

# **Cancer Screening Evidence Review Report**

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**Working Group Co-Chair**

**Rebecca Fitzgerald Professor of Cancer Prevention & Interim Director of the MRC Cancer Unit, University of Cambridge**

**Working Group Chair**



Science Advice for Policy by European Academies

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# Background

**Cancer is a leading cause of suffering and death across the European Union, with 2.7 million people diagnosed with cancer and 1.3 million people losing their lives to it every year. Not only does cancer carry great personal cost for individuals and their loved ones, but it also represents a significant financial and social burden on society.**

**The earlier cancer is diagnosed and treated, the greater the chances of survival. Early detection of cancer through population-based screening therefore offers a significant opportunity to save lives and reduce the personal and societal burden of the disease across the EU.**



# Methodology

**3 rapid reviews, one for each workshop conducted by methodology and subject experts at Cardiff University and University of Cambridge**

## **Workshop 1 (21st September)**

**Key Question: What is the scientific basis of extending screening programmes to other cancers, e.g., lung, prostate and gastric cancers, and ensuring their feasibility throughout the EU?**

## **Workshop 2 (19th October)**

**Key Question: How can cancer screening programmes targeting breast, cervical and colorectal cancers, be improved throughout the EU?**

## **Workshop 3 (8th November)**

**Key Question: Which are the main scientific elements to consider, and best practices to promote, for optimizing risk-based cancer screening and early diagnosis throughout the EU?**



**Key Question: What is the scientific basis of extending screening programmes to other cancers, e.g., lung, prostate and oesophago-gastric cancers, and ensuring their feasibility throughout the EU?**

**These cancers were selected based on disease burden measured by:**

- overall mortality**
- disability-adjusted life-years**
- screening test performance evaluated in large-scale trials.**

**Consideration of other cancer types where more targeted screening of high-risk individuals may be beneficial, such as liver or pancreatic cancer, is not considered here but general findings may be relevant.**

**These and less prevalent cancer types should be kept under consideration for the future.**



# Should we extend screening programmes?

## Lung cancer

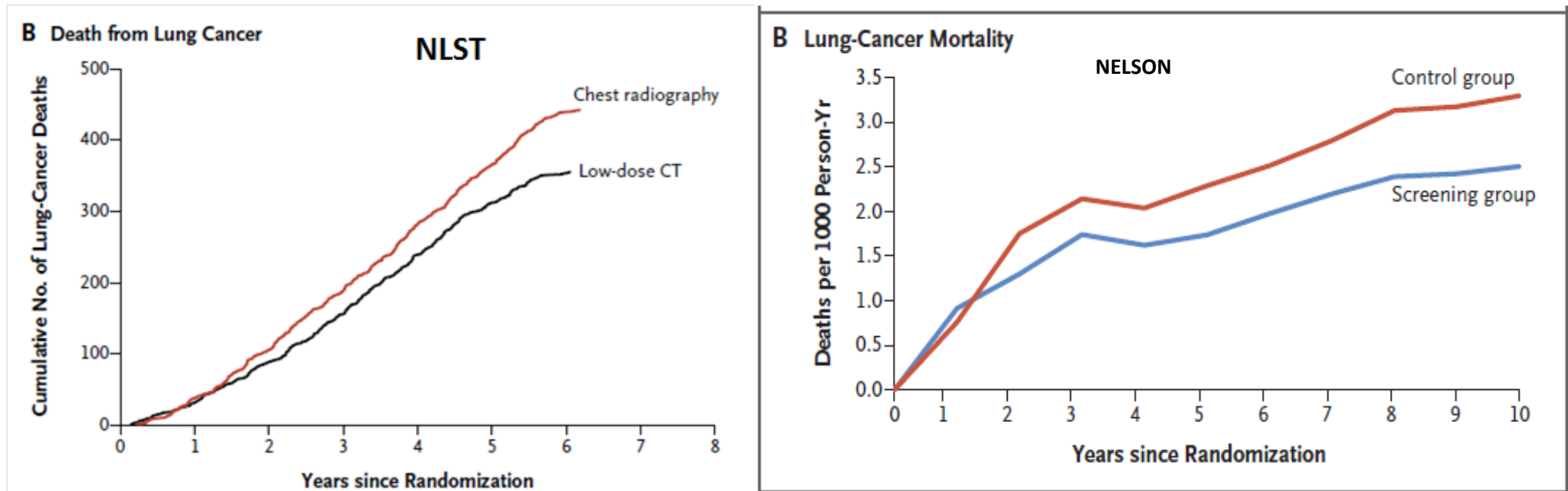
- **High disease burden accounting for 20% cancer deaths in EU**
- **Two large-scale RCTs show low dose CT scanning (LDCT) reduce cancer mortality for smokers and ex-smokers aged 50 to 80 years**
- **Burden and possible harms of low dose scanning are limited**
- **Two systematic reviews (12 studies) suggest cost-effective strategies**
- **US Preventative Service Task Force are recommending LDCT for >50 years at least 20 pack-years and ex-smokers <15 years**
- **Pilots in UK and some EU countries suggest broad acceptance and provide an opportunity for effective smoking cessation advice**



