Demystifying Breast Cancer

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Faculty/Presenter Disclosure

- **Faculty:** Anna Wilkinson

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  - Ontario College of Family Physicians Speaker Honoraria (ASA)
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  - CPAC- travel to one day meeting in Toronto
  - CFPC- travel to MIG meetings
  - CFPC Grant for Breast Cancer Survivorship Tool

Learning Objectives

- Describe screening guidelines and the diagnostic workup for breast cancer
- List and discuss potential adjuvant therapies for breast cancer, including surgery, chemotherapy, targeted therapy, radiotherapy, and endocrine therapy
- Identify appropriate survivorship care for breast cancer patients

Objectives

1) Screening
2) Diagnosis
3) Treatment
4) Survivorship Care

1) Screening

Canadian Task Force on Preventive Health Care: Breast Cancer Screening Guidelines

Recommendations on screening for breast cancer in women aged 40–74 years who are not at increased risk for breast cancer

Scott Klarenbach MD MSc, Nicki Sims-Jones RN MScN, Gabriela Lewin MD, Harminder Singh MD MPH, Guylène Thériault MD, Marcello Tonelli MD SM, Marion Doull PhD, Susan Courage RN BScN, Alejandra Jaramillo Garcia MSc, Brett D. Thombs PhD; for the Canadian Task Force on Preventive Health Care

Cite as: *CMAJ* 2018 December 10;190:E1441-51. doi: 10.1503/cmaj.180463

This guideline is available in French at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.180463/-/DC1

CMAJ Podcasts: interview in English at https://soundcloud.com/cmajpodcasts/180463-guide-eng; entrevue en français au https://soundcloud.com/cmajpodcasts/180463-guide-fre

See related article at www.cmaj.ca/lookup/doi/10.1503/cmaj.181538

Breast cancer mortality rates among Canadian women have declined from 41.7 per 100 000 in 1988 to an estimated 23.2 per 100 000 in 2017, while age-standardized incidence has remained relatively stable, at around 130 per 100 000 since 2004.[1] Declining mortality with stable incidence

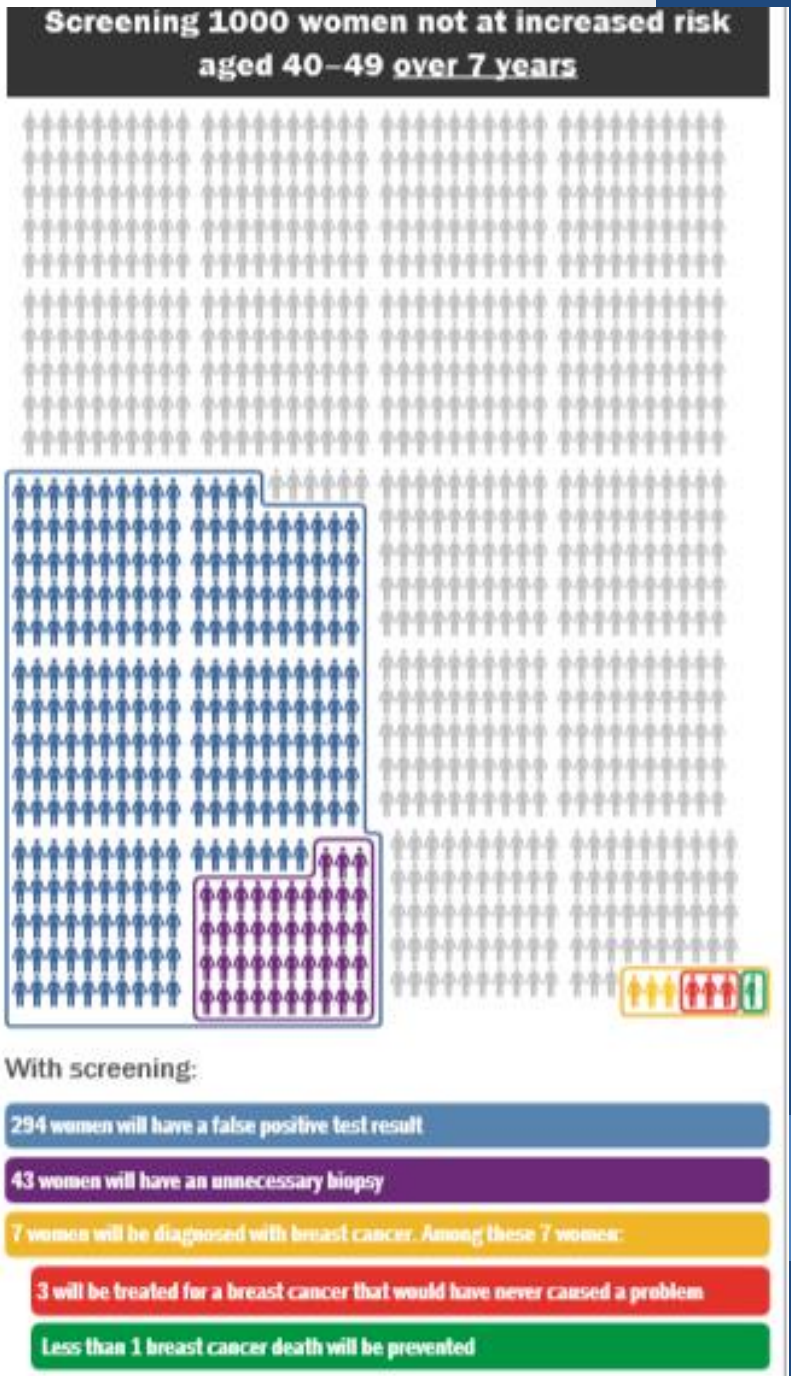
KEY POINTS

- Low-certainty evidence indicates that screening for breast cancer with mammography results in a modest reduction in breast cancer mortality for women aged 40 to 74 years; the

https://canadiantaskforce.ca/guidelines/published-guidelines/breast-cancer-update/

2018 CTPHC Guidelines:

- Age 40-49
  - No screening recommended
  - *Conditional recommendation; low certainty evidence*
    - NNS (Number needed to screen to prevent one death): 1724



https://canadiantaskforce.ca/tools-resources/breast-cancer-update/1000-person-tool-age-40-49/

2018 CTPHC Guidelines:

- Age 50-74
  - Mammography every 2 to 3 years
  - *Conditional recommendation; very low certainty evidence*
    - NNS 50-59: 1333
    - NNS 60-69: 1087
    - NNS 70-74: 645
- the decision to undergo screening is conditional on the relative value a woman places on possible benefits and harms from screening.

https://canadiantaskforce.ca/guidelines/published-guidelines/breast-cancer-update/

Other Screening Modalities

- No Role for:

