

Can Guidelines for Breast Cancer Treatment in Developing Countries Improve Outcome ?



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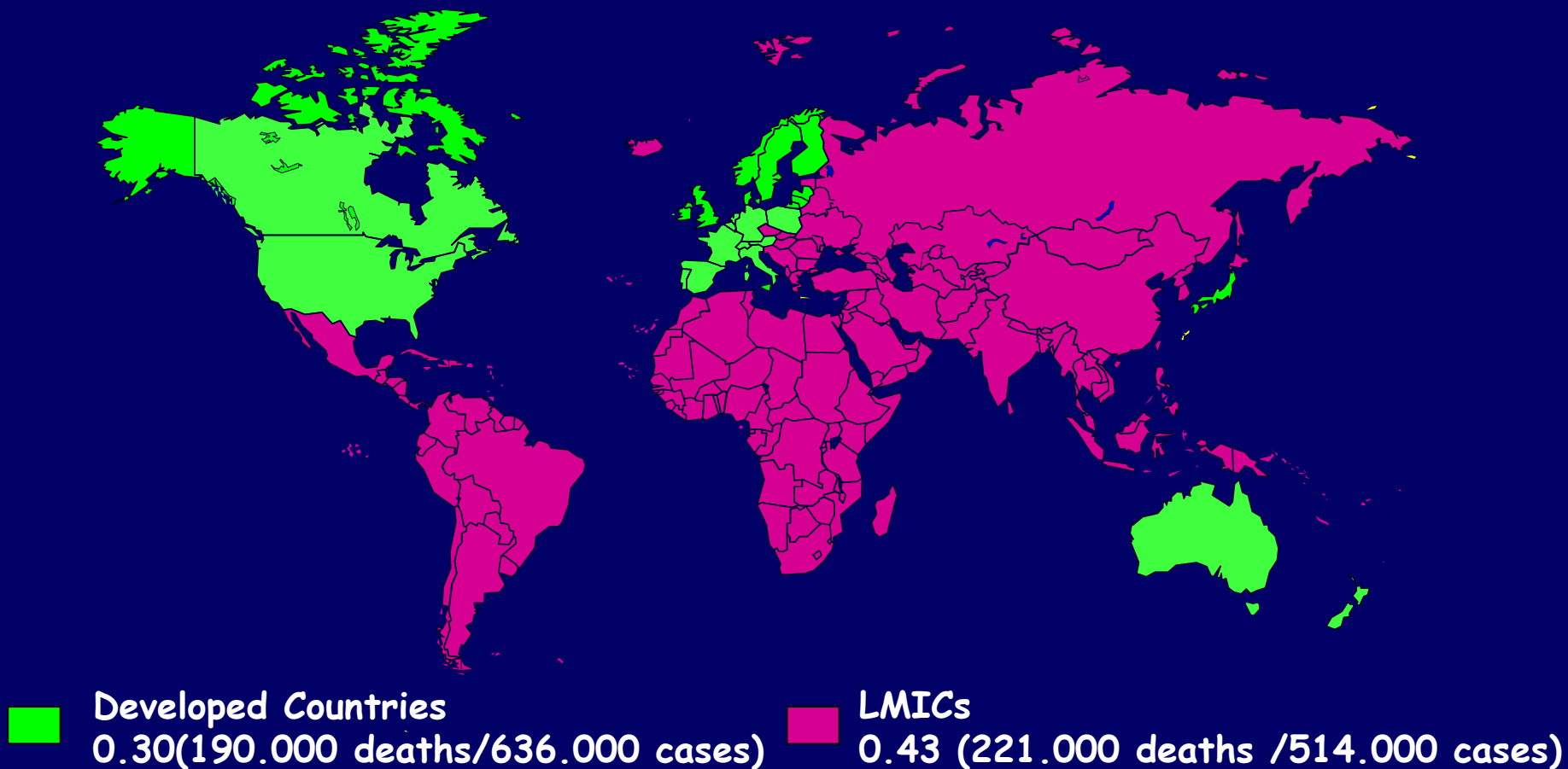
- ✓ Breast cancer in developed and low-middle income countries (LMIC)
- ✓ Guidelines for breast cancer treatment in developed countries
- ✓ The Breast Health Global Initiative (BHGI), and Guidelines for breast cancer treatment in LMICs

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Breast Cancer Incidence / Mortality



Parkin DM et al. *CA Cancer J Clin.* 2005
Globocan 2002 (IARC)

- ✓ The breast cancer burden in LMICs predictably will continue to increase in coming years on the basis of
 - 1) increasing life expectancy and,
 - 2) shifting reproductive and behavioral patterns associated with heightened breast cancer risk.

