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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**

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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.

Member Societies

European Association of Urology
EANM
ECL Association of European Cancer Leagues
EASL The Home of Hepatology
European Hereditary Tumour Group
European Oncology Nursing Society
ERS European Respiratory Society
ESHI MT
EUSOMA
EUSOBI
European Society of Pathology
ESSRF
EUROSKIN
esso The European Society of Surgical Oncology
ipvs International Papillomavirus Society
IPOS International Psycho-Oncology Society
UNITED EUROPEAN GASTROENTEROLOGY ueg

Patient Organisations

Childhood Cancer International EUROPE
DIGESTIVE CANCERS EUROPE
EUROPA DONNA The European Breast Cancer Coalition
EUROPA UOMO
Lung Cancer Europe
European Cancer Patient Coalition
LYMPHOMA COALITION EUROPE
MPNE
MPe Myeloma Patients Europe

Invited Stakeholders

Cardio Oncology
International Agency for Research on Cancer (IARC)
Wonca
ESC European Society of Cardiology
Wonca Vasco da Gama Movement
EGPRN
EQuiP
EHNS European Head & Neck Society

Community 365 INITIATIVE OF THE EUROPEAN CANCER ORGANISATION

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

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Early Detection for All Cancers

Matti Aapro

President
European Cancer Organisation

Cindy Perettie

Head of Roche Molecular Lab

Early Detection and the Power of Molecular Therapies

Early Detection

Targeted Treatment Earlier

Post Treatment Monitoring

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Multi-cancer early detection: rationale and application

Paul Limburg, MD

Chief Medical Officer, Screening
Exact Sciences

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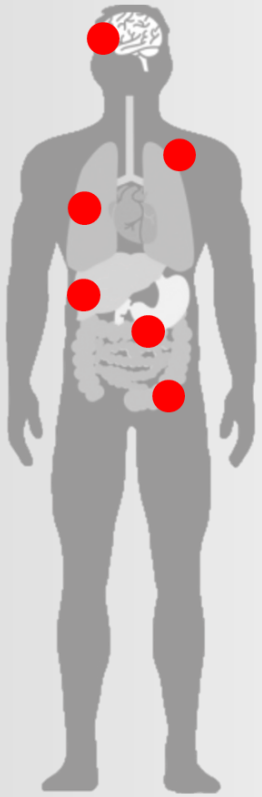
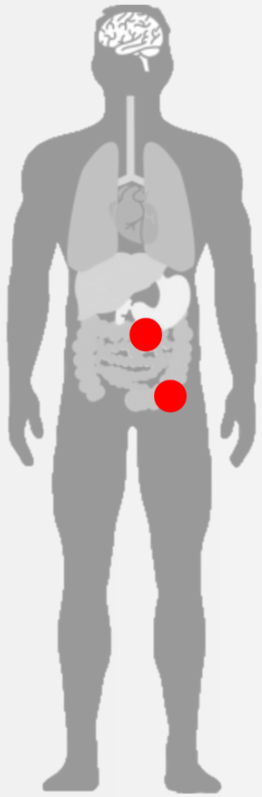
Earlier cancer detection saves lives



