Named inventor on a number of patents and patent applications relating to the evaluation of diseases of the chest including measurement of nodules. Some of these, which are owned by Cornell Research Foundation (CRF) are non-exclusively licensed to General Electric.

A shareholder in Accumetra LLC

Medical Advisory Board Grail
Topics

Large RCTs

Continuous Screening

Women and Lung Cancer
Lung Cancer Incidence and Mortality with Extended Follow-up in the National Lung Screening Trial National Lung Screening Trial Writing Team

William C. Black, Caroline Chiles, Timothy R. Church, Ilana F. Gareen, David S. Gierada, Irene Mahon, Eric A. Miller, Paul F. Pinsky, JoRean D. Sicks
Mortality Reduction

- Relative reduction fell from 20% to 8%
- Absolute reduction (NNS) 320 to 303
- Different between men and women

<table>
<thead>
<tr>
<th></th>
<th>LDCT # (per 1,000 subjects)</th>
<th>CXR # (per 1,000 subjects)</th>
<th>Difference across arms (95% CI) [CXR minus LDCT]</th>
<th>RR (95% CI)</th>
<th>P-value Interaction$^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All lung cancer deaths</strong></td>
<td></td>
<td></td>
<td>per 1,000 subjects</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All subjects</td>
<td>1147 (42.9)</td>
<td>1236 (46.2)</td>
<td>3.3 (-0.2 – 6.8)</td>
<td>0.92 (0.85 -1.00)</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>733 (46.5)</td>
<td>755 (47.9)</td>
<td>1.4 (-3.3 – 6.1)</td>
<td>0.97 (0.87-1.07)</td>
<td>0.17</td>
</tr>
<tr>
<td>Women</td>
<td>414 (37.8)</td>
<td>481 (43.9)</td>
<td>6.1 (0.8 – 11.3)</td>
<td>0.86 (0.75-0.98)</td>
<td></td>
</tr>
<tr>
<td>Current Smoker</td>
<td>724 (56.3)</td>
<td>818 (63.4)</td>
<td>7.1 (1.3-12.9)</td>
<td>0.88 (0.80-0.97)</td>
<td>0.12</td>
</tr>
<tr>
<td>Former Smoker</td>
<td>423 (30.5)</td>
<td>418 (30.2)</td>
<td>-0.3 (-4.3-3.8)</td>
<td>1.01 (0.88-1.15)</td>
<td></td>
</tr>
<tr>
<td>Age 55-64 at randomization</td>
<td>641 (32.7)</td>
<td>739 (37.7)</td>
<td>5.0 (1.3-8.6)</td>
<td>0.86 (0.78-0.96)</td>
<td>0.051</td>
</tr>
<tr>
<td>Age 65-74 at randomization</td>
<td>506 (71.2)</td>
<td>497 (69.9)</td>
<td>-1.3 (-9.7-7.2)</td>
<td>1.01 (0.90-1.15)</td>
<td></td>
</tr>
</tbody>
</table>
American College of Chest Physicians (ACCP) and the American Society of Clinical Oncology (ASCO)

The role of CT screening for Lung Cancer in clinical practice

• Components of a conversation about CT screening
  – “4 out of 5 people who are going to die of lung cancer will die of it even if they are screened. Screening prevents one in five deaths from lung cancer.”

Bach et al.  JAMA 2012
Further explanation

• “only about 1 in 5 individuals that were, if you will, destined to die from lung cancer had their deaths prevented (that is what that relative risk reduction means). Which means that 4 out of 5 of the lung cancers in laymen’s terms snuck through and were incurable despite the routine screening.”
Overdiagnosis

- Overall fell from 18% to 3%
- Excluding “BAC” virtually 0%
- 79% for “BAC”
Effects of volume CT lung cancer screening

Mortality results of the NELSON randomised-controlled population-based screening trial

