Research into Overdiagnosis and Overtreatment

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Is it important to do research in these topics?

Content of presentation

- Defining overdiagnosis
- Types of overdiagnosis
- Experiences of being overdiagnosed
- The degree of overdiagnosis
- Consequences of overdiagnosis
- Drivers to overdiagnosis
Content of presentation

- Defining overdiagnosis
- Types of overdiagnosis
- Experiences of being overdiagnosed
- The degree of overdiagnosis
- Consequences of overdiagnosis
- Drivers to overdiagnosis
What is overdiagnosis?

Talk 2 & 2 for 2 minutes
Mammography screening
Lung cancer screening with CT
Overdiagnosis - definition

“Overdiagnosis is the diagnosis of ‘illnesses’ that would never have caused patients harm but potentially exposes them to treatments where the risks outweigh the benefits.”

Doust & Glasziou. Is the problem that everything is a diagnosis? Australian Family Physician 42:856-859, 2013.
Overdiagnosis - description

“Overdiagnosis occur when individuals are diagnosed with conditions that will never cause symptoms or death.”

“...the ultimate criterion for overdiagnosis: at the end of life, if the person never developed a problem from her condition, she has been overdiagnosed.”

Overdiagnosis – my own definition

Overdiagnosis is the diagnosis of deviations, abnormalities, risk factors and/or pathology that never in itself will: cause symptoms (applies only to risk factors and pathology), lead to morbidity or be the cause of death.
Overdiagnosis – Søren Kierkegaard

"Life can only be understood backwards; but it must be lived forwards"

Søren Kierkegaard
(Danish philosopher 1813-55)
Overdiagnosis – therefore

- Individual level: never sure when the patient is actually overdiagnosed
- At the end of life the GP can be certain if the diagnosis was correct or iatrogenic
What is overtreatment?

- Treatment of overdiagnosed conditions is one category of overtreatment.
- Another type of overtreatment is when best available external evidence shows that the treatment has no beneficial effect on the diagnosed condition.
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- Types of overdiagnosis
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- Consequences of overdiagnosis
- Drivers to overdiagnosis
Types of overdiagnosis

- Overdetection – screening
- Disease mongering
- Expanding disease definitions or changing disease boundaries
Content of presentation

- Defining overdiagnosis
- Types of overdiagnosis
- Experiences of being overdiagnosed
- The degree of overdiagnosis
- Consequences of overdiagnosis
- Drivers to overdiagnosis
How is it to be overdiagnosed?

- Subjects: Conditions and diagnoses where the likelihood of overdiagnosis is large
- Material & Methods: Interviews, observational field work, documents etc.
Osteoporosis 1

16 healthy women with no chronic or disabling conditions and who had been (over)diagnosed with osteoporosis via a population-based cohort study

Osteoporosis 2

- appeared to take the scan literally
- planned their lives accordingly
- believed that the 'pictures' revealed some truth
- interpreted the scan result to mean bodily fragility, which they incorporated into their bodily perception

“A ticking bomb inside your stomach”

15 men (over)diagnosed
- median aortic diameter: 32 mm
- 15 single interviews
- 3 group interviews
one year later


**FIGURE 3** Aneurysm growth rate by 5-mm size ranges of baseline aneurysm diameter: random-effect meta-analyses conducted within subgroups.
Heterogeneity in growth rate in AAA diagnosed via screening


FIGURE 3 Aneurysm growth rate by 5-mm size ranges of baseline aneurysm diameter: random-effect meta-analyses conducted within subgroups.
Drop in incidens of AAA: 77%

Opening Pandora's box

The men expressed ambivalence towards the diagnosis: “they appreciated having the knowledge but it was accompanied by worry, feelings of anxiety and existential thoughts about the fragility and finiteness of life”

COS-AAA, part I

- Anxiety
- Sense of dejection
- Negative impact on behaviour
- Negative impact on sleep
- Change in body perception
- Guilt
- Fear and powerlessness
- Negative experiences from the examination
- Negative emotional reactions
- Change in lifestyle
- Better not knowing
- Fear of rupture
- Negative impact on sexuality
- Lack of information
- Stigmatised
- Self-blame for smoking
- Still regretful smoking

COS-AAA, part II

- More or less relaxed/calm
- Social relationship
- Existential values
- Empathy
- Impulsivity

To what degree and for how long?

