Le dépistage du cancer bronchique: Où en est-on?

Toulouse 7-10-2019

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Conflicts of Interest disclosure

I have the following potential conflicts of interest to report:
- Grants received from Belgian Cancer League & from Foundation Against Cancer for participation in NELSON trial
Lung cancer screening: time for implementation?

Toulouse 7-10-2019

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Lung
Source: Globocan 2018

Number of new cases in 2018, both sexes, all ages

- Lung: 2,093,876 (11.6%)
- Other cancers: 7,753,946 (42.9%)
- Cervix uteri: 569,847 (3.2%)
- Oesophagus: 572,034 (3.2%)
- Liver: 841,080 (4.7%)
- Breast: 2,088,849 (11.6%)
- Colorectum: 1,849,518 (10.2%)
- Prostate: 1,276,106 (7.1%)
- Stomach: 1,033,701 (5.7%)

Total: 18,078,957 cases

Number of deaths in 2018, both sexes, all ages

- Lung: 1,761,007 (18.4%)
- colorectum: 880,792 (9.2%)
- Stomach: 782,685 (8.2%)
- Liver: 781,631 (8.2%)
- Other cancers: 3,422,417 (35.8%)
- Prostate: 358,989 (3.8%)
- Pancreas: 432,242 (4.5%)
- Oesophagus: 508,585 (5.3%)
- Breast: 626,679 (6.6%)

Total: 9,555,027 deaths
Early detection of lung cancer

Figure 3.2 Lung cancer (males & females): Stage by histological type, Belgium 2004-2005

Stages I-II
Persons at high risk for lung cancer

- Smoking: 83%
- Asbestos: 6%
- Second-hand smoke: 3%
- Other: 6.7%
- Radon: 0.5%
- Radiotherapy: 0.8%
Persons at high risk for lung cancer

Belgium 2017

Data source: http://www.kankerregister.org
Persons at high risk for lung cancer

Predicted number of deaths
Figure 4 – Age-adjusted 5-year survival from lung cancer in selected European countries among patients diagnosed 2000–2002 relative to that of the general population. Survival for the UK has been derived from estimates for England, Scotland, Wales and Northern Ireland and the average independently calculated. Data from EUROCARE-4 study (www.eurocare.it).
Curative lung cancer treatment

Lung Cancer Overall Survival by clinical stage

<table>
<thead>
<tr>
<th>Proposed</th>
<th>Events / N</th>
<th>MST</th>
<th>24 Month</th>
<th>60 Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA1</td>
<td>68 / 781</td>
<td>NR</td>
<td>97%</td>
<td>92%</td>
</tr>
<tr>
<td>IA2</td>
<td>505 / 3105</td>
<td>NR</td>
<td>94%</td>
<td>83%</td>
</tr>
<tr>
<td>IA3</td>
<td>546 / 2417</td>
<td>NR</td>
<td>90%</td>
<td>77%</td>
</tr>
<tr>
<td>IB</td>
<td>560 / 1928</td>
<td>NR</td>
<td>87%</td>
<td>68%</td>
</tr>
<tr>
<td>IIA</td>
<td>215 / 585</td>
<td>NR</td>
<td>79%</td>
<td>60%</td>
</tr>
<tr>
<td>IIB</td>
<td>605 / 1453</td>
<td>66.0</td>
<td>72%</td>
<td>53%</td>
</tr>
<tr>
<td>IIIA</td>
<td>2052 / 3200</td>
<td>29.3</td>
<td>55%</td>
<td>36%</td>
</tr>
<tr>
<td>IIIB</td>
<td>1551 / 2140</td>
<td>19.0</td>
<td>44%</td>
<td>26%</td>
</tr>
<tr>
<td>IIIC</td>
<td>831 / 986</td>
<td>12.6</td>
<td>24%</td>
<td>13%</td>
</tr>
<tr>
<td>IVA</td>
<td>336 / 484</td>
<td>11.5</td>
<td>23%</td>
<td>10%</td>
</tr>
<tr>
<td>IVB</td>
<td>328 / 398</td>
<td>6.0</td>
<td>10%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Curative lung cancer treatment

Postmus PE et al Early and Locally Advanced NSCLC: ESMO Clinical Practice Guidelines Ann Oncol 2017
“Lung cancer screening aims to reduce lung cancer related mortality with relatively limited harm through early detection and treatment”
Annual or biennial repeat CT’s (UKLS and NELSON modelling)

