THE BREAST HEALTH GLOBAL INITIATIVE

SUMMARY TABLES FROM THE GUIDELINES FOR INTERNATIONAL BREAST HEALTH AND CANCER CONTROL-IMPLEMENTATION

Excerpt from Anderson BO, Yip CH, Smith RA, et al. Cancer 2008;113(8 suppl):2221-43

The Breast Health Global Initiative

Pan American Health Organization

Regional Office of the World Health Organization

This document includes summary tables extracted from the Guidelines for International Breast Health and Cancer Control Implementation in low- and middle-income countries developed by The Breast Health Global Initiative (BHGI) (*1-5*). For this purpose, the BHGI invited international experts to review and revise previously developed BHGI resource-stratified guideline tables for early detection, diagnosis, treatment and healthcare systems (*6-9*). The resulting evidence-based breast healthcare guidelines are oriented to countries or regions of the world with limited financial resources, establishing the best standard of care that is practical in a given setting to improve breast cancer outcomes. Therefore, interventions are proposed on the bases of a stratification scheme that includes four levels of resources, defined as follows:

Basic level—Core resources or fundamental services that are absolutely necessary for any breast healthcare system to function; basic-level services typically are applied in a single clinical interaction.

Limited level—Second-tier resources or services that are intended to produce major improvements in outcome such as increased survival, and 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 should produce further improvements in outcome and 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 and/or may be recommended by breast care guidelines that do not adapt to resource constraints but that nonetheless should be considered a lower priority than those resources or services listed in the basic, limited, or enhanced categories on the basis of extreme cost and/or impracticality for broad use in a resource-limited environment; to be useful, maximal-level resources typically depend on the existence and functionality of all lower level resources.

The summary tables presented in this document are an excerpt from the complete guidelines that have been published elsewhere (*1*). It is important to note that the table stratification scheme implies incrementally increasing resource allocation at the basic, limited, and enhanced levels. An empty matrix box indicates that additional resource allocation is not mandated beyond those resources required at lower levels. Maximal level resources should not be targeted for implementation in LMCs, even though they may be used in some higher income settings.

The **Breast Health Global Initiative (BHGI)** is a global health alliance of organizations and individuals. The BHGI strives to develop, implement and study evidence-based, economically feasible, and culturally appropriate guidelines for international breast health and cancer control for low- and middle-income countries to improve breast health outcomes.

1. Anderson BO, Yip CH, Smith RA, et al. Guideline Implementation for Breast Healthcare in Low-Income and Middle-Income Countries. Cancer 2008;113(8 suppl):2221–43.

2. Yip CH, Smith RA, Anderson BO, Miller AB, Thomas DB, Ang E-S, Caffarella RS, Corbex M, Kreps GL, McTiernan A: Guideline implementation for breast healthcare in low-income and middle-income countries: Early detection resource allocation. Cancer 2008;113(8 suppl.):2244-56.

3. Shyyan R, Sener SF, Anderson BO, Fernandex Garrote LM, Hortobagyi GN, Ibarra JA, Ljung B-M, Sancho-Garnier H, Stalsberg H: Guideline implementation for breast healthcare in low-income and middle-income countries: Diagnosis resource allocation. Cancer 2008;113(8 suppl.):2257-68.

4. Eniu A, Carlson RW, El Saghir NS, Bines J, Bese NS, Vorobiof D, Masetti R, Anderson BO: Guideline implementation for breast healthcare in low-income and middle-income countries: Treatment resource allocation. Cancer 2008;113(8 suppl.):2269-81.

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6. Smith RA, Caleffi M, Albert US, et al. Breast cancer in limited-resource countries: early detection and access to care. Breast J. 2006;12(1 suppl):S16-S26.