# Should we extend screening programmes?

## Lung cancer

- High disease burden accounting for 20% cancer deaths in EU
- Two large-scale RCTs show low dose CT scanning (LDCT) reduce cancer mortality for smokers and ex-smokers aged 50 to 80 years



*The experts therefore find a strong scientific basis for extending cancer screening programmes in EU to lung cancer screening based on effectiveness and burden*



# Should we extend screening programmes?

## Prostate cancer

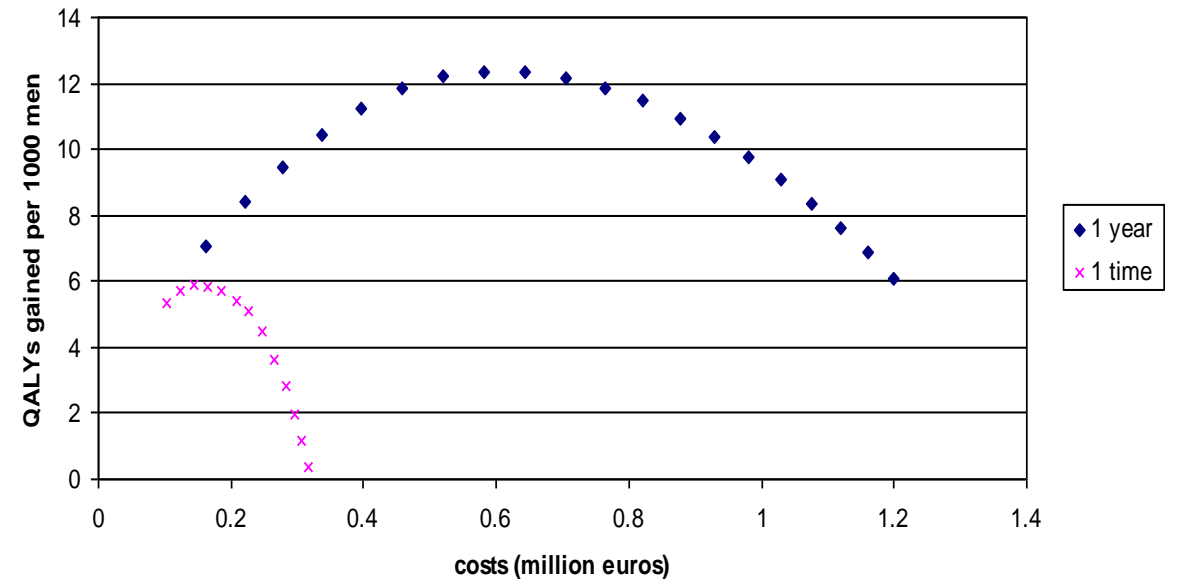
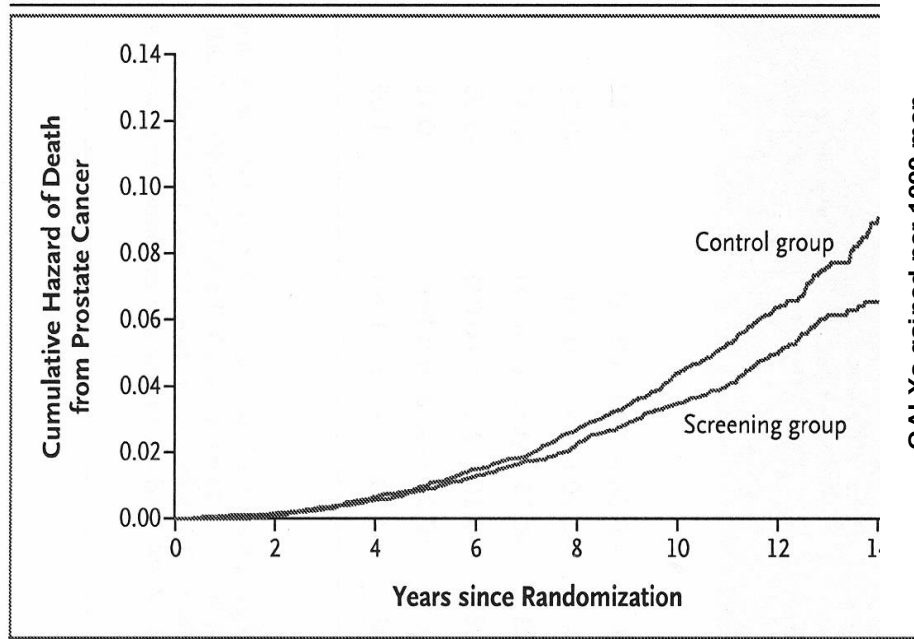
- **Prostate cancer is the most commonly diagnosed cancer and the leading cause of cancer death in non-smoking European men**
- **Large European powered RCT and meta-analysis shows screening via low threshold prostate specific antigen (PSA) reduces prostate cancer mortality in men aged 55-69**
- **Burden and possible harms of testing for individuals can be substantial, but additional tests such as MRI (reflex testing), and existing guidelines on Active Surveillance are likely to reduce harms or overdiagnosis**
- **Securing enough MRI scanning resource and quality may be challenging in some EU member states. Bi-parametric MRI maybe more feasible and cost-effective**
- **Opportunistic PSA testing outside of organized screening can lead to harms**