- Cost effectiveness NLST $81K/QALY: UKLS Modeling ~£12k/QALY.
- Mortality data – only available for NLST – await NELSON & pooled NELSON & UKLS

Patient at risk of developing lung cancer

- Evidence for a validated screening test
- Smoking Cessation

Recruitment of Hard to Reach

- Risk Prediction modeling (LLP$_{v2}$)
- Screen age range 60-75 years

Decision to treat – 1st option Surgery / consider radiotherapy

Identify ‘Indeterminate’ nodules - Care Pathway

LDCT scan – utilizing volumetrics and VDT

Referral to MDT in Center of Excellence - Work-up by NICE standards
Lung Cancer Screening PROs

• Early detection (stage I-II) of lung cancer
• In persons at high(est) risk
• Curative treatment
• Improved lung cancer specific survival
• Smoking cessation
Lung Cancer Screening **CONs**

- Selection of screening (‘highest risk’) participants
- Cost/Benefit of lung cancer screening
- Cumulative Radiation risk (serial CT’s)
- Risks of harm (invasive examinations) in screening-positive participants
- False positive screening results
- Overdiagnosis
- No screening BUT Smoking cessation!
Improved Lung Cancer specific survival

Total number of deaths due to lung cancer:
247 vs 309 deaths/100.000 pers.yrs (CT vs RX group)

- Relative reduction in LC mortality of 20.0% or HR=0.80 (95%CI 0.73-0.93)
- Reduction in all cause mortality of 6.7% or HR=0.93 (95% CI 0.86-0.99)

Number Needed to Screen with LDCT to prevent 1 death: 320

Table 1: Large-scale randomised controlled lung cancer screening trials

<table>
<thead>
<tr>
<th>Sample size</th>
<th>Recruitment</th>
<th>Follow-up (years)</th>
<th>Comparison (nodule measurement)</th>
<th>Smoking history</th>
<th>Smoking cessation</th>
<th>Age group (years)</th>
<th>Screening interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>NLST (USA, 2002)</td>
<td>53,454 Volunteers</td>
<td>6.4*</td>
<td>CT vs chest radiography (D)</td>
<td>≥30 pack-years</td>
<td>&lt;15 years</td>
<td>55-74</td>
<td>Three annual screenings</td>
</tr>
<tr>
<td>NELSON (Netherlands/Belgium, 2004)</td>
<td>15,822 Population-registry</td>
<td>7.4*</td>
<td>CT vs usual care (V)</td>
<td>≥15 cigarettes per day for ≥25 years or ≥10 cigarettes per day for ≥30 years</td>
<td>≤10 years</td>
<td>50-75</td>
<td>Four screenings with different screening intervals: 1 year, 2 years, and 2.5 years</td>
</tr>
<tr>
<td>DLCST (Denmark, 2004)</td>
<td>4104 Volunteers</td>
<td>9.8*</td>
<td>CT vs usual care (V)</td>
<td>≥20 pack-years</td>
<td>≤10 years</td>
<td>50-70</td>
<td>Five annual screenings</td>
</tr>
<tr>
<td>MILD (Italy, 2000 and 2005)</td>
<td>1035 (pilot) and 4099 (main study) Volunteers</td>
<td>4.4*</td>
<td>CT vs usual care (V)</td>
<td>≥20 pack-years</td>
<td>≤10 years</td>
<td>≥49</td>
<td>Five annual vs three biennial screenings</td>
</tr>
<tr>
<td>UKLS (UK, 2011-12)</td>
<td>4055 Population-registry</td>
<td>--</td>
<td>CT vs usual care (V)</td>
<td>Predicted risk of ≥5% of lung cancer diagnosis within 5 years, and 5-year risk for lung cancer</td>
<td>≤10 years</td>
<td>50-75</td>
<td>One screening</td>
</tr>
<tr>
<td>LUSI (Germany, 2007)</td>
<td>4052 Population</td>
<td>3-6.5</td>
<td>CT vs usual care (D)</td>
<td>≥15 cigarettes per day for ≥25 years or ≥10 cigarettes per day for ≥30 years</td>
<td>≤10 years</td>
<td>50-69</td>
<td>Four annual screenings</td>
</tr>
<tr>
<td>ITALUNG (Italy, 2003)</td>
<td>3206 General practitioners</td>
<td>6</td>
<td>CT vs usual care (D)</td>
<td>≥20 pack-years</td>
<td>≤10 years</td>
<td>55-69</td>
<td>Four annual screenings</td>
</tr>
<tr>
<td>DANTE (Italy, 2005)</td>
<td>2450 Volunteers</td>
<td>8.4</td>
<td>CT vs clinical review (D)</td>
<td>≥20 pack-years</td>
<td>≤10 years</td>
<td>60-74</td>
<td>Four annual screenings</td>
</tr>
</tbody>
</table>

