions, and it is considered the gold standard. Surgical biopsy provides tissue for histologic diagnosis and takes advantage of techniques and pathology expertise currently available in most countries. The disadvantages of this method

include its invasive nature and substantial cost when performed in an operating room. However, costs are reduced if it is performed in the outpatient setting.

In countries with limited resources, a majority of women with breast cancer have large primary tumors at the time they seek medical care. A surgical biopsy under local anesthesia is more expensive, time-consuming, and traumatic than minimally invasive biopsy, but provides the greatest amount of histologic information. The panel concluded that this procedure should be introduced at the basic-resource level, provided a country also meets the pathology requirements for that level.

Record Keeping

Note: The recommendations of this panel were integrated with those of the Health Care Systems and Public Policy panel and are presented in the matrix guideline Table 1 in the companion document, "Breast Cancer in Limited-Resource Countries: Health Care Systems and Public Policy" (see "Availability of Companion Documents" field).

All Global Summit panels identified the need for a system of record keeping in countries with limited resources to document the clinical stage of the breast cancer and clinical outcomes, among other information.

Medical Records

Permanent, quality medical records are essential for documenting diagnostic findings, treatments given, and patient outcomes, and for communicating this information to other health care providers. In addition, well-kept medical records are useful for generally assessing the prevailing patterns of breast cancer presentation and care, which can be helpful for planning resource allocation and monitoring changes as additional resources are applied. The panel agreed that medical records should be available at the basic-resource level.

In terms of diagnosis and pathology, the medical record should document the patient's name and unique medical record number, dates, clinical findings, imaging findings, types of biopsies performed (including needle used, whether guidance was used, and number of samples obtained), pathologic findings reported according to the pathologic Tumor Node Metastasis (TNM) (pTNM) system, whether a cytologist was onsite during the procedure (for FNAB), and the patient's outcome (clinical, imaging, and surgical pathology information, when available). The panel endorsed the use of the clinical TNM (cTNM) staging system and, because tumor size substantially affects prognosis and a given T stage applies to a wide range of sizes, the panel also encourages documentation of tumor size. Quality pathology reports, discussed below, should become part of the medical record.

Follow-Up

In addition to its obvious benefits in terms of continuity of care and support for patients, follow-up is essential for assessing and improving diagnostic performance, as previously noted. The frequency of insufficient samples with a

diagnostic method should be documented at the time of the procedure and the outcome data collected during follow-up should be analyzed to assess a given method's true-negative, false-negative, true-positive, and false-positive rates. This follow-up information should help to optimize biopsy procedures based on outcome data. The panel recommends that some form of follow-up be in place at the basic-resource level, recognizing that the method and frequency of follow-up will vary by setting.

Pathology Report

Elaboration of the pathology or cytology report is the responsibility of the pathologist, but requires close collaboration with surgeons and radiologists. Accurate pathologic diagnosis starts with the clinician, who provides relevant historical and physical examination information. The need for the triple test to minimize errors in diagnosis is particularly important when minimally invasive biopsy (FNAB or core needle biopsy) is used.

Prognostic and predictive parameters are useful to guide treatment because there is significant variability in the natural history of breast cancer. Predictive factors, in contrast, are clinical, pathologic, and biologic characteristics that are used to estimate the likelihood of response to a particular type of therapy. Features such as tumor size, lymph node status, histopathologic type, and tumor grade should be universally documented because of their limited cost and important prognostic significance. Conceptually, these features are useful in providing patients an estimate of prognosis, which facilitates their education, involvement in their therapy, and respect for their autonomy.

In the limited-resource setting, assessment of the expression of estrogen receptors, progesterone receptors, or both is recommended only if hormonal therapy such as tamoxifen, aromatase inhibitors, or surgical or medical ovarian ablation is possible. The panel recommends introduction of this assessment at the limited level, although some panelists favored introducing it at the basic level instead.

Measurement of HER-2/*neu* is problematic because the cost of immunohistochemical analysis, fluorescence in situ hybridization, and trastuzumab therapy is prohibitively expensive in the limited-resource setting; therefore the panel recommends introducing this test only at the maximal-resource level. Such important pathologic pieces of information as the status of the microscopic margin of resection and the status of the sentinel node are recommended at the limited level and maximal level, respectively, where resources also allow breast conservation and sentinel lymph node biopsy.

Registries

Whereas medical records provide critical information about breast health and breast care for individual patients, registries provide such information for the populations they cover. Depending on their coverage, registries may be resource intensive. The panel therefore recommends introduction of local, regional, and national registries at the limited, enhanced, and maximal levels, respectively.