# Should we extend screening programmes?

## Prostate cancer

- Prostate cancer is the most commonly diagnosed cancer and the leading cause of cancer death in non-smoking European men



*The experts find the scientific basis for organised prostate cancer screening quite strong provided that the age criteria are appropriate. The high levels of opportunistic PSA testing at older ages can lead to overdiagnosis and harm. Likely that MRI (and active surveillance) will become part of prostate screening protocols to further improve net-benefit for individuals.*





# Should we extend screening programmes?

## Ovarian cancer

- **Large RCT and 1 systematic review on screening for ovarian cancer using serial CA125 with transvaginal ultrasound or ultrasound alone did not find a beneficial effect**
- **Neither the experts nor the literature found scientific grounds to recommend ovarian cancer screening for EU Member States at the current time**

*Further research is needed to identify improved technological approaches for this lethal cancer*



# Should we extend screening programmes?

## **Gastric cancer**

- **Gastric cancer rates are falling with improvements in living conditions and reduction in H. pylori infection rates**
- **Insufficient evidence to recommend endoscopic screening of the gastric mucosa across all EU member states**
- **The screen and treat strategy for reducing H. pylori infection provides good opportunity to prevent gastric cancer in EU member countries with intermediate to high gastric cancer incidence**

## **Oesophageal cancer**

- **Poor outcome cancer with variable prevalence of two main subtypes across EU Member states**
- **Insufficient scientific grounds to recommend population-wide endoscopic oesophageal cancer screening currently**
- **More could be done to ensure endoscopy referrals for high-risk groups**
- **New non-endoscopic technologies are emerging with encouraging evidence from RCT in UK**



