Clinical Practice Guidelines for the Management of Breast Cancer in Malaysia

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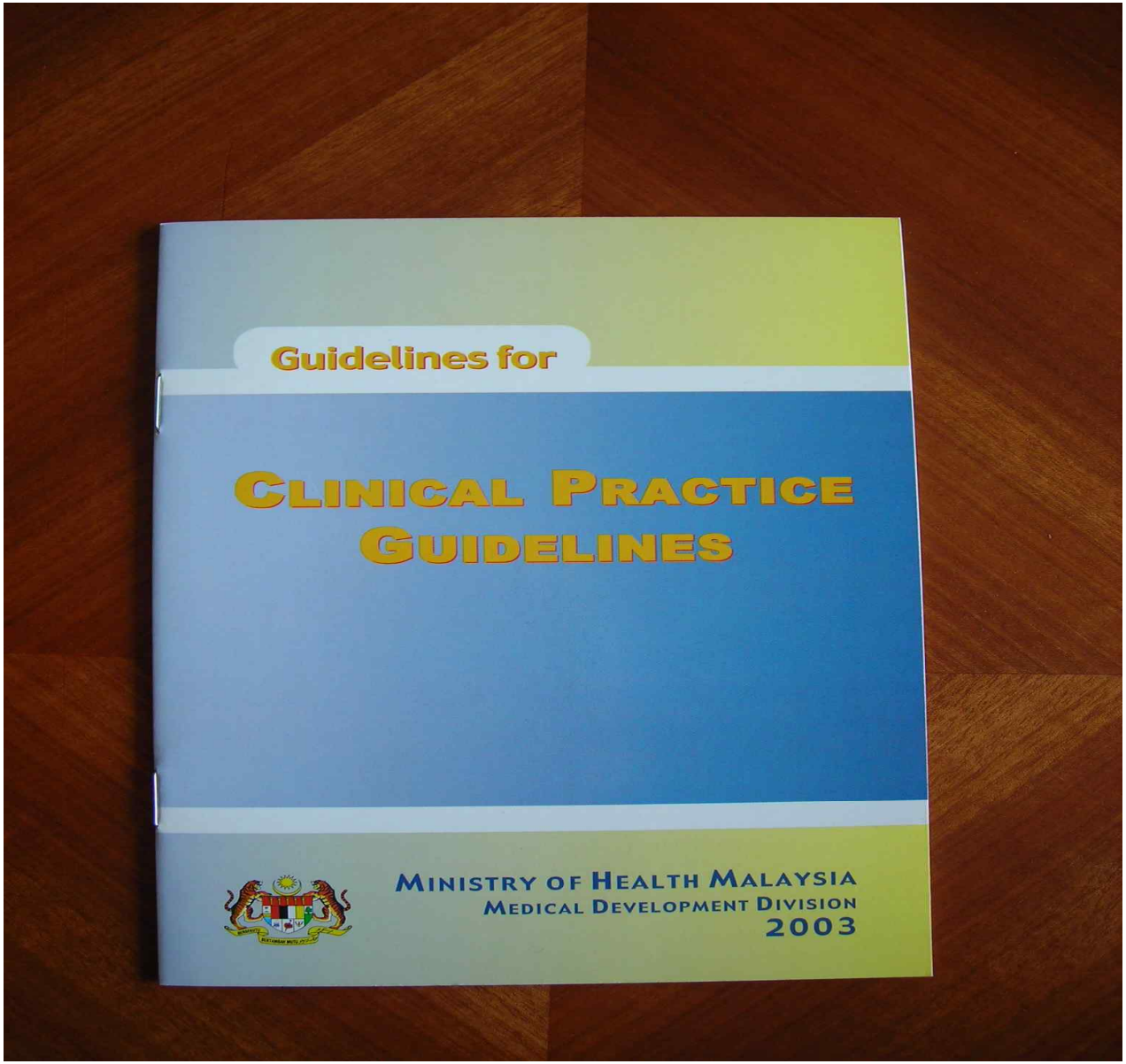
ABCS and GBCC