- ✓ There could be a nearly 50% increase in global incidence and mortality between 2002 and 2020 due to demographic changes alone.

Ferlay J, Bray F, Pisani P, Parkin DM. GLOBOCAN 2002: Cancer Incidence, Mortality and Prevalence Worldwide. IARC CancerBase Available at:<http://www-dep.iarc.fr/>. Accessed on August 26, 2008..

✓ Breast cancer incidence has been increasing in Turkey, and the estimated number of breast cancer cases in 2007 was 44,253.

✓ The breast cancer incidence in Western Turkey (50/100,000) is more than two times that of Eastern Turkey (20/100,000) due to 'Westernized' lifestyles in the last two decades.

Fidaner C, Parkin EJCancer 1993

Ozmen V, Anderson BO US Oncology 2008

Ozmen V, Breast cancer in the world and Turkey, J Breast Health, 2008

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American Society of Clinical Oncology
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NCCN

st. gallen oncology
primary therapy of early breast cancer conferences

NCCN Clinical Practice
Guidelines in Oncology™

- ✓ Evidence based guidelines for breast cancer treatment have been developed for countries with high-level health-care resources.
- ✓ The aims of these guidelines are to find the most effective but, usually expensive treatments of BC.

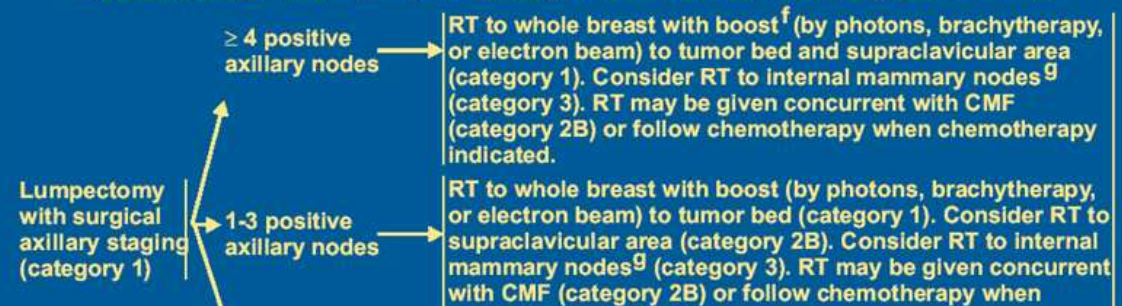
clinical recommendations

Annals of Oncology 18 (Supplement 2): iii-iiiB, 2007
doi:10.1093/annonc/mdm015

Primary breast cancer: ESMO Clinical Recommendations for diagnosis and follow-up



LOCOREGIONAL TREATMENT



special article

Annals of Oncology 18: 1133-1144, 2007
doi:10.1093/annonc/mdm277

Progress and promise: highlights of the international expert consensus on the primary therapy of early breast cancer 2007