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		LEVEL OF AVAILABLE RESOURCES			
		BASIC	**LIMITED**	**ENHANCED**	**MAXIMAL**
EARLY DETECTION	**Public Education and Awareness**	• Development of culturally sensitive, linguistically appropriate local education programs for target populations to teach value of early detection, breast cancer risk factors and breast health awareness (education + self-examination)	• Culturally and linguistically appropriate targeted outreach/ education encouraging CBE for age groups at higher risk administered at district/provincial level using healthcare providers in the field	• Regional awareness programs regarding breast health linked to general health and women's health programs	• National awareness campaigns regarding breast health using media
	Detection Methods	• Clinical history and CBE	• Diagnostic breast US +/- diagnostic mammography in women with positive CBE • Mammographic screening of target group[1]	• Mammographic screening every 2 years in women ages 50-69[1] • Consider mammographic screening every 12-18 months in women ages 40-49[1]	• Consider annual mammographic screening in women ages 40 and older • Other imaging technologies as appropriate for high-risk groups[2]
	Evaluation Goal	• Breast health awareness regarding value of early detection in improving breast cancer outcome	• Downsizing of symptomatic disease	• Downsizing and/ or downstaging of asymptomatic disease in women in highest yield target groups	• Downsizing and/ or downstaging of asymptomatic disease in women in all risk groups
DIAGNOSIS	**Clinical**	• History • Physical examination • CBE • Tissue sampling for cancer diagnosis (cytologic or histologic) prior to initiation of treatment	• US-guided FNAB of sonographically suspicious axillary nodes • Sentinel lymph node (SLN) biopsy with blue dye[3]	• Image guided breast sampling • Preoperative needle localization under mammo and/or US guidance • SLN biopsy using radiotracer[3]	
	Imaging and Lab Tests	See footnote 4	• Diagnostic breast US • Plain chest & skeletal radiography • Liver US • Blood chemistry profile[4] • CBC[4]	• Diagnostic mammography • Specimen radiography • Bone scan, CT scan • Cardiac function monitoring	• PET scan, MIBI scan, breast MRI, BRCA 1/2 testing • Mammographic double reading
	Pathology	• Pathology diagnosis obtained for every breast lesion by any available sampling procedure • Pathology report containing appropriate diagnostic and prognostic/predictive information to include tumor size, lymph node status, histologic type and tumor grade • Process to establish hormone receptor status possibly including empiric assessment of response to therapy[5] • Determination and reporting of TNM stage	• Determination of ER status by IHC[5] • Determination of margin status, DCIS content, presence of LVI • Frozen section or touch prep SLN analysis[6]	• Measurement of HER-2/ neu overexpression or gene amplification[6] • Determination of PR status by IHC	• IHC staining of sentinel nodes for cytokeratin to detect micrometastases • Pathology double reading Gene profiling tests

NOTES

Resource allocation for early detection for breast cancer. CBE indicates clinical breast examination; **US**: ultrasound; +/-, with or without. **1:** Target group selection for mammographic screening should consider breast cancer demographics and resource constraints within the population. Please see text for complete discussion. **2:** It has been demonstrated that breast magnetic resonance imaging is more sensitive than mammography in detecting tumors in asymptomatic women who have an inherited susceptibility to breast cancer.

Diagnosis resource table for breast cancer. CBE indicates clinical breast examination; **TNM**, classification of malignant tumor system; **US**, ultrasound; **FNAB**, fine-needle aspiration biopsy; **SLN**, sentinel lymph node; **CBC**, complete blood count; **ER**, estrogen receptor; **IHC**, immunohistochemistry; **DCIS**, ductal carcinoma in situ; **LVI**, lymphovascular invasion; mammo, mammography; **CT**, computed tomography; **HER-2**, human epidermal growth factor receptor 2; **PR**, progesterone receptor; **PET**, positron emission tomography; **MIBI**, methoxy-isobutyl-isonitrile; **BRCA1/2**, breast cancer genes 1 and 2. **3:** The use of SLN biopsy requires clinical and laboratory validation of the SLN technique. **4:** Systemic chemotherapy requires blood chemistry profile and CBC testing for safety. When chemotherapy is available at the basic level, these tests also should be provided. **5:** ER testing by IHC is preferred for establishing hormone receptor status and is cost effective when tamoxifen is available. When tamoxifen is available at the basic level, IHC testing of ER status also should be provided. **6:** If the costs associated with trastuzumab were substantially lower, trastuzumab would be used as a limited-level. In this case, measurement of HER-2/neu overexpression and/or gene amplification would also need to be available at the limited level in order to properly select patients for this highly effective but expensive HER-2/neu targeted biological therapy.

		TREATMENT	LEVEL OF AVAILABLE RESOURCES: BASIC	LIMITED	ENHANCED	MAXIMAL
STAGE I	Local-regional treatment	Surgery	Modified radical mastectomy	Breast conserving surgery[1] Sentinel lymph node (SLN) biopsy with blue dye[2]	SLN biopsy using radiotracer[2] Breast reconstruction surgery	
		Radiation Therapy			Breast-conserving whole-breast irradiation as part of breast-conserving therapy[1]	
	Systemic treatment	Chemotherapy		Classic CMF[3] AC, EC, or FAC[3]	Taxanes	Growth factors Dose-dense chemotherapy
		Endocrine Therapy	Oophorectomy in premenopausal women Tamoxifen[4]		Aromatase inhibitors LH-RH agonists	
		Biological therapy		See footnote 5	Trastuzumab for treating HER-2/neu positive disease[5]	
STAGE II	Local-regional treatment	Surgery	Modified radical mastectomy	Breast c onserving surgery[1] Sentinel lymph node (SLN) biopsy with blue dye[2]	SLN biopsy using radiotracer[2] Breast reconstruction surgery	
		Radiation Therapy	See footnote 6	Postmastectomy irradiation of chest wall and regional nodes for high-risk cases[6]	Breast-conserving whole-breast irradiation as part of breast-conserving therapy[1]	
	Systemic treatment	Chemotherapy	Classic CMF[3] AC, EC, or FAC[3]		Taxanes	Growth factors Dose-dense chemotherapy
		Endocrine Therapy	Oophorectomy in premenopausal women Tamoxifen[4]		Aromatase inhibitors LH-RH agonists	
		Biological therapy		See footnote 5	Trastuzumab for treating HER-2/neu positive disease[5]	