Seoul 6 Oct 2009



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WORK PROCESS -12 steps

1. Define topic/issue
2. Develop appropriate CLINICAL questions and CPG protocol
3. Determine mode of formulation of guidelines
4. Retrieve literature
5. Critical appraisal of literature
6. Analysis of evidence
7. Synthesize and develop guidelines
8. Consultation & peer review (CPG TAC and HTA & CPG Council)
9. Disseminate guidelines
10. Develop patient version of guidelines quick reference guide and training module
11. Monitor & evaluate guidelines
12. Updating CPG

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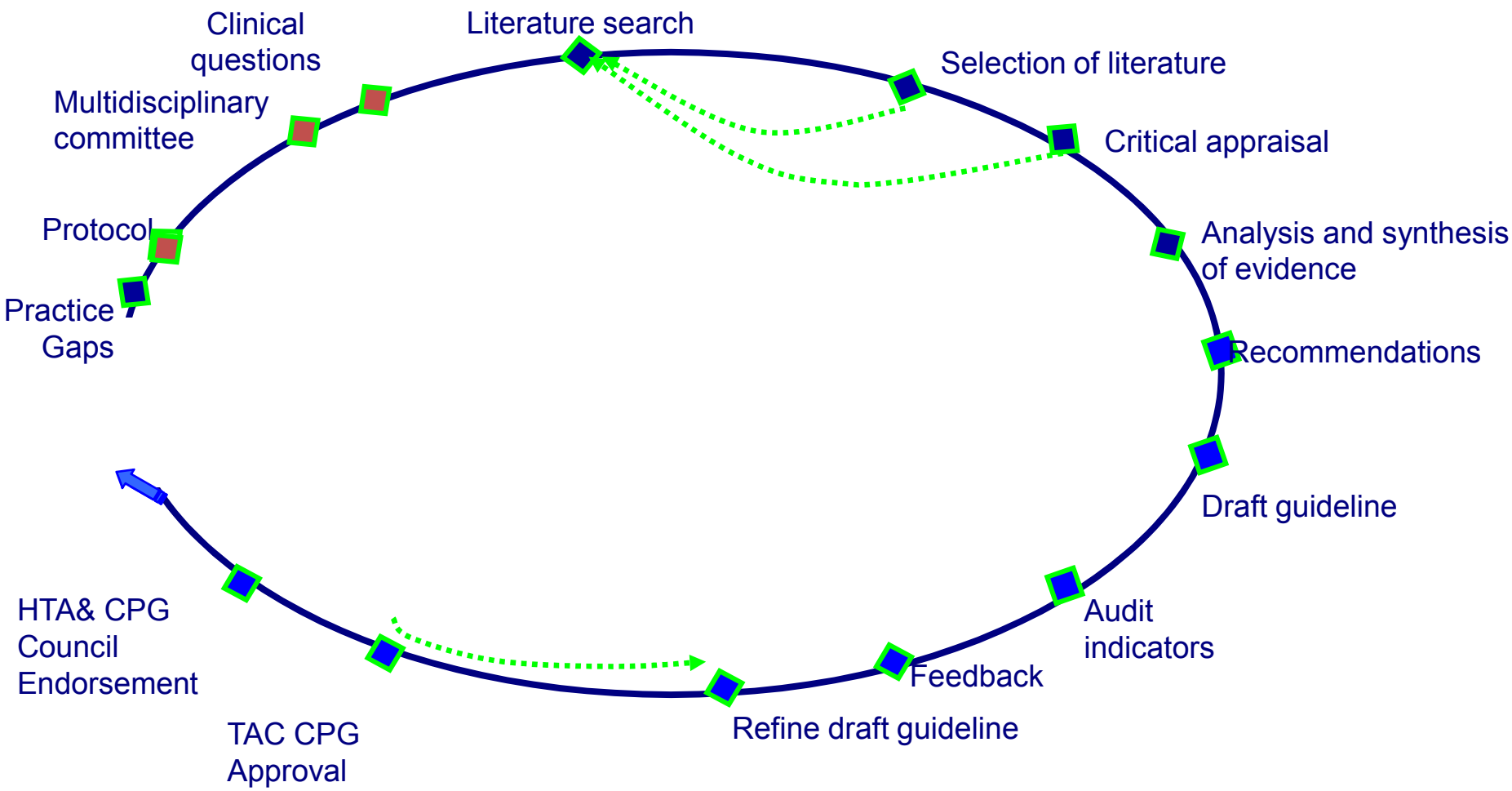
CPG development work process