A. Goldhirsch^{1*}, W. C. Wood², R. D. Gelber³, A. S. Coates⁴, B. Thürlimann⁵, H.-J. Senn⁶ & Panel Members[†]

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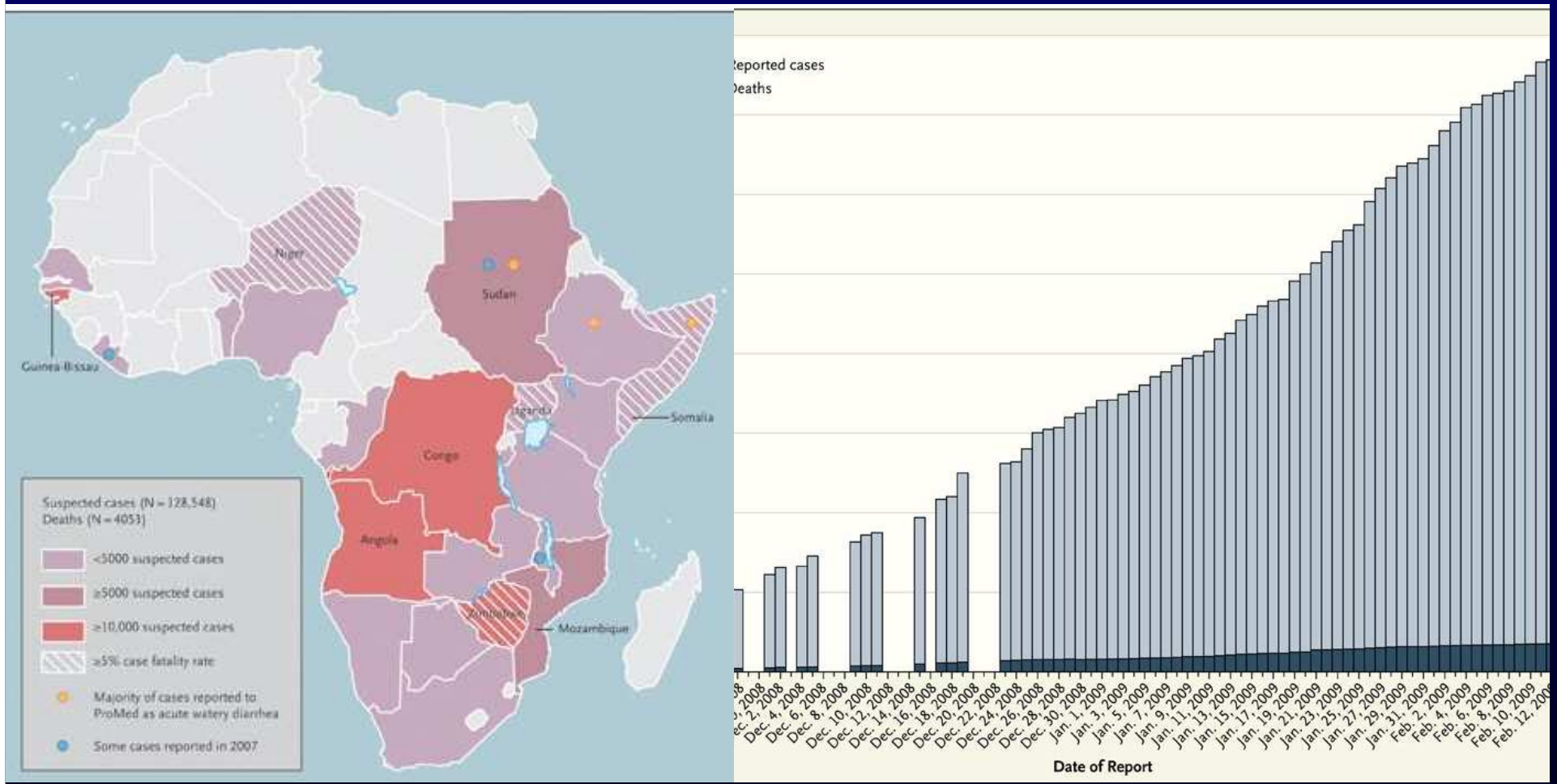
Why another consensus guidelines are necessary for breast cancer treatment in LMICs ?

•While guidelines have been created in the U.S. and Europe for breast cancer treatment, most of them cannot be realistically applied in low-middle income countries (LMICs).

Reasons:

- limited funding,
- infrastructure, staffing and training,
- insufficient health-care systems

A Lion in Our Village – The Unconscionable Tragedy of Cholera in Africa, with as many as one in five persons with severe illness dying for lack of safe drinking water and sanitation and a simple therapy consisting of salt, sugar, and water.