Strong recommendation; no evidence

- MRI
- Tomosynthesis
- Ultrasound

Conditional recommendation; no evidence

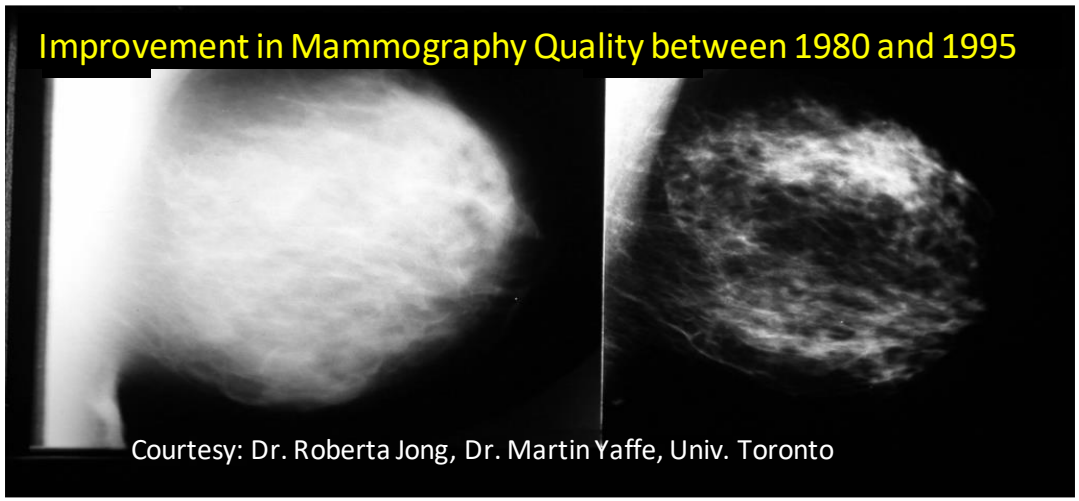
- Clinical breast examination

Conditional recommendation; low-certainty evidence

- Breast self-examination

Mortality benefit of screening

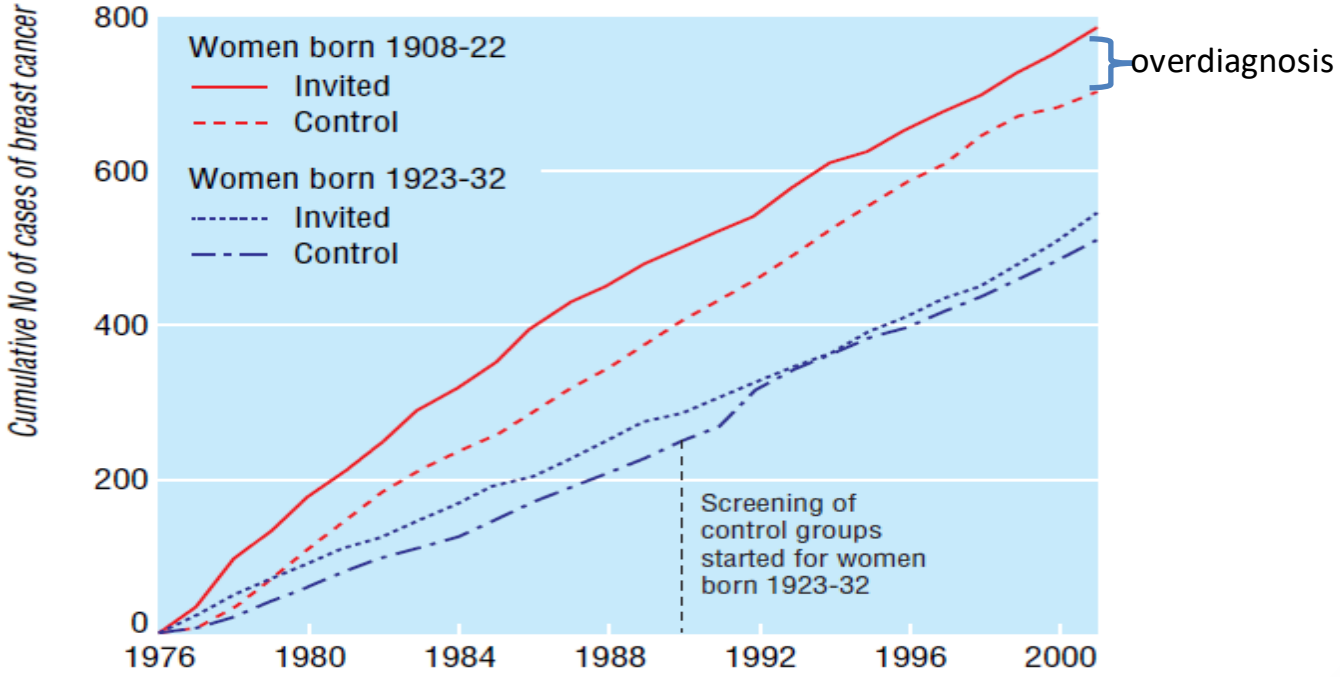
- Studies used in 2018 CTFPHC guidelines to derive mortality benefit began between 1963 and 1991
- Significant advances in technology/treatment since this time
- Earlier diagnosis = less treatment- morbidity impact?
- CTFPHC mortality benefit 15%-21%; other studies suggest ~40%



Seely and Alhassan. Curr Oncol. 2018 Jun; 25(Suppl 1): S115–S124.
Andrew Coldman, Norm Phillips, Christine Wilson et al, 2014. JNCI J Natl Cancer Inst (2014) 106(11)

Overdiagnosis

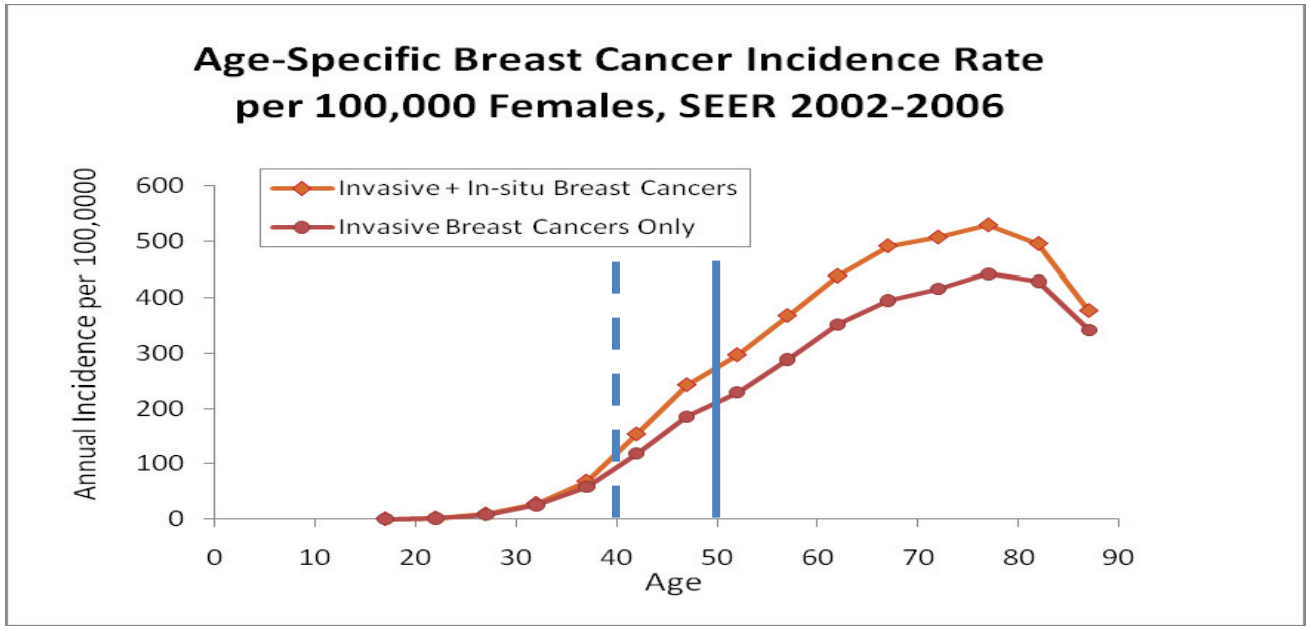
- Diagnosis of a cancer that would not cause a problem in a person's lifetime
- Estimates of overdiagnosis vary widely from 0-57% (?validity)
  - Canadian Task force states is ~50%
  - Other RCT's state ~10%



Puliti D, Duffy SW, Miccinesi G et al, J Med Screen 2012;19 Suppl1:42–56
Zackrisson S, Andersson I, Janzon L, Manjer J, Garne JP. Rate of over-diagnosis of breast cancer 15 years after end of Malmö mammographic screening trial: follow-up study. BMJ, doi:10.1136/bmj.38764.572569.7C

Age of Initiation

- 1 in 5 breast cancers diagnosed are women in their 40's
- 33% of lives lost to breast cancer occur in women in 40s
- There is no abrupt change at age 50
- Earlier initiation of screening in US, UK, Sweden

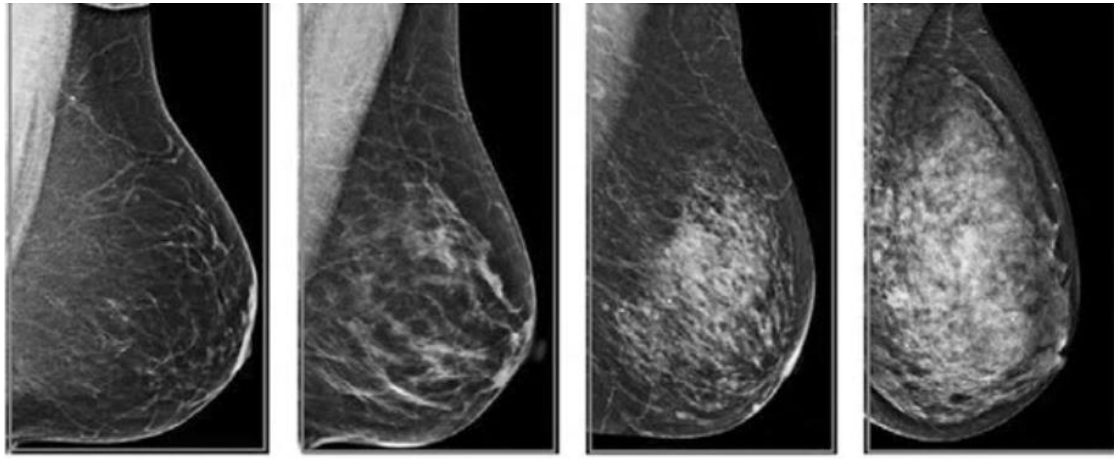


Moss et al, UK Ages trial, *The Lancet Oncology*, July 2015
Coldman et al, Pan Canadian study, *J Natl Cancer Inst* 2014
Tabar L, et al. *Cancer*, Nov. 2018

https://www.mayoclinic.org/breast-density-mdash-the-four-levels/img-20008862

Breast Density

- Dense (C) or extremely dense (D) breast tissue increases risk of developing breast cancer (odds ration ~4.0)
- Dense breast tissue limits cancer detection with mammography
- Woman with dense breast are at increased risk of developing interval cancers



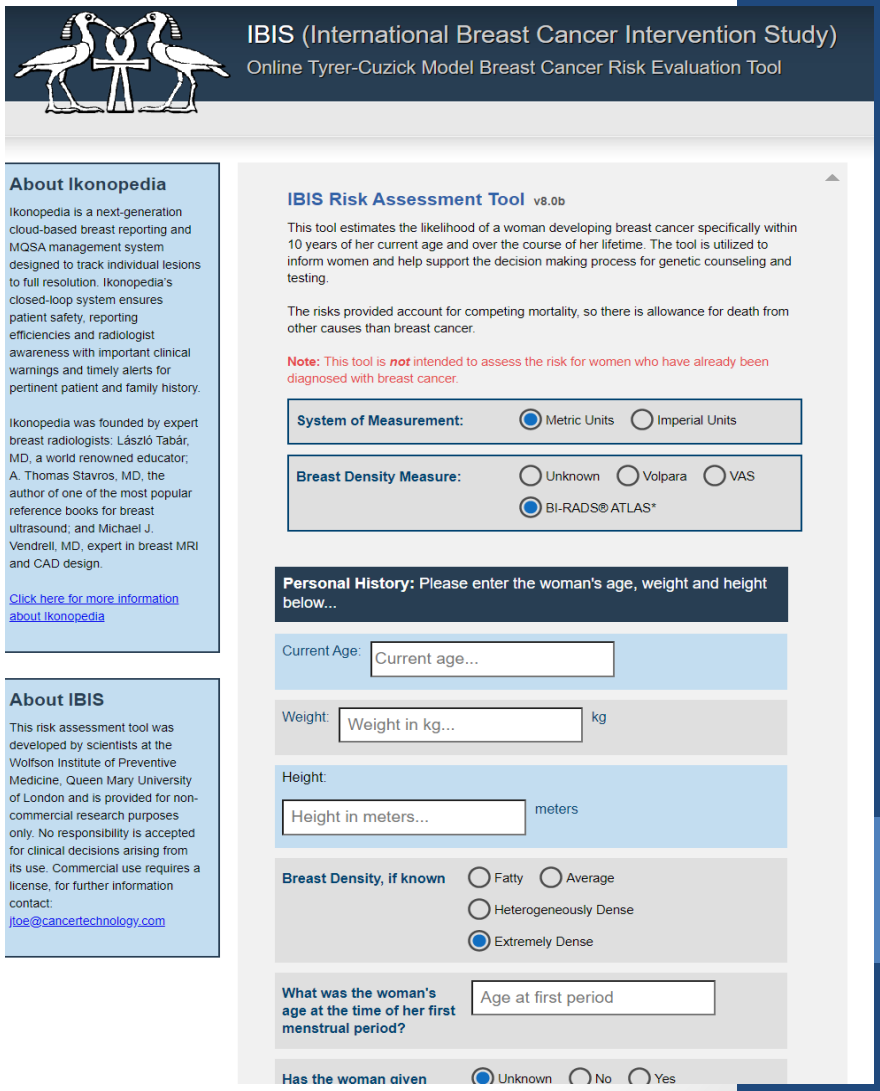
Boyd et al. Mammographic denisty and the risk and detection of breast cancer. N Engl J Med 2007; 356:227-236
Bakker et al. Supplmental MRI screening for women with extremely dense breast tissue. N Engl J Med 2019; 381(22): 2091-2102.
Harvey, J. A., & Bovbjerg, V. E. (2004). Quantitative assessment of mammographic breast density: relationship with breast cancer risk. *Radiology*, *230*(1), 29-41.

