The prevalence of incidental breast cancer and neoplastic precursors: A systematic review of autopsy studies

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Increasing incidence of breast cancer

- Deaths have decreased 35% (uncertain how much is due to earlier detection)
- Breast cancer increased 50% in 30 years;

Figure 2: Age-standardised incidence rates for breast cancer 1982–2012 and age-standardised mortality rates for breast cancer 1968–2013


Source: Australian Institute of Health and Welfare¹
Overdiagnosis: cancers diagnosed that would never have caused symptoms or death

Source: NCI Division of Cancer Prevention

Adapted from a figure provided courtesy of H. Gilbert Welch, Dartmouth Medical School
What is the prevalence of incidental breast cancer and neoplastic precursor lesions found in autopsies?

Previous systematic review undertaken in 1997

• How large is the reservoir of undetected:
  1. Invasive breast cancer
  2. Carcinoma-in-situ (DCIS/LCIS)
  3. Atypical hyperplasia

• Variations of these lesions with age?

• Any other predictors of breast cancer prevalence?
Systematic review of autopsy studies

SEARCH FOR:
Autopsy studies of women with no known breast cancer or pathology

FOUND:
13 studies includable
Published 1949 to 2010
Overall incidental cancer and precursor prevalence

• 0.8% Invasive (no adjustment)
• 8.9% In-situ (less thorough studies adjusted up)
• 9.8% Atypical hyperplasia (less thorough studies adjusted up)

Total = 19.5%
Prevalence over time
Thoroughness of examination: Invasive breast cancer

Prevalence of invasive breast cancer 0.8%
Thoroughness of examination: In-situ carcinoma

Prevalence of in-situ breast cancer (%) vs. Mean number of sections examined per woman.

Prevalence of in-situ cancer 8.9%
Thoroughness of examination: Atypical hyperplasia

Prevalence of atypical hyperplasia 9.8%
Predictors of breast cancer and precursor prevalence

<table>
<thead>
<tr>
<th>Thoroughness of examination</th>
<th>Invasive cancer</th>
<th>In-situ cancer (DCIS + LCIS)</th>
<th>Atypical hyperplasia (ADH + ALH)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;20 sections taken on average</td>
<td>OR 1.1 (0.5-2.7)</td>
<td>P 0.75</td>
<td>OR 126.8 (20.2-793.0)</td>
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### Relative size of prevalence pool

<table>
<thead>
<tr>
<th><strong>Invasive breast cancer</strong></th>
<th><strong>In-situ cancer</strong></th>
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<tr>
<td>Rate of incidental <em>invasive cancer</em> in autopsies (1%):</td>
<td>Rate of incidental <em>in-situ cancer</em> in autopsies (9%)</td>
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<tr>
<td>Lifetime risk of diagnosis of invasive breast cancer for women is 12.7%*</td>
<td>Lifetime risk of diagnosis of in-situ breast cancer for women is 2%*</td>
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<td>Half of the number of women die from breast cancer (2.7%)</td>
<td>4 x larger than number of cases currently diagnosed in life</td>
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<td>much more likely to be overdiagnosed</td>
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Based on 2010-2012 data
Conclusions

• Latent cancer and precursors detected in all studies since 1948

• Small reservoir of incidental invasive cancer (approx 1%) found in even the least thorough studies.

• Large reservoir of cancer in-situ and atypical hyperplasia especially in more thorough studies (approx 19%).
Clinical Implications

Over-detection of latent in-situ breast cancer or atypical hyperplasia by screening is highly likely to increase with newer, more sensitive technologies (e.g. digital and 3D mammography).

Expansion of screening programs will also increase risk of overdiagnosis (especially for older women, as they are more likely to die WITH than BECAUSE of cancer).

SDM: Harms, benefits and personal preferences