Map of Cholera Outbreaks in Sub-Saharan Africa in 2008, Showing Numbers of Suspected Cases per Country, and Cholera Cases and Deaths in Zimbabwe (November 20, 2008-February 12, 2009)

Mintz E and Guerrant R. N Engl J Med 2009;360:1060-1063

✓ Significantly limited health care resources pose unique challenges

- Unavailable parameters prohibit the use of guidelines

- Because of lack of resources, we are forced sometimes to make decisions against our best medical knowledge

- Clinician= manager of scarce resources



Mission

The Breast Health Global Initiative (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.



- ✓ The BHGI guidelines are intended to assist ministers of health, policymakers, administrators, and institutions in prioritizing resource allocation as breast cancer treatment programs are implemented and developed in their resource-constrained countries.

BHGI 2007 AWARDS PILOT RESEARCH AND DEMONSTRATION PROJECTS

SOUTHEAST ASIA	Health Care Systems Project
Project 1 PI	Kardinah, MD, Dharmais Hospital, National Cancer Center Jakarta, Indonesia
Project 1 Title	"Early breast cancer detection through clinical breast examination training for midwives in rural Jakarta, Indonesia" Approved FUNDED
SOUTH AMERICA	Early Detection Projects
Project 2 PI	Raul Murillo, MD, Instituto Nacional de Cancerologia de Colombia (National Cancer Institute of Colombia), Bogota, Colombia
Project 2 Title	"Pilot introduction of breast cancer early detection programs in Colombia" Approved FUNDED
EAST EUROPE	Early Detection Projects
Project 3 PI	Vahit Özmen, MD, FACS, Professor of Surgery, Istanbul University, Department of Surgery, Istanbul, Turkey
Project 3 Title	"Survey on a pilot mammographic screening program in Bahcesehir Istanbul, Turkey" Approved FUNDED
Project 4 PI	Alexandru Eniu, MD, Cancer Institute "I. Chiricuta", Dept. of Breast Tumors (oncology) Cluj-Napoca, Romania
Project 4 Title	"What do you need to participate in cancer clinical studies as a research center: A Checklist - based recommendation" Approved FUNDING
EAST AFRICA	Health Care Systems Project
Project 5 PI	William Mbabazi, MD, National Program Officer (NPO), Epid-surveillance/ Integrated disease surveillance and response (EPI/IDSR) Officer, World Health Organization, Uganda Country Office / (WHO Uganda/UNEPI) Kampala, Uganda
Project 5 Title	"Establishing a breast health initiative for Uganda" Approved FUNDING

To successfully implement the BHGI guidelines in LMICs, 3 goals must be addressed.

- ✓ First, dissemination and implementation strategies need to be studied and developed in different LMIC environments, so that guideline adoption takes place.
- ✓ Second, education of the public, of healthcare providers, and of health system administrators is necessary for guideline adoption to be successful and sustained.
- ✓ Third, effective and affordable technology for detection, diagnosis, and treatment must be achieved in target LMICs so that cancer diagnosis and treatment is performed correctly.

BHGI GLOBAL SUMMIT 2005:

Resource Stratification

- ✓ **Basic level** — Core resources or fundamental services necessary for any breast health care system to function.
- ✓ **Limited level** — Second-tier resources or services that produce major improvements in outcome such as survival.
- ✓ **Enhanced level** — Third-tier resources or services that are optional but important, because they increase the number and quality of therapeutic options and patient choice.
- ✓ **Maximal level** — Highest-level resources or services used in some high resource countries that have lower priority on the basis of extreme cost and/or impracticality.

