Early Detection and Diagnosis
Early Detection and Diagnosis

- **Versions 2005–2019:**
  Albert / Blohmer / Fallenberg / Fersis / Junkermann / Maass / Müller-Schimpfle / Scharl / Schreer

- **Version 2021**
  Fallenberg / Gerber
## Early Detection with Mammography

<table>
<thead>
<tr>
<th>Age</th>
<th>Interval</th>
<th>Oxford</th>
<th>LOE</th>
<th>GR</th>
<th>AGO</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 40</td>
<td>na</td>
<td>-</td>
<td>-</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
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<td>1b</td>
<td>B</td>
<td>-</td>
<td>#</td>
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<td>24-36</td>
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<td>B</td>
<td>+#</td>
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<tr>
<td>50–69*</td>
<td>24</td>
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<td>A</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>70–74</td>
<td>24</td>
<td>1a</td>
<td>A</td>
<td>+#</td>
<td></td>
</tr>
<tr>
<td>&gt; 75**</td>
<td>24</td>
<td>4</td>
<td>C</td>
<td>+/-#</td>
<td></td>
</tr>
</tbody>
</table>

* National Mammography-Screening-Program
** health status + life expectancy more than 10 years
# clear indication necessary
Early Detection in Asymptomatic Women
Digital Breast Tomosynthesis

The complete DBT dataset of images has to be available for evaluation/reporting, the synthetic mammography only is not sufficient.

- Sign. higher sensitivity, heterogeneous specificity, and higher costs [machine, evaluation, archiving] of DBT in comparison to Full-Field Digital Mammography (FFDM)
- Dose reduction due to calculated synthetic 2D mammography (SM) instead of FFDM

** Evaluation for Germany in a randomized prospective trial (TOSYMA)

<table>
<thead>
<tr>
<th>Digital Breast Tomosynthesis (DBT in addition to FFDM or SM)*</th>
<th>Oxford</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LOE</td>
</tr>
<tr>
<td></td>
<td>GR</td>
</tr>
<tr>
<td></td>
<td>AGO</td>
</tr>
<tr>
<td>Replacing FFDM by synthetic MG in addition to DBT**</td>
<td>1a</td>
</tr>
<tr>
<td></td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Replacing FFDM by synthetic MG in addition to DBT**</td>
<td>2a</td>
</tr>
<tr>
<td></td>
<td>B</td>
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<tr>
<td></td>
<td>++</td>
</tr>
</tbody>
</table>
## Breast Cancer Mortality Reduction

### Meta-Analysis

<table>
<thead>
<tr>
<th>Study</th>
<th>RR 95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Independent UK Panel, 2012</strong></td>
<td>0.80 (0.73–0.89)</td>
</tr>
<tr>
<td>13-year metaanalysis</td>
<td></td>
</tr>
<tr>
<td><strong>Cochrane Review, 2011</strong></td>
<td>0.81 (0.74–0.87)</td>
</tr>
<tr>
<td>Fixed-effect metaanalysis of 9 RCT-trials</td>
<td></td>
</tr>
<tr>
<td>As above, but excluding women &lt;50 years</td>
<td>0.77 (0.69–0.86)</td>
</tr>
<tr>
<td><strong>Canadian Task Force, 2011</strong></td>
<td>0.79 (0.68–0.90)</td>
</tr>
<tr>
<td>Women aged 50–69 years</td>
<td></td>
</tr>
<tr>
<td><strong>Duffy et al, 2012</strong></td>
<td>0.79 (0.73–0.86)</td>
</tr>
<tr>
<td>Review of all trials and age groups</td>
<td></td>
</tr>
<tr>
<td><strong>Duffy et al, 2020</strong></td>
<td>0.59 (0.51-0.68) mortality</td>
</tr>
<tr>
<td>Review of 549,091 Women (30% eligible Swedish screening population)</td>
<td>0.75 (0.66-0.84) advanced BC</td>
</tr>
</tbody>
</table>
# Breast Cancer Mortality Reduction