- **Subjects**: Conditions and diagnoses where people are overdiagnosed for at shorter period of time and/or the likelihood of overdiagnosis is large
- **Material & Methods**: Survey
Cumulative risk of false-positive screening mammography

<table>
<thead>
<tr>
<th>Country</th>
<th>Age Group</th>
<th>Cumulative risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>US</td>
<td>40-49 y</td>
<td>61.3% (10 rounds in 10 years)</td>
</tr>
<tr>
<td>US</td>
<td>40-69 y</td>
<td>49.1% (10 rounds in 10 years)</td>
</tr>
<tr>
<td>US</td>
<td>40-69 y</td>
<td>43.1% (9 rounds in 9 years)</td>
</tr>
<tr>
<td>Australia</td>
<td>50-69 y</td>
<td>37.5% (10 rounds in 20 years)</td>
</tr>
<tr>
<td>Spain</td>
<td>50-69 y</td>
<td>32.4% (10 rounds in 20 years)</td>
</tr>
<tr>
<td>Norway</td>
<td>50-69 y</td>
<td>20.8% (10 rounds in 20 years)</td>
</tr>
<tr>
<td>Denmark</td>
<td>50-69 y</td>
<td>8.1-21.5% (10 rounds in 20 years)</td>
</tr>
</tbody>
</table>
## Focus groups: content validity

<table>
<thead>
<tr>
<th>Examinations</th>
<th>Ultrasound &amp; clinical mammography</th>
<th>Plus needle biopsy</th>
<th>Plus surgical biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of women</td>
<td>5</td>
<td>7</td>
<td>7</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Examinations</th>
<th>Plus early recall</th>
<th>Plus needle biopsy</th>
<th>Plus surgical biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of women</td>
<td>5</td>
<td>5</td>
<td>7</td>
</tr>
</tbody>
</table>

COS-BC part I

Psychosocial consequences of abnormal false-positive screening mammography

- Anxiety
- Negative impact on behaviour
- Sense of dejection
- Negative impact on sleep
- Breast examination
- Negative impact on sexuality
- 2 single items

COS-BC part II

Long-term psychosocial consequences of false-positive screening mammography

- Anxious about/belief in (not) having breast cancer
- More or less relax
- Social relationship
- Existential values

J. Brodersen. Measuring psychosocial consequences of false-positive screening results - breast cancer as an example, Department of General Practice, Institute of Public Health, Faculty of Health Sciences, University of Copenhagen: Månedsskrift for Praktisk Lægegerning, Copenhagen. ISBN: 87-88638-36-7, 2006.
Longitudinal survey

- 3 June 2004 - 2 June 2005
- 1,318 women consecutively recruited
- 2 screening centres
- 5 assessments: 0, 1, 6, 18 & 36 months after screening/diagnosis
- COS-BC:
  - 12 psychosocial outcomes

Population screened in 1 year
Approx. 30,000

Abnormal results
590

Not invited or refused to participate: 136 (23.1%)
Participants with abnormal results: 454 (76.9%)

Excluded: 8 (1.8%)
Participants with breast cancer: 174 (38.3%)
Participants with false positive result: 272 (59.9%)
Participants with normal result: 864 (95.2%)

5 abnormal results with unknown conclusion
Baseline: 174 (100.0%)
1 month: 152 (87.4%)
6 months: 139 (79.9%)
18 months: 138 (79.3%)
36 months: 136 (78.2%)

3 abnormal results with cancer other than BC
Baseline: 272 (100.0%)
1 month: 234 (86.0%)
6 months: 201 (73.9%)
18 months: 216 (79.4%)
36 months: 209 (76.8%)

Baseline: 863 (99.9%)
1 month: 703 (81.4%)
6 months: 642 (74.3%)
18 months: 666 (77.1%)
36 months: 719 (83.2%)
False Positives: invasiveness?

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The Screening Cascade

People who are screened

Negative screening result

Positive screening result

Incidental finding

Separate cascade

Workup

True positive

False positive

Indeterminate finding

Surveillance

Treatment

Rapidly progressive disease; person would die even if treated

Mild, easily treatable disease; person would do well even if treated later

Person would never have developed symptoms, even if untreated

Delayed Benefit

No Benefit

Modified slide: Professor Russ Harris
Model: what happens at cancer screening?

