WHO Perspective on Cancer Screening

Understanding the Impact & Potential Harms

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Why Cancer Matters

1 in 6 global deaths
1 in 2 M, 1 in 3 F lifetime risk

Lower-middle-income country

<table>
<thead>
<tr>
<th>Country</th>
<th>Financial catastrophe</th>
</tr>
</thead>
<tbody>
<tr>
<td>India</td>
<td>32%</td>
</tr>
<tr>
<td>Haiti</td>
<td>&gt;66%</td>
</tr>
<tr>
<td>VietNam</td>
<td>78%</td>
</tr>
<tr>
<td>China</td>
<td>21-75%</td>
</tr>
<tr>
<td>South Korea</td>
<td>40%</td>
</tr>
<tr>
<td>US</td>
<td>12%</td>
</tr>
</tbody>
</table>

Graph: Financial burden due to cancer and other conditions in lower-middle-income countries from 2011 to 2016.
Outline

• Understanding the policy objective
  – Disease criteria for effective screening
  – Organized screening programmes

• Potential harms of screening

• Public health decision-making
Outline

• Understanding the policy objective
  – Disease criteria for effective screening
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• Public health decision-making
• Public health goals
  – Public health surveillance
    • Prevent disease when possible
    • Detect disease as early as possible
  ➔ Maximize lives saved and reduce burden of disease for population
**Early detection:**
Aims to identify cancer in early stages or pre-cancerous lesions;

Two strategies: screening & early diagnosis
Goal = early identification
→ Reduce mortality / improve survival
→ Less morbid treatment
→ Reduced costs of care
Early Detection of Cancer

Key Considerations:

1. What diseases should be screened?
2. What type of programme should be implemented?
Screening vs. Early Diagnosis

• Screening:
  – Presumptive identification of unrecognized disease in general population
  – *More than a test*

Key considerations:
(1) What diseases should be screened?
(1) What type of programme should be implemented?

Awareness of symptoms
Screenable Disease: Wilson and Jungner criteria

“The central idea of early disease detection and treatment is essentially simple. However, the path to its successful achievement ... is far from simple though sometimes it may appear deceptively easy.”

- Wilson JMG, Junger G (Principles and Practice of Screening for Disease. WHO, 1968)
Cancers to be Considered

**Key considerations:**

(1) What diseases should be screened?

(1) What type of programme should be implemented?

What can be screened?  ➡️  What should be screened?
Screenable Disease: Implementation

Cancer Control
Knowledge into Action
WHO Guide for Effective Programmes

Early Detection
Disease- & test-based criteria

PRINCIPLES AND PRACTICE OF SCREENING FOR DISEASE

J. M. G. WILSON & G. JUNGNER

WORLD HEALTH ORGANIZATION
GENEVA
WHO screening targets:

1. Organized (vs opportunistic):
   a. Greatest impact
   b. Fewest harms
   c. Equitable

2. >70% participation

<table>
<thead>
<tr>
<th>Criteria for Organized Screening</th>
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<tbody>
<tr>
<td>National program to make service available</td>
</tr>
<tr>
<td>Coordination, centralized at national/regional level</td>
</tr>
<tr>
<td>Protocol for screening frequency, target population</td>
</tr>
<tr>
<td>Mechanism of inviting target population systematically</td>
</tr>
<tr>
<td>Functioning health information system including registries</td>
</tr>
<tr>
<td>Monitoring &amp; Evaluation program</td>
</tr>
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• Public health decision-making
Outline

• Understanding the policy objective
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• **Potential harms of screening**

• Public health decision-making and epidemiology

1. Overdiagnosis
2. False (+) result
3. Inefffectual service
Breast Cancer Screening

Population sensitized to screening test

High quality, accurate, accessible screening test

Confirmatory pathologic diagnosis & staging

Referral for definitive treatment

Treatment accessible, high quality

Sample population: 1 million

55,000 women screened with mammography each year

5,000 with abnormal screening test

350 with confirmed cancer found on screening

4,720 require follow-up & found to have no abnormality

450 women will require treatment

340 women will survive without screening

20 women avoid death from breast ca due to screening

30 women will not receive any major benefit (due to overdiagnosis)

Breast ca screening costs in HIC: ~$10mil per 1mil population

Breast treatment costs in HIC: ~ $15mil per 1mil population
Lung Cancer Screening

Population sensitized to screening test
High quality, accurate, accessible screening test
Confirmatory pathologic diagnosis & staging
Referral for definitive treatment
Treatment accessible, high quality

Sample population: 1 million
53,000 women screened with LDCT each year
13,000 with abnormal screening test
500 with confirmed cancer found on screening
12,500 require follow-up & found to have no abnormality
350 require treatment

50 will survive without screening
250 will die regardless
50 avoid death from lung ca due to screening
50 will not receive any major benefit (due to overdiagnosis)