Principles for allocation of resources (WHO)

- ✓ Rational use
- ✓ Equity in access to treatment
- ✓ "Minimum standard of care"
- ✓ Build a strategy for improving care
- ✓ Incremental, step-by-step allocation
- ✓ Multidisciplinary breast centers
- ✓ Optimal care to all is the ultimate goal, BUT...
- ✓ Resource constraints may necessitate intermediate steps

Level of resources (2)

- ✓ = level on which *the health unit functions*
- ✓ To pass to next level, all resources for the preceding level(s) have to be *available to all patients* in the health unit
- ✓ different levels may coexist within a country
- ✓ short-term goal : advance to the next-higher level
- ✓ long-term goal : advance to the optimal level

Breast Cancer Surgery Checklist

Therapy	Strengths	Weaknesses	Required Resources
MRM	Rapid treatment Curative for early breast cancer Technology to perform widely available	Disfiguring	Staff: Surgeon, anesthesiologist, pathologist, nurses, physiotherapist, medical social worker/counselor Surgical resources: Operating theater, anesthetics, postoperative care system
BCS with axillary dissection	Rapid surgical treatment	Technically demanding Not appropriate for all patients Requires ability to assess margin status by breast imaging and pathology Requires application of postoperative radiation therapy as potentially curative therapy for breast cancer	Surgical staff and resources as above under MRM Resources included in Table 2
SLN with blue dye	Allows for accurate identification of SLN Minimizes postsurgical morbidity in women with negative axillary lymph nodes	Requires experienced SLN team Rare allergic reactions	Staff: Experienced surgeon, experienced pathologist
SLN with radiotracer	Allows for accurate identification of SLN Minimizes postsurgical morbidity in women with negative axillary lymph nodes	Requires experienced SLN team Special handling of radiotracer	Staff: Experienced surgeon, experienced pathologist Other resources: Procedures, equipment, and facilities for radiotracer handling (nuclear medicine)

MRM indicates modified radical mastectomy; SLN, sentinel lymph node; BCS, breast-conserving surgery.

Breast conserving therapy: Limited or Enhanced?

Treatment Resource Allocation: Stage II Breast Cancer					
Level of resources	Local-regional treatment		Systemic treatment (adjuvant)		
	Surgery	Radiation therapy	Chemotherapy	Endocrine therapy	Biological therapy
Limited	Breast conserving surgery§ Sentinel lymph node (SLN) biopsy with blue dye†	Postmastectomy irradiation of chest wall and regional nodes for high-risk cases§§			***
Enhanced	SLN biopsy using radiotracer† Breast reconstruction surgery	Breast-conserving whole-breast irradiation as part of breast-conserving therapy§	Taxanes	Aromatase inhibitors LH-RH agonists	Trastuzumab for treating HER-2/neu positive disease***

§ Breast conserving surgery can be provided as a limited-level resource, but requires radiation therapy. If radiation therapy is unavailable, patients should be transferred to a higher level facility

Radiationtherapy Checklist: Postlumpectomy Irradiation of the Breast

Strengths	Weaknesses	Required Resources
<ul style="list-style-type: none">•A four- to five-fold reduction in local recurrence and improvement in survival•When added to breast conserving surgery, survival is equivalent to MRM•Preservation of the body-image	<ul style="list-style-type: none">•Overall survival benefit has not been shown in individual trials•Requires access to radiotherapy facility•The treatment course is prolonged (6- 7 weeks)•Close follow-up of the patient for early detection of the local recurrences	<p>Equipment</p> <ul style="list-style-type: none">• Megavoltage tele-therapy equipment• Conventional simulator• Dosimetry equipment• Accessories for immobilization, shielding and dose distribution <p>Quality Assurance</p> <p>Staff</p> <ul style="list-style-type: none">• Radiation oncologist• Medical physicist• Radiotherapy technologists/positioning <p>Support systems that allow receipt of radiotherapy for a period of several weeks</p>

Chemotherapy checklist: Trastuzumab

Strengths	Weaknesses	Required Resources
<p>In HER2-positive breast cancer substantially reduces risks of disease recurrence and death as a component of adjuvant therapy</p> <p>In metastatic HER2 positive breast cancer provides substantial palliation and control of disease as a single agent and in combination with chemotherapy</p> <p>Limited acute and chronic toxicity</p>	<p>Requires availability of reliable method for determining HER2 over-expression or gene amplification</p> <p>Administered in combination with cytotoxic therapy</p> <p>Optimal duration of treatment unknown</p> <p>Associated with increased risk of symptomatic congestive heart failure, especially when given with an anthracycline containing chemotherapy regimen</p> <p>Occasional allergic infusion reactions</p> <p>Very high drug cost</p>	<p>Pathology</p> <ul style="list-style-type: none"> • reliable HER2 status <p>Ability to monitor cardiac function</p> <ul style="list-style-type: none"> • Echocardiography • Radionuclide left ventricular ejection fraction <p>Pharmacy services to compound drug</p> <p>Physical facilities to administer IV chemotherapeutic drug infusions</p> <p>Resources to administer cytotoxic chemotherapy</p>

Trastuzumab adjuvant therapy: Limited or enhanced?

