Community 365
Roundtable Meeting
Early Detection and Screening

22 June 2021
Prevention, Early Detection and Screening Network

• Established in June 2020

• Bringing together 45+ stakeholder organisations, including E.C.O. Member Societies, Patient Advisory Committee, Community 365 and invited stakeholders

• Aims to drive fresh and stronger consensus in areas of primary and secondary cancer prevention

• New name: Prevention, Early Detection and Screening Network
Prevention, Early Detection and Screening Network

The Prevention, Early Detection and Screening Network brings together a wide range of experts and stakeholders, from the European Cancer Organisation Member Societies, Patient Advisory Committee and other stakeholders, with the aim of driving fresh and stronger consensus in areas chosen by its participants for focus.
Advocacy Paper

• Advocacy Paper on Early Detection and Screening will be published in September, based on this meeting’s presentations and discussions. It will outline today’s key recommendations in the context of the implementation of Europe’s Beating Cancer Plan and the EU Cancer Mission

• If you wish to input into the Advocacy Paper, contact Norbert Couespel
  norbert.couespel@europeancancer.org

• This Advocacy Paper will be used for further engagement with the European Parliament (including the Special Committee on Beating Cancer), the European Commission and EU agencies to take these recommendations forward

• Paper will also form the basis of our session at the European Cancer Summit 2021 on 17 November at 9:15-10:45 CET
Early Detection for All Cancers
Early Detection and the Power of Molecular Therapies

- Early Detection
- Targeted Treatment Earlier
- Post Treatment Monitoring
Multi-cancer early detection: rationale and application

Paul Limburg, MD
Chief Medical Officer, Screening Exact Sciences
Earlier cancer detection saves lives

About half of new cases in Europe have limited or no early screening

Number of new cancer cases per year

- Screening available for average risk: 1,062,837 (40%)
- Screening available for high risk: 379,261 (14%)
- Limited/no screening available: 1,240,439 (46%)

Number of cancer deaths per year

- Screening available for average risk: 331,313 (26%)
- Screening available for high risk: 311,162 (25%)
- Limited/no screening available: 619,247 (49%)

Number of deaths per year for cancers with limited/no screening

- Kidney: 34,409
- Brain/CNS: 34,713
- Non-Hodgkin: 34,892
- Leukaemia: 43,435
- Bladder: 49,185
- Stomach: 52,085
- Pancreatic: 89,256
- All others: 281,272

The power of aggregate prevalence

Multi-cancer screening is more effective and cost efficient

Source: Ahlquist, Nature Precision Oncology (2018) 2:23; doi:10.1038/s41698-018-0066-x
There are several approaches to multi-cancer early detection

**Ideal features**
- Effective early-stage detection
  - Sensitivity
  - Compliance
  - Access
- High specificity
- Accurate site prediction
- Non-invasive
- Affordability

**Sampling options**
- Imaging with clearer vision
- Target the circulation
  - Blood
  - Urine
  - Breath
  - Saliva
- Capitalize on tumor exfoliation
  - Stool
  - Tampon

**Potential markers**
- Whole cells
- Proteins
- Metabolites (e.g. VOCs)
- RNA
- DNA
  - Genetic (e.g. mutations)
  - Epigenetic (e.g. aberrant methylation)
CancerSEEK is our approach to multi-cancer early detection

Our Proprietary Integrated Service Model

- **Multiple unscreened cancers:** In an interventional study of 10,006 women, CancerSEEK identified 26 cancers: 23 of which wouldn’t have been screened for

- **Reflex testing:** A “rule-in” approach that pairs high specificity testing with confirmatory PET-CT

- **Focused on the patient:** Participants were counselled about test implications and educated on their need to continue SOC cancer protection

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Source: A. M. Lennon et al., Science (2020). 1 Cancers identified with screening alternatives were breast (1), colorectal (2). There were 9 lung cancers identified, but lung screening is only available for high-risk individuals, who were not enrolled in the DETECT-A study.
WHO estimates 11M annual cancer cases diagnosed in LMICs by 2030

Prohibitive cost
Lack of infrastructure
Limited education on cancer screening
Insufficient screening
Reluctance to get tested
Shortage of medical workers
Lack of downstream resources to treat

What’s needed to get there?