Breast Density- Supplemental Screening?

- Consider yearly mammogram to decrease interval cancers
- Calculate risk:
  - IBIS calculator:

https://ibis.ikonopedia.com/

  - Intermediate Risk: 15-20% Lifetime risk
    - consider supplemental US
  - High Risk: >=20- 25% Lifetime risk
    - may be eligible for MRI screening- refer to high risk program



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2) Diagnosis

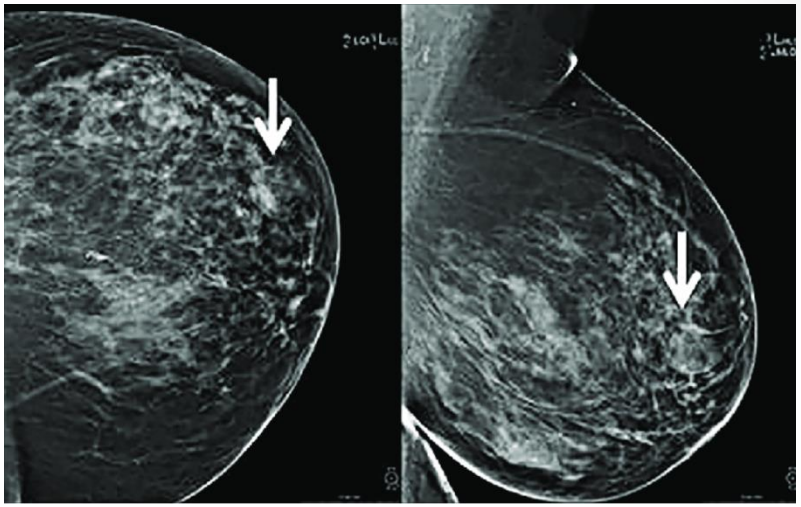
Presenting symptoms

- Not all breast cancers present as “lumps”
- Palpable breast mass
- Nipple discharge without mass
  - Concerning if: persistent, reproducible, spontaneous, unilateral, serous/serosanguinous or sanguineous
- Asymmetric thickening or nodularity
- Skin changes
- Axillary mass
  - Can be associated with an occult breast cancer
- Breast pain
  - Up to 6.7% will be dx breast cancer

NCCN Clinical Practice Guidelines in Oncology. Version1.2018-March 2018. Retrieved from: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf Aug 31, 2018

Work-up

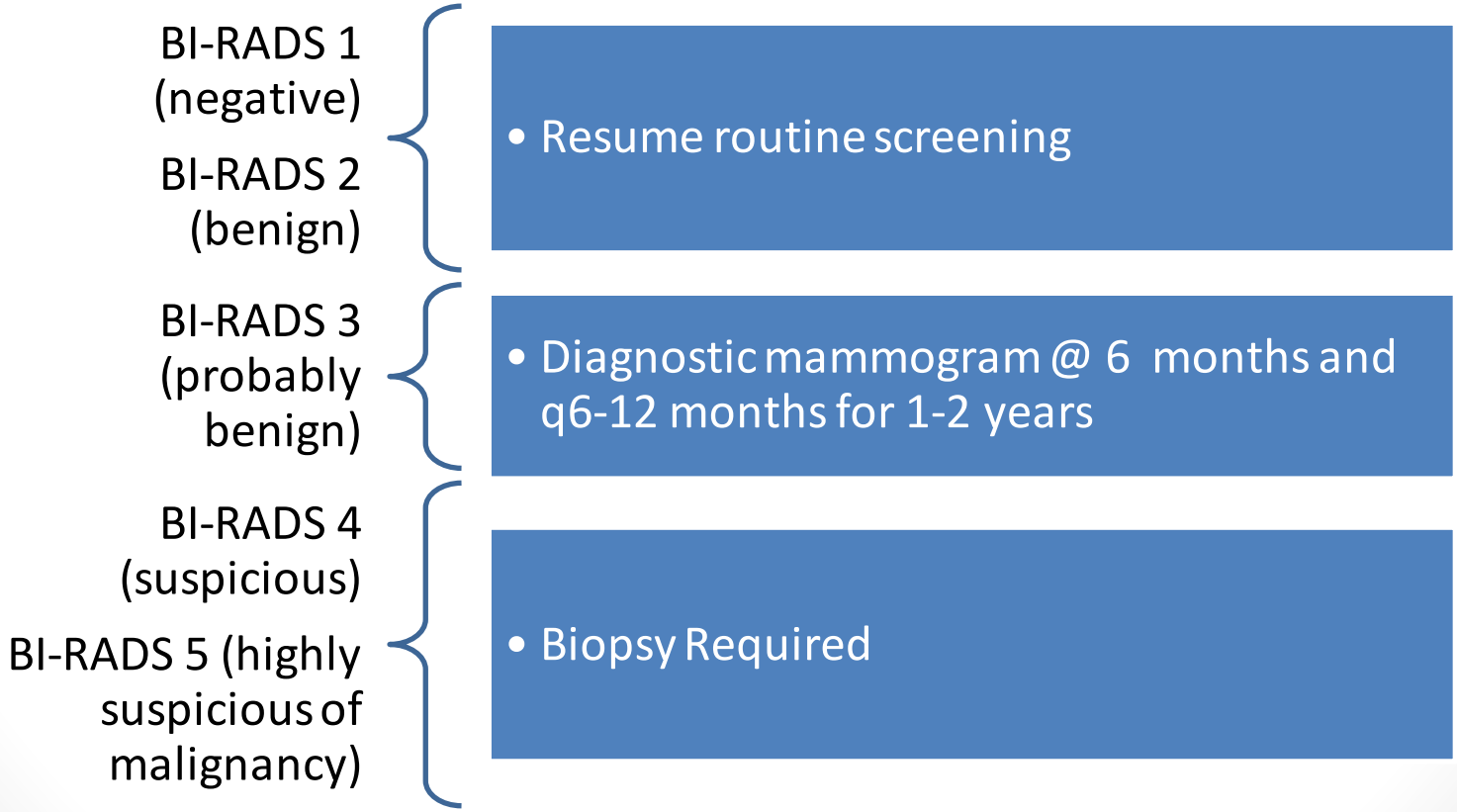
https://www.researchgate.net/figure/A-66-year-old-female-with-abnormal-screening-mammogram-showing-a-mixed-density_fig2_332838144



- Mammogram
  - Screening
    - 2 views each breast
  - Diagnostic
    - Additional views, magnification
- Ultrasound
  - Does not detect microcalcifications
  - Good for cysts
  - Often first investigation in woman <30
- MRI
  - Suspicion of inflammatory breast cancer- skin changes with negative biopsy
  - Suspicious nipple discharge when mammo or u/s non-diagnostic

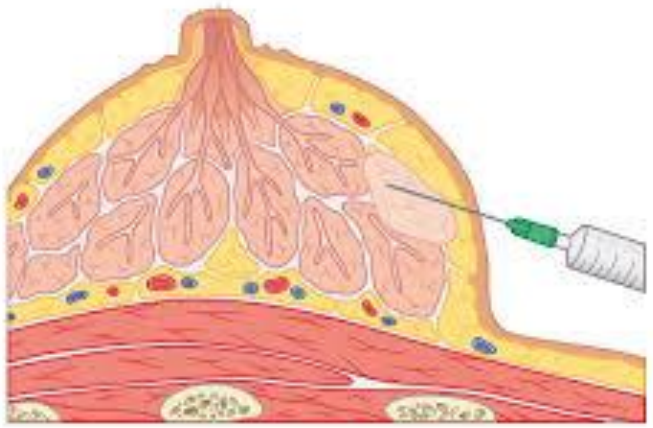
BI-RADS

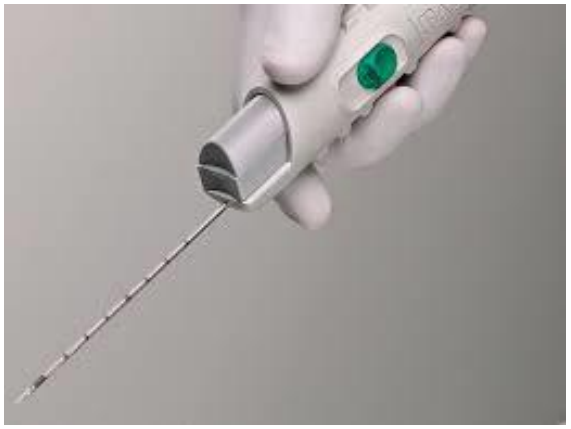
- Breast Imaging-Reporting and Data System
- a quality assurance tool used to categorise findings and provide recommendations for follow up



Biopsy

- Fine Needle Aspiration (FNA)
  - Small bore needle
  - Less invasive
  - Less tissue
- Core
  - Multiple cores of tissue
  - More accurate than FNA
  - More tissue
- Excisional
  - Removal of entire breast mass in OR
  - Usually needle/wire localization prior
- Skin biopsy
  - If changes with skin or nipple

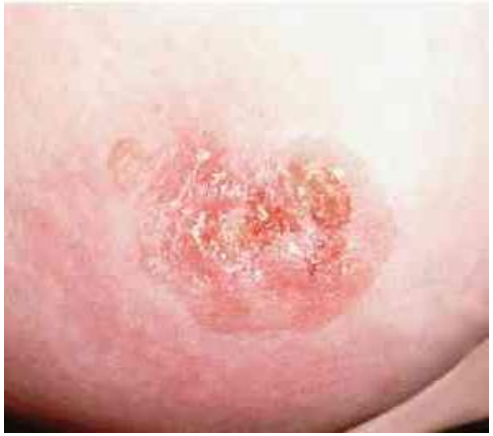




poliklinikahuman.rs

Don’t be fooled….