# Experts from workshop 1 (21<sup>st</sup> September)



**Prof David Baldwin**  
Consultant Respiratory Physician and Honorary Professor of Medicine, Respiratory Medicine Unit, Nottingham University Hospitals and University of Nottingham (United Kingdom)



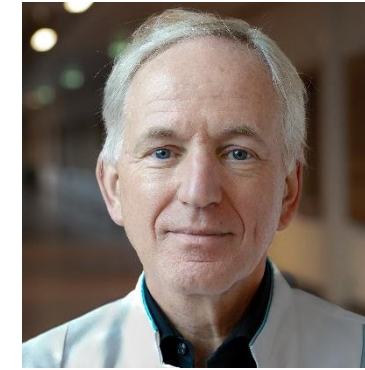
**Dr Iris Lansdorp-Vogelaar**  
Associate Professor-Department of Public Health, Erasmus MC University Medical Center, Rotterdam (Netherlands)



**Prof Rudolf Kaaks** Division of Cancer Epidemiology, German Cancer Research Centre, Heidelberg (Germany)



**Prof Linda Rabeneck**  
Vice President, Prevention and Cancer Control, Ontario Health and Professor of Medicine, University of Toronto (Canada)



**Prof Jelle Barentsz**  
Professor of Radiology and Chair of the Prostate MR Expert Centre, Radboudumc (Netherlands)



**Prof Matthew Callister**  
Consultant Respiratory Physician, Leeds Teaching Hospitals NHS Trust (United Kingdom)



**André Deschamps** Chairman, EUROPA UOMO-The Voice of Men with Prostate Cancer in Europe, Antwerp (Belgium)



**Prof Usha Menon**  
Professor of Gynaecological Cancer, MRC Clinical Trials Unit, Institute of Clinical Trials and Methodology, University College London (United Kingdom)



**Prof Michal Kaminski**  
Head of Department of Cancer Prevention and Head of Endoscopy Unit, Department of Gastroenterological Oncology at the Maria-Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Warsaw (Poland)



**Dr Urska Ivanus**  
Assistant Professor, Head of Screening Department, Institute of Oncology Ljubljana and Head on National Cancer Screening Committee (Slovenia)



**Prof Martin Tammemagi**  
Senior Scientist- Prevention and Cancer Control, Faculty of Health Sciences, Brock University (Canada)