- Finalize assay and algorithm
- Define optimal target population
- Standardize case management approach
- Support access to diagnostic follow-up and appropriate treatment
- Perform rigorous cost-effectiveness analyses
- Work with academia, professional societies, regulatory bodies and payors
Early detection for all cancers: The early detection of treatment intervention targets in all cancers from the pathologist’s perspective

Holger Moch
President
European Society of Pathology
Department of Pathology and Molecular Pathology
UZH
The role of a pathologist is evolving.

Molecular testing is evolving towards precision medicine.

Conventional:
- Tumour 1
- Tumour 2
- Tumour 3

Standard therapy
Helpful for 1 of 3 patients

Personalised:
- Tumour 1
- Tumour 2
- Tumour 3

Molecular pathology
More effective
Less toxic
Less costly

Therapy 1
Therapy 2
Therapy 3
# Advanced diagnostics inform therapy selection in lung cancer

## Targetable mutations in lung cancer

### EGFR
- **sensitising** 17%
- **other** 4%
- **sensitising and other** 21%
- **Non-sensitising** 83%

### ALK
- **7%** of patients

### EGFR
- **sensitising** 17%
- **sensitising and other** 21%
- **Non-sensitising** 83%

### MET
- **3%** of patients

### ROS1
- **2%** of patients

### BRAF
- **2%** of patients

### RET
- **2%** of patients

### NTRK
- **1%** of patients

### PIK3CA
- **1%** of patients

### MEK1
- **<1%** of patients

### KRAS
- **25%** of patients

### No oncogenic driver detected
- **31%** of patients

## Identifying actionable mutations with broad genomic profiling

### Approved drugs

<table>
<thead>
<tr>
<th>EGFR</th>
<th>ALK</th>
<th>BRAF</th>
<th>RET</th>
<th>HER2</th>
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<tbody>
<tr>
<td>• Arafatinib</td>
<td>• Alectinib</td>
<td>• Binimetinib</td>
<td>• Pralsetinib</td>
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<tr>
<td>• Dacomitinib</td>
<td>• Brigatinib</td>
<td>• Cobimetinib</td>
<td>• Selumetinib</td>
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<tr>
<td>• Erlotinib (± anti-VEGF / VEGFR)</td>
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<td>• Cotinib</td>
<td>• Sotorasib</td>
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<tr>
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<td>• Crizotinib</td>
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<td>• Nectatumab</td>
<td>• Lorlatinib</td>
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### Investigational drugs

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</table>

## Notes

1. *Some drugs are approved for cancer types other than lung cancer with alterations in the indicated gene with clinical trials investigating efficacy in lung cancer.
2. *Some drugs are investigational and not approved in any indication. Some non-investigational drugs are only approved for use in specific indications in Europe and / or USA and / or Japan. Therapies marked with ▼ are subject to additional monitoring. Reporting suspi product is important. Adverse events should be reported to your respective local office (see slide notes for full listing).
4. Reporting suspi product is important. Adverse events should be reported to your respective local office (see slide notes for full listing).

## Acknowledgments

All drugs listed are included in NSCLC NCCN Guidelines unless otherwise indicated. Some therapies listed target specific variants of the indicated gene.
Pembrolizumab is the first FDA approved cancer treatment based on a common biomarker

- Traditionally in oncology approvals were based on a tumour type or a biomarker within a tumour type
- For the first time, the FDA has ‘approved a drug based on a tumour’s biomarker without regard to the tumour’s original location’
- Pembrolizumab is indicated for the treatment of patients with unresectable or metastatic solid tumours possessing a microsatellite instability-high (MSI-H) biomarker