- Inflammatory Breast Cancer
  - Rare aggressive form of breast caner
  - Dermal edema (peau d’orange) and breast erythema
- Paget's
  - Neoplastic cells in areola or nipple
  - Presents as eczema of nipple, bleeding, ulcer or itching
  - Occult on mammogram, requires skin biopsy



http://www.aboutcancer.com/paget.htm

Sampling Error

- If clinical/imaging/biopsy results discordant consider:
  - re-biopsy *or*
  - close observation clinically *or*
  - close observation with imaging

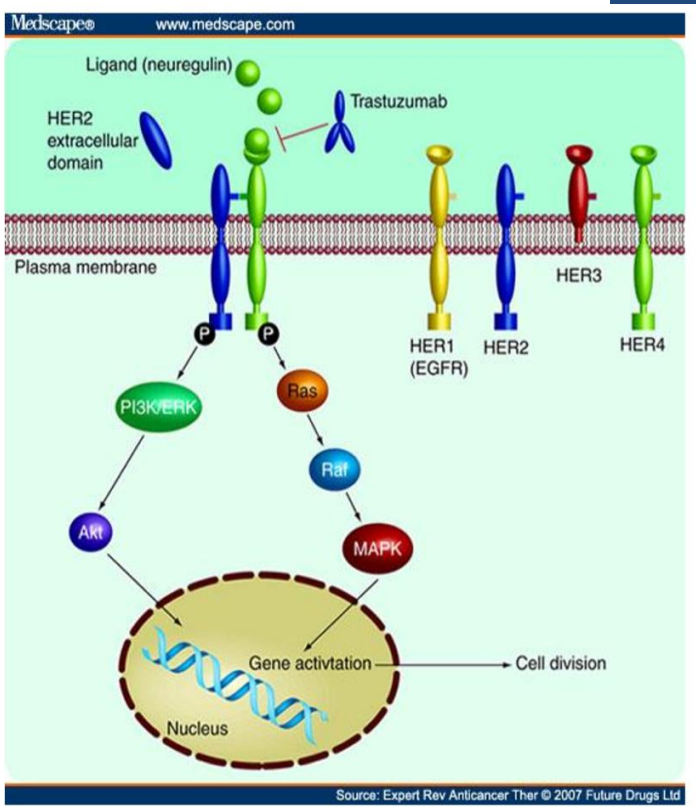
3) Treatment

Breast Cancer Pathology

- **Cell type**
- **Grade**

Grade 1	Grade 2	Grade 3
• Well differentiated		• Poorly differentiated

- **ER/PR**
  - Estrogen receptor status
  - Progesterone receptor status
- **HER2**
  - human epidermal growth factor receptor 2, a transmembrane tyrosine kinase receptor
  - *HER2* + breast cancers have a gene amplification or HER2 protein overexpression= uncontrolled cell growth
  - HER2 can be targeted by Trastuzumab



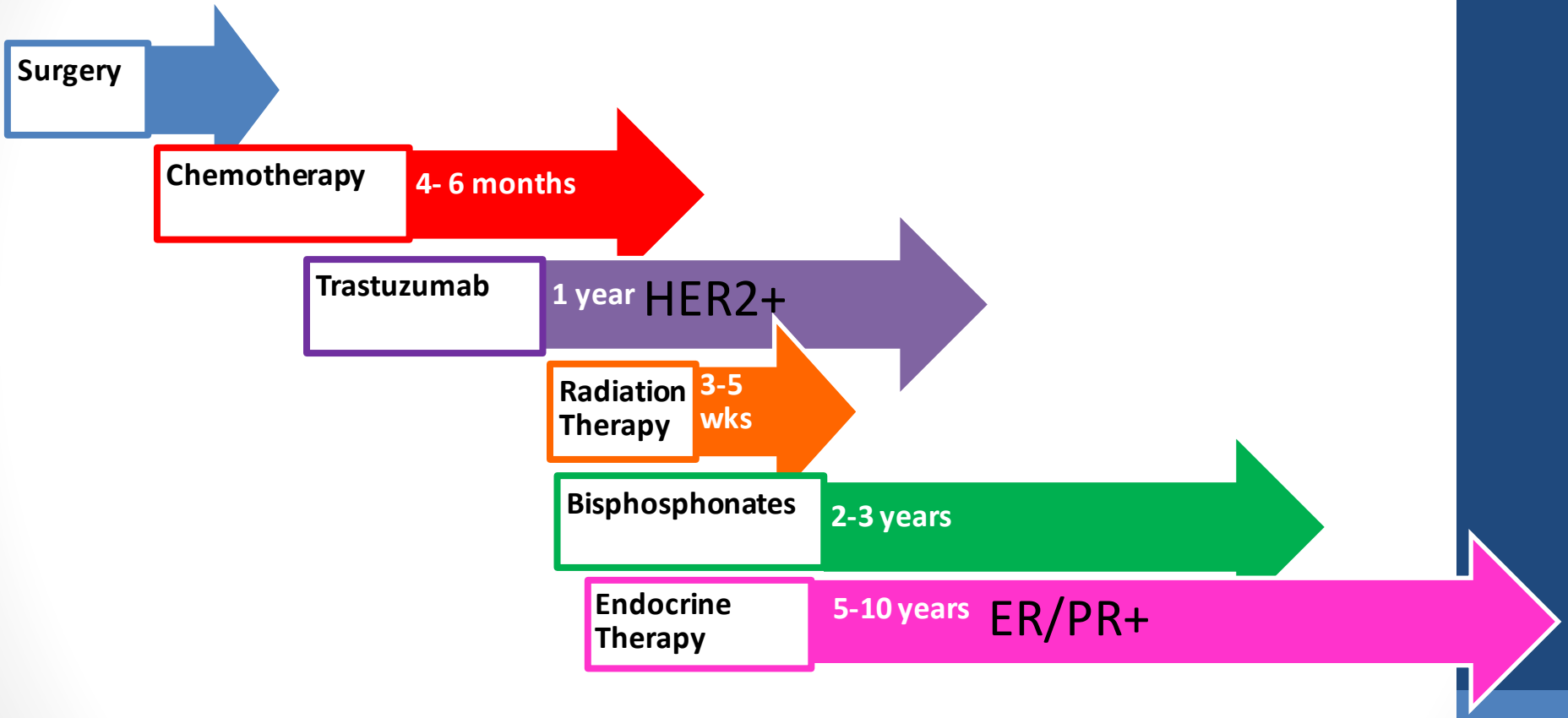
Staging

Stage 0	• LCIS/DCIS
Stage 1-2	• Operable- Adjuvant Therapy **Tumour <5cm, up to 3 nodes**
Stage 3	• Non-operable- Neoadjuvant Therapy **Tumour >5cm or >4 nodes**
Stage 4	• Metastatic

No staging investigations required for Stage 0, 1 or 2 breast cancer in absence of clinical symptoms and normal LFT's, ALP

LCIS= Lobular Carcinoma in Situ
DCIS= Ductal Carcinoma in Situ

Overview of Treatment



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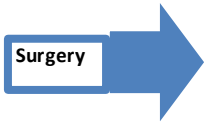
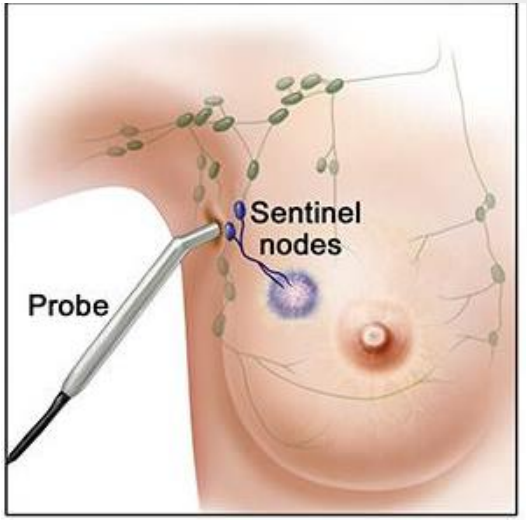
Surgery



- **Lumpectomy vs Mastectomy**?
  - **Lumpectomy**
    - For tumours <5cm
    - Margins must be negative
    - Must able able to receive XRT post
  - **Mastectomy**
    - Equivalent to lumpectomy +radiation
    - If underlying genetic mutation

Axillary staging



https://www.cancer.gov/news-events/cancer-currents-blog/2017/breast-cancer-lymph-node-removal

- **Sentinel Node vs Axillary dissection**?
  - No nodes clinically= **sentinel node**
    - Further nodal resection if sentinel node positive
    - Decreased arm/shoulder pain, lymphedema
  - Clinically positive nodes= **axillary dissection**
    - Pathologic confirmation with FNA/core biopsy
    - At least 10 nodes should be examined

Who Gets Chemotherapy?