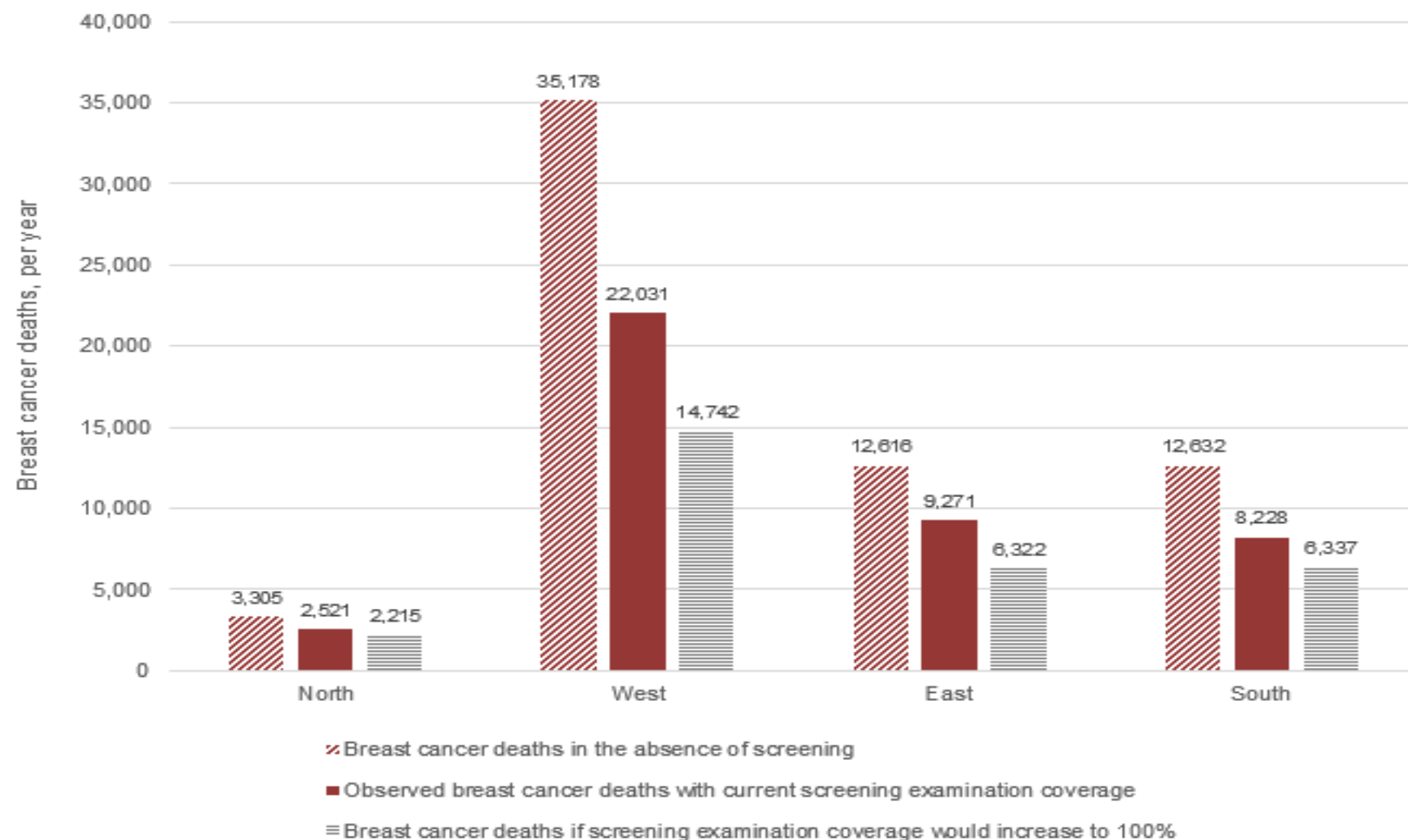
## Workshop 2

**Key Question: How can cancer screening programmes targeting breast, cervical and colorectal cancers, be improved throughout the EU?**

**Despite the EU-wide commitment to cancer screening, significant inequalities in access to the current types of screening still exist between individual member states, as well unequal coverage within countries.**



**Figure 2:** Annual number of observed and preventable breast cancer deaths, ages 50-74, per European region



**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



# Can we improve existing screening programmes?

## Breast cancer screening

- 25 out of 28 member states have some kind of population-based breast screening programme; 95% eligible EU women aged 50-69 have access
- Evidence suggests risk for aggressive breast cancer increasing in younger women and effectiveness in women screened from age 45 years
- Trial evidence supports supplemental regimens for women to include MRI for women with dense breasts (DENSE trial)
- Modelling suggests more risk adapted screening could improve outcomes (high and low risk) and be cost-effective. Randomised trials are underway to test this.

***The experts therefore find a strong scientific basis for extending breast cancer screening programmes to initiate screening around age 45.***

***MRI is effective in earlier detection and less interval cancer rates in women with dense breasts***

***Adaptations of programmes to risk levels subgroups (“risk stratified screening”) would seem a logic next implementation step.***



# Can we improve existing screening programmes?

## **Colorectal cancer screening**

- **23 out of 28 member states have some kind of population-based breast screening programme. Full roll-out in 11 states**
- **72% eligible EU residents aged 50-69 have access**
- **FIT testing is optimal triage test for colonoscopy based on accuracy and public preferences**
- **Uptake and compliance needs to be improved**
- **More research to determine optimal FIT thresholds based on age, sex, time since previous test**
- **Research could be conducted in parallel to implementation programmes**

***FIT testing is the preferred stool test***



# Can we improve existing screening programmes?

## **Cervical cancer screening and HPV eradication**

- Although very long established only 22 out of 28 member states have population-based screening programme, full roll-out in 12 with substantial variability across EU; 72% eligible EU residents aged 30-59 have access

***We have an unprecedented opportunity to eliminate cervical cancer***

- A meta-analysis suggests better protection from HPV screening v. conventional cytology testing. This is cost-effective
- HPV vaccination and testing should be rolled out to replace/complement cytology testing
- For under-screened women self-sampling for HPV may increase uptake
- Research should elucidate the social and cultural determinants affecting HPV vaccination uptake, including religious beliefs and vaccine hesitancy and develop strategies to address them.