Dates provided are trial start dates. D=diameter, V=volume. * Median.

<table>
<thead>
<tr>
<th>Year</th>
<th>Control arm n=7,892</th>
<th>Screen arm n=7,900</th>
<th>Usual care (no screening)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year 1</td>
<td>CT screening</td>
<td>n=7,557</td>
<td>95.6% uptake</td>
</tr>
<tr>
<td>Year 2</td>
<td>CT screening</td>
<td>n=7,295</td>
<td>92.3% uptake</td>
</tr>
<tr>
<td>Year 4</td>
<td>CT screening</td>
<td>n=6,922</td>
<td>87.6% uptake</td>
</tr>
<tr>
<td>Year 6.5</td>
<td>CT screening</td>
<td>n=5,279</td>
<td>66.8% uptake</td>
</tr>
<tr>
<td>Year 10</td>
<td>CT screening</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**NATIONAL LINKAGES**
- Statistics Netherlands/ Belgium
- Dutch/ Belgium Cancer Registry
- Centre for Genealogy

**CAUSE OF DEATH REVIEW**

*de Koning H. et al J Thorac Oncol 2018;13(10):S185 PL02.05*
Lung Cancer Stage (males NL) 7th TNM

Cancer Registry NL - Control Arm - Screen Arm

up to December 2011

Stage

Yousaf-Khan et al., in preparation
Cumulative lung cancer deaths (men only)

- **Control arm**: 214 lung cancer deaths
- **Screen arm**: 157 lung cancer deaths

Cumulative absolute number of first lung cancers

- **Control**: 214 lung cancer deaths
- **Screen**: 157 lung cancer deaths

**Years since randomisation**
- 0
- 50
- 100
- 150
- 200
- 250
- 300
- 350
- 400
- 450

**Cumulative lung cancer deaths**
- 0
- 50
- 100
- 150
- 200
- 250

**Control arm**: 214 lung cancer deaths
**Screen arm**: 157 lung cancer deaths
<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>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>FEMALES</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>

FU: 23-12-2003 – 31-12-2015
FU 94% complete year 10
Improved Lung Cancer specific survival

Prolonged lung cancer screening reduced 10-year mortality in the MILD trial: new confirmation of lung cancer screening efficacy

Cumulative Overall mortality by arm, over 10 yrs of FU
Reduction of 20%

Cumulative Lung Cancer Mortality by arm, over 10 yrs of FU
Reduction of 39%

Pastorino U et al Ann Oncol 2019
Improved Lung Cancer specific survival

Lung cancer mortality reduction by LDCT screening—Results from the randomized German LUSI trial

Cumulative LC mortality over 5 yrs of FU
Reduction of 26% (p=0.21 NS)

Cumulative LC Mortality by sex over 5 yrs of FU
HR 0.31 p=0.04 in women
HR 0.94 p=0.81 in men

Becker N et al Int J Cancer 2019
Smoking Cessation in Lung Cancer Screening

YOU STOPPED SMOKING
NOW START SCREENING

EVA-MARIE
QUIT AFTER SMOKING 15,000 PACKS OF CIGARETTES OVER 15 YEARS

Now there's a new screening that can catch lung cancer early and could save lives.
Talk to your doctor or learn more at SavedByTheScan.org

www.lung.org
Interventions for Smoking Cessation

• **Non-pharmacologic**
  - Self help (also Internet)  **NNT 50**
  - Advice/information  **NNT 50**
  - Individual counselling  **NNT 25**
  - Group counselling  **NNT 20**
  - Telephone counselling  **NNT 40**

• **Pharmacologic**
  - NRT  **NNT 20**
  - Bupropion  **NNT 15**
  - Varenicline  **NNT 8**

• **Alternative interventions**
  - hypnosis, acupuncture, laser therapy ??