- Based on careful review of treatment benefit/toxicity, patient co-morbidities and preference. Generally:

- **No chemotherapy**
  - Tumour <0.5cm and no node involvement
  - Tumour >0.5cm, no node involvement with favourable prognostic factors
    - Her2-
    - ER/PR+
    - Low grade
  - Genomic Profiling: low-intermediate risk

- **Chemotherapy**
  - Positive lymph nodes
  - Tumour >0.5cm, no node involvement but unfavourable prognostic factors
    - HER2 +
    - ER/PR-
    - High grade
  - Genomic Profiling: high risk

Genomic Profiling: Personalized Therapy

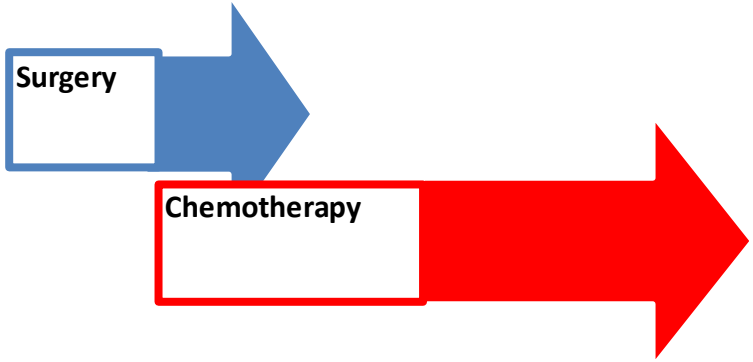
- 21 gene assay (OncotypeDx): "Recurrence Score"
- No benefit for chemotherapy for low/intermediate risk breast cancer
- Up to 70% of woman with early stage, favourable dz (ER/PR+, HER2-, No Nodes) don't need chemo
- Shows treatment benefit primarily from endocrine therapy
- Compliance!

Sparano et al. Adjuvant chemotherapy guided by a 21-gene expression assay in breast cancer. NEJM. 2018:379(2): 111-121

Neoadjuvant Chemotherapy

- Chemotherapy given for large (>5 cm) or high risk (N2 or N3) tumours preoperatively, especially “triple negative”

- Benefits
  - Inoperable tumours become operable
  - Time for genetic testing prior to surgery
  - Facilitates breast conservation
  - Pathological response gives prognostic information



Chemotherapy Regimes

- Within 8 (up to 12) weeks from surgery
- Choice of chemotherapy regime depends on comorbidities, known toxicities

- **AC+T**
  - Adriamycin/Cyclophosphamide q 2-3 wks x 4 + Taxane q2-3wks x 4 or weekly x 12

or

- **FEC/Docetaxol**
  - 5-FU/Epirubicin/Cyclophosphamide q3wks x 3 +Taxotere q3wks x3

or

- **TC**
  - Taxotere/Cyclophosphamide q3 wks x 4

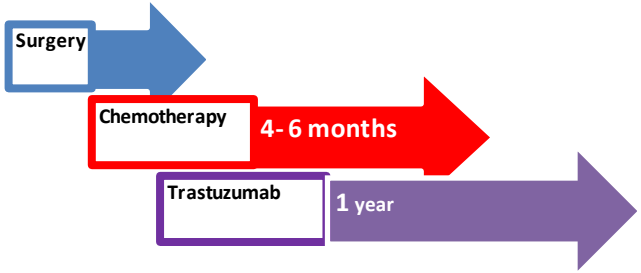
- Adriamycin + Epirubicin= Anthracyclines

Anthracycline Cardiotoxicity

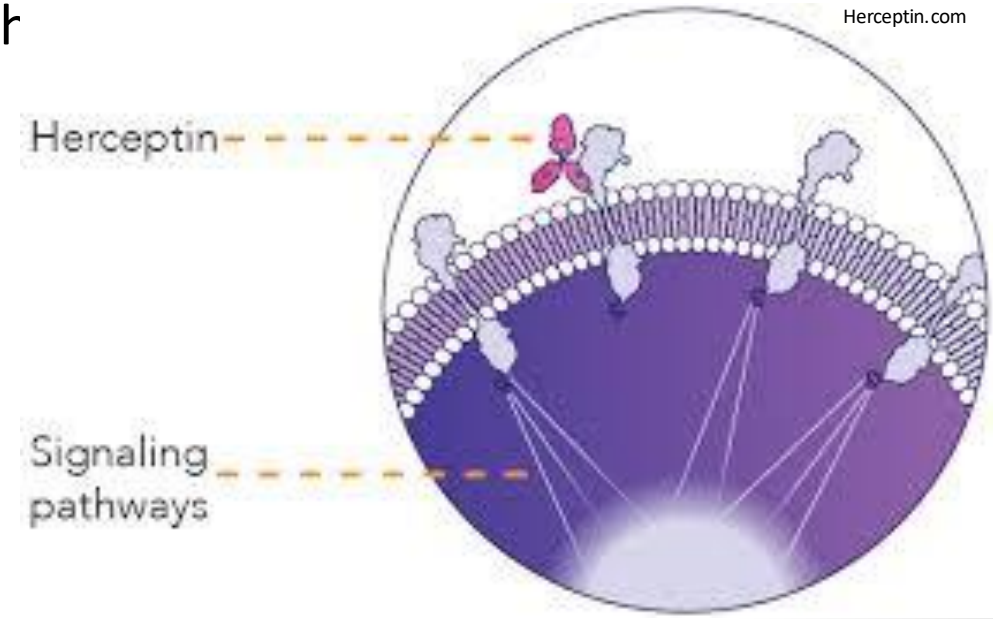
- Months to > 20 years after treatment
- Additive with cardiotoxicity from other therapies (XRT/trastuzumab)
- Incidence ~2%
- Decreased EF or CHF
- Low threshold for investigation of dyspnea
- Prevention
  - Aggressively address CV risk factors
  - Consider **ace-inhibitor or ARB** for tx of hyperte
- Management
  - As per heart failure guidelines

Adriamycin + Epirubicin= Anthracyclines

Trastuzumab

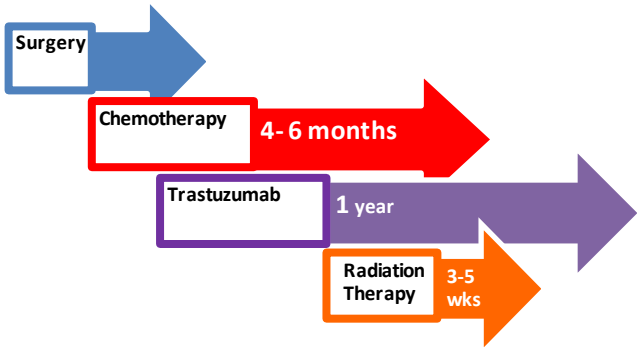


- Trastuzumab (Herceptin)
  - monoclonal antibody for extracellular domain of HER2 receptor
- For patients who are HER2+
- Q3wks x 1 yr, given concomitantly with non-anthracycline chemotherapy
- 48% reduction in risk of recurrence
- 39% reduced risk of death
- Adverse Effects
  - decreased EF



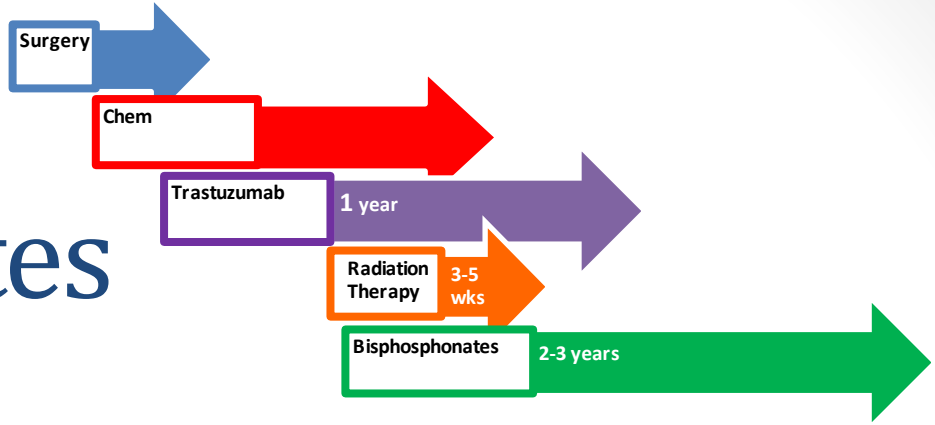
Romond, E. H., Perez, E. A., Bryant, J., Suman, V. J., Geyer Jr, C. E., Davidson, N. E., ... & Swain, S. M. (2005). Trastuzumab plus adjuvant chemotherapy for operable HER2-positive breast cancer. *New England Journal of Medicine*, *353*(16), 1673-1684.

Radiation Therapy



- Lumpectomy
  - Whole breast: *50 Gy in 25 # (5 weeks) or 40 Gy in 15 # (2-3 weeks)*
  - If high risk (Age <50, high grade, positive margins) may also get:
    - Boost to tumour bed: *10-16 Gy in 4-8#*
    - Regional nodes (infra/supraclavicular, axillary, internal mammary): *50 Gy in 25#*
- Mastectomy
  - If high risk (Large tumour (>5cm), LN+, positive margins)
    - Chest wall: *50 Gy in 25#*
    - Nodes: *50 Gy in 25#*
- If age >70 and Stage 1, can potentially forego XRT

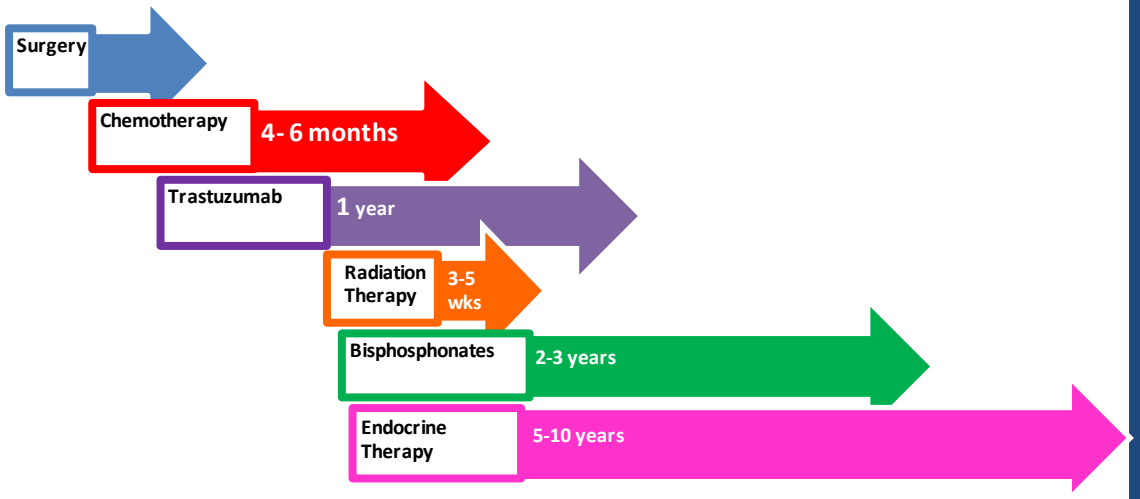
Bisphosphonates



- Intermediate/high risk cancers, postmenopausal
- Zoledronic acid q6mon x 2-3 yrs.
- Significantly decreases in bone recurrence (RR 0.86) and breast cancer mortality (RR 0.85)
- Avoid invasive dental procedures where possible