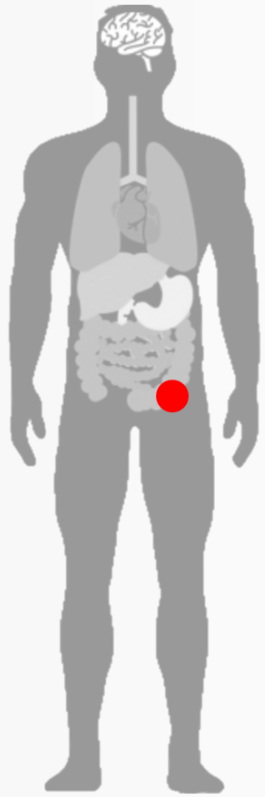
DISTANT
METASTASIS
STAGE IV

14%
5-Year Survival
POST-DIAGNOSIS



REGIONAL
STAGE III

71%
5-Year Survival
POST-DIAGNOSIS

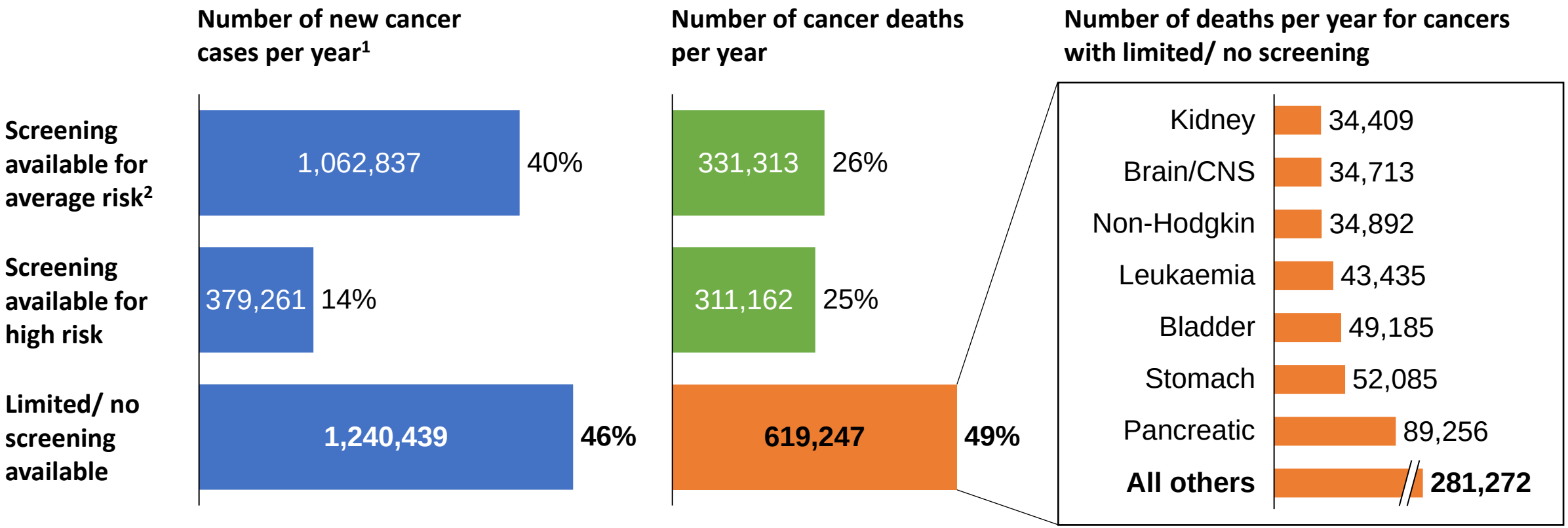


LOCAL
STAGE I & II

90%
5-Year Survival
POST-DIAGNOSIS

Sources: https://www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/cancer-facts-figures-2020.html; https://seer.cancer.gov/; https://www.cancer.net/;

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



1 EU-27 2020 numbers 2 Calculated using US screening standards: Average risk screening for CRC, breast, cervical, prostate; High risk for lung, liver; Limited/no screening available for all others. Source: ECIS - European Cancer Information System from https://ecis.jrc.ec.europa.eu, accessed on 11/06/2021; © European Union, 2021

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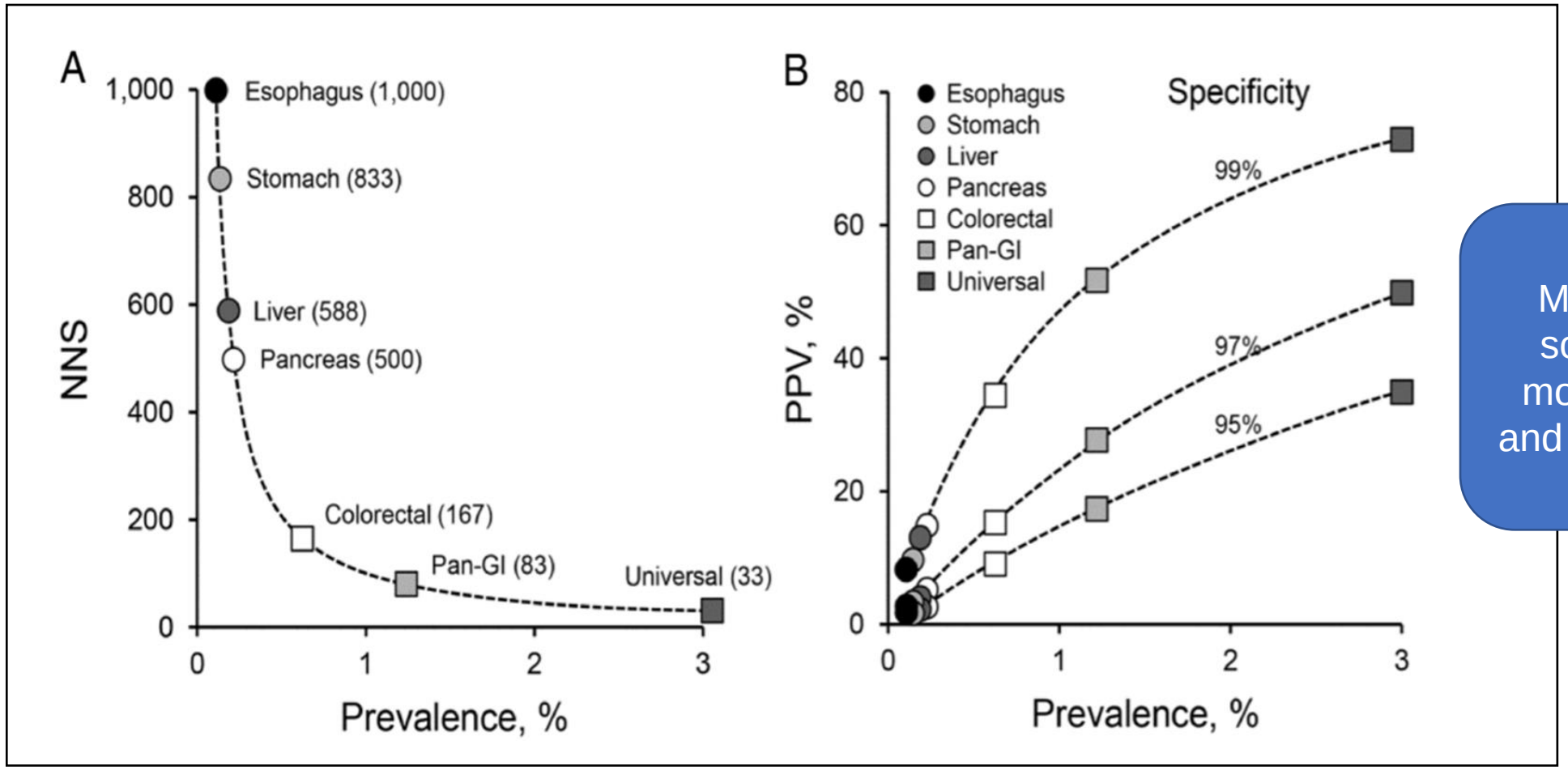
The power of aggregate prevalence



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)

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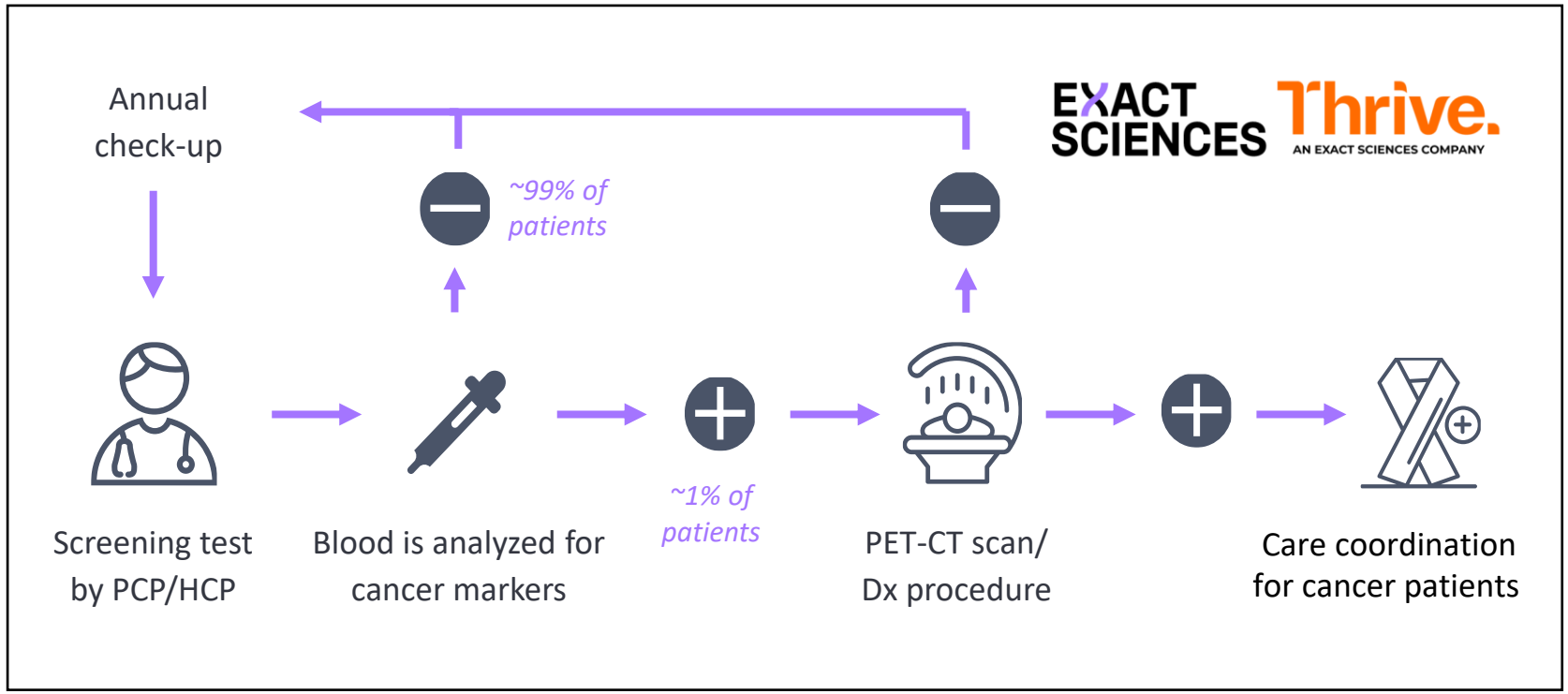
CancerSEEK is our approach to multi-cancer early detection

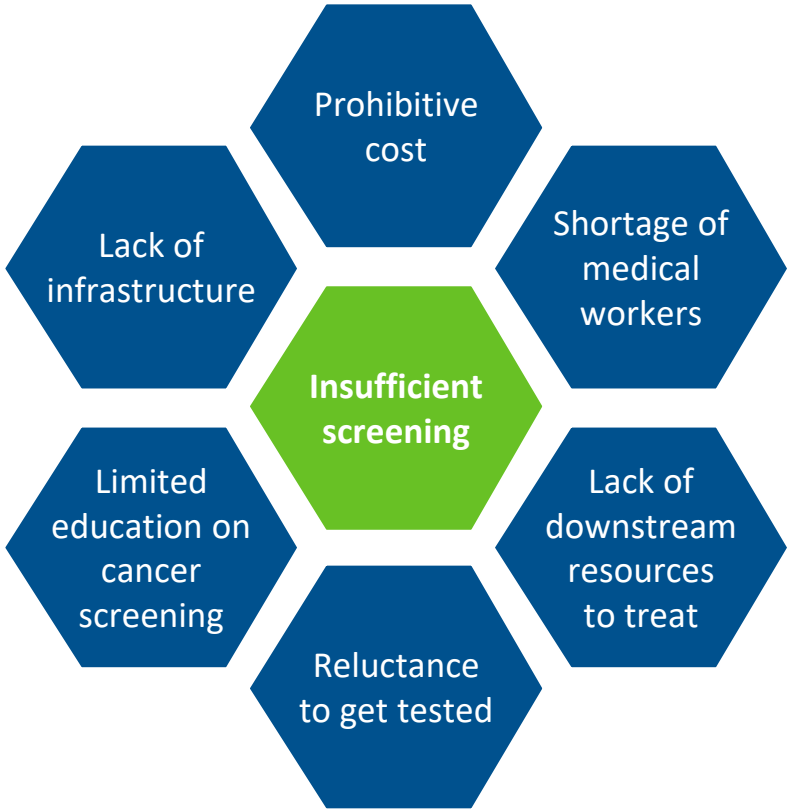
Our Proprietary Integrated Service Model

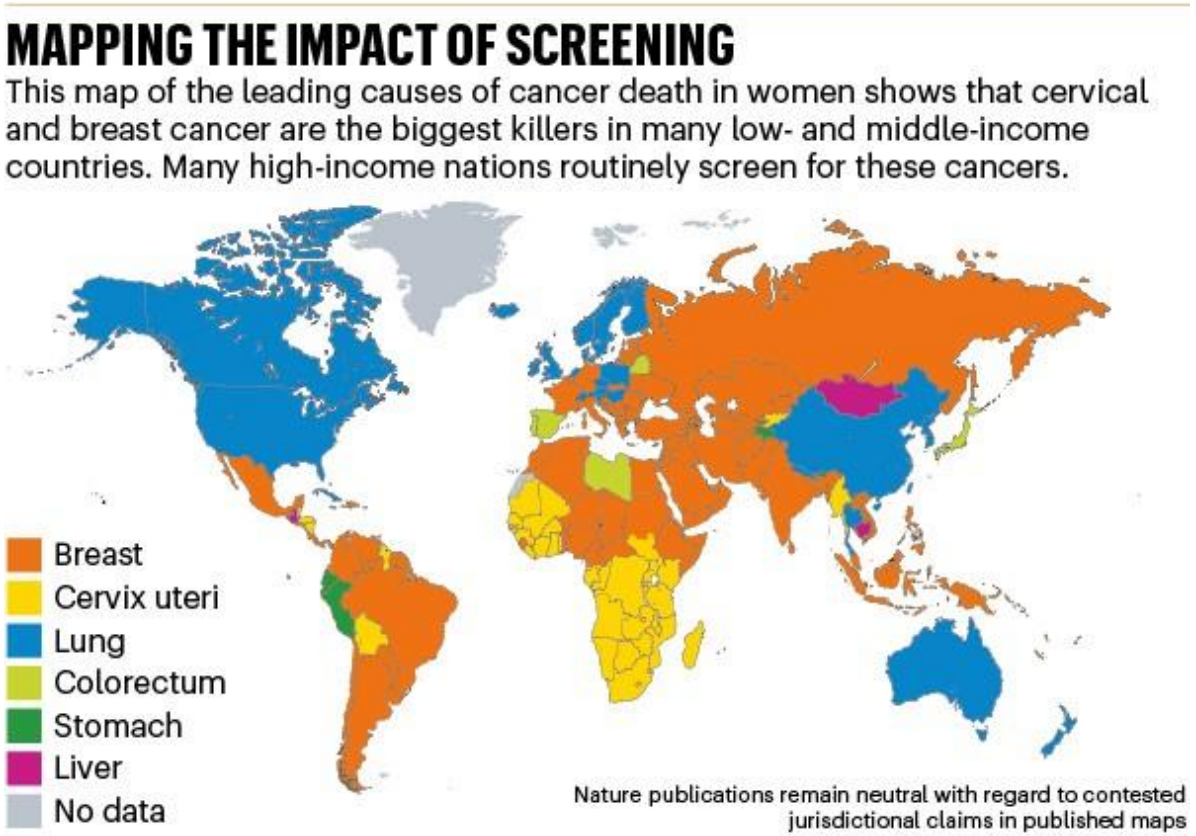


- **Multiple unscreened cancers:** In an interventional study of 10,006 women, CancerSEEK identified 26 cancers: 23 of which wouldn't have been screened for[1]
- **Reflex testing:** A "rule-in" approach that pairs high specificity testing with confirmatory PET-CT
- **Focused on the patient:** Participants were counselled about test implications and educated on their need to continue SOC cancer protection

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





Source: E. Sohn. Nature 579, S17-S19 (2020) doi: https://doi.org/10.1038/d41586-020-00848-1; F. Bray et al. Ca. Cancer J. Clin. 68, 394–424 (2018);

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

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USZ Universitäts Spital Zürich

Universität Zürich[UZH]

Early detection for all cancers: The early detection of treatment intervention targets in all cancers from the pathologist's perspective

Holger Moch

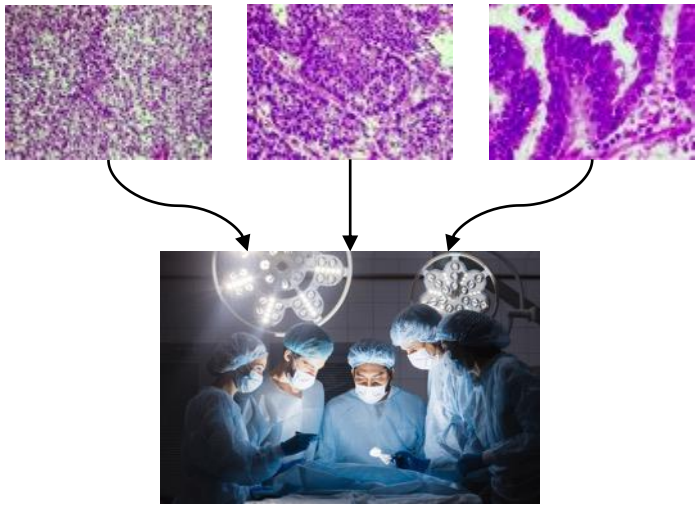
President
European Society of Pathology

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



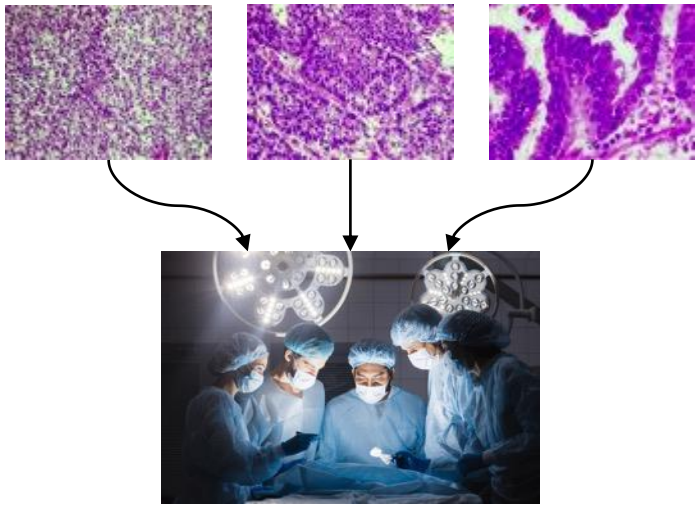
Standard therapy

Helpful for 1 of 3 patients

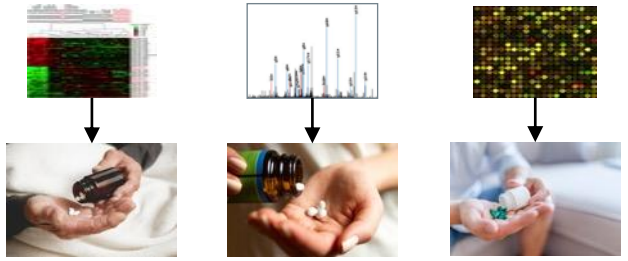
More effective
Less toxic
Less costly

Personalised

Tumour 1 Tumour 2 Tumour 3



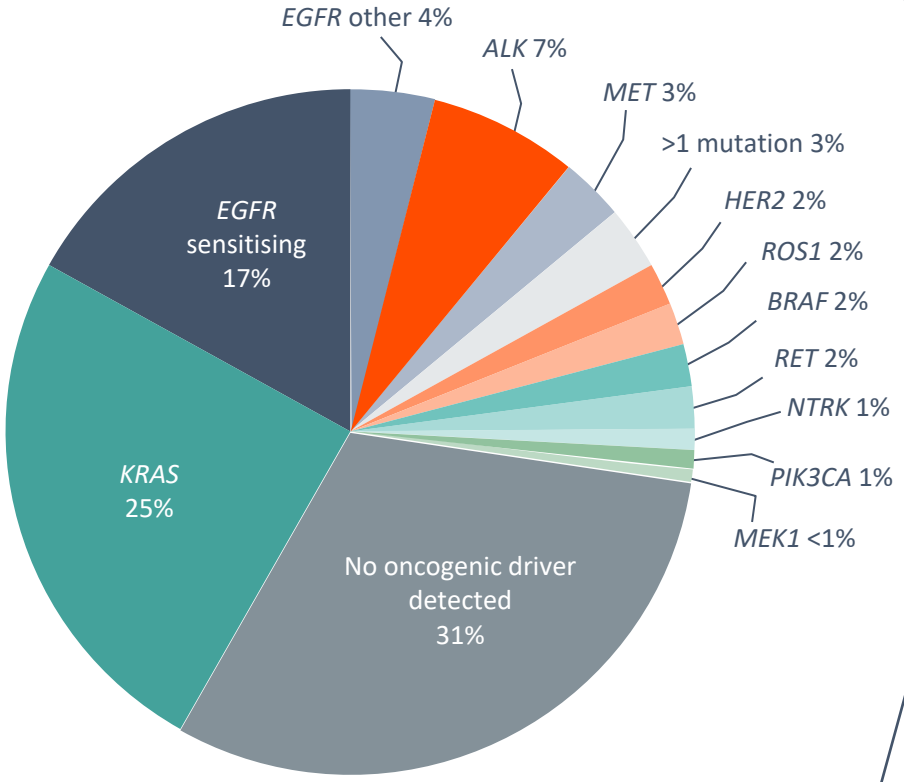
Molecular pathology



Therapy 1 Therapy 2 Therapy 3

Advanced diagnostics inform therapy selection in lung cancer

Targetable mutations in lung cancer[1]



Identifying actionable mutations with broad genomic profiling[2]

Approved drugs*

Investigational drugs†

EGFR

- Afatinib
- Dacomitinib ▼
- Erlotinib (± anti-VEGF / VEGFR)
- Gefitinib
- Necitumumab ▼[1]
- Osimertinib ▼
- Amivantamab[2]
- Avitinib[3]
- Cabozantinib ▼[4]
- CK-101[5]
- Icotinib[6]
- JNJ-372[7]
- Lazertinib[8]
- Mobocertinib[9]
- Nazartinib[10]
- Neratinib ▼[11]
- Olaparib + Durvalumab ▼[12]
- Olmutinib[13]
- Pirotinib[14]
- Poziotinib[15]
- Tarloxotinib[16]
- U3-1402[17]
- Zorifertinib[18]

PIK3CA

- Alpelisib ▼[19]
- Copanlisib[20]
- Ipatasertib[21]
- MK-2206[22]

ALK

- Alectinib ▼
- Brigatinib ▼
- Ceritinib ▼
- Crizotinib
- Lorlatinib ▼
- Cobimetinib + Alectinib ▼[23]
- Ensartinib[24]
- Repotrectinib[25]
- TQ-B3139[26]

KRAS

- Adagrasib[27]
- Binimetinib ▼[19]
- Binimetinib ▼ + Palbociclib ▼[28]
- Erlotinib + Tivantinib[29]
- JDQ443 (+ TNO155)[30]
- Selumetinib[22]
- Sotorasib[31]
- Trametinib[32]
- VS-6766 (+ Defactinib)[33]

MEK1

- Cobimetinib[1]
- Trametinib[1]
- Selumetinib[1]

BRAF

- Binimetinib ▼[34]
- Cobimetinib[21]
- Encorafenib ▼[34]
- Dabrafenib (+ trametinib)
- Vemurafenib
- Selumetinib[22]

HER2

- Dacomitinib ▼[1]
- Neratinib ▼[35]
- Pertuzumab + trastuzumab ▼[36]
- Trastuzumab emtansine[1] / deruxtecan[37]
- Afatinib[1]
- Lapatinib[22]
- Mobocertinib[9]
- Poziotinib[15]
- Pyrotinib Maleate[14]
- Tarloxotinib[16]
- TAS0728[38]

NTRK

- Entrectinib ▼
- Larotrectinib ▼
- Cabozantinib ▼[1]
- Ensartinib[14]
- Repotrectinib[25]
- Selitrectinib[39]

RET

- Pralsetinib
- Selpercatinib
- Alectinib ▼[40]
- Apatinib[1]
- Cabozantinib ▼
- Lenvatinib ▼[1]
- Ponatinib ▼[1]
- TPX-0046[41]
- Vandetanib ▼

MET

- Capmatinib[42]
- Tepotinib[43]
- Bozitinib[44]
- Cabozantinib ▼[1,45]
- Crizotinib
- Ensartinib[14]
- Glesatinib[46]
- Glumetinib[47]
- Merestinib[48]
- Savolitinib + Osimertinib[49]
- Sym015[50]

ROS1

- Crizotinib
- Entrectinib ▼
- Ceritinib ▼
- Ensartinib[14]
- Lorlatinib ▼
- Repotrectinib[25]
- Taletrectinib[51]

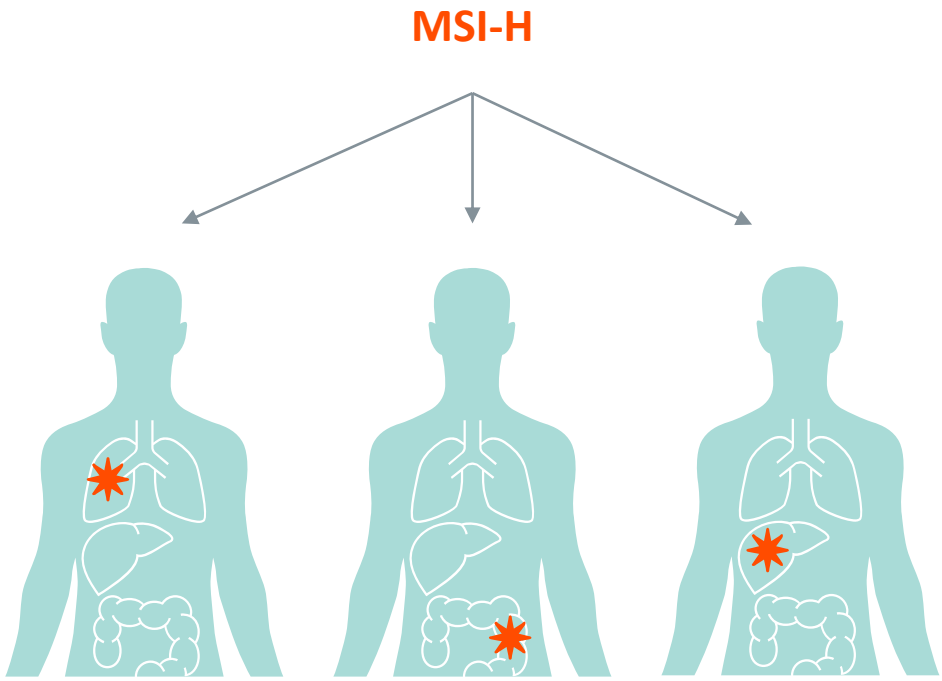
All drugs listed are included in NSCLC NCCN Guidelines unless otherwise indicated. Some therapies listed target specific variants of the indicated gene.

*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.

†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 suspe product is important. Adverse events should be reported to your respective local office [see slide notes for full listing]. 1. Adapted from Tsao, A.S., et al. (2016) J Thorac Oncol 11:613-38; 2. NCT04599712; 3. NCT03300115; 4. NCT01708954; 5. NCT02926768; 6. NCT03595644; 7. NCT02609776; 8. NCT04248829; 9. NCT02716116; 10. NCT03292133; 11. NCT00266877; 12. NCT04538378; 13. NCT02485652; 14. NCT03574402; 15. NCT03318939; 16. NCT03805841; 17. NCT03260491; 18. NCT03653546; 19. NCT02276027; 20. NCTC NCT03202940; 24. NCT02767804; 25. NCT03093116; 26. NCT04009317;
27. NCT04685135; 28. NCT03170206; 29. NCT01395758; 30. NCT04699188; 31. NCT04303780; 32. NCT01362296; 33. NCT04620330; 34. NCT04585815; 35. NCT01827267; 36. NCT03845270;
37. NCT03505710; 38. NCT03410927; 39. NCT03206931; 40. NCT03445000.; 41. NCT04161391; 42. NCT03693339; 43. NCT02864992; 44. NCT04258033; 45. NCT03911193; 46. NCT02544633;
47. NCT04270591; 48. NCT02920996; 49. NCT03778229; 50. NCT02648724; 51. NCT04395677.

Pembrolizumab is the first FDA approved cancer treatment based on a common biomarker

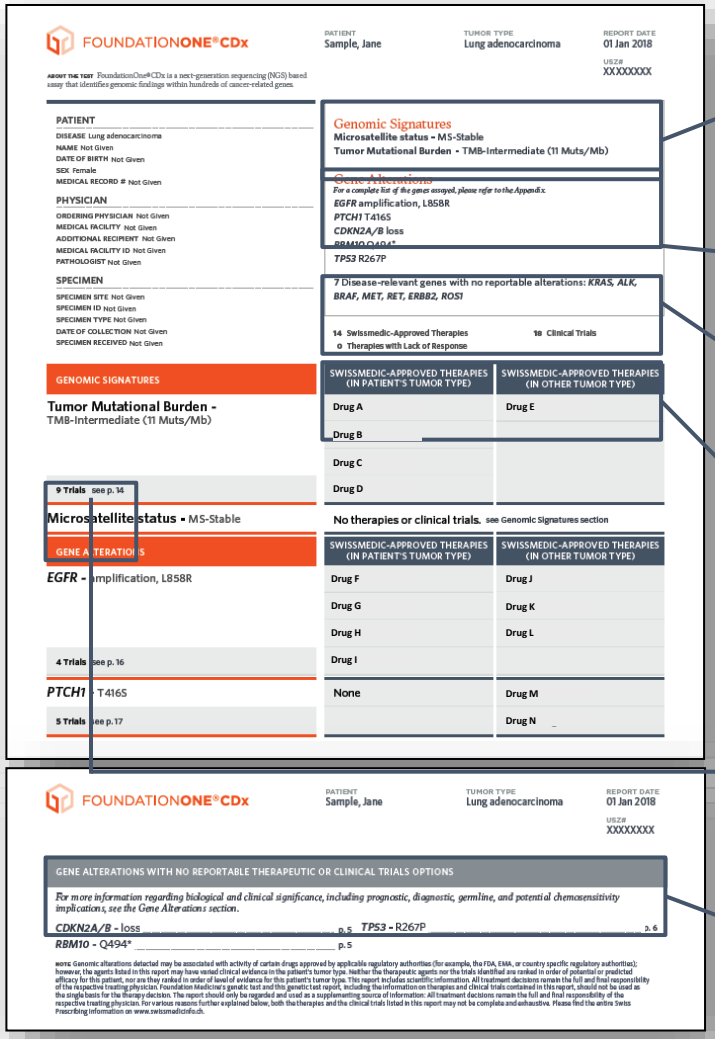
- Traditionally in oncology **approvals were based on a tumour type or a biomarker within a tumour type**
- For the first time, the FDA has **‘approved a drug based on a tumour's biomarker without regard to the tumour’s original location’**
- Pembrolizumab is indicated for the treatment of patients with 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 microsatellie instability status, which may predict response to immunotherapy[1–4]

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

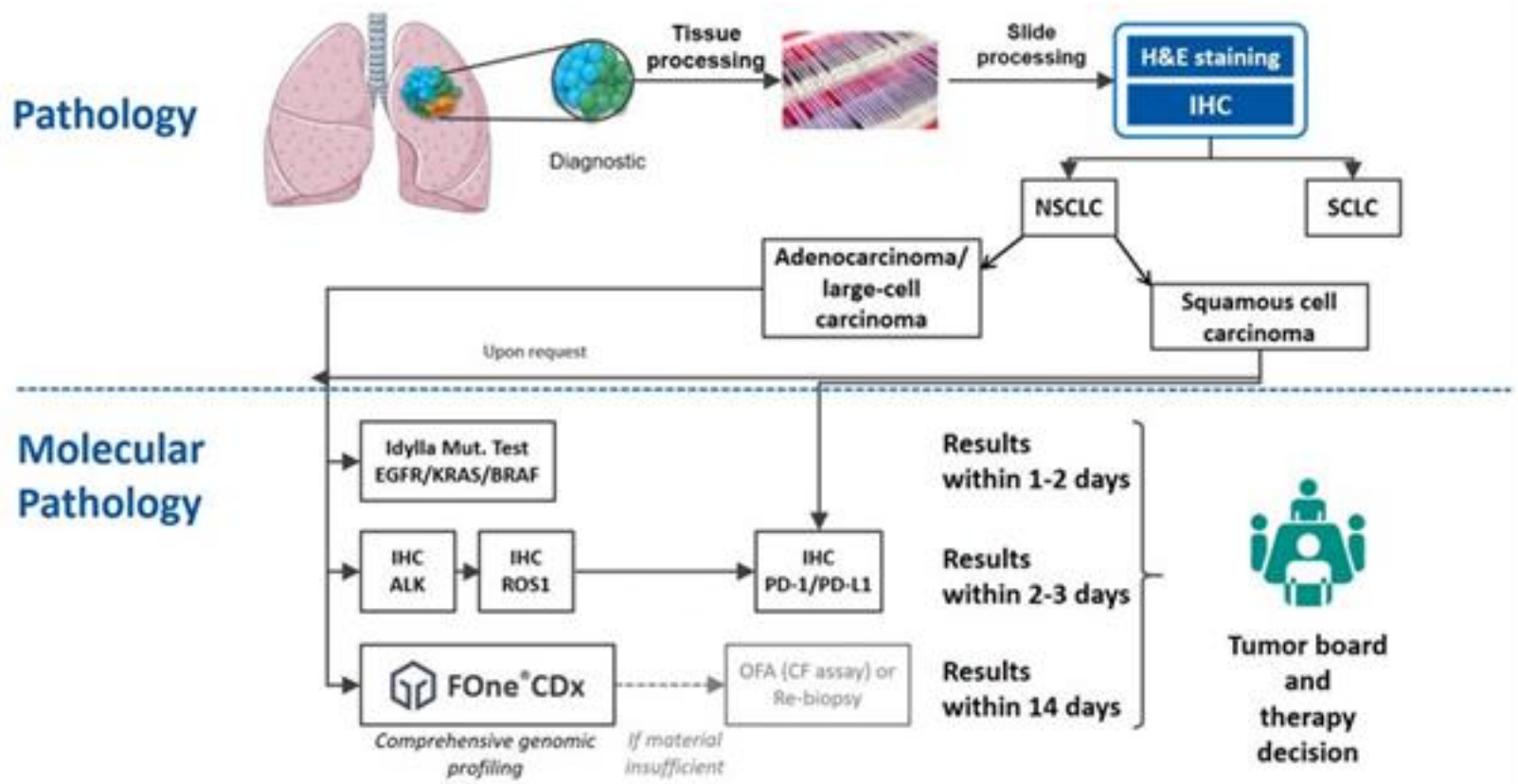
Genomic findings with no reportable options

To help you rule out uncertainty and determine the appropriate course of action

1. Chalmers ZR et al. Analysis of 100,000 humancancer genomes reveals the landscape of tumor mutational burden. Genome Med 2017;9(1):34. **2.** Johnson DB et al. Targeted next generation sequencing identifies markers of response to PD-1 blockade. Cancer Immunol Res 2016;4(11):959–967. **3.** Carbone DP et al. First-line nivolumab in stage IV or recurrent non-small-cell lung cancer. N Engl J Med 2017;376(25):2415–2426. **4.** Gatalica Z et al. High microsatellite instability (MSI-H) colorectal carcinoma: a brief review of predictive biomarkers in the era of personalized medicine. Fam Cancer 2016;15(3):405–412.

University Hospital Zurich Approach

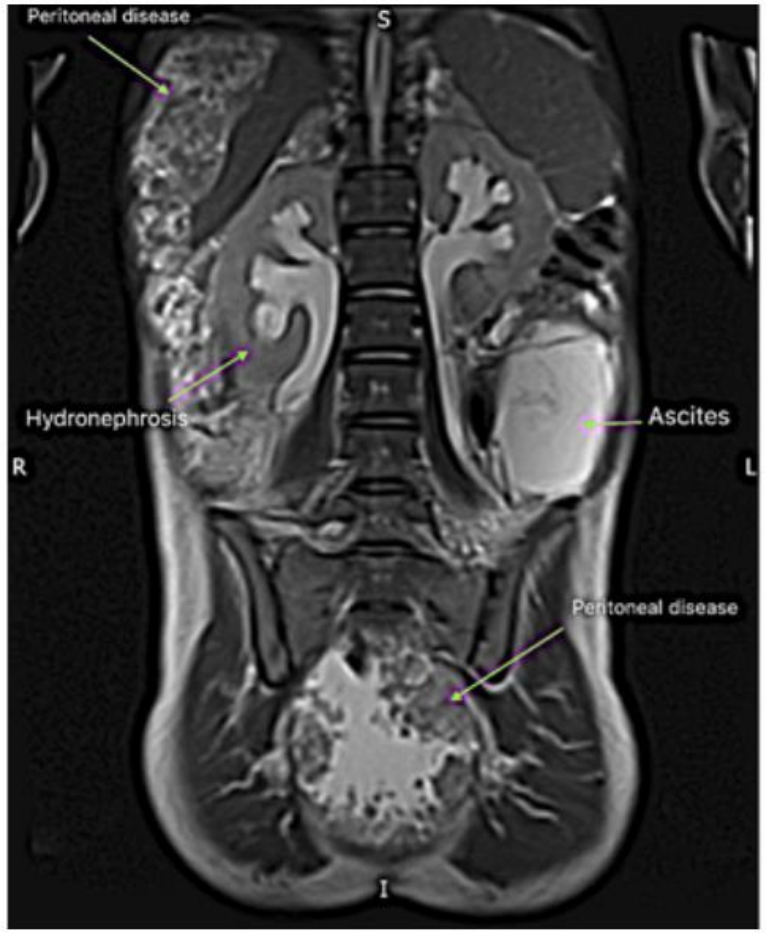
First Diagnosis