Modified with permission from the NZ guidelines group

Details of work process

Preparing draft protocol	HTA Section
Reviewing draft protocol	All development group members
Presenting draft protocol to Review Committee	**Chairperson**
Defining the clinical questions	All development group members
Selecting papers for review	All development group members
Reviewing individual papers	Subgroup members working in pairs

Details of work process contd…

Analysing evidence tables	Subgroups
Summarising evidence and agreeing levels of evidence	Subgroups
Presenting analysis of the evidence to the Review Committee	All development group members
Drafting the guideline	Subgroups, coordinated by the chair
Merging the draft guideline	**HTA section**
Presenting draft to Review Committee	Chairman of the development group

Details of work process contd…

Considering feedback from external reviewers, TAC and draft on webpage	All development group members
Editing	Chair, subgroup leaders, HTA section
Presenting to the HTA & CPG Council	Chairman of the development group
Disseminating CPG	**HTA section**
Implementation of CPG	**Few members of the development group**

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CPG DEVELOPMENT/ REVIEW COMMITTEE

- Multi-disciplinary will depend on the nature of the guideline, designed to encourage expressions of diverse interest group
  - Clinicians with expertise from relevant disciplines
  - Involvement of all sectors – public, academic, private
  - Representatives of professional groups like Academy of Medicine/ Societies
  - Public health specialist
  - Representatives of relevant consumer groups
  - Experts in research methods relevant to guideline development e.g. epidemiologist, biostaticians

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MODE OF DEVELOPMENT

- **ADOPT**
- **ADAPT** link
  - *update*
  - *combine guidelines from different agencies*
  - *add local data - epidemiological, clinical patterns, costing*
- **NEW**

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Consider adapting/updating other guidelines

- Ideal source guideline is:
  - Valid: systematically produced
  - Transparent (evidence clearly referenced and graded, evidence tables provided)
  - Up-to-date (recent search)
  - Applicable: to your population and users
  - Useful (questions relevant, advice specific, outcomes measurable)

Step 4

RETRIEVAL OF LITERATURE

- Carry out a systematic search
- Search strategies
- Evidence tables
- Guidance & assistance provided by secretariat – full articles