Lung ca screening costs in HIC: ?
Cost-effectiveness: $2,000 - $250,000 per QALY
Harm #1: Overdiagnosis = finding extra cancers

- Finding “extra” tumors – that would never cause problem

<table>
<thead>
<tr>
<th></th>
<th>Incidence</th>
<th>Mortality</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Per 100 000</td>
<td>% Change</td>
</tr>
<tr>
<td>Breast (New cases)</td>
<td>140</td>
<td>120</td>
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- Key message: negative consequences of overdiagnosis:
  1. Results unnecessary treatment, complications of treatment
  2. Inflates benefits of screening
Harm #2: False Positive Findings

• Consequences
  – Individual

  Key message:
  1) False + & overdiagnosis: cause significant personal & system costs (~$USD 4 billion/yr in US)
  2) Low quality screening tests result in greater harm

  – Can be 10-50% of programme costs
  – In US, expenditure for false (+) ~ USD$1-2 bil/yr
Harm #3: Ineffectual Services

- Organized cancer screening

Benchmarks:
- High participation
- Quality assured
- Link to treatment
Harm #3: Ineffectual Services

<table>
<thead>
<tr>
<th>Situation</th>
<th>Women screened</th>
<th>Abnormal screening results</th>
<th>False positives</th>
<th>Women benefitting from screening</th>
<th>Program costs</th>
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<tr>
<td>Optimal conditions</td>
<td>40,000</td>
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<td>2,920</td>
<td>20</td>
<td>$ 300,000</td>
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<tr>
<td>(Efficacy)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low participation</td>
<td>20,000</td>
<td>1,500</td>
<td>1,460</td>
<td>10</td>
<td>$ 150,000</td>
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## Harm #3: Ineffectual Services

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**Benchmarks**

- Optimal conditions (Efficacy)
  - Women screened: 40,000
  - Abnormal screening results: 3,000
  - False positives: 2,920
  - Women benefiting from screening: 20
  - Program costs: $300,000
- Low quality
  - Women screened: 40,000
  - Abnormal screening results: 5,000
  - False positives: 4,930
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  - Program costs: $500,000
## Harm #3: Ineffectual Services

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**Harm #3: Ineffectual Services, where are we now?**

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<tr>
<th>Cancer</th>
<th>Participation</th>
<th>Opportunistic</th>
<th>Co-payment</th>
<th>Inequities</th>
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<tr>
<td>Breast</td>
<td>35-80% (Canton-specific)</td>
<td>Yes</td>
<td></td>
<td>Yes (SES, region, education)</td>
</tr>
<tr>
<td>Colorectal</td>
<td>22%</td>
<td>Yes</td>
<td>10% after deductible</td>
<td>Yes (SES)</td>
</tr>
<tr>
<td>Cervical</td>
<td>70-80%</td>
<td>Yes</td>
<td></td>
<td>Yes (SES, region)</td>
</tr>
<tr>
<td>Prostate</td>
<td>~70$ (from 50% in 1992)</td>
<td>Yes</td>
<td></td>
<td>Yes (SES, region, education)</td>
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**Key message:** Consider public health priorities, budgetary impact, health system capacity when proposing screening programme. High participation and quality are critical.
### Efficacy vs. Effectiveness

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Outline

• Understanding the policy objective
  – Disease criteria for effective screening
  – Organized screening programmes

• Potential harms of screening

• Public health decision-making
Public Health Decision-Making

• Cancer screening
  – Must ensure favorable benefit-harm ratio
  – Decision-making options
    1. Regulatory framework
    2. Public funding for programme
  – Considerations
    • Limited data for evidence-based policies
    • Context-specific with acceptable risks for population
    • Mechanism for M&E critical
Emotional Epidemiology

ALL-NITE DRIVE-THRU
SCREENING CLINIC

I'm obliged to inform you:
You have the right to remain anxious.

Anything you say will be used to further test you.

If you do not already have a diagnosis, one will be provided for you.

Statistically-funny.blogspot.com
Interpreting the Results

• Screening is balance of benefits & harms

• Estimations of benefits vs harms, vary
  ➔ Impact value of screening

• Modeling impact challenging
Variables to consider:

- Appropriate target population (age of exposure, dose, gender)
- Test quality
- Test frequency
- Effectiveness of treatment