<table>
<thead>
<tr>
<th>Meta-Analysis</th>
<th>RR 95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Case-Control Studies</strong></td>
<td></td>
</tr>
<tr>
<td>Broeders et al</td>
<td>Screening Mx</td>
</tr>
<tr>
<td></td>
<td>Corr. for self selection</td>
</tr>
<tr>
<td></td>
<td>Invited for screening</td>
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<tr>
<td><strong>Incidence-based Mortality Studies</strong></td>
<td></td>
</tr>
<tr>
<td>Broeders et al</td>
<td>Screening Mx</td>
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<tr>
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<td>Invited to screening</td>
</tr>
<tr>
<td><strong>Randomized Clinical Trials</strong></td>
<td></td>
</tr>
<tr>
<td>Gotsche and Jorgenson</td>
<td>Screening Mx</td>
</tr>
<tr>
<td><strong>ECIBC</strong></td>
<td>Screening MX</td>
</tr>
<tr>
<td></td>
<td>45–49</td>
</tr>
<tr>
<td></td>
<td>50–69</td>
</tr>
</tbody>
</table>
Breastcancer: incidence and mortality

- **Annual incidence of breast cancer and mortality in the EU (GLOBOCAN 2012)**

<table>
<thead>
<tr>
<th>Age</th>
<th>Incidence/1000</th>
<th>Mortality/1000</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 to 44</td>
<td>1,2</td>
<td>0,1</td>
</tr>
<tr>
<td>45 to 49</td>
<td>1,7</td>
<td>0,2</td>
</tr>
<tr>
<td>50 to 69</td>
<td>2,7</td>
<td>0,5</td>
</tr>
<tr>
<td>70 to 74</td>
<td>3,0</td>
<td>0,8</td>
</tr>
</tbody>
</table>

From: http://gco.iarc.fr/
# Mammography-Screening
## Benefit and Harm

Data background: Breast Cancer Surveillance Consortium Registry Data per 10,000 Women screened over 10 years

<table>
<thead>
<tr>
<th>Age</th>
<th>40-49</th>
<th>50-59</th>
<th>60-69</th>
<th>70-74</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast cancer death avoided (CI95%)</td>
<td>3 (0-9)</td>
<td>8 (2-17)</td>
<td>21 (11-32)</td>
<td>13 (0-32)</td>
</tr>
<tr>
<td>False-positive (n)</td>
<td>1212</td>
<td>932</td>
<td>808</td>
<td>696</td>
</tr>
<tr>
<td>Breast biopsies (n)</td>
<td>164</td>
<td>159</td>
<td>165</td>
<td>175</td>
</tr>
<tr>
<td>False-negative (n)</td>
<td>10</td>
<td>11</td>
<td>12</td>
<td>13</td>
</tr>
</tbody>
</table>

Siu Al on behalf of the USPSTF 2016, 164:279–296

Early Detection and Diagnosis
**Early Detection (normal risk) Sonography/MRI**

<table>
<thead>
<tr>
<th>Oxford</th>
<th>LoE</th>
<th>GR</th>
<th>AGO</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5</td>
<td>D</td>
<td>--</td>
</tr>
<tr>
<td></td>
<td>3a</td>
<td>C</td>
<td>--</td>
</tr>
</tbody>
</table>

- **Screening-Breast Sonography allone**
  - Automated 3D-Sonography

- **Breast sonography as an adjunct:**
  - Dense mammogram (heterogeneously dense, extremely dense)
  - Elevated risk
  - Mammographic lesion
  - Second-look US (MRI-only detected lesions)

- **MRI if screening MG is negative and breast composition: extremely dense* 50–75 y**

* Definition of extremely dense corresponds to BIRADS-density category D, heterogeneously dense to BIRADS-category C according to ACR BI-RADS-Atlas 5th ed. 2013

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in der DGGG e.V.
sowie
in der DKG e.V.
Guidelines Breast
Version 2021.1E

www.ago-online.de

Early Detection and Diagnosis
# Early Detection (normal risk) Clinical Breast Examination (CBE)

As a stand-alone procedure

- **Self-examination**
- **Clinical breast examination (CBE) by health professionals outside checkup for cancer**
- **Clinical breast examination (CBE) by health professionals during checkup for cancer**
- **Medical palpation thru blind/optically disabled persons**