Quality Assurance and Standardization

Because treatment decisions and estimations of prognosis are based on the results of diagnostic and pathology tests, these tests must be done at a level that ensures that the information they provide is reliable and useful. Therefore the panel recommends consideration of formal quality assurance procedures whereby diagnostic findings are recorded and the accuracy of these findings is monitored over time. Such procedures help identify areas for improvement. Standardization of pathology procedures and reports is important for better characterizing breast lesions and improving communication among health care providers. A pathology service should provide not only diagnostic information, but also prognostic and predictive information, whenever possible.

Diagnostic capacity is critical to the success of a comprehensive breast health care program in countries with limited resources. This central role of diagnosis highlights the importance of training health care providers in pathology and its subspecialties (e.g., cytopathology). The availability of pathologists with expertise in breast pathology differs around the globe. Approaches for improving breast pathology include training pathologists, establishing pathology services in centralized facilities, and organizing international pathology services. Panelists expressed opposing viewpoints about the advisability of training nonpathologist health care providers (such as nurses) to perform preliminary steps in diagnostic procedures, such as obtaining aspirates for FNAB.

Summary of Recommendations

The panel's consensus guidelines for stratification of diagnostic and pathology methods by level of resources are summarized in the table below.

Resource Allocation for Diagnosis and Pathology			
Level of Resources	Clinical	Pathology	Imaging and Laboratory Tests
Basic	<ul style="list-style-type: none"> • History • Physical examination • Clinical breast examination • Fine-needle aspiration biopsy • Surgical biopsy 	<ul style="list-style-type: none"> • Interpretation of biopsies • Cytology report categorizing cells as malignant, benign or not diagnostic • Surgical or pathology report categorizing lesion as malignant vs. benign, invasive vs. in situ and describing tumor size, lymph node status, histologic type, tumor grade and margin status 	
Limited	<ul style="list-style-type: none"> • Core needle biopsy • Image-guided 	<ul style="list-style-type: none"> • Determination and reporting of ER and PR status 	<ul style="list-style-type: none"> • Diagnostic breast ultrasound

Resource Allocation for Diagnosis and Pathology			
Level of Resources	Clinical	Pathology	Imaging and Laboratory Tests
	sampling (ultrasonographic \pm mammographic)	<ul style="list-style-type: none"> Determination and reporting of margin status 	+/- diagnostic mammography <ul style="list-style-type: none"> Plain chest radiography Liver ultrasound Blood chemistry profile/CBC
Enhanced	<ul style="list-style-type: none"> Preoperative needle localization under mammographic or ultrasound guidance 	<ul style="list-style-type: none"> Onsite cytopathologist 	<ul style="list-style-type: none"> Diagnostic mammography Bone scan
Maximal	<ul style="list-style-type: none"> Stereotactic biopsy Sentinel node biopsy 	<ul style="list-style-type: none"> HER-2/<i>neu</i> status IHC staining of sentinel nodes for cytokeratin to detect micrometastases 	<ul style="list-style-type: none"> CT scanning, PET scan, MIBI scan, breast MRI

Abbreviations: 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.

The requirements for competent performance of each of these methods are shown in a checklist format in Table 2 in the original guideline document. The personnel suggested in this table refer to those generally used in countries with a maximal-resource level; the panel agreed that creative use of existing personnel, cross-training individuals to perform different tasks, and development of incentives to attract and maintain trained personnel may be useful for meeting personnel requirements in the limited-resource setting.

Although there was generally agreement as to the diagnostic and pathology methods that were feasible in countries with limited resources, there was some debate within and between panels regarding the level at which specific methods should be introduced. The panel noted that the resource level applied in a given health unit will depend on factors such as available personnel, equipment, and facilities; the needs of the population served; and competing health care priorities. Such health system considerations are discussed in the companion document "Breast Cancer in Limited-Resource Countries: Health Care Systems and Public Policy" (see the "Availability of Companion Documents" field.).

Basic Level

Minimal diagnostic and pathology requirements include the ability to take a history, perform CBE and physical examination, make a pathology diagnosis of breast cancer by interpreting the specimens obtained by surgical biopsy or FNAB, determine clinical and pathologic stage, and record this information in the medical record. The panel emphasized that even at the basic level, the availability of accurate information regarding breast cancer size and stage at presentation, and breast cancer treatment and outcome is invaluable to determine the next steps required to decrease breast cancer mortality.