→ Consider study methodology & biases
<table>
<thead>
<tr>
<th>Study</th>
<th>Setting</th>
<th>Outcome</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>NLST (National Lung Screening Trial)</td>
<td>USA 55-74yo &gt;30pk-yr hx</td>
<td>20% relative mortality</td>
<td>Younger age</td>
</tr>
<tr>
<td>NELSON</td>
<td>Belgium/Netherlands 1, 2, 2.5yr interval</td>
<td>TBD Higher interval rate w/ 2.5yrs vs 1,2yr</td>
<td>Comparison w/ no screening 84% male</td>
</tr>
<tr>
<td>DANTE</td>
<td>Italy (n=2472) 60-74yo Annual</td>
<td>No impact ? Small sample size</td>
<td>Male only</td>
</tr>
<tr>
<td>DLSCT (Danish Randomized Lung Cancer CT screening trial)</td>
<td>Denmark 50-60</td>
<td>No impact ? Greater mass size ? Sample size</td>
<td>Lower risk population</td>
</tr>
<tr>
<td>MILD (Multicentric Italian Lung Detection)</td>
<td>Italy</td>
<td>No impact ? Low quality</td>
<td>Lower risk population</td>
</tr>
<tr>
<td>MILD (Multicentric Italian Lung Detection)</td>
<td>Italy</td>
<td>Inadequate randomized</td>
<td>Lower risk population</td>
</tr>
<tr>
<td>LUSI (Lung Cancer Screening Intervention)</td>
<td>Germany 50-69yo</td>
<td>TBD</td>
<td>Recall rates decline with each interval Results end of 2018</td>
</tr>
<tr>
<td>UKLS (Lung Cancer Screening Intervention)</td>
<td>UK 50-75yo</td>
<td>TBD</td>
<td>Evaluating risk prediction model</td>
</tr>
<tr>
<td>Case for</td>
<td>Case against</td>
<td></td>
<td></td>
</tr>
<tr>
<td>------------------------------------------------------------------------</td>
<td>------------------------------------------------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• ↓ BCa specific mortality</td>
<td>• Personal, financial cost of false +</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• ↓ morbidity for diagnosed</td>
<td>• Financial impact of overdiagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Discomfort</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Radiation (in high-risk subgroups)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Case for/against Lung cancer screening

<table>
<thead>
<tr>
<th>Case For</th>
<th>Case Against</th>
</tr>
</thead>
<tbody>
<tr>
<td>• ↓ Lung ca-specific mortality</td>
<td>• Focus should remain on prevention (&gt;1000x more cost-effective)</td>
</tr>
<tr>
<td>• ↓ overall mortality</td>
<td>• High rates of false +, incidental findings</td>
</tr>
<tr>
<td>? ✷ morbidity for diagnosed ?</td>
<td>– Patient distress</td>
</tr>
<tr>
<td>? Impact on tobacco use ?</td>
<td>– ↑ cost</td>
</tr>
<tr>
<td></td>
<td>• ↑ incidental findings</td>
</tr>
<tr>
<td></td>
<td>• Radiation exposure</td>
</tr>
<tr>
<td></td>
<td>• Overdiagnosis (13-27%)</td>
</tr>
<tr>
<td></td>
<td>• ? Impact on tobacco use ?</td>
</tr>
</tbody>
</table>
Modeling the Impact: Breast Cancer

Scenario #1 (Euroscreen)

**Benefits**
- 40 breast cancer deaths avoided
- Less morbid treatment

**Harms**
- 10 Potential overdiagnosis
- 2,000 false (+)

Per 1,000,000 population

- 50,000 screened
- Incidence 100/100,000
- Study sensitivity high
- High quality treatment
Modeling the Impact: Breast Cancer

Scenario #2
(Cochrane)

Benefits

- 6 breast cancer deaths avoided

Harms

- 100 Potential overdiagnosis
- 5,000 false (+)

Per 1,000,000 population

- 50,000 screened
- Incidence 100/100,000
- Study sensitivity high
- High quality treatment
Modeling the Impact: Lung Cancer

Scenario #1
(High risk)

25,000 screened

Incidence 50/100,000

Specificity high (low FP, 5mm mass)

Benefits

- 20 lung cancer deaths avoided
- Reduced overdiagnosis

Harms

- Missed cancer in population
- Higher programmatic costs
Modeling the Impact: Lung Cancer

Scenario #2
(Expanded criteria)

Benefits

- 50,000 screened
- 40 lung cancer deaths avoided

Harms

- 20,000 false positives
- 100+ overdiagnosis

Key message: selecting the appropriate target population (high risk, high incidence) and facilitating favourable conditions → increases the effectiveness of screening programme
Providing Integrated People-Centred Care

• Informed decision-making
  – Expert guidance
    • Bias toward intervention, benefits

Key message: screening requires balance of all medical ethics principles: autonomy, beneficence, non-maleficence, justice

Summary

• Just because it can be screened, doesn’t mean it should
  – Strict criteria when deciding whether to screen
  – Routine M&E required to ensure programme effectiveness

• Screening can cause real harm to individuals and to health system
  – Communicate balance of benefit/harm to all stakeholders
  – Engagement in public sphere critical
THANK YOU

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Next Steps for Lung Cancer Screening

• Additional data pending:
  – 2+ trials pending
  – Cost data / health system impact TBD

• Improving outcomes
  – Screen positive criteria / reduce false +
  – Quality of radiology review
  – Use of biomarkers
  – Review target population