<table>
<thead>
<tr>
<th>CBE because of mammographic/sonographic lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBE in combination with imaging</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Oxford</strong></th>
<th><strong>LoE</strong></th>
<th><strong>GR</strong></th>
<th><strong>AGO</strong></th>
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</thead>
<tbody>
<tr>
<td>1a</td>
<td>A</td>
<td>-*</td>
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</tr>
<tr>
<td>1a</td>
<td>C</td>
<td>-*</td>
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<tr>
<td>1a</td>
<td>B</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>3b</td>
<td>C</td>
<td>-</td>
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</tr>
<tr>
<td>5</td>
<td>D</td>
<td>++</td>
<td></td>
</tr>
<tr>
<td>1a</td>
<td>A</td>
<td>++</td>
<td></td>
</tr>
</tbody>
</table>

* May increase breast awareness
### Assessment of Breast Symptoms or Lesions

- **Clinical examination**
- **Mammography**
  - Tomosynthesis***
  - Contrast-enhanced mammography (alone or as an adjunct)
- **Sonography**
  - Elastography (shear-wave) *
  - Automated 3D-sonography
- **Minimally invasive biopsy**
- **MRI**

<table>
<thead>
<tr>
<th>Method</th>
<th>Oxford</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>LoE</td>
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<tr>
<td>Clinical examination</td>
<td>3b</td>
</tr>
<tr>
<td>Mammography</td>
<td>1b</td>
</tr>
<tr>
<td>Tomosynthesis***</td>
<td>2b</td>
</tr>
<tr>
<td>Contrast-enhanced mammography (alone or as an adjunct)</td>
<td>2a</td>
</tr>
<tr>
<td>Sonography</td>
<td>2b</td>
</tr>
<tr>
<td>Elastography (shear-wave) *</td>
<td>2b</td>
</tr>
<tr>
<td>Automated 3D-sonography</td>
<td>3b</td>
</tr>
<tr>
<td>Minimally invasive biopsy</td>
<td>1b</td>
</tr>
<tr>
<td>MRI**</td>
<td>3a</td>
</tr>
</tbody>
</table>

* Adjunct assessment

**If clinical examination, mammography and sonography incl. needle biopsy do not allow a definite diagnosis

*** replacement of FFDM with SM
Pre-therapeutic Assessment of Breast and Axilla

- Clinical examination
- Mammography
  - + Tomosynthesis (DBT)***
  - Contrast-enhanced mammography (alone or as adjunct)
- Sonography (breast and axilla)
- MRI*
- Minimally invasive biopsy**
  - Axilla CNB, if lymph node is suspect
- Breast-CT

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Oxford LoE</th>
<th>GR</th>
<th>AGO</th>
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<td>Clinical examination</td>
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<td>D</td>
<td>++</td>
</tr>
<tr>
<td>Mammography</td>
<td>2b</td>
<td>B</td>
<td>++</td>
</tr>
<tr>
<td>+ Tomosynthesis (DBT)***</td>
<td>2b</td>
<td>B</td>
<td>+</td>
</tr>
<tr>
<td>Contrast-enhanced mammography</td>
<td>2a</td>
<td>B</td>
<td>+</td>
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<tr>
<td>Sonography (breast and axilla)</td>
<td>2b</td>
<td>B</td>
<td>++</td>
</tr>
<tr>
<td>MRI*</td>
<td>1b</td>
<td>B</td>
<td>+</td>
</tr>
<tr>
<td>Minimally invasive biopsy**</td>
<td>1b</td>
<td>A</td>
<td>++</td>
</tr>
<tr>
<td>Axilla CNB, if lymph node is suspect</td>
<td>2b</td>
<td>B</td>
<td>++</td>
</tr>
<tr>
<td>Breast-CT</td>
<td>5</td>
<td>D</td>
<td>-</td>
</tr>
</tbody>
</table>

* MRI-guided vacuum biopsy is mandatory in case of MRI-detected additional lesions (in house or with cooperations). Individual decision for patients at high familiar risk, with dense breast (density C/D), lobular invasive tumors, suspicion of multilocular disease. No reduction in re-excision rate.