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Step 5

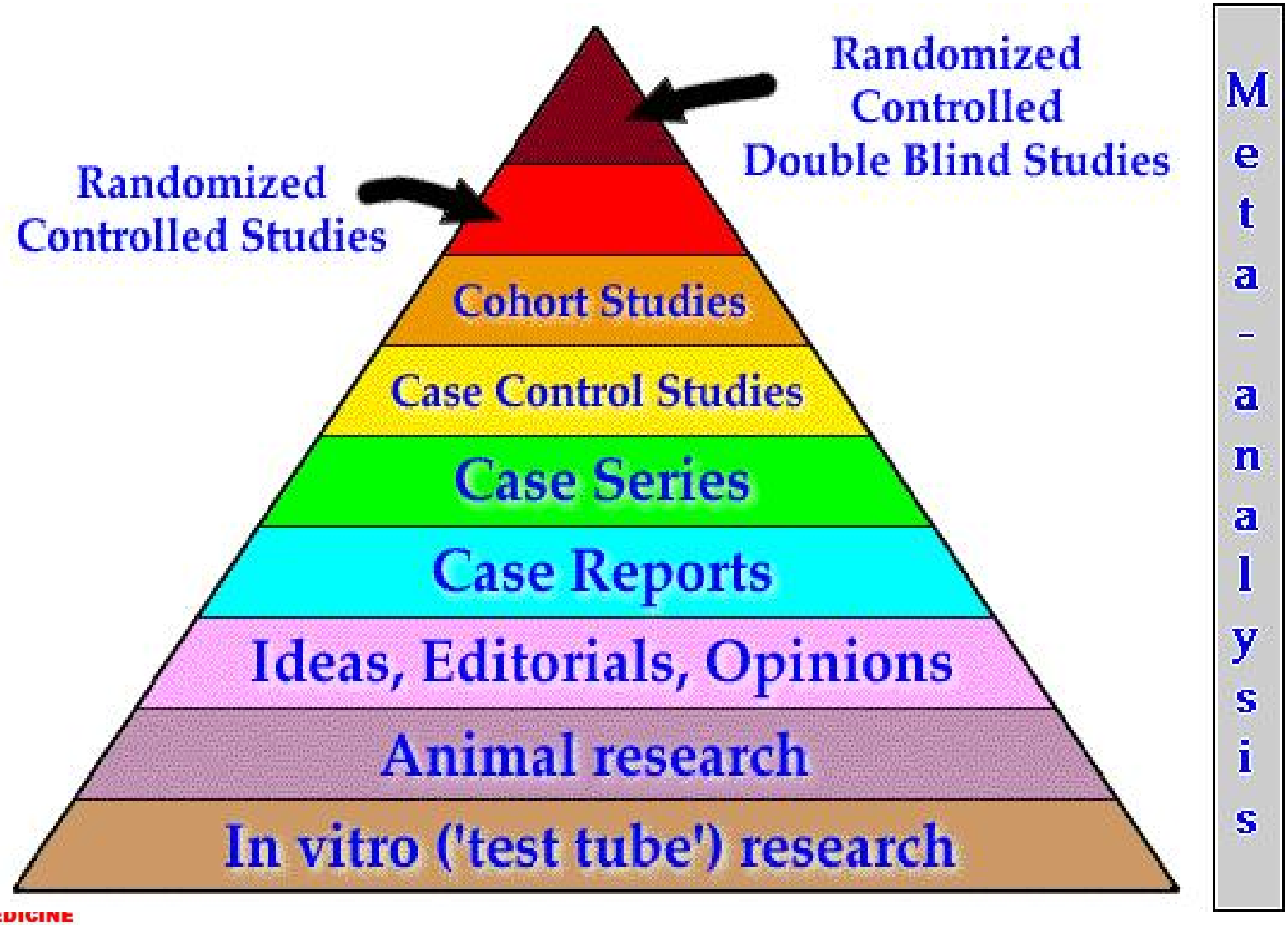
CRITICAL APPRAISAL

- Should be carried out for all literature
- Hierarchy of evidence looking for meta-analysis, systematic reviews & RCT -first
- Each piece of literature to be read by 2 members (preferably)

GRADING OF EVIDENCE

- Option to use grading scale from Canadian/ US Preventive Task Force
- Suggested that all members use similar grading scale
- Grade can be indicated in body of report

Levels of Evidence



LEVELS OF EVIDENCE
(US/ CANADIAN PREVENTIVE SERVICES TASK FORCE)

I	evidence from at least properly randomized controlled trial
II -1	evidence obtained from well-designed controlled trials without randomisation
II-2	evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one centre or group
II-3	evidence from multiple time series with or without intervention
III	opinions of respected authorities based on clinical experience; descriptive studies & case reports; or reports of expert committees

GRADING OF RECOMMENDATION

Translate evidence into recommendations

Graded A, B, C depending on strength of evidence

A	At least one meta analysis, systematic review or RCT or evidence rated as good and directly applicable to the target population
B	Evidence from well conducted clinical trials, directly applicable to the target population, and demonstrating overall consistency of results; or evidence extrapolated from meta analysis, systematic reviews or RCT
C	Evidence from expert committee reports, or opinions and or clinical experiences of respected authorities; indicates absence of directly applicable clinical studies of good quality

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Decision on Pharmaceutical Involvement in Guideline Development

HTA AND CPG Council 1/06

15 August 2006

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PHARMACEUTICAL INVOLVEMENT

- **allow drug companies to fund externally developed CPG**
- **pharmaceutical companies are not allowed to act as secretariat for the guidelines being developed**
- **logo of the drug company should not appear**
- **the *Source of Funding* will be mentioned in the CPG**
- **all members of the CPG development group will have to fill in a *Disclosure Form***

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CLINICAL PRACTICE GUIDELINES – MANAGEMENT OF BREAST CANCER

Malaysia 2002

Development team

Chairman: **Yip Cheng Har**

Co-Chairman: **Noor Hisham Abdullah**

Secretary: **S. Sivalal**

- **Surgery**
- **Pathology**
- **Radiology**
- **Oncology**
- **Public Health**
- **Palliative Care**

2009:

PLUS **Family Medicine**

Clinical Genetics

Patient Advocate

Clinical Psychology

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1. INTRODUCTION

- **1.1. Incidence of Breast Cancer**

- **1.2 Aetiology of Breast Cancer**

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2. Diagnosis of Breast Cancer