FDA: US food and drug administration; MSI-H: microsatellite instability-high.
FDA press release (2017)
https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm560167.htm
Molecular profiling provides actionable insights

**Genomic signatures**
Tumour mutational burden and microsatellite instability status, which may predict response to immunotherapy¹⁻⁴

**Gene alterations**
Clinically relevant alterations in 324 tested cancer-related genes

**Pertinent negative results**
Rules out important alterations that are not present

**Therapies with clinical benefit**
Swissmedic-approved therapies for your patient’s genomic signatures and gene alterations

**Clinical trials**
Relevant trials for which your patient may be eligible, based on their genomic profile and geographic location

**Genomic findings with no reportable options**
To help you rule out uncertainty and determine the appropriate course of action

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University Hospital Zurich
Approach

First Diagnosis
Patient 2: 13 yo female patient

**Patient History:**
- Abdominal girth for 4 months
- Slightly reduced appetite

MRI Scan on admission date:
- Large volume ascites
- Bilateral hydro-nephrosis
- Widespread peritoneal deposits
Patient: Biopsy
Patient: Comprehensive Genomic Profiling

**PATIENT RESULTS**

- 3 genomic findings
- 3 therapies associated with potential clinical benefit
- 0 therapies associated with lack of response
- 10 clinical trials

**TUMOR TYPE: PEDIATRIC PERITONEUM MESOTHELIOMA**

- Genomic Alteration Identified:
  - **ALK** STRN-ALK fusion

- Additional Findings:
  - **Microsatellite status**: MS-Stable
  - **Tumor Mutational Burden**: TMB-Low; 3 Muts/Mb

---

**INFORMATION REGARDING PHARMACEUTICAL PRODUCTS AND CLINICAL TRIALS**

<table>
<thead>
<tr>
<th>Genomic Findings Detected</th>
<th>Swissmedic-Approved Therapies (in patient's tumor type)</th>
<th>Swissmedic-Approved Therapies (in another tumor type)</th>
<th>Potential Clinical Trials</th>
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<tr>
<td><strong>ALK</strong> STRN-ALK fusion</td>
<td>None</td>
<td>Alectinib</td>
<td>Yes, see clinical trials section</td>
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<tr>
<td></td>
<td></td>
<td>Ceritinib</td>
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</tr>
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<td><strong>Microsatellite status</strong></td>
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<td>None</td>
<td>None</td>
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<td>MS-Stable</td>
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<tr>
<td><strong>Tumor Mutational Burden</strong></td>
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<td>None</td>
<td>None</td>
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<tr>
<td>TMB-Low; 3 Muts/Mb</td>
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</table>
Patient: Treatment and Follow-Up

Before treatment

6 weeks of treatment

12 weeks of treatment
Potential applications of liquid biopsies throughout the disease journey

Cancer detection: screening or earlier diagnosis
Molecular profiling or prognostication
Detection of residual disease
Monitoring response
Monitoring clonal evolution or acquired resistance

Quantitative analysis
• Disease staging
• Response monitoring
• Prognostication

Genomic analysis
• Mutation profiling
• Treatment selection
• Monitoring clonal evolution

EU Level Screening Initiatives: What have we learned so far?

Isabel Rubio
Co-Chair of the Prevention, Early Detection and Screening Network
European Cancer Organisation
Developments in Breast Cancer Screening since 2003

Prof. Harry J. de Koning, MD PhD
Prof & Deputy Head Public Health
Erasmus MC, Rotterdam, the Netherlands
“Every day of delay is a missed opportunity to catch a person’s cancer or disease at an earlier point, and potentially save their life ”

Sir Richard
Cancer & cancer screening

Estimated incidence and mortality per cancer site

- Lung cancer
- Breast cancer
- Colorectal cancer
- Cervical cancer

Number of cases (x 1,000)
Mammography screening

Model estimates for women aged 40 years and older who were invited to screening between 50 and 74 years, followed over their lifetimes (participation rate: 80%).