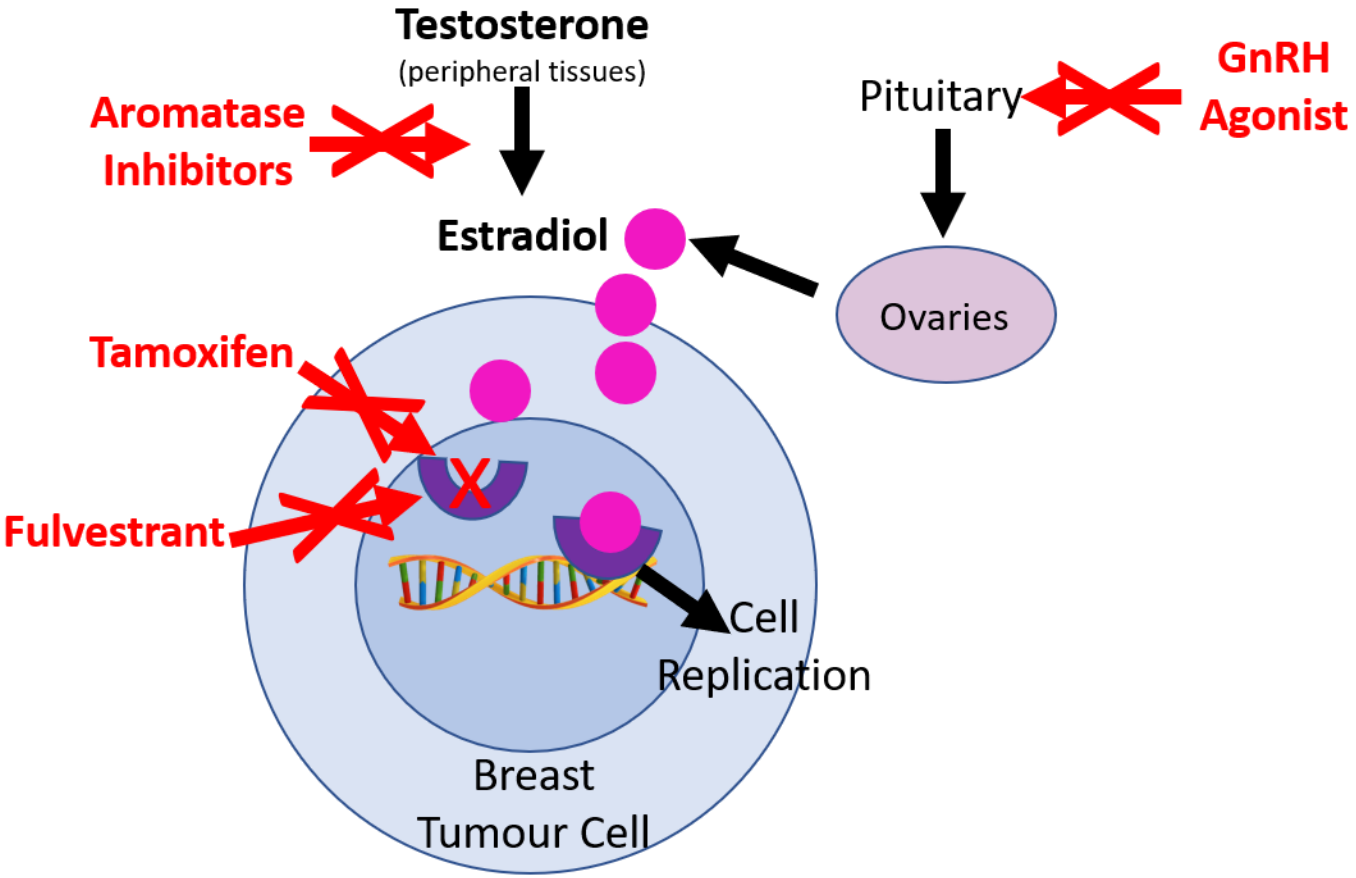
Early Breast Cancer Trialists' Collaborative Group. (2015). Adjuvant bisphosphonate treatment in early breast cancer: meta-analyses of individual patient data from randomised trials. *The Lancet*, *386*(10001), 1353-1361.
https://www.cda-adc.ca/jcda/vol-74/issue-7/617.pdf
https://www.cmaj.ca/content/172/13/1684

Endocrine Therapy



- For ER/PR + disease
- Tamoxifen
- Aromatase Inhibitors
  - Letrozole
  - Anastrozole
  - Exemestane
- GnRH agonists
- Fulvestrant

Mechanism of Action of Endocrine Therapy



Tamoxifen

- Selective Estrogen Receptor Modulator (SERM)
- Can be used in both pre and post menopausal women
- Efficacy
  - Reduces recurrence by 39%
  - Reduces 10 yr mortality by 31%
- Side Effects
  - VTE
  - Endometrial cancer (risk 3.1%)
  - Vaginal dryness and hot flashes
- *Caution with SSRI's: Fluoxetine and Paroxetine decrease efficacy of Tamoxifen*

Davies, C., Pan, H., Godwin, J., Gray, R., Arriagada, R., Raina, V., ... & Bradbury, J. (2013). Long-term effects of continuing adjuvant tamoxifen to 10 years versus stopping at 5 years after diagnosis of oestrogen receptor-positive breast cancer: ATLAS, a randomised trial. *The Lancet*, *381*(9869), 805-816.

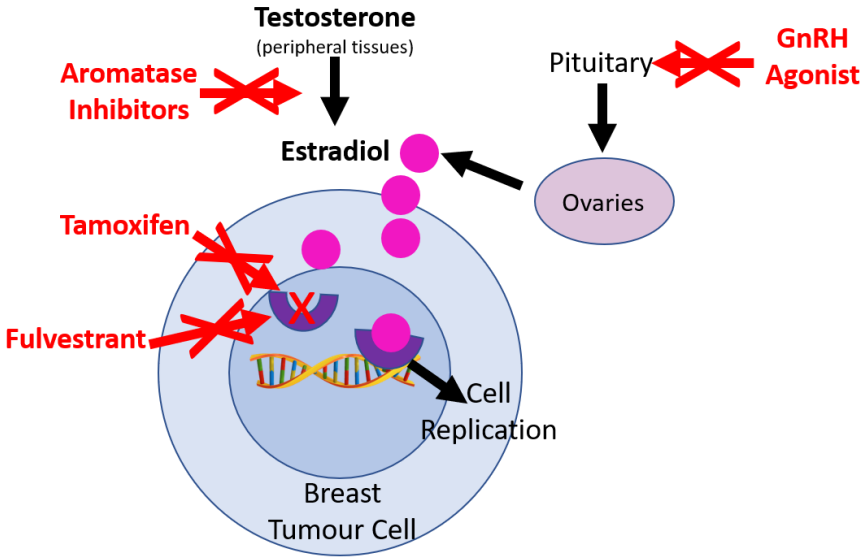
Aromatase Inhibitors

- Post menopausal women only
- Efficacy
  - 10 yr mortality decreased by an additional 10% (in addition to 31% from tamoxifen)
- Side Effects
  - Hyperlipidemia
  - Osteoporosis
  - Arthralgias and myalgias
  - Vaginal dryness and hot flashes
- Compliance ~70%

Arimidex, T. (2008). Effect of anastrozole and tamoxifen as adjuvant treatment for early-stage breast cancer: 100-month analysis of the ATAC trial. *The lancet oncology*, *9*(1), 45-53.
Crivellari, D., Sun, Z., Coates, A. S., Price, K. N., Thürlimann, B., Mouridsen, H., ... & Gelber, R. D. (2008). Letrozole compared with tamoxifen for elderly patients with endocrine-responsive early breast cancer: the BIG 1-98 trial. *Journal of clinical oncology*, *26*(12), 1972-1979.

Menopausal Status- Why does it matter?

- Aromatase Inhibitors (AI) block peripheral conversion of androgens to estrogen
- In premenopausal women with functioning ovaries, decreased circulating estrogen with AI's will cause ovaries to be stimulated to make more estrogen
- Estrogen levels are therefore higher than without treatment



Endocrine Therapy Options

- **Premenopausal**
  - Tamoxifen
  - Ovarian Suppression (GnRH agonist/Ablation/Oophorectomy) + tamoxifen
  - Ovarian Suppression (GnRH agonist/Ablation/Oophorectomy) + AI
- **Post Menopausal**
  - Tamoxifen
  - Tamoxifen followed by AI
  - AI
- **Duration**
  - At least 5 yrs
  - If node positive/high risk continue to 7 yrs
  - No survival benefit beyond 7 yrs, but prevents new breast cancers up to 10 yrs

Adjuvant Treatment- What's in the Pipeline???

- **Immunotherapy**
  - ?role in triple negative breast cancer? Studies ongoing

- **CDK4/6 Inhibitors**
  - Used in conjunction with endocrine therapy
  - "molecular brakes"-stop or slow cell division
    - Palbociclib
    - Ribociclib
    - Abemaciclib
  - 3.5% improvement in disease free survival rate.
  - $$$

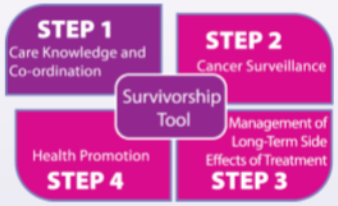
Johnston, S. R., Harbeck, N., Hegg, R., Toi, M., Martin, M., Shao, Z. M., ... & Sohn, J. (2020). Abemaciclib combined with endocrine therapy for the adjuvant treatment of HR+, HER2−, node-positive, high-risk, early breast cancer (monarchE). *Journal of Clinical Oncology*, JCO-20.