Overdiagnosis in RCT

Overdiagnosis in RCT
Overdiagnosis in DLCST at 5 year follow-up

Cumulative incidence of lung cancer

- Screening group
- Control group

Cumulative incidence

Follow-up since randomisation (years)
Overdiagnosis in DLCST at 5 year follow-up

Cumulative incidence of lung cancer

- Screening group
- Control group

Cumulative incidence

Follow-up since randomisation (years)

- 24
- 68
- 96
- 53
Overdiagnosis in DLCST at 5 year follow-up

Cumulative incidence of lung cancer
Overdiagnosis in DLCST at 5 year follow-up

Cumulative incidence of lung cancer

- Screening group
- Control group

Cumulative incidence

Follow-up since randomisation (years)
Overdiagnosis in DLCST at 5 year follow-up

- Extra number of LC: 43 (96-53)
- ODx: \( \frac{43}{68} = 63\% \) [95% CI; 33%-88%]

Strength & limitations

- No screening in control group
- Minor contamination in control group
- Participation bias in DLCST?
- Too short follow-up?
- Uneven distribution of high risk heavy smokers after randomisation?

Heterogeneity in growth rate in AAA diagnosed via screening

<table>
<thead>
<tr>
<th>Author</th>
<th>n</th>
<th>AAA growth, cm (range)</th>
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<tbody>
<tr>
<td>30–34 mm</td>
<td></td>
<td></td>
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<tr>
<td>Brown 2003\textsuperscript{29}</td>
<td>191</td>
<td>2.80 (2.21–3.39)</td>
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<tr>
<td>Lindholt 2000\textsuperscript{35}</td>
<td>86</td>
<td>2.00 (1.67–2.33)</td>
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<tr>
<td>McCarthy 2003\textsuperscript{37}</td>
<td>330</td>
<td>1.60 (1.40–1.80)</td>
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<tr>
<td>Santilli 2002\textsuperscript{36}</td>
<td>578</td>
<td>1.50 (1.34–1.66)</td>
</tr>
<tr>
<td>Solberg 2005\textsuperscript{38}</td>
<td>87</td>
<td>1.80 (1.31–2.29)</td>
</tr>
<tr>
<td>Vega de Céniga 2006\textsuperscript{32}</td>
<td>155</td>
<td>1.65 (1.28–2.02)</td>
</tr>
<tr>
<td>Overall (I\textsuperscript{2}=78.3%)</td>
<td></td>
<td>1.81 (1.55–2.07)</td>
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<tr>
<td>35–39 mm</td>
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<td></td>
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<tr>
<td>Brown 2003\textsuperscript{29}</td>
<td>204</td>
<td>3.40 (2.81–3.99)</td>
</tr>
<tr>
<td>Lindholt 2000\textsuperscript{35}</td>
<td>34</td>
<td>3.20 (2.02–4.38)</td>
</tr>
<tr>
<td>McCarthy 2003\textsuperscript{37}</td>
<td>166</td>
<td>3.20 (2.79–3.61)</td>
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<tr>
<td>Santilli 2002\textsuperscript{36}</td>
<td>212</td>
<td>2.00 (1.75–2.25)</td>
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<tr>
<td>Solberg 2005\textsuperscript{38}</td>
<td>58</td>
<td>1.75 (1.48–2.02)</td>
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<tr>
<td>Vega de Céniga 2006\textsuperscript{32}</td>
<td>91</td>
<td>2.80 (1.94–3.66)</td>
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<tr>
<td>Overall (I\textsuperscript{2}=91.0%)</td>
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<td>2.66 (2.06–3.27)</td>
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<td>40–44 mm</td>
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<td>Brown 2003\textsuperscript{29}</td>
<td>306</td>
<td>4.50 (3.91–5.09)</td>
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<tr>
<td>Lindholt 2000\textsuperscript{35}</td>
<td>24</td>
<td>4.20 (3.00–5.40)</td>
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<td>Solberg 2005\textsuperscript{38}</td>
<td>23</td>
<td>2.31 (1.37–3.25)</td>
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<tr>
<td>Vega de Céniga 2006\textsuperscript{32}</td>
<td>62</td>
<td>4.50 (3.17–5.83)</td>
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<tr>
<td>Overall (I\textsuperscript{2}=81.0%)</td>
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<td>3.86 (2.75–4.97)</td>
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<tr>
<td>45–49 mm</td>
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<tr>
<td>Brown 2003\textsuperscript{29}</td>
<td>194</td>
<td>5.20 (4.42–5.98)</td>
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<tr>
<td>Lindholt 2000\textsuperscript{35}</td>
<td>7</td>
<td>5.30 (3.77–6.83)</td>
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<tr>
<td>Solberg 2005\textsuperscript{38}</td>
<td>11</td>
<td>3.36 (1.50–5.22)</td>
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<tr>
<td>Vega de Céniga 2006\textsuperscript{32}</td>
<td>44</td>
<td>5.02 (3.04–7.00)</td>
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<tr>
<td>Overall (I\textsuperscript{2}=11.2%)</td>
<td></td>
<td>4.96 (4.25–5.66)</td>
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</table>