<table>
<thead>
<tr>
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<th>1000 women without screening</th>
<th>1000 women with screening</th>
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</thead>
<tbody>
<tr>
<td>Women who died from breast cancer</td>
<td>45</td>
<td>32</td>
</tr>
<tr>
<td>Women with a false-positive test result</td>
<td>-</td>
<td>143</td>
</tr>
<tr>
<td>Women who were unnecessarily diagnosed and treated</td>
<td>-</td>
<td>5</td>
</tr>
<tr>
<td>Remaining women</td>
<td>955</td>
<td>820</td>
</tr>
</tbody>
</table>
The potential of breast cancer screening in Europe

Nadine Zielonke1 | Lindy M. Kregting2 | Eveline A. M. Heijnsdijk1 | Piiret Veerus2 | Sirpa Heinävaara3 | Martin McKee4 | Inge M. C. M. de Kok2 | Harry J. de Koning4 | Nicolien T. van Ravesteyn | the EU-TOPIA collaborators5

1Department of Public Health, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands
2National Institute for Health Development, Tallinn, Estonia
3Finish Cancer Registry, Helsinki, Finland
4London School of Hygiene and Tropical Medicine, London, UK
5The EU-TOPIA collaborators are listed in the Appendix

Abstract
Currently, all European countries offer some form of breast cancer screening. Nevertheless, disparities exist in the status of implementation, attendance and the extent of opportunistic screening. As a result breast cancer screening has not yet reached its full potential. We examined how many breast cancer deaths could be prevented if all European countries would biennially screen all women aged 50 to 69 for breast cancer. We calculated the number of breast cancer deaths already prevented due to screening as well as the number of breast cancer deaths which could be additionally prevented if the total examination coverage (organised plus opportunistic) would reach 100%. The calculations are based on total examination coverage in women aged 50 to 69, the annual number of breast cancer deaths for women aged 50 to 74 and the maximal possible mortality reduction from breast cancer, assuming similar effectiveness of organised and opportunistic screening. The total examination coverage ranged from 49% (East), 62% (West), 67% (North) to 69% (South). Yearly 21 080 breast cancer deaths have already been prevented due to mammography screening. If all countries would reach 100% examination coverage, 12 404 additional breast cancer deaths could be prevented annually, with the biggest potential in Eastern Europe. With maximum coverage, 23% of their breast cancer deaths could be additionally prevented, while in Western Europe it could be 21%, in Southern Europe 13% and in Northern Europe 9%. Our study illustrates that by further optimising screening coverage, the number of breast cancer deaths in Europe can be lowered substantially.

KEYWORDS
breast cancer mortality, breast cancer mortality reduction, breast cancer screening, screening coverage, screening guidelines
Figure 2: Annual number of observed and preventable breast cancer deaths, ages 50-74, per European region

Breast cancer deaths, per year

- Breast cancer deaths in the absence of screening
- Observed breast cancer deaths with current screening examination coverage
- Breast cancer deaths if screening examination coverage would increase to 100%

Northern Europe: Denmark, Estonia, Finland Iceland, Latvia, Lithuania, Norway and Sweden.
Western Europe: Austria, Belgium, France, Germany, Ireland, Luxembourg, The Netherlands, United Kingdom and Switzerland.
Eastern Europe: Bulgaria, Czech Republic, Croatia, Hungary, Poland, Romania, Slovakia and Slovenia.
Southern Europe: Cyprus, Gibraltar, Greece, Italy, Malta, Portugal and Spain.
These analyses illustrate that breast cancer screening in Europe already has a substantial impact by preventing nearly 21,700 breast cancer deaths per year.

Through introducing a hypothetical 100% coverage of screening in the advised target age groups, the number of breast cancer deaths of European women could be further reduced by almost 12,500 per year.