NOTES

Treatment resource allocation table for stage I and stage II breast cancer. SLN indicates sentinel lymph node; **CMF**, cyclophosphamide, methotrexate, and 5-fluorouracil; **AC**, doxorubicin and cyclophosphamide; **EC**, epirubicin and cyclophosphamide; **FAC**, 5-fluorouracil, doxorubicin, and cyclophosphamide; **LH-RH**, luteinizing hormone-releasing hormone; **HER-2/neu**, human epidermal growth factor receptor 2.

1: Breast-conserving surgery can be provided as a limited-level resource but requires breast-conserving radiation therapy. If breast-conserving radiation is unavailable, then patients should be transferred to a higher level facility for postlumpectomy radiation. **2:** The use of SLN biopsy requires clinical and laboratory validation of the SLN technique. **3:** Systemic chemotherapy requires blood chemistry profile and complete blood count testing for safety. When chemotherapy is available at the basic level, these tests also should be provided. **4:** ER testing by IHC is preferred for establishing hormone receptor status and is cost effective when tamoxifen is available. When tamoxifen is available at the basic level, then IHC testing of ER status also should be provided. **5:** If the costs associated with trastuzumab were substantially lower, trastuzumab would be used as a limited-level. In this case, measurement of HER-2/neu overexpression and/or gene amplification would also need to be available at the limited level in order to properly select patients for this highly effective but expensive HER-2/neu targeted biological therapy. **6:** Chest wall and regional lymph node irradiation substantially decreases the risk of postmastectomy local recurrence. If available, it should be used as a basic-level resource.

		TREATMENT	LEVEL OF AVAILABLE RESOURCES: BASIC	LIMITED	ENHANCED	MAXIMAL
LOCALLY ADVANCED	Local-regional treatment	Surgery	Modified radical mastectomy		Breast conserving surgery Breast reconstruction surgery	
		Radiation Therapy	See footnote 1	Postmastectomy irradiation of chest wall and regional nodes[1]	Breast-conserving whole-breast irradiation as part of breast-conserving therapy	
	Systemic treatment (Adjuvant and neoadjuvant)	Chemotherapy	Preoperative chemotherapy with AC, EC, FAC, or CMF[2]		Taxanes	Growth factors Dose-dense chemotherapy
		Endocrine Therapy	Oophorectomy in premenopausal women Tamoxifen[3]		Aromatase inhibitors LH-RH agonists	
		Biological therapy		See footnote 4	Trastuzumab for treating HER-2/neu positive disease[4]	
METASTASIC & RECURRENT	Local-regional treatment	Surgery	Total mastectomy for ipsilateral breast tumor recurrence after breast conserving surgery			
		Radiation Therapy		Palliative radiation therapy		
	Systemic treatment	Chemotherapy		Classic CMF[2] Anthracycline monotherapy or in combination[2]	Sequential single agent or combination chemotherapy Trastuzumab Lapatinib	Bevacizumab
		Endocrine Therapy	Oophorectomy in premenopausal women Tamoxifen[3]		Aromatase inhibitors	Fulvestrant
		Biological therapy	Nonopioid and opioid analgesics and symptom management		Bisphosphonates	Growth factors

NOTES

Treatment resource allocation table for locally advanced breast cancer, metastatic (stage IV) and recurrent breast cancer . AC indicates doxorubicin and cyclophosphamide; **EC**, epirubicin and cyclophosphamide; **FAC**, 5-fluorouracil, doxorubicin, and cyclophosphamide; **CMF**, cyclophosphamide, methotrexate, and 5-fluorouracil; **LH-RH**, luteinizing hormone-releasing hormone; **HER-2/neu**, human epidermal growth factor receptor 2.

1: Chest wall and regional lymph node irradiation substantially decreases the risk of postmastectomy local recurrence. If available, it should be used as a basic-level resource. **2:** Systemic chemotherapy requires blood chemistry profile and complete blood count testing for safety. When chemotherapy is available at the basic level, these tests also should be provided. **3:** ER testing by IHC is preferred for establishing hormone receptor status and is cost effective when tamoxifen is available. When tamoxifen is available at the basic level, then IHC testing of ER status also should be provided. **4:** If the costs associated with trastuzumab were substantially lower, trastuzumab would be used at a limited level. In this case, measurement of HER-2/neu overexpression and/or gene amplification would also need to be available at the limited level in order to properly select patients for this highly effective but expensive HER-2/neu targeted biological therapy.

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