***HPV vaccination coupled with HPV screening is more effective than conventional cytology testing alone***





# Experts from Workshop 2 (19<sup>th</sup> October)



**Prof Marc Arbyn**  
Coordinator of the Unit of Cancer  
Epidemiology, Belgian Cancer Centre  
(Belgium)



**Dr Iris Lansdorp-Vogelaar** Associate  
Professor-Department of Public Health,  
Erasmus MC  
University Medical Center, Rotterdam  
(Netherlands)



**Prof Zoltán Voko**  
Director and Professor of Epidemiology at  
Centre for Health Technology Assessment,  
Semmelweis University, Budapest and  
Medical Director at Syreon Research  
Institute (Hungary)



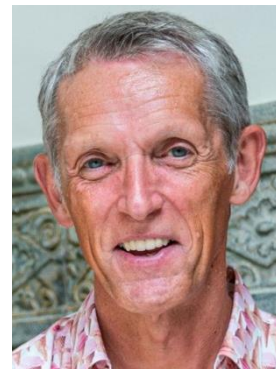
**Dr Partha Basu**  
Deputy Head of Early Detection,  
Prevention and Infection Branch,  
International Agency for Research on  
Cancer, World Health Organisation  
(France)



**Dr Sirpa Heinävaara**  
Senior Researcher at Finnish Cancer  
Registry (Finland)



**Dr Mirza Balaj**  
(CHAIN Research Coordinator,  
Norwegian University of Science and  
Technology, Trondheim (Norway))



**Prof Patrick M Bossuyt** (Professor of  
Clinical Epidemiology, University of  
Amsterdam (Netherlands))



**Zbrana Maravic**  
(CEO at Europe, Brussels (Belgium))



**Prof Joakim Dillner**  
Professor in infectious disease  
epidemiology at Karolinska Institutet  
(Sweden)



## Workshop 3

**Key Question: Which are the main scientific elements to consider, and best practices to promote, for optimizing risk-based cancer screening and early diagnosis throughout the EU?**



*Figure taken from Pashayan et al., 2020*



## **Workshop 3: Is there new technology to enhance future screening programmes?**

- **Lots of exciting developments including in:**
  - **ctDNA and other liquid biopsy technology to detect multiple cancer types**
  - **Molecular technologies applied to proximal tissue sampling e.g. oesophagus, nasopharynx, biomarker additions to FIT for stool**
  - **Artificial intelligence can augment radiology and pathology to reduce bottlenecks and harmonise quality control standards**
- **These new tests are not yet ready for prime time**
- **Further research is recommended and EU should be at forefront of this**



# Experts from Workshop 3 (8<sup>th</sup> November)



**Dr Liesbeth Lenaerts**  
Research Expert, Cancer in Pregnancy group,  
Department of Oncology,  
KU Leuven, Leuven,  
Belgium



**Prof Mozziyar Etemadi**  
Medical Director,  
Advanced Technologies,  
Northwestern  
Medicine, Chicago, (USA)



**Prof Nickolas Papadopoulos**  
Professor of Oncology and  
Pathology and Director of  
Translational Genetics at Ludwig  
Center for Cancer Genetics and  
Therapeutics, Sidney Kimmel  
Comprehensive Cancer Center,  
(USA)



**Dr Nitzan Rosenfeld**  
Group leader at the Cancer  
Research UK Cambridge  
Institute, University  
of Cambridge (United Kingdom)



**Prof Nadir Arber**  
Director, Integrated Cancer  
Prevention Centre, Tel Aviv  
(Israel)



**Prof Linda Rabeneck**  
Vice President,  
Prevention and Cancer  
Control, Ontario Health  
and Professor of  
Medicine, University of  
Toronto (Canada)