*NNT = number needed to treat*

Report from Federaal Kenniscentrum voor de Gezondheidszorg (KCE), Belgium 2004
Trends in Tobacco Use and Lung Cancer Death Rates in the U.S.


Does smoking cessation lead to a decrease in lung cancer deaths? YES
Since 2008 smoking prevalence barely declined
LDCT Lung Cancer Screening

Benefits
LC mortality reduction
Reduction in stages III-IV

Harms
False positives
Overdiagnosis
Overtreatment
Radiation exposure
Costs
QOL
Smoking behaviour
The step-wise decision-making concerning potential new cancer screening programmes include the establishment of evidence of effectiveness, benefits that outweigh the harms, and cost-effectiveness.
Selection of screening (‘highest risk’) participants

Best selection of screening participants

- USPSTF Age (55-80 yrs) & smoking behaviour (30PY)
- PLCOm2012 model
- LLPv2 Liverpool Lung Project risk prediction model, used in RCT, Subjects selected with a ≥ 5% risk of developing LC in next 5 yrs
- Using other inclusion criteria (biological data, …)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio (95% CI)</th>
<th>P Value</th>
<th>Beta Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, per 1-yr increase†</td>
<td>1.081 (1.057–1.105)</td>
<td>&lt;.001</td>
<td>0.0778868</td>
</tr>
<tr>
<td>Race or ethnic group‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>1.000</td>
<td>Reference group</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>1.484 (1.083–2.033)</td>
<td>.01</td>
<td>0.3944778</td>
</tr>
<tr>
<td>Hispanic</td>
<td>0.475 (0.195–1.160)</td>
<td>.10</td>
<td>−0.7434744</td>
</tr>
<tr>
<td>Asian</td>
<td>0.627 (0.332–1.185)</td>
<td>.15</td>
<td>−0.466585</td>
</tr>
<tr>
<td>American Indian or Alaskan Native</td>
<td>1</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Native Hawaiian or Pacific Islander</td>
<td>2.793 (0.992–7.862)</td>
<td>.05</td>
<td>1.027152</td>
</tr>
<tr>
<td>Education, per increase of 1 level‡§</td>
<td>0.922 (0.874–0.972)</td>
<td>.003</td>
<td>−0.0812744</td>
</tr>
<tr>
<td>Body-mass index, per 1-unit increase‡</td>
<td>0.973 (0.955–0.991)</td>
<td>.003</td>
<td>−0.0274194</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease (yes vs. no)</td>
<td>1.427 (1.162–1.751)</td>
<td>.001</td>
<td>0.3553063</td>
</tr>
<tr>
<td>Personal history of cancer (yes vs. no)</td>
<td>1.582 (1.172–2.128)</td>
<td>.003</td>
<td>0.4589971</td>
</tr>
<tr>
<td>Family history of lung cancer (yes vs. no)</td>
<td>1.799 (1.471–2.200)</td>
<td>&lt;.001</td>
<td>0.587185</td>
</tr>
<tr>
<td>Smoking status (current vs. former)</td>
<td>1.297 (1.047–1.605)</td>
<td>.02</td>
<td>0.2597431</td>
</tr>
<tr>
<td>Smoking intensity†</td>
<td>–1.822606</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of smoking, per 1-yr increase†</td>
<td>1.032 (1.014–1.051)</td>
<td>.001</td>
<td>0.0317321</td>
</tr>
<tr>
<td>Smoking quit time, per 1-yr increase†</td>
<td>0.970 (0.950–0.990)</td>
<td>.003</td>
<td>−0.0308572</td>
</tr>
<tr>
<td>Model constant</td>
<td>−4.532506</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Overdiagnosis

The excess of lung cancers detected by LDCT divided by all lung cancers detected by screening in a LDCT arm

- In NLST about 18.5% overdiagnosis in screen-detected LCs
- Expected to be less in NELSON (results awaited)