Limited Level

At the limited level, characterized by increasing but still constrained resources, the panel recommends that diagnostic breast imaging with ultrasound or mammography be available. Core needle biopsy, as a minimally invasive method for obtaining histological diagnosis, can be performed on palpable masses at low cost, and can provide tissue for immunohistochemical staining to determine hormone receptor status prior to surgical intervention. At the high end of limited resources, the panel also suggests introducing image-guided needle sampling. Panelists agreed that ultrasound guidance for needle biopsy has the advantages of lower cost and multipurpose use of the equipment; in contrast, stereotactic guidance was considered to require a higher (maximal) level of resources. The accompanying guidelines addressing treatment recommend breast-conserving surgery at the limited-resource level; if breast conservation is offered, diagnostic breast imaging is essential. Although the panel uniformly agreed about the importance of assessing hormone receptor status, which in the context of limited resources is practical only if hormonal therapy is available, it disagreed as to whether such assessments should be introduced at the basic or limited level. Also at the limited level, the health unit may have the capability for determining and reporting the margin status and better assessment for metastatic disease with plain chest radiography, liver ultrasound, and blood chemistry profile/ complete blood count.

Enhanced Level

At the enhanced level, the level at which breast conservation is available, the panel recommends introduction of core needle biopsy with mammographic or ultrasound guidance and preoperative needle localization under mammographic or ultrasound guidance. Improved pathology services may involve the presence of an onsite cytopathologist. Higher-level resources should also allow the use of more sophisticated methods of metastatic examination, such as bone scanning.

Maximal Level

The panel's main focus was on developing guidelines for diagnosis and pathology in countries with less than maximal resources. However, maximal resources make available additional diagnostic and related methods that can further improve outcomes in patients with breast cancer, including (but not limited to) stereotactic biopsy, sentinel node biopsy, determination of HER-2/*neu* status, use of immunohistochemical staining to detect micrometastases, and advanced imaging studies. Panelists agreed that although resource constraints may limit the

methods that can be applied in the short term, the maximal level should be the goal for the long term.

Resource Stratification Definitions

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.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is not specifically stated for each recommendation.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Improved timeliness and accuracy of breast cancer diagnosis in limited resource countries
- Improved breast cancer morbidity and mortality in limited-resource countries

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

Although there was generally agreement as to the diagnostic and pathology methods that were feasible in countries with limited resources, there was some debate within and between the 2005 Breast Health Global Initiative panels regarding the level at which specific methods should be introduced. The Diagnosis and Pathology panel noted that the resource level applied in a given health unit will depend on factors such as available personnel, equipment, and facilities; the needs of the population served; and competing health care priorities. Such health system considerations are discussed in the companion document, "Breast Cancer in Limited-Resource Countries: Health Care Systems and Public Policy" (see the "Availability of Companion Documents" field).

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

See the original guideline document and companion document, "Breast Cancer in Limited-Resource Countries: Health Care Systems and Public Policy" (see "Availability of Companion Documents" field) for implementation strategies.

IMPLEMENTATION TOOLS

Chart Documentation/Checklists/Forms
Quick Reference Guides/Physician Guides

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Shyyan R, Masood S, Badwe RA, Errico KM, Liberman L, Ozmen V, Stalsberg H, Vargas H, Vass L. Breast cancer in limited-resource countries: diagnosis and pathology. *Breast J* 2006 Jan-Feb;12 Suppl 1:S27-37. [45 references] [PubMed](#)

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2006 Jan

GUIDELINE DEVELOPER(S)

Breast Health Global Initiative - Professional Association
Fred Hutchinson Cancer Research Center - Private Nonprofit Research Organization
Susan G. Komen Breast Cancer Foundation - Private Nonprofit Research Organization

SOURCE(S) OF FUNDING

Breast Health Global Initiative

GUIDELINE COMMITTEE

Global Summit Diagnosis and Pathology Panel

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the [Fred Hutchinson Cancer Research Center Web site](#).

Print copies: Roman Shyyan, MD, MSc, Surgical Oncology, Lviv Cancer Center, Hasheka St. 2a, 79000, Lviv, Ukraine; E-mail: roma@txnet.com.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Breast cancer in limited resource countries: an overview of the breast health global initiative 2005 guidelines. Breast J 2006 Jan-Feb;12 Suppl 1:S3-15. Available in Portable Document Format (PDF) from the [Fred Hutchinson Cancer Research Center Web site](#).
- Breast cancer in limited-resource countries: health care systems and public policy. Breast J 2006 Jan-Feb;12 Suppl 1:S54-69. Available in Portable Document Format (PDF) from the [Fred Hutchinson Cancer Research Center Web site](#).
- The Breast Health Global Initiative (BHGI) resource-stratified matrix guidelines. Breast J 2006 Jan-Feb;12 Suppl 1:S117-20. Available in Portable Document Format (PDF) from the [Fred Hutchinson Cancer Research Center Web site](#).

Print copies: Available from Benjamin O. Anderson, MD, Department of Surgery, Box 356410, University of Washington, Seattle, WA 98195, USA, or e-mail: banderso@u.washington.edu.

Additionally, a checklist of the requirements for competent performance of the recommended diagnostic and pathology methods can be found in the [original guideline document](#).

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on July 28, 2006. The information was verified by the guideline developer on August 28, 2006.

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