- **2. 1 Clinical Diagnosis**
- Triple Assessment emphasized:

- Clinical assessment
- Radiological investigations
- Biopsy
- **2.2 Baseline Staging Investigations**
- **2.3 Laboratory Diagnosis**

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2.2 Baseline Staging Investigations

- **The AJCC (American Joint Committee on Cancer) Cancer Staging Manual (6th Edition) has been used for staging of cancers in this guideline**
- **The recommended work-up and staging tests of invasive breast cancer includes a complete blood count, liver function tests, chest radiograph and bilateral mammography.**
- **Patients with Stage III and IV breast cancer clinically should undergo a chest X-ray, liver ultrasound or CT scan, and bone scan.**
- **In other stages, the performance of a bone scan is not required unless in the presence of bone pains or an elevated alkaline phosphatase**

2.2 Baseline Staging Investigations

- In women with no symptoms, physical signs or biochemical evidence of metastases, the recommendation depends on the pathological stage of the cancer. This guideline proposes:
- In women with pathological Stage I tumours, routine bone scan and liver imaging are not indicated
- In women with pathological Stage II tumours, a post-operative bone scan may be considered as part of baseline staging. Routine liver imaging may also be considered for patients with 4 or more positive.
- In women with pathological Stage III tumours, bone scanning and liver imaging are recommended post-operatively.
- However, the decision for a staging bone scan in individual patients may need to be influenced by the availability of resources.

3. MANAGEMENT OF BREAST CANCER

- 3.1 Counseling
- 3.2 Surgery
  - 3.2.1 Choice of operation for Stage 1 and 2
  - 3.2.2 Management of the axilla
- 3.3 Management of DCIS
- 3.4 Management of LCIS
- 3.5 Management of Locally advanced breast cancer
- 3.6 Breast reconstruction
- 3.7 Management of metastatic breast cancer
- 3.8 Adjuvant radiotherapy
- 3.9 Adjuvant chemotherapy
- 3.10 Adjuvant hormone therapy
- 3.11 Bisphosphonates in adjuvant therapy
- 3.12 Follow-up
- 3.13 Management of bone metastases in breast cancer
- 3.14 Management of malignant hypercalcemia
- 3.15 Palliative care

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3.2 Surgery

- ***3.2.1 The Choice of Operation for Stage I And II***
- Breast conservation surgery (BCS) followed by radiotherapy is an appropriate method of primary therapy for the majority of women with Stage I or II breast cancer, and is preferable ***because it provides survival equivalent to total mastectomy and axillary clearance while preserving the breast*** In the absence of special reasons for selecting mastectomy, the choice between BCS and mastectomy can be made according to the patient's circumstances and personal preferences (*Level I)*.

3.2.2 Management of the Axilla

- Axillary node biopsy may fail to detect metastases in 42% of patients and axillary node sampling may miss 14% of patients with axillary metastases
- For accurate staging, at least level I and II nodes should be removed (Level II-1).
- A full clearance of up to Level III should be carried out in the presence of clinically involved nodes
- In an adequate clearance, the number of nodes retrieved should be at least 10 (Level III).

3.2.2 Sentinel lymph node biopsy

- **Sentinel lymph node biopsy (SLNB) is appropriate if an experienced sentinel lymph node team is available with facilities for both the dye and albumin radiocolloid technique**
- **Candidates for sentinel node biopsy should have clinically negative axillary lymph nodes, solitary T1 or small T2 primary, no large haematoma or seroma in the breast, and no prior neoadjuvant chemotherapy.**
- **The SLN can be identified in over 97% of patients if both the dye and radiocolloid technique are used together, with a false negative rate of 5%**

3.9 Adjuvant chemotherapy

- **Adjuvant chemotherapy should be offered to all patients in the *high-risk* category:**
- **· All node positive patients**
- **· Patients with tumours 2 cm or more**
- **· Patients with ER negative tumours**
- **It *may* be considered in the following patients in the *moderate risk* category*:***
- **· All patients with tumours 1-2 cm**
- **· Patients with high grade (Grade 3) tumours**
- **· Patients with tumours with lymphovascular invasion**
- **Adjuvant chemotherapy *is not required* in patients in the *low-risk category*, that include**
- **· All patients with tumours less than 1 cm**
- **· Patients with tumours of special types of histology (tubular, mucinous and cribriform) less than 2 cm.**