Estimates of $P_A$ and $P_S$

<table>
<thead>
<tr>
<th>Lung Cancer Type</th>
<th>Overdiagnosis, % (95% CI)</th>
<th>$P_A$</th>
<th>$P_S$</th>
</tr>
</thead>
<tbody>
<tr>
<td>All lung cancers</td>
<td></td>
<td>11.0 (3.2 to 18.2)</td>
<td>18.5 (5.4 to 30.6)</td>
</tr>
<tr>
<td>All NSCLC, including BAC and NOS</td>
<td></td>
<td>14.4 (6.1 to 21.8)</td>
<td>22.5 (9.7 to 34.3)</td>
</tr>
<tr>
<td>All NSCLC, excluding BAC and including NOS</td>
<td></td>
<td>7.1 (−2.3 to 15.6)</td>
<td>11.7 (−3.7 to 25.6)</td>
</tr>
<tr>
<td>BAC only</td>
<td></td>
<td>67.6 (53.5 to 78.5)</td>
<td>78.9 (62.2 to 93.5)</td>
</tr>
</tbody>
</table>

Abbreviations: BAC, bronchioloalveolar cell carcinoma; NOS, not otherwise specified; NSCLC, non-small cell lung cancer.

$P_A$ : the total amount of excess LC cases between LDCT and CXR arm over the total number of LCs diagnosed in the screen arm

$P_S$ : the total amount of excess LC cases between LDCT and CXR arm over all screen-detected LCs in LDCT screening arm
### False positive screening results

**Low rate of false positive screening scans**

<table>
<thead>
<tr>
<th></th>
<th>High referral protocol</th>
<th>Low referral protocol with published mortality analyses</th>
<th>Low referral protocol with no published mortality analyses</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NELST(^{15}) (n=53454)</td>
<td>DLCST(^{13}) (n=4104)</td>
<td>DANTE(^{10}) (n=2450)</td>
</tr>
<tr>
<td><strong>Interval lung cancers</strong></td>
<td>44</td>
<td>32</td>
<td>38</td>
</tr>
</tbody>
</table>

#### Positive screening tests (%)

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>24.7%</th>
<th>3.8%</th>
<th>37.3%</th>
<th>...</th>
<th>2.0%</th>
<th>8.8%</th>
<th>19.6%</th>
<th>5.7%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>At least one test</strong></td>
<td></td>
<td>39.1%</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>6.0%</td>
<td>...</td>
<td>52.7%</td>
<td>...</td>
</tr>
<tr>
<td><strong>T</strong>(_0)</td>
<td></td>
<td>27.3%</td>
<td>8.7%</td>
<td>...</td>
<td>...</td>
<td>2.6%</td>
<td>22.2%</td>
<td>30.3%</td>
<td>5.7%</td>
</tr>
<tr>
<td><strong>T</strong>(_1)</td>
<td></td>
<td>27.9%</td>
<td>2.3%</td>
<td>...</td>
<td>...</td>
<td>1.8%</td>
<td>4.7%</td>
<td>17.3%</td>
<td>...</td>
</tr>
<tr>
<td><strong>T</strong>(_2)</td>
<td></td>
<td>16.8%</td>
<td>2.7%</td>
<td>...</td>
<td>...</td>
<td>2.4%</td>
<td>4.0%</td>
<td>16.1%</td>
<td>...</td>
</tr>
<tr>
<td><strong>T</strong>(_3)</td>
<td></td>
<td>2.2%</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>2.0%</td>
<td>5.7%</td>
<td>13.7%</td>
<td>...</td>
</tr>
<tr>
<td><strong>T</strong>(_4)</td>
<td></td>
<td>2.8%</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>2.2%</td>
<td>5.7%</td>
<td>...</td>
<td>...</td>
</tr>
</tbody>
</table>

#### False-positives (%)

<table>
<thead>
<tr>
<th></th>
<th>Of all scans</th>
<th>17,497/75,126 (23.3%)</th>
<th>302/9800 (3.1%)</th>
<th>...</th>
<th>...</th>
<th>...</th>
<th>355/29735 (1.2%)</th>
<th>747/9121 (8.2%)</th>
<th>1002/5333 (18.8%)</th>
<th>72/1994 (3.6%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Of all positive scans</td>
<td>17,497/18146 (96.4%)</td>
<td>302/371 (81.4%)</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>355/598 (59.4%)</td>
<td>747/805 (92.8%)</td>
<td>1002/1044 (96.1%)</td>
<td>72/114 (63.2%)</td>
</tr>
<tr>
<td></td>
<td>Per participant basis</td>
<td>...</td>
<td>22.9 %</td>
<td>...</td>
<td>...</td>
<td>...</td>
<td>273/7582 (3.6%)</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
</tbody>
</table>