This represents an additional 23% in Eastern Europe, 21% in Western Europe, 15% in Southern Europe and 9% in North.
Risk-based screening ("patient centric") is the best concept

Risk assessment  Stratification  Intervention based on risk
Risk stratification in breast cancer screening: Cost-effectiveness and harm-benefit ratios for low-risk and high-risk women

Valérie D. V. Sankatsing | Nicolien T. van Ravesteyn
Eveline A. M. Heijnsdijk | Mireille J. M. Broeders | Harry J. de Koning
Optimal screening scenario and corresponding outcomes by risk group

<table>
<thead>
<tr>
<th></th>
<th>Current screening RR = 1</th>
<th>Low risk RR = 0.75</th>
<th>High risk RR = 1.8</th>
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<tr>
<td>(Optimal) scenario</td>
<td>B 50-74</td>
<td>T 50-71</td>
<td>B 40-74</td>
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<tr>
<td>Screening rounds</td>
<td>13</td>
<td>8</td>
<td>18</td>
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<tr>
<td>Screening outcomes*</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>False positives</td>
<td>187</td>
<td>102</td>
<td>371</td>
</tr>
<tr>
<td>Overdiagnosis</td>
<td>5</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>BC deaths averted</td>
<td>16</td>
<td>10</td>
<td>26</td>
</tr>
<tr>
<td>Life-years gained</td>
<td>206</td>
<td>134</td>
<td>380</td>
</tr>
<tr>
<td>Harm-benefit ratios</td>
<td></td>
<td></td>
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<tr>
<td>False-positives/deaths averted</td>
<td>11.8</td>
<td>10.1</td>
<td>14.5</td>
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<tr>
<td>False-positives/life-years gained</td>
<td>0.90</td>
<td>0.76</td>
<td>0.98</td>
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<tr>
<td>Overdiagnosis/deaths averted</td>
<td>0.34</td>
<td>0.31</td>
<td>0.29</td>
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<tr>
<td>Overdiagnosis/life-years gained</td>
<td>0.03</td>
<td>0.02</td>
<td>0.02</td>
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</table>

*Screening outcomes are presented per 1,000 women, aged 40 years followed over their lifetime invited for screening.

T: triennial (3-year interval)
B: biennial (2-year interval)
### PRS & Family history
(van den Broek et al., JNCI 2020)

<table>
<thead>
<tr>
<th>Guideline*</th>
<th>Screening strategy</th>
<th>Number of screens</th>
<th>Life years gained</th>
<th>Breast cancer deaths averted</th>
<th>Over-diagnosis</th>
<th>False positives</th>
<th>LYG/screen</th>
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<td>United States Preventive Services Task Force</td>
<td>Biennial 50-74</td>
<td>11182</td>
<td>118</td>
<td>6.7</td>
<td>14.5</td>
<td>920</td>
<td>0.0106</td>
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<tr>
<td>Risk-based</td>
<td>Family history</td>
<td>11840</td>
<td>125</td>
<td>6.9</td>
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<td>1000</td>
<td>0.0105</td>
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<td>Risk-based</td>
<td>Polygenic risk</td>
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<td>141</td>
<td>7.4</td>
<td>16.0</td>
<td>1156</td>
<td>0.0109</td>
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<td>Family history &amp; polygenic risk</td>
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<td>154</td>
<td>7.9</td>
<td>16.6</td>
<td>1169</td>
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<td>Sensitivity analysis</td>
<td>Polygenic risk</td>
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<td>135</td>
<td>7.1</td>
<td>14.0</td>
<td>946</td>
<td>0.0124</td>
</tr>
</tbody>
</table>
Future of risk-based BC screening?