COUNTRY	Italy		USA	Turkey
Description	Cost(EUR)	Description of Reference	Cost(USD)	Cost(EUR)
Trastuzumab(single dose)	675	Hospital acquisition cost	767	605
IV drug administration	40	Local charge for	50	50
Paclitaxel (overall cost)	2.716	4 doses+4 drug adm.	7.592	3.200
Adj. Trastuzumab (overall cost)	40.100	53 doses+48 drug adm.+4 echocardiographi	44.881	37.325
Aromatase inhibitors	2.117/yr	Local cost	2.701/yr	1.175
Echocardiography	60	Local charge	420	215
Symptomatic cardiac dysfunction	375/3months	Local cost	1.750/3months	1475
Asymptomatic cardiac dysfunction	186/3months	Local cost+charges	1.000/3months	975
Early follow-up(<5years)	96/year	4 visits+1mmg(43.9)	700/year	435
Late follow-up(>5years)	56/year	1 visit+1 mmg	700/year	285
Local relapse(overall cost)	3.780	Local costs+charges	16.200	3.660
Metastatic disease	15.600	Local costs+charges	20.280	11.325

Adjuvant treatment cost

Trastuzumab adjuvant therapy: Limited or enhanced?

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*** If the costs associated with trastuzumab were substantially lower, trastuzumab would be used as a limited-level therapy.

Process metrics : Appropriate quality-assurance and quality-control measures should be integrated into cancer care programs at all levels of early detection, diagnosis, and treatment.

- ✓ measure the effectiveness of a process
- ✓ not a treatment recommendation !
- ✓ identifies a homogeneous subgroup of patients for which consensus exist on treatment recommendation
- ✓ should be simple and inexpensive
- ✓ may provide a way to establish the threshold to be met to move the unit to the next level of resource allocation, based on local conditions

Level of resources	Process Metrics
Basic	<p>Pts diagnosed with cancer underwent MRM (min 75%, target 90%)</p> <p>Chemotherapy for premeno pts with ER- disease within 120d (min 75%, target 90%)</p> <p>Tamoxifen for postmeno pts with ER+ tumors >1 cm within 1 year of diagnosis (min 75%, target 90%)</p>
Limited	<p>Post mastectomy chest wall radiation therapy for high risk women <70 years within 1 year of mastectomy: minimum 75%, target 90%</p> <p>Sentinel node identification (min 75%, target 90%)</p>
Enhanced	<p>Sentinel node identification (min 90%, target 95%)</p> <p>Chemo for premeno pts w/ ER- ca w/i 120d (min 90%, target 95%)</p> <p>Hormone tx for pts with ER+ ca w/i 1 yr (min 90%, target 95%)</p> <p>XRT post BCT for pts <70 yrs w/i 1 yr (min 75%, target 90%)</p>



CONCLUSIONS-1

- ✓ Breast cancer incidence and mortality rates have been increasing in LMICs.
- ✓ Guidelines created in the U.S. and Europe for breast cancer treatment cannot be realistically applied in low-middle income countries (LMICs).
- ✓ Resource constraints impose alterations of the multidisciplinary pattern of care, such as limitation of breast conserving surgery, targeted therapy, etc.



CONCLUSIONS-2

✓ BHGI guidelines can improve breast cancer treatment results in LMICs, but each country should evaluate national diagnostic and treatment resources that establish a minimum standard of care and promote the rational use of existing resources and greater equity in access to treatment.

✓ And also, there should be awareness of the burden of the disease, and good collaborations among ministers of health, policymakers, administrators, and institutions in these countries.

Thank you for your attentions!