- False positives of all scans: 1.2%(NELSON) - 23.3%(NLST)
- False positives of all positive scans: 59.4%(NELSON) – 96.4%(NLST)

Van der Aalst CM et al Lancet Respir Med 2016
Nodule management

- NELSON nodule management plan

Results: nodule volume algorithm based on LC probability

<table>
<thead>
<tr>
<th>Screening result</th>
<th>Nodule volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>negative</td>
<td>&lt; 100 mm³</td>
</tr>
<tr>
<td>indeterminate*</td>
<td>≥ 100 to 300 mm³</td>
</tr>
<tr>
<td>positive</td>
<td>≥ 300 mm³</td>
</tr>
</tbody>
</table>

*Follow-up CT for VDT assessment:
- final screening result negative for VDT ≥ 600 days
- final screening result positive for VDT < 600 days
End-to-end lung cancer screening with three-dimensional deep learning on low-dose chest computed tomography

Fig. 1 | Overall modeling framework. For each patient, the model uses a primary LDCT volume and, if available, a prior LDCT volume as input. The model then analyzes suspicious and volumetric ROIs as well as the whole-LDCT volume and outputs an overall malignancy prediction for the case, a risk bucket score (LUMAS) and localization for predicted cancerous nodules.
Risks of harm (invasive examinations)

Maximal protection of screening participants

- Unintended harms of screening (radiation exposure)
- Psychosocial consequences of false positives and overdiagnosis
- Invasive examinations for screen-detected lung nodules
Cumulative Radiation risk (serial CT’s)

<table>
<thead>
<tr>
<th>Radiation exposition to screening participants</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Table 5</strong> Recently reported effective dose values from lung cancer screening LDCT studies</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Report (year of publication)</th>
<th>Effective dose</th>
<th>Method of estimation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rampineli et al. (2017) [23]</td>
<td>1.2</td>
<td>DLP</td>
</tr>
<tr>
<td>Lee et al. (2017) [33]</td>
<td>2.01-2.80</td>
<td>Organ doses [NLST]</td>
</tr>
<tr>
<td>Messerli et al. (2017) [34]</td>
<td>0.13*</td>
<td>DLP</td>
</tr>
<tr>
<td></td>
<td>0.3*</td>
<td>DLP+SSDE**</td>
</tr>
<tr>
<td>Jacobs et al. (2017) [35]</td>
<td>1.3</td>
<td>DLP</td>
</tr>
<tr>
<td></td>
<td>3.8</td>
<td>DLP+SSDE**</td>
</tr>
<tr>
<td>Miao et al. (2017) [36]</td>
<td>0.67*</td>
<td>DLP</td>
</tr>
<tr>
<td></td>
<td>1.20</td>
<td>DLP</td>
</tr>
<tr>
<td>Current study</td>
<td>0.71</td>
<td>Organ doses</td>
</tr>
<tr>
<td></td>
<td>0.52</td>
<td>DLP+SSDE</td>
</tr>
</tbody>
</table>

*Described as ultra-low dose chest CT protocol

**DLP-derived effective dose corrected for body size to provide size specific dose estimates (SSDE)

Key Points

- Effective dose from lung cancer screening low-dose CT may be <1 mSv.
- Screening with modern low-dose CT minimally aggravates lifetime cancer induction intrinsic risk.
- Dosimetry of lung cancer screening low-dose CT should encounter the radiation burden from the localizing scan projection radiography.
- DLP method may underestimate effective dose from low-dose chest CT by 27%.