Harry J. de Koning, MD PhD

PI NELSON
Professor & Deputy Head
Department of Public Health
Erasmus MC, University Medical Center Rotterdam, the Netherlands
<table>
<thead>
<tr>
<th>Lung cancer mortality rate ratio (95% CI)</th>
<th>Year 8</th>
<th>Year 9</th>
<th>Year 10</th>
</tr>
</thead>
<tbody>
<tr>
<td>MALES</td>
<td></td>
<td></td>
<td><strong>0.74</strong> (0.60-0.91)</td>
</tr>
<tr>
<td>Lung cancer mortality rate ratio (95% CI)</td>
<td>Year 8</td>
<td>Year 9</td>
<td>Year 10</td>
</tr>
<tr>
<td>------------------------------------------</td>
<td>-----------</td>
<td>-----------</td>
<td>------------</td>
</tr>
<tr>
<td>MALES</td>
<td>0.75</td>
<td>0.76</td>
<td>0.74</td>
</tr>
<tr>
<td></td>
<td>(0.59-0.95)</td>
<td>(0.60-0.95)</td>
<td>(0.60-0.91)</td>
</tr>
</tbody>
</table>

Harry J. de Koning, Erasmus MC, Public Health Rotterdam
<table>
<thead>
<tr>
<th>Lung cancer mortality rate ratio (95% CI)</th>
<th>Year 8</th>
<th>Year 9</th>
<th>Year 10</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MALES</strong></td>
<td>0.75</td>
<td>0.76</td>
<td>0.74</td>
</tr>
<tr>
<td></td>
<td>P=0.015 (0.59-0.95)</td>
<td>P=0.012 (0.60-0.95)</td>
<td>P=0.003 (0.60-0.91)</td>
</tr>
<tr>
<td><strong>FEMALES</strong></td>
<td>0.39</td>
<td>0.47</td>
<td>0.61</td>
</tr>
<tr>
<td></td>
<td>P=0.0037 (0.18-0.78)</td>
<td>P=0.0069 (0.25-0.84)</td>
<td>P=0.0543 (0.35-1.04)</td>
</tr>
</tbody>
</table>
NELSON Volume CT screening

- MALES at high risk for lung cancer have a reduced risk of dying from lung cancer of 26% in the screen arm compared to the male control arm (95% CI 9-40%)

- In WOMEN, reductions are consistently more favourable: 39-61%

- These results are more favourable than the NLST-results & suggest gender differences

- Volume CT lung cancer screening of high risk former and current smokers results in low referral rates (2.3%), and a very substantial reduction in lung cancer mortality (in both genders)
### Table 3: Stage distribution of screening-detected lung cancers of all rounds

<table>
<thead>
<tr>
<th>Stage</th>
<th>Round 1</th>
<th></th>
<th></th>
<th>Round 2</th>
<th></th>
<th></th>
<th>Round 3</th>
<th></th>
<th></th>
<th>Round 4</th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Per cent</td>
<td>Cumulative %</td>
<td>p Value*</td>
<td></td>
<td></td>
<td>p Value†</td>
<td></td>
<td></td>
<td>p Value‡</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ia</td>
<td>44</td>
<td>59.5</td>
<td>59.5</td>
<td></td>
<td>43</td>
<td>74.1</td>
<td>74.1</td>
<td>0.37</td>
<td></td>
<td>50</td>
<td>64.9</td>
<td>64.9</td>
</tr>
<tr>
<td>Ib</td>
<td>4</td>
<td>5.4</td>
<td>64.9</td>
<td></td>
<td>1</td>
<td>1.7</td>
<td>75.9</td>
<td></td>
<td>6</td>
<td>7.8</td>
<td>72.7</td>
<td></td>
</tr>
<tr>
<td>IIa</td>
<td>7</td>
<td>9.5</td>
<td>74.3</td>
<td></td>
<td>4</td>
<td>6.9</td>
<td>82.8</td>
<td></td>
<td></td>
<td></td>
<td>76.6</td>
<td></td>
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<tr>
<td>IIb</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3</td>
<td>3.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IIIa</td>
<td>10</td>
<td>13.5</td>
<td>87.8</td>
<td></td>
<td>6</td>
<td>10.3</td>
<td>93.1</td>
<td></td>
<td>14</td>
<td>18.2</td>
<td>94.8</td>
<td></td>
</tr>
<tr>
<td>IIIb</td>
<td>4</td>
<td>5.4</td>
<td>93.2</td>
<td></td>
<td>2</td>
<td>3.4</td>
<td>96.6</td>
<td></td>
<td>1</td>
<td>1.3</td>
<td>96.1</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>5</td>
<td>6.8</td>
<td>100</td>
<td></td>
<td>2</td>
<td>3.4</td>
<td>100</td>
<td></td>
<td>3</td>
<td>3.9</td>
<td>100</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>74</td>
<td>100</td>
<td></td>
<td></td>
<td>58</td>
<td>100</td>
<td></td>
<td>77</td>
<td>100</td>
<td></td>
<td>46</td>
<td>100</td>
</tr>
</tbody>
</table>