**age**

40  SNPtest: PRS RR > 2 --> start screening

45  baseline mammogram: extremely dense --> start screening
    questionnaire: RR > 1.5 --> start screening

50  questionnaire: RR < 0.7 --> start triennial screening
    RR > 0.7 --> start biennial screening
    extremely dense breasts --> MRI screening

69/74  dependent on risk? Remaining life expectancy?
Breast cancer screening’s future

The right invite, at the right interval, with the right information

This means (EU-TOPIA) tools to evaluate, quantify and change

Age extensions to 44 / 74

Screening intervals and test modalities by risk

More equity by (less) diversity
EU Level Screening initiatives: Progress Made on Colorectal Cancer Screening Since 2003

Luigi Ricciardiello
Professor
Chair, Research Committee
United European Gastroenterology
Aiming to improve digestive health

Uniting 30,000 specialists from every field in digestive health
Coordinating European Action against Colorectal Cancer

Call to policymakers:
United European Gastroenterology (UEG) calls for the implementation of organised, population-based screening programmes across the entirety of the EU and for Member States to improve the coverage and quality of existing programmes to reduce colorectal cancer (CRC) rates.
Estimated CRC Incidence by Country

Effect of screening programs

Global trends in incidence and mortality from CRC over the period 2000-2015

Incidence: -25.5%

Mortality rates: -52.4%

Levin TR et al, Gastroenterology, 2018
Vast inequalities in colorectal cancer screening programmes design and participation across Europe

Bulgaria, Greece, Latvia, Romania and the Slovak Republic currently do not have population-based CRC screening programmes\(^3\)

Prevention and treatment strategies, including the implementation of screening programmes could reduce CRC mortality by 27% by 2030\(^6\)

CRC has a 5-year survival rate of 90% when detected at stage 1 and 71% at stage 2\(^7\)
Innovate on screening techniques & strategies

- Identify & better understand the barriers for screening experienced by disadvantaged groups
- COVID-19 → significant disruption of existing CRC screening programs → define protected path for CRC screening
- Next generation screening tools with robust biomarkers for the identification of patients at risks
- Innovate the screening of upper digestive cancers (oesophageal, gastric), to enable screening with adapted tools for risk individuals and/or high incidence European countries
UEG calls on the EU and all Member States to:

- Incentivise Member States to improve the organisation of their existing programmes to further increase the coverage and quality of CRC screening across Europe.

- Encourage the implementation of organised CRC screening programmes across the entirety of the EU in accordance with EU screening guidelines.

- Undertake updates of European CRC screening guidelines and screening progress reports every two years, which reflect scientific evidence from current best practice.
Q&A with Speakers and Co-Chairs
The Development of New Screening and Tumor-specific Strategies

Jan van Meerbeeck
Co-Chair of the Prevention, Early Detection and Screening Network
European Cancer Organisation

Karl Matussek
Head of Oncology Germany
AstraZeneca
Challenges in the implementation of lung cancer screening

Emma O’Dowed
Consultant Respiratory Physician
Nottingham University Hospitals NHS Trust
Challenges in the implementation of lung cancer screening

- Harm minimisation
- Benefit
- Recruitment/eligibility optimisation
- Cost effectiveness
- Workforce/capacity
- Participation
- Quality assurance
- Add on health interventions
- Incidental findings
- Lung cancer screening
## False positives

### Cervical screening (England 2018)

<table>
<thead>
<tr>
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<th>Routine screening</th>
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<tr>
<td><strong>Negative</strong></td>
<td></td>
</tr>
<tr>
<td>Low-grade changes/</td>
<td>Repeat smear</td>
</tr>
<tr>
<td>inadequate (3%)</td>
<td></td>
</tr>
<tr>
<td><strong>Positive</strong></td>
<td>Colposcopy/ surgery</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th><strong>Routine screening</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Negative</strong></td>
<td></td>
</tr>
<tr>
<td>Indeterminate</td>
<td>Repeat LDCT at 3 months</td>
</tr>
<tr>
<td><strong>Positive</strong></td>
<td>Lung MDT referral</td>
</tr>
</tbody>
</table>

- \( \approx 92\% \) \( \approx 83\% \)
- \( \approx 7\% \) \( \approx 13\% \)
- \( \approx 1\% \) \( \approx 5\% \)
- \( \ast \) \( 52\% \) lung cancer

Overdiagnosis

LDCT

CXR

Excess lung cancer

3.3%

Hospital anxiety and depression score and Cancer Worry Score were measured in control (non-screened) and intervention group at baseline, 2 weeks, and up to 2 years.