Persinakis K et al Eur Radiol 2018; Figure from: [http://www.aboutcancer.com/radiation_imaging_risks_0311.htm](http://www.aboutcancer.com/radiation_imaging_risks_0311.htm) (accessed 2019)
Cost/Benefit of lung cancer screening

Cost per country

- Influence of smoking eligibility criteria for screening trial on Cost effectiveness
- But also the amount of CT’s and CT detected nodule management plan (volumetry)
- Tobacco cessation measures

- NLST: 81,000 US dollars/QALY
- UKLS modeling study: 12,000 Pound/QALY
- Canada: 52,000 CAD dollars/QALY
- Switzerland (MISCAN Modeling study): less than 50,000 € per LYG (Life Year gained) or less than 70,000 € per QALY

Impact of low-dose CT screening on smoking cessation among high-risk participants in the UK Lung Cancer Screening Trial

Kate Brain,¹ Ben Carter,¹,² Kate J Lifford,¹ Olivia Burke,¹ Anand Devaraj,³ David R Baldwin,⁴ Stephen Duffy,⁵ John K Field⁶

...or screening AND Smoking Cessation!

Key messages

What is the key question?
What is the effect on smoking cessation of taking part in the UK randomised pilot trial of low dose CT lung screening?

What is the bottom line?
CT lung cancer screening does not appear to falsely reassure smokers or reduce their motivation to stop smoking.

Why read on?
For clinicians and policy makers who are considering implementation of risk-stratified lung cancer screening, this study adds to evidence suggesting that integrating CT screening with evidence-based smoking cessation interventions could prompt quitting in motivated high-risk smokers.
Cancer

Screening for lung cancer is a controversial idea

But the evidence now suggests it can work

LUCSO-1—French pilot study of LUng Cancer Screening with low-dose computed tomography in a smokers population exposed to Occupational lung carcinogens: study protocol


Figure 3  Organisation of lung cancer screening in subjects at high risk of lung cancer in France.
Thank you for your attention … on lung cancer screening!

&

NELSON-investigators
NEderlands-LeuvenS Longkanker Screenings ONderzoek

Erasmus MC, University Medical Center Rotterdam, University Medical Center Utrecht, Spaarne Gasthuis Haarlem, University Medical Center Groningen, University Hospital Leuven, Belgium, Maasstad Hospital Rotterdam, University Medical Center Amsterdam, Radboud University Medical Center Nijmegen
Table 6  Lung nodule and cancer prevalence in series of incidentally detected nodules and screening trials

<table>
<thead>
<tr>
<th></th>
<th>Studies (n)</th>
<th>Patients (n)</th>
<th>Nodule prevalence (%)</th>
<th>Lung cancer prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidental</td>
<td>13 5 7 13−18 31 32</td>
<td>11 683</td>
<td>13 (2−24)</td>
<td>1.5 (0−4.0)</td>
</tr>
<tr>
<td>Screening</td>
<td>21 4 6 8−12 19−30 34 35</td>
<td>116 300</td>
<td>33 (17−53)</td>
<td>1.4 (0.5−2.7)</td>
</tr>
</tbody>
</table>

The reported prevalence of malignant nodules is similar in screening studies and in studies reporting nodules as incidental findings. Evidence level 3
Persons at high risk for lung cancer

**Cumulative Lung Cancer Risk**

![Graph showing cumulative lung cancer risk by age and smoking status.](image-url)
LUNG CANCER SCREENING

Current Smoker?

YES

Are you between the ages of 55 and 80?

YES

Do you smoke at least one pack a day for 30 years or two packs a day for 15 years?

YES

Talk to your doctor about smoking cessation.

TALK TO YOUR DOCTOR ABOUT GETTING SCREENED.

NO

NO

Talk to your doctor about smoking cessation.

TALK TO YOUR DOCTOR ABOUT GETTING SCREENED.

NO

NO

Did you ever smoke?

YES

Did you quit more than 15 years ago?

YES

NO

DO YOU HAVE A FAMILY HISTORY OF LUNG CANCER OR, HISTORY OF ASBESTOS OR OTHER ENVIRONMENTAL EXPOSURE?

YES

SCREENING NOT LIKELY RECOMMENDED.

NO

NO

TALK TO YOUR DOCTOR.

NO

NO

SCREENING NOT LIKELY RECOMMENDED.
OVERVIEW OF NELSON SCREENING PROTOCOL

NELSON : 5,5 YEARS CALCULATIONS

<table>
<thead>
<tr>
<th>1st screening result</th>
<th>Risk screen-detected lung cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>1,0%</td>
</tr>
<tr>
<td>Indeterminate</td>
<td>5,7%</td>
</tr>
<tr>
<td>Positive</td>
<td>48,3%</td>
</tr>
</tbody>
</table>