3.9 Adjuvant chemotherapy

- **Adjuvant chemotherapy should be started 4-6 weeks after surgery, since there is no benefit in administering delayed chemotherapy (*Level III).***
- **Acceptable adjuvant chemotherapy regimes are:**
- **· CMF for 6 cycles (Cyclophosphamide, Methotrexate and 5-Fluorouracil)**
- **· AC for 4 cycles (Adriamycin and Cyclophosphamide)**
- **· FAC or FEC for 4-6 cycles (5-Fluorouracil, Adriamycin or Epirubicin and Cyclophosphamide)**

- **The role of Taxanes in the adjuvant setting is still investigational (NCCN Practice Guidelines in Oncology, 2002).**

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3.10 Adjuvant Hormone Therapy

- **Adjuvant Tamoxifen 20 mg daily for 5 years should be offered to all patients with ER positive tumours and in patients where ER status is unknown as it has been shown to improve recurrence free survival and overall survival Level I).**
- **It may also be considered in post-menopausal patients with ER negative tumours.**
- **The effects of use of Tamoxifen in ER negative but PR positive patients are not known, while its use in ER negative, pre-menopausal patients is not recommended**
- **The role of Aromatase inhibitors in postmenopausal patients in the adjuvant setting is still in the investigational stage, while its use in pre-menopausal patients is contra-indicated**
- **(END POINT – significant OS and not DFS)**

3.12 Follow-up

- All patients with breast cancer should be followed up, since most recurrences occur in the interval of follow-up.
- The objectives of follow-up are to:
- · provide patients with support and counselling
- · detect potentially curable conditions such as local recurrence of cancer in the breast following BCS, and to detect new cancers in the opposite breast
- · manage patients in whom metastatic disease develops, and to determine outcome

- The suggested follow-up schedule is as follows:
- · 3 monthly for the first 2 years
- · 6-monthly for the next 3 years
- · Yearly thereafter

3.12 Follow-up

- **History and physical examination**
- **Blood tests and diagnostic imaging have not been found to improve survival or quality of life more than does physical examination for detecting distant metastases. The patient is also advised to carry out monthly breast self-examination *(Level I).***
- **While there is no data to show that mammography improves survival when used for detection of local recurrence or contra-lateral breast cancer, it has been suggested that annual mammography after therapy for primary breast cancer makes good sense *(Level I)*.**
- **After breast conservation surgery, the first mammogram of the affected breast should be performed 6 months after completion of radiotherapy**

4. Breast cancer in special circumstances

- 4.1 Breast cancer in Pregnancy
- 4.2 Male breast cancer
- 4.3 Breast cancer in the elderly
- 4.4 Pregnancy after breast cancer
- 4.5 Hormone replacement therapy after breast cancer

- **5. Screening for breast cancer**
  - **5.1 Evaluation of the non-palpable breast abnormality on screening**

- **6 Complementary and alternative medicine therapies**

- **7 Prevention of breast cancer**

Conclusion

- **Many therapeutic options in the management of breast cancer**
- **These guidelines were prepared to provide assistance to the medical practitioners on how to manage breast cancer. The aim of this guideline is to assist the medical practitioner in clinical decision making by providing well balanced information on how to arrive at a diagnosis of cancer without undue delay, achieve both local and systemic control of disease by a multidisciplinary approach with reduction of the risk of recurrence to improve survival and maintain a good quality of life for the patient.**
- ***However optimum treatment of breast cancer can be expensive and cost effectiveness as measured by QALY is important before any recommendation and the QALY may differ between countries and even within countries***
- ***Hence resource stratification may be necessary***

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Resource stratification
(Breast Health Global Initiative)

- **Basic level - core resources absolutely necessary for any breast health programme**
- **Limited level - these are second tier resources or services which would produce a major improvement in outcome**
- **Enhanced level - these third-tier resources or services are optional and may produce minor improvements in survival.**
- **Maximal level - these are high-level resources that may not even be affordable in high-resource countries.**

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The Breast Health Global Initiative

Finally….

- Each country should adapt established guidelines to cater for its individual requirements and available resources

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