Any medical intervention:  
Balance of benefits & harms
Any medical intervention: 
Balance of benefits & harms

Harms

Low risk  High risk
Any medical intervention: Balance of benefits & harms
Any medical intervention: Balance of benefits & harms
AAA screening: 38-44% ODx

http://www.bmj.com/content/350/bmj.h825/infographic
Any medical intervention: Balance of benefits & harms
PSA-screening

Figure 2: Cumulative incidence of prostate cancer in the screening group and in the control group

Hugosson J et al. Mortality results from the Göteborg randomised population-based prostate-cancer screening trial. www.thelancet.com/oncology Published online July 1, 2010
NORCCAP: 7 years follow-up

Results:
Participation rate: 63%
Incidence: HR 1.02 [95% CI 0.83-1.25]
NORCCAP: 11 years follow-up

Results:
Participation rate: 63%
Incidence: HR 0.80 [95% CI 0.70-0.92]
ODx in observational studies
ODx in observational studies

Esserman L., Shieh Y., & Thompson I.  
Rethinking Screening for Breast Cancer and Prostate Cancer.  
Cancer death and invasive cancer diagnosis with and without screening

*Lung, breast and prostate. France 1980-2010*

- **Lung**
  - Without screening
  - Death
  - Diagnosis

- **Breast** (women)
  - Increasing screening

- **Prostate**
  - Increasing screening

Cases per year

- 60000
- 50000
- 40000
- 30000
- 20000
- 10000

Years

- 1980
- 1985
- 1990
- 1995
- 2000
- 2005
- 2010
Malignant melanoma in DK

Danmark
Modermærkekræft, hud
ASR (W) alder 0-85+

![Graph showing malignant melanoma incidence and mortality in Denmark from 1943 to 2008.](image)

NORDCAN © Association of the Nordic Cancer Registries (19.5.2014)
Cardio-vascular Overdiagnosis

CVD diseases and number of risk factors

Content of presentation

- Defining overdiagnosis
- Types of overdiagnosis
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- Consequences of overdiagnosis
- Drivers to overdiagnosis
Harmful consequences of ODx

- financial strain
- hassles/inconveniences
- medical costs
- opportunity costs
- physical harms
- psychological harms
- societal costs
+ work-related costs

Harris R.P. et al. The Harms of Screening: A Proposed Taxonomy and Application to Lung Cancer Screening, JAMA 2014
 Costs in the DLCST

## Costs in the DLCST

<table>
<thead>
<tr>
<th>Diagnostic groups</th>
<th>Cumulative effect</th>
</tr>
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<tbody>
<tr>
<td>Controls</td>
<td>1.00</td>
</tr>
<tr>
<td>True negative</td>
<td>0.96</td>
</tr>
<tr>
<td>False positive</td>
<td>1.66</td>
</tr>
<tr>
<td>True positive</td>
<td>10.61</td>
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## Costs in the DLCST

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<td>True positive</td>
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</tbody>
</table>

Psychosocial consequences of lung cancer screening

Participation bias in a randomised trial of screening for lung cancer

Mie Sara Hestbech\textsuperscript{a,\,*}, Volkert Siersma\textsuperscript{b}, Asger Dirksen\textsuperscript{c}, Jesper H. Pedersen\textsuperscript{d}, John Brodersen\textsuperscript{b}

Conclusion:...substantial socio-demographic and psychosocial participation bias...
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Drivers of Overdiagnosis

Survivors stories drive screening towards more overdiagnosis

More Intensive Screening

More Useful Screening Appears To Be

More "Survivor" Stories

More Overdiagnosis

Popularity paradox
BARCELONA 2016 – 20th to 22nd September 2016

Following successful conferences in Dartmouth in 2013, the University of Oxford in 2014 and the NIH in 2015, we are pleased to announce the dates for the 2016 international Preventing Overdiagnosis conference, to be held in Barcelona. Please let your colleagues and networks know about the announcement of these dates, and that abstract submission and registration will be open soon. Innovations to … Read More....

September 2017: Quebec, Montreal
September 2018: Denmark, Copenhagen?