Cancer distress was higher in participants with positive results at 2 weeks but not at longer follow-up.
Harms associated with referral/ treatment

- Pooled data from UKLS, LSUT, Nottingham, Liverpool and Manchester (unpublished)- 11815 participants

<table>
<thead>
<tr>
<th>Description</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number with major complication from invasive testing/treatment(^#) for lung cancer</td>
<td>3</td>
<td>0.03</td>
</tr>
<tr>
<td>Number of deaths as a result of investigation/management(^#) with lung cancer</td>
<td>2</td>
<td>0.02</td>
</tr>
<tr>
<td>Number undergoing invasive testing(^*) for benign disease (not including surgery)</td>
<td>61</td>
<td>0.5</td>
</tr>
<tr>
<td>Number undergoing lung resection for benign disease (5% benign resection rate)</td>
<td>9</td>
<td>0.07</td>
</tr>
<tr>
<td>Number with major complication from invasive testing/treatment(^#) for benign disease</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Number deaths as a result of invasive testing/treatment(^#) for benign disease</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

* Bronchoscopy or biopsy  \#Bronchoscopy, biopsy or surgery
Eligibility optimisation and participation

- How to identify the ‘high risk’
- Risk models versus age and smoking status alone
  - No consensus on which model/ threshold to use
- Participation promising in UK pilots (30-50%)
  - LSUT 53% participation
  - Compared with 3-4% in US

Recruitment

NELSON

Images courtesy of Carlijn van der Aalst & Mat Callister

YLST
Workforce

Number of practicing radiologists per 100,000 population

CT scanning capacity

Data from Organisation for Economic Co-operation and Development - available via https://stats.oecd.org
## Cost Effectiveness

<table>
<thead>
<tr>
<th>Method</th>
<th>Result ICER per QALY gained</th>
</tr>
</thead>
<tbody>
<tr>
<td>Villante¹</td>
<td>£22,592</td>
</tr>
<tr>
<td>NLST²</td>
<td>£64,800 (41,000 to 149,000)</td>
</tr>
<tr>
<td>UKLS³</td>
<td>£8,466 (5,542 to 12,569 )</td>
</tr>
<tr>
<td>HTA⁴</td>
<td>£28,169</td>
</tr>
<tr>
<td>Manchester pilot⁵</td>
<td>£10,069</td>
</tr>
<tr>
<td>Canada⁶</td>
<td>£12,560</td>
</tr>
</tbody>
</table>

### References

Service implementation and quality assurance

- Capacity and Infrastructure
- Governance
- Selection, risk assessment, consent, clinical pathways
- Low dose CT technical standards
- Smoking cessation
- Scan intervals
- Non-attendance and exiting programme
- Management of findings
- Communication
- Data management and evaluation
Implementation challenges

- Lung cancer screening
- Incidental findings
- Harm minimisation
- Benefit
- Add on health interventions
- Cost effectiveness
- Recruitment/eligibility optimisation
- Quality assurance
- Participation
- Workforce/capacity
- Incidental findings
Evidence for risk-adapted screening in prostate cancer

Peter Albers, MD
Professor of Urology
Division Head, C130 Personalized Prevention and Early Detection of Prostate Cancer
German Cancer Research Center (DKFZ) Heidelberg, Germany
Chair, Department of Urology, Düsseldorf University Hospital Heinrich-Heine-University, Düsseldorf, Germany
No conflict of interest regarding this talk.
Prostate cancer specific mortality (ERSPC)

RR 0.80 (95% CI, 0.72-0.89, p=0.001)

Hugosson J et al. Eur Urol 2019
Due to screening:

- no lives will be saved
- around 20 men will be diagnosed with cancers that would not have caused any harm

https://scienceblog.cancerresearchuk.org
Individualised Early Detection of PCA

Potential Methods

• age-adapted risk groups
• hereditary risk
• mpMRI before biopsy
• kallikreins (4K)
• molecular serum markers (SNPs, MSI)
• urine markers (HOXC6, DLX1, T2:ERG)
• combinations (risk calculators from ERSPC and PCPT)
Individualised Early Detection of PCA

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Prediction of PCA metastasis by „baseline“ PSA

PSA at 45 yrs risk for metastasis after 25 yrs

PSA < 1.1 ng/ml 1.38%

PSA > 1.6 ng/ml up to 9.82%

~ 10x higher risk > 1.6 ng/ml

Vickers A et al. BMJ 2013
Risk-adapted prostate cancer (PCa) early detection study based on a “baseline” PSA value in young men – a prospective multicenter randomized trial (PROBASE)
Study Design

"baseline" PSA

< 1.5 ng/ml
PSA after 5 years
90%

1.5 - 2.99 ng/ml
PSA after 2 years
8%

≥ 3.0 ng/ml
mpMRI and biopsy
2%
Study Design

Arm A
- Immediate PSA value at age 45
- Informed consent, and validated questionnaires
- Risk-adapted screening

Arm B
- Deferred PSA value at age 50
- Informed consent, validated questionnaires, and DRE
- After 5 years: "baseline" PSA
- Risk-adapted screening

N = 50,000
45-yr old men
Random sample from population registries
Randomization
Accrual Feb 2014 – Dec 2019: 46,642 participants
Summary of the First Screening Round

- prevalence of prostate cancers at age 45 is very low (0.19%)
- prevalence of unfavorable prostate cancers is even lower (0.05%)
- prevalence of DRE - detected PCA is extremely low
Platinum Opinion

Early Detection of Prostate Cancer in 2020 and Beyond: Facts and Recommendations for the European Union and the European Commission

Hendrik Van Poppel\textsuperscript{a,\dagger,*}, Renée Hogenhout\textsuperscript{b,\dagger}, Peter Albers\textsuperscript{c,d}, Roderick C.N. van den Bergh\textsuperscript{e}, Jelle O. Barentsz\textsuperscript{f,\dagger}, Monique J. Roobol\textsuperscript{b,\dagger}
Risk Stratification (RC, MRI) avoids > 50% of biopsies and > 50% of radical surgery
Take Home Messages

population-based PCa screening with PSA alone is obsolete

risk-adapted screening is possible and effective

> 50% of biopsies and overtreatment can be avoided
Thank you for your attention!

Further information on www.dkfz.de
The Next Steps – Progressing the Agenda with the JRC and FEAM

Richard Price
EU Affairs Policy Manager
European Cancer Organisation

Ciaran Nichol
Head of the Health in Society Unit, Joint Research Centre (JRC)

Stefan Constantinescu
President
Federation of European Academies of Medicine (FEAM)
Advocacy Paper

• Advocacy Paper on Early Detection and Screening will be published in September, based on this meeting’s presentations and discussions. It will outline today’s key recommendations in the context of the implementation of Europe’s Beating Cancer Plan and the EU Cancer Mission

• If you wish to input into the Advocacy Paper, contact Norbert Couespel norbert.couespel@europeancancer.org

• This Advocacy Paper will be used for further engagement with the European Parliament (including the Special Committee on Beating Cancer), the European Commission and EU agencies to take these recommendations forward

• Paper will also form the basis of our session at the European Cancer Summit 2021 on 17 November at 9:15-10:45 CET
Save the Date!
Session on Prevention, Early Detection & Screening
17 November 2021 at 9:15-10:45 CET
The Prevention, Early Detection and Screening Network brings together a wide range of experts and stakeholders, from the European Cancer Organisation Member Societies, Patient Advisory Committee and other stakeholders, with the aim of driving fresh and stronger consensus in areas chosen by its participants for focus. Please contact our CEO, Mike Morrissey, if you would like to join the Prevention, Early Detection and Screening Network (free-of-charge).