4) Survivorship Care

Breast Cancer Survivorship Tool

Patient Identification

STEP 1 Know Your Patient



THE COLLEGE OF FAMILY PHYSICIANS OF CANADA | LE COLLÈGE DES MÉDECINS DE FAMILLE DU CANADA

Patient Profile

Age at diagnosis: _____

Date of diagnosis: _____

Breast cancer site: ○ L ○ R ○ BL

Type: _____

Grade: _____ Margins: _____

Lymph nodes involved: _____

☐ ER+/ ER- ☐ PR+/PR- ☐ HER2+/ HER2-

TNM: _____ Stage: _____

Genetic testing: _____

Menopausal status: _____

Date of last mammogram: _____

Health Care Team

Family physician: _____

Medical oncologist: _____

Radiation oncologist: _____

General surgeon: _____

Plastic surgeon: _____

The first step of survivorship care is understanding what breast cancer treatments an individual has received.

Print this form and complete it by hand or fill in the blanks online.

Print document

How to cite this document:
College of Family Physicians of Canada. Breast Cancer Survivorship Tool. Mississauga, ON: College of Family Physicians of Canada; 2019.

Treatment History

Surgery ☐ Lumpectomy ☐ Mastectomy ☐ Sentinel node biopsy ☐ Axillary dissection

Reconstruction ☐ Implant ☐ Tissue flap ☐ Other

Chemotherapy Drug Regimen: _____

♥ Anthracycline (doxorubicin/epirubicin) given: ○ Yes ○ No

Radiation therapy Total dose: _____ Location: _____

Herceptin ♥ ○ Yes ○ No

Bisphosphonate ○ Yes ○ No

Ovarian suppression ○ Medical ○ Surgical

Endocrine therapy Drug: _____ Start date: _____

Intended treatment duration: _____

Drug: _____ Start date: _____

Intended treatment duration: _____

Date treatment completed: _____

♥ Potential for cardiotoxicity

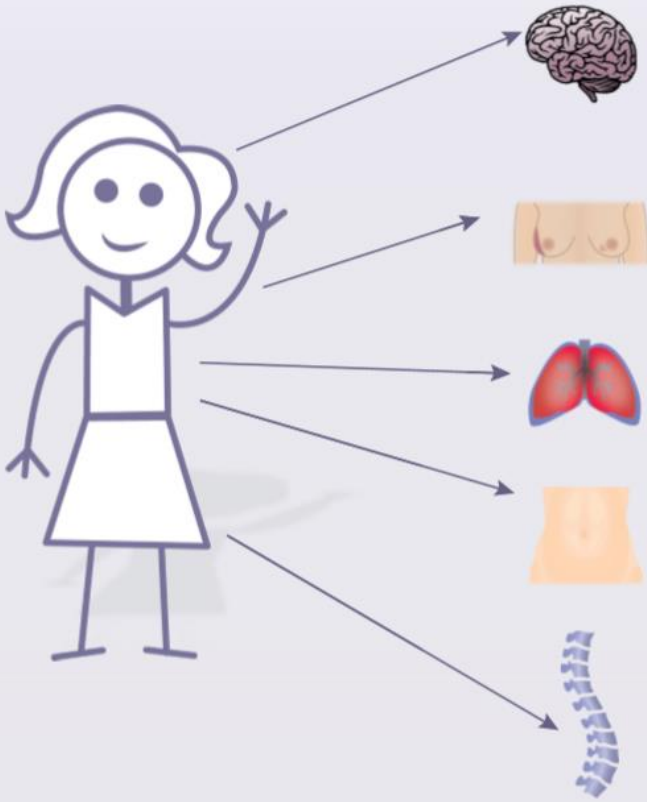
https://www.cfpc.ca/uploadedFiles/Directories/Committees_List/BCS_Tool_Eng_Sep30_2019.pdf

Survivorship Care- 4 stages

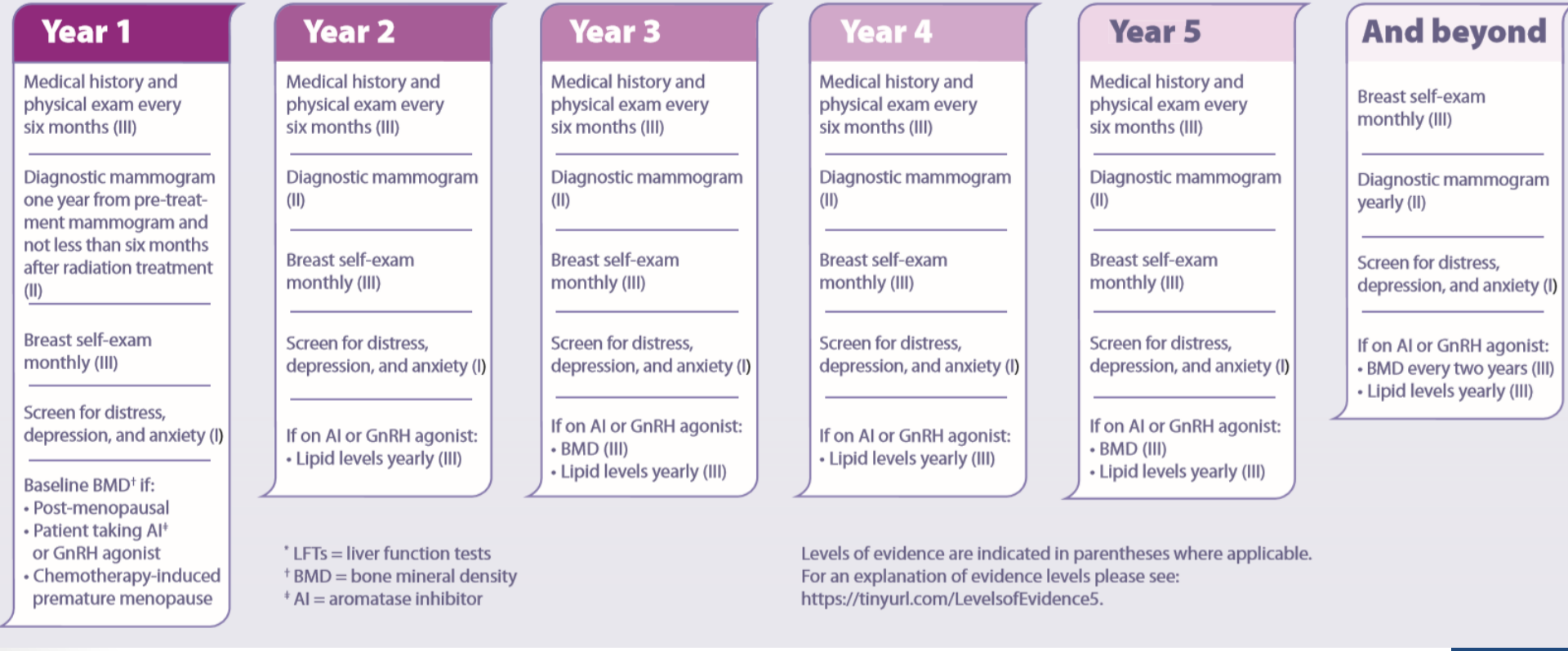
STEP 2 **Cancer Surveillance: Cancer Recurrance** [3,9,10,11]

Common Sites of Disease Recurrence: local, lung, liver, bone, brain

Always consider the possibility of a new primary cancer and the need for biopsy in addition to referral.



	Further Steps
New neurological symptoms • Headache • Seizures • Nausea and vomiting • New weakness/paresthesia	• MRI (if available) or CT head with contrast • Refer to radiation/medical oncology and/or neurosurgery
New breast/axillary symptoms • Dimpling of the skin • Discharge from the nipple • New palpable breast mass • New palpable lymph node • New lymphedema	• Mammogram, ultrasound • Refer to breast surgeon and/or breast diagnostic centre • Refer to medical oncology
New respiratory symptoms • Coughing • Hemoptysis • Shortness of breath	• Chest X-ray, CT thorax • Refer to medical oncology
New abdominal symptoms • Nausea and vomiting • New somatic and visceral pain • Abdominal distension • Jaundice	• Consider LFTs, ultrasound, or CT abdomen/pelvis • Refer to medical oncology
New bone pain • Acute or progressive bone pain	• Consider X-ray, bone scan, or CT/MRI axial skeleton • Refer to medical oncology/radiation oncology



* LFTs = liver function tests
† BMD = bone mineral density
‡ AI = aromatase inhibitor

Levels of evidence are indicated in parentheses where applicable.
For an explanation of evidence levels please see:
https://tinyurl.com/LevelsofEvidence5.

STEP 3 Long-Term Side Effects of Treatment

Long-term side effects will depend on which therapies your patient has had. Surgery, radiation, chemotherapy, and endocrine therapies all have different possible long-term effects.