** Histopathology of additional lesions if relevant for treatment

*** replacement of FFDM with SM
## Sensitivities CESM

<table>
<thead>
<tr>
<th>Author</th>
<th>n</th>
<th>MG</th>
<th>CESM</th>
<th>MRI</th>
<th>US</th>
<th>Analyse</th>
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<tr>
<td>Dromain 2011</td>
<td>110</td>
<td>78</td>
<td>92</td>
<td></td>
<td></td>
<td>Per patient</td>
</tr>
<tr>
<td>Fallenberg 2014</td>
<td>118</td>
<td>77.9</td>
<td>94.7</td>
<td></td>
<td></td>
<td>Per patient</td>
</tr>
<tr>
<td>Mokhtar 2014</td>
<td>60</td>
<td>93.2</td>
<td>97.7</td>
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<td>Per patient</td>
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<tr>
<td>Lobbes 2014*</td>
<td>113</td>
<td>96.9</td>
<td>100</td>
<td></td>
<td></td>
<td>Per patient</td>
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<tr>
<td>Perez 2015 ECR</td>
<td>98</td>
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<td>78</td>
<td>66</td>
<td></td>
<td>Per lesion</td>
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<tr>
<td>Luczinska 2014</td>
<td>152</td>
<td>91</td>
<td>100</td>
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<tr>
<td>Jochelson 2012</td>
<td>52</td>
<td>81</td>
<td>96</td>
<td>96</td>
<td>93</td>
<td>Per patient</td>
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<tr>
<td></td>
<td></td>
<td>59</td>
<td>83</td>
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<td></td>
<td>Per lesion</td>
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<tr>
<td>Fallenberg 2013</td>
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<td>81</td>
<td>100</td>
<td>97</td>
<td></td>
<td>Per patient</td>
</tr>
<tr>
<td>Fallenberg 2016</td>
<td>155</td>
<td>81</td>
<td>94</td>
<td>95</td>
<td>76</td>
<td>Index Per Lesion</td>
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<tr>
<td>Lalji 2016*</td>
<td>199</td>
<td>93</td>
<td>96,9</td>
<td></td>
<td></td>
<td>Per patient</td>
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<tr>
<td>Tennant 2016</td>
<td>100</td>
<td>84</td>
<td>95</td>
<td></td>
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<tr>
<td>Luczynska 2016</td>
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<td>90</td>
<td>100</td>
<td>92</td>
<td></td>
<td></td>
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<tr>
<td>Xing 2019</td>
<td>235</td>
<td></td>
<td>91,5</td>
<td>91,5</td>
<td></td>
<td>Per lesion</td>
</tr>
</tbody>
</table>

CESM is comparable to MRI regarding index, a bit inferior for additional lesions

* Recall from Screening
Pre-therapeutic Staging

History and clinical examination

Additional diagnosis for patients with tumors of high metastatic potential and/or symptoms and/or indication for (neo-)adjuvant chemotherapy and/or antibody-therapy):

- CT scan of thorax/abdomen
- Bone scan
- Chest X-ray
- Liver ultrasound
- In case of suspicious lesions further diagnosis (e.g. liver-MRI, CEUS*, biopsy etc.)
- FDG-PET or FDG-PET /CT**
- Whole body MRI

* Contrast enhanced ultrasound

**especially in patients with high tumor stage (III) if available

<table>
<thead>
<tr>
<th>Oxford</th>
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<tbody>
<tr>
<td></td>
<td>2a</td>
<td>B</td>
<td>+</td>
</tr>
<tr>
<td>CT scan of thorax/abdomen</td>
<td>2b</td>
<td>B</td>
<td>+</td>
</tr>
<tr>
<td>Bone scan</td>
<td>5</td>
<td>C</td>
<td>+/-</td>
</tr>
<tr>
<td>Chest X-ray</td>
<td>5</td>
<td>D</td>
<td>+/-</td>
</tr>
<tr>
<td>Liver ultrasound</td>
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<td>B</td>
<td>+</td>
</tr>
<tr>
<td>FDG-PET or FDG-PET /CT**</td>
<td>2b</td>
<td>B</td>
<td>+/-</td>
</tr>
<tr>
<td>Whole body MRI</td>
<td>4</td>
<td>C</td>
<td>+/-</td>
</tr>
</tbody>
</table>