**Prof Nora Pashayan**  
Professor of Applied Cancer  
Research and Hon Consultant of  
Public Health Medicine at  
University College London  
(United Kingdom)



**Prof Klaus Pantel**  
Chairman of Institute of Tumour  
Biology at the University Medical  
Centre, Hamburg, Eppendorf,  
(Germany)



**Dr Suzette Delaloge**  
Medical Oncologist and Director  
of Interception Programme at  
Department of Cancer Medicine,  
Institut Gustave Roussy, (France)



**Dr Nicolas Wentzensen**  
Head of Clinical Epidemiology Unit,  
Deputy Chief, Clinical Genetics  
Branch, Division of Cancer  
Epidemiology and Genetics at  
National Cancer Institute, Bethesda,  
(USA)



**Prof Attila Lorincz**  
Emeritus Professor of  
Molecular Epidemiology,  
Queen Mary University of  
London, (United Kingdom)





## Additional expert speakers

- **Professor Mark Dobrow** (Associate Professor, Institute of Health Policy, Management and Evaluation, University of Toronto, Canada)
- **Professor Ruth Etzioni** (Public Health Sciences Division-Fred Hutchinson Cancer Research Centre, Seattle, USA)
- **Professor/Chief Physician Jonas Hugosson** (Department of Urology, University of Gothenburg, Sweden)
- **Professor Marcis Leja** (Professor, Faculty of Medicine, University of Latvia, Latvia)
- **Dr Carmen Ungurean** (Cancer screening coordinator, National Institute of Public Health, Romania)
- **Professor Arnaud Villers** (Urologist, Department of Urology, Centre Hospitalier Universitaire of Lille, Lille University, France)
- **Professor Solveig Hofvind** (Cancer Registry of Norway and Department of Health and Care Sciences, Faculty of Health Sciences, The Arctic University of Norway, Tromsø, Norway)
- **Professor Anne Mackie** (Director of Screening at Public Health England, United Kingdom)
- **Professor Peter Sasieni** (Academic Director of King's Clinical Trials Unit and Professor of Cancer Prevention, King's College London, United Kingdom)
- **Professor Robert Smith** (Cancer Epidemiologist and Senior Director, Cancer Control at the National Office of the American Cancer Society in Atlanta, Georgia, USA)
- **Professor Carla H. van Gils** (Professor of Clinical Epidemiology of Cancer, UMC Utrecht, Netherlands)
- **Professor Gareth Evans** (Professor in Medical Genetics and Cancer Epidemiology at University of Manchester, United Kingdom)



# General learnings from all workshops

- **Much can be done to harmonise screening guidelines and implementation across the EU to ensure access, equity, quality control and uniformity.**
- **Continuous evaluation are needed to e.g., assist EU states lagging behind and learn from best practices.**
- **Local and regional build-ups of new programs could be encouraged, followed by scaling up**
- ***Ad hoc* offers of screening tests outside of organised programmes should be discouraged**
- **EU should be primed to do implementation research**
- **Living guidelines approach is recommended to facilitate changes rapidly**



**The expert group finds that an upper age limit on cancer screening at population level can address the issue that the number of cancers that will be found with no or marginal net-benefit for the individual will increase with age.**

**Further research is needed to determine the age at which cancer screening should stop, and whether this should be the same for all individuals and cancer types.**

**Research is also needed to determine whether there is a minimum level of individual risk for a given type of cancer that is required to take part in a screening programme in the first place, and how this should be measured and implemented in practice.**

**This expert evidence review shows there are a small number of crucial opportunities available to the EU Commission and member states to optimise existing breast, cervical and colorectal cancer screening programmes, along with a sound scientific basis for introducing lung and prostate cancer screening programmes.**

**Promising emerging tests and novel multi-cancer screening technologies are not yet ready for primetime, but research is moving fast.**

**Adding all this together has the potential to make a real impact in ensuring uniformity, quality and equity in cancer screening across the EU, minimising harms and maximising the health benefits for all.**