Cognitive dysfunction [1,12,13,14]
Chemotherapy
- Mild cognitive impairment or "chemo brain"

Psychological distress [3,5,15]
All therapies

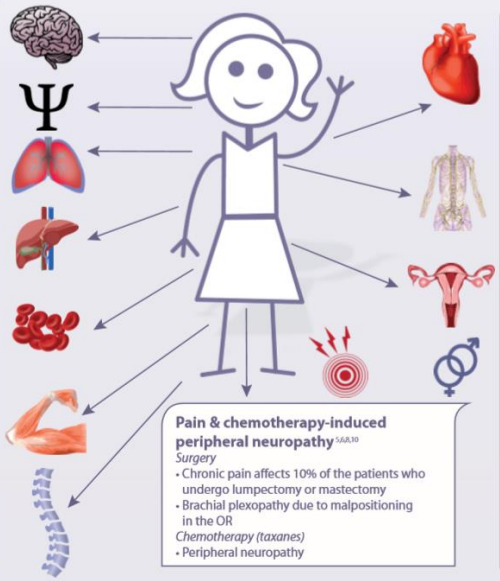
Pulmonary fibrosis [16,17,18]
Radiation
- Increased shortness of breath

Fatty liver disease [8,19]
Endocrine (tamoxifen)
- May develop in up to 33% of patients

Venous thromboembolism [8,20]
Endocrine (tamoxifen)
- Relative risk of VTE is two to three times higher
- Pulmonary embolism risk of 0.2% over five years

Arthralgia, musculoskeletal symptoms [8,21,22,23,24]
Endocrine (AI)
- Affects 45% to 50% of patients on AI

Osteoporosis [3,5,8,25]
Chemotherapy, Endocrine (AI, GnRH agonist)
- Relative risk of fractures increases by 47% +/- 13%; absolute increase of 2%



Pain & chemotherapy-induced peripheral neuropathy [5,6,8,10]
Surgery
- Chronic pain affects 10% of the patients who undergo lumpectomy or mastectomy
- Brachial plexopathy due to malpositioning in the OR

Chemotherapy (taxanes)
- Peripheral neuropathy

Cardiovascular health [3,5,8,26]
Chemotherapy (anthracyclines; trastuzumab)
- Heart failure, MI, arrhythmias

Endocrine (AI)
- Hypertension, hyperlipidemia

Radiation
- Fibrosis

Lymphedema
Surgery [3,5,27]
- Lymphedema can develop post sentinel node dissection (9%) and axillary dissection (40%)

Gynecological, sexual health [3,8,25,28]
Chemotherapy, Endocrine
- Anxiety with intimacy due to psychological and physical changes

Chemotherapy
- Premature ovarian failure: Affects 30% of wo… 90%

Endoc…
- Vagi…

Endoc…
- Hot f… of wo…
- Endo…

Eleva… seco…
Chem…

STEP 3 Managment of Long-Term Side Effects of Treatment

Cognitive dysfunction [1,5,13,14,15]
- Ask about cognitive difficulties (III)
- Assess for reversible factors and treat when possible (I)
- Refer for neurocognitive assessment and rehab if there are signs of impairment (I)
- Suggest coping strategies (relaxation, stress management, routine exercise) (III)

Psychological distress [3,5,9,15]
- Assess frequently for distress, depression, anxiety (I)
- Refer to counselling and/or start pharmacotherapy (II)
- Avoid paroxetine, fluoxetine where possible due to potential interaction with tamoxifen

Pulmonary fibrosis [16,17,18]
- Assess for shortness of breath
- Order chest X-ray, pulmonary function test, consider CT chest
- Refer to respirology

Fatty liver disease [8,19]
- If LFTs increase to more than double the upper limit of normal, stop tamoxifen, recheck LFTs, and re-evaluate. If restarted, repeat LFTs every three to six months. Refer to liver specialist if LFTs persistently elevated.

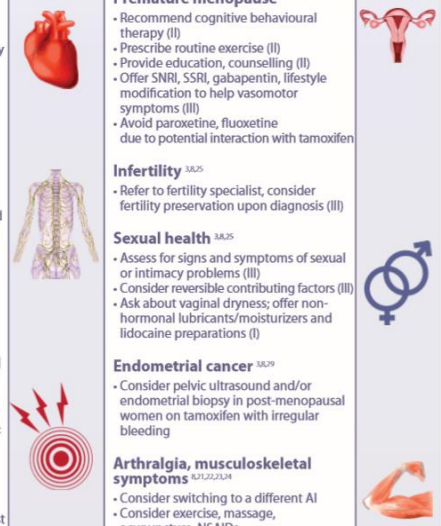
Venous thromboembolism [8,20]
- Treat VTE as per guidelines

Osteoporosis [3,5,8,25]
- Send for BMD scan every two years if patient on AI or GnRH agonist (III)
- Manage as per osteoporosis guidelines

Cardiovascular [3,5,8,26]
- Encourage lifestyle modifications (diet, exercise, smoking cessation)
- Monitor lipid levels (III)
- Manage cardiac risk factors appropriately
- Initiate cardiac workup if patient is symptomatic, including stress test and echocardiogram
- Refer to cardiology if any signs of cardiotoxicity

Lymphedema [3,5,27]
- Consider weight loss (III)
- Educate about lymphedema signs and symptoms (III)
- If no lymphedema can give injection and measure BP; if patient has lymphedema, avoid injection and BP measurement in the affected arm
- Keep the skin clean and avoid injury
- Try a compression sleeve
- Prescribe massage therapy
- Refer to lymphedema specialist if available (III)

Pain and chemotherapy-induced peripheral neuropathy [5,6,8,10,27]
- Assess for pain and contributing factors with pain scale and history (III)
- Prescribe non-pharmacologic treatment: physical activity (I), acupuncture (III), TENS (III)
- Prescribe pharmacologic treatment: acetaminophen, NSAIDs, duloxetine, pregabalin (I)
- Provide education about phantom breast syndrome
- Consider referral to pain specialist (III)



Premature menopause [3,8,25]
- Recommend cognitive behavioural therapy (II)
- Prescribe routine exercise (II)
- Provide education, counselling (II)
- Offer SNRI, SSRI, gabapentin, lifestyle modification to help vasomotor symptoms (III)
- Avoid paroxetine, fluoxetine due to potential interaction with tamoxifen

Infertility [3,8,25]
- Refer to fertility specialist, consider fertility preservation upon diagnosis (III)

Sexual health [3,8,25]
- Assess for signs and symptoms of sexual or intimacy problems (III)
- Consider reversible contributing factors (III)
- Ask about vaginal dryness; offer non-hormonal lubricants/moisturizers and lidocaine preparations (I)

Endometrial cancer [3,8,29]
- Consider pelvic ultrasound and/or endometrial biopsy in post-menopausal women on tamoxifen with irregular bleeding

Arthralgia, musculoskeletal symptoms [8,21,22,23,24]
- Consider switching to a different AI
- Consider exercise, massage, acupuncture, NSAIDs

STEP 4 Health Promotion

Weight management [3,25,30,31]

Breast cancer survivors who have BMIs higher than 30 are at an increased risk of disease recurrence and the development of new primary malignancies. Primary care physicians should encourage:

- Healthy dietary habits (III)
- Physical activity (III)
- Weight loss (III)

Physical activity [5,10,31]

Physical activity is recommended for all breast cancer survivors. Evidence shows that survivors who participate in daily physical activity have a decreased risk of death, less fatigue, less pain, lower rates of depression, and a better quality of life. Primary care physicians should:

- Recommend returning to daily activities as soon as possible after the initial diagnosis (II)
- Recommend 150 minutes of moderate exercise per day or 75 minutes of high-intensity exercise weekly (I)
- Recommend twice-a-week strength training (I)

Nutrition [5]

Although there is no scientific evidence demonstrating that nutrition alone can prevent cancer recurrence, primary care providers should emphasize the importance of a diet that has a positive impact on cardiovascular health. This includes:

- A diet rich in fruit, legumes, and whole grains and low in saturated fat (I)
- Limited amounts of processed meat and red meat (I)
- Vitamin and iron supplementation only if deficiencies are demonstrated (III)
- Daily intakes of calcium (1,200 mg/day) and vitamin D (800 IU/day)

Smoking cessation [3,8]

Breast cancer survivors who stop smoking have significantly lower all-cause mortality. (II)
Primary care physicians should therefore:

- Encourage smoking cessation (I)
- Offer smoking cessation resources and support (I)

Concerning marijuana, there is no evidence addressing its use and health implications in breast cancer survivors.

Preventative health [3,33]

A Canadian study demonstrated that 65% of eligible breast cancer survivors were not screened for colorectal cancer and 40% were not screened for cervical cancer over a four-year follow-up period. Primary care physicians should continue recommended routine screening during and after cancer treatment.

Alcohol [3,8,25,30,32]

Cancer survivors who have a greater alcohol intake have an increased rate of cancer recurrence. Breast cancer survivors should limit their consumption to no more than three or four standard drinks (14 g of alcohol/drink) a week.

Questions?

Bisphosphonates can be used in the adjuvant treatment of breast cancer.

a) True
b) False

Anthracycline cardiotoxicity can manifest more than 20 yrs post treatment.

a) True
b) False

Aromatase Inhibitors can be used in:

a) Premenopausal women with functioning ovaries
b) Postmenopausal women
c) Premenopausal women with supressed ovarian function
d) B + D
e) All of the above

Follow up care for breast cancer patients should include the following:

a) Mammography
b) Breast MRI
c) Bone Scan
d) LFT's
e) All of the above

Who should be referred to Genetics?

- Breast cancer diagnosis at age < 50 (especially < 35)
- Triple-negative breast cancer age < 60
- Ovarian cancer at any age
- Bilateral breast cancer
- Breast and ovarian cancer in the same woman or family
- Multiple breast cancers on same side of family (paternal or maternal)
- Male breast cancer
- Ashkenazi Jewish ethnicity

Fertility Preservation

- Childbearing after treatment of invasive breast cancer does not increase rates of recurrence
- There is no increased risk of birth defects/serious illnesses after treatment for breast cancer
- Treatment for breast cancer may impair fertility
- Consider discussing fertility with newly diagnosed patients and referring to fertility specialist before treatment starts

Menopausal Status

- Use LH, FSH, estradiol to determine menopausal status
- Amenorrhea post chemo not reliable especially if on tamoxifen

Pagani, O., Regan, M. M., Walley, B. A., Fleming, G. F., Colleoni, M., Láng, I., ... & Ciruelos, E. (2014). Adjuvant exemestane with ovarian suppression in premenopausal breast cancer. *New England Journal of Medicine*, *371*(2), 107-118

Francis, P. A., Regan, M. M., Fleming, G. F., Láng, I., Ciruelos, E., Bellet, M., ... & Martino, S. (2015). Adjuvant ovarian suppression in premenopausal breast cancer. *New England Journal of Medicine*, *372*(5), 436-446.

Investigations not routinely indicated

- Breast MRI
- Blood work
  - CBC, LFT, tumour markers
- Imaging
  - CXR, CT, Bone scan
- Cardiac markers, ECHO