* p Value: comparison of stage distribution of the screening-detected lung cancers of round 1 vs round 4.
† p Value: comparison of stage distribution of the screening-detected lung cancers of round 2 vs round 4.
‡ p Value: comparison of stage distribution of the screening-detected lung cancers of round 3 vs round 4.

Yousaf-Khan U: Thorax 2016

75.9 vs. 72.7 vs 60.9
NELSON: Interval Cancers

1 year  2 years  2.5 years

5 (8%) vs. 19 (20%) vs 28 (38%)

Yousaf-Khan U: Thorax 2016
Miettinen O: Lancet 2007
Prolonged lung cancer screening reduced 10-year mortality in the MILD trial: new confirmation of lung cancer screening efficacy

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\textsuperscript{1}Unit of Thoracic Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan; \textsuperscript{2}Section of Radiology, Unit of Surgical Sciences, Department of Medicine and Surgery (IDMEC), University of Padua, Padua; \textsuperscript{3}Tumour Genomics Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan; \textsuperscript{4}Division of Biostatistics, Department of Statistics and Quantitative Methods, Epidemiology and Public Health, University of Milano-Bicocca, Milan; \textsuperscript{5}Department of Radiology, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy

*Correspondence to: Dr. Michele Silva, Thoracic Surgery Unit, Fondazione IRCCS Istituto Nazionale dei Tumori, Via Venezian 1, 20133 Milan, Italy. Tel: +39-02-816-3903; Fax: +39-02-816-2107; E-mail: ugo.pastorino@iunito.cnr.it

\textbf{Background:} The National Lung Screening Trial showed that lung cancer (LC) screening by three annual rounds of low-dose computed tomography (LDCT) reduces LC mortality. We evaluated the benefit of prolonged LDCT screening beyond 5 years, and its impact on overall and LC specific mortality at 10 years.

\textbf{Design:} The Multicentric Italian Lung Detection (MILD) trial prospectively randomized 4099 participants, to a screening arm ($n = 2378$), with further randomization to annual ($n = 1190$) or biennial ($n = 1188$) LDCT for a median period of 6 years, or control arm ($n = 1723$), without intervention. Between 2005 and 2013, 39,293 person-years of follow-up were accumulated. The primary outcomes were 10-year overall and LC specific mortality. Landmark analysis was used to test the long-term effect of LC screening, beyond 5 years by exclusion of LCs and deaths that occurred in the first 5 years.

\textbf{Results:} The LDCT arm showed a 39\% reduced risk of LC mortality at 10 years (hazard ratio (HR) 0.61, 95\% confidence interval (CI) 0.39–0.95), compared with control arm, and a 20\% reduction of overall mortality (HR 0.80, 95\% CI 0.62–1.03). LDCT benefit improved beyond the 5th year of screening, with a 58\% reduced risk of LC mortality (HR 0.42, 95\% CI 0.22–0.79), and 32\% reduction of overall mortality (HR 0.68, 95\% CI 0.49–0.94).

\textbf{Conclusions:} The MILD trial provides additional evidence that prolonged screening beyond 5 years can enhance the benefit of early detection and achieve a greater overall and LC mortality reduction compared with NLST trial.
Lung cancer mortality

Log-rank test $P = 0.0172$

HR (95%CI) = 0.61 (0.39-0.95)
Lung cancer mortality

Log-rank test $P=0.0037$

HR (95%CI)=0.42 (0.22-0.79)
Women and Lung Cancer: Screening, Treatment and Beyond

Moderator: James L. Mulshine, MD
Professor Chair, Screening and Early Detection Committee, IASLC
Rush University, Chicago

Mary Pasquinelli, DNP, FNP-BC
Adjunct Clinical Instructor - UIC College of Nursing
Director, Lung Cancer Screening Program
Advanced Practice Nurse, Pulmonary and Medical Oncology
University of Illinois Hospital & Health Science System (UI Health)

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Andrea S. Wolf, MD, MPH
Associate Professor
Director, New York Mesothelioma Program
Department of Thoracic Surgery
The Icahn School of Medicine at Mount Sinai
New York, NY

This program is sponsored by:

[Logos of sponsoring organizations]

AMERICAN LUNG ASSOCIATION
GO2 FOUNDATION FOR LUNG CANCER
PREVENT CANCER FOUNDATION
Prior publications

• American Health Foundation database indicated that for every level of exposure to cigarette smoke
  – odds ratio is consistently higher for women than for men for the major lung cancer cell-types.

• A Canadian case–control study of gender differences in lung cancer from 1981 to 1985, for smokers with at least 40 pack-years of smoking compared to lifelong never smokers
  – The odds ratio for women is 27.9
  – The odds ratio for men is 9.6

• The risk of lung cancer is 2.5 times higher for women who never smoked in their lifetime compared to men who never smoked

NELSON Lung Cancer Mortality Rates at Year 10
Baseline + 3 AR rounds for people 50-74 yrs of age and at least 15 pk-yrs.

<table>
<thead>
<tr>
<th>LC MRR (95% CI)</th>
<th>Year 10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td></td>
</tr>
<tr>
<td>0.75 (0.59-0.95)</td>
<td>0.74 (0.60-0.91)</td>
</tr>
<tr>
<td></td>
<td>P = 0.003</td>
</tr>
<tr>
<td>Women</td>
<td></td>
</tr>
<tr>
<td>0.39 (0.18-0.78)</td>
<td>0.61 (0.35-1.04)</td>
</tr>
<tr>
<td></td>
<td>P = 0.0543</td>
</tr>
</tbody>
</table>

Mortality reduction

Men: 26%

Women: 39%

The mortality reduction remains greater for women than men
In North America, 
N=41263 screenees: 18451 (45%) women AND 22812 (55%) men
Smokers aged 40 years and older
All rounds of screening
I-ELCAP in North America 1992-2018: Susceptibility of women compared with men

- OR=1.7 (95%CI: 1.4-2.0), conditioned on smoking history and age

• Hazard Ratio (HR) from survival analysis comparing women and men, adjusting for age, smoking history, and resection.

• HR = **0.60** (95%CI: 0.4-0.9)

• This means that the risk of dying of lung cancer among women is **40% lower** than that of men when adjusted for age, smoking history, and resection.

• Otherwise said: men are 1.67 (1/0.60) times more likely to die of lung cancer when adjusted for age, smoking history, and resection.
Guiding Principle for Screening

**Women** are at **higher** risk of lung cancer and have **higher** cure rates, if found early by screening.

**THEREFORE**

Women should be screened at a younger age and lower pack-years than men.
Conclusion

Large randomized trials show mortality reduction

Magnitude of the benefit as demonstrated by continuous screening is higher than in stop screen studies approaching cure rates

Overdiagnosis is minimal

Women have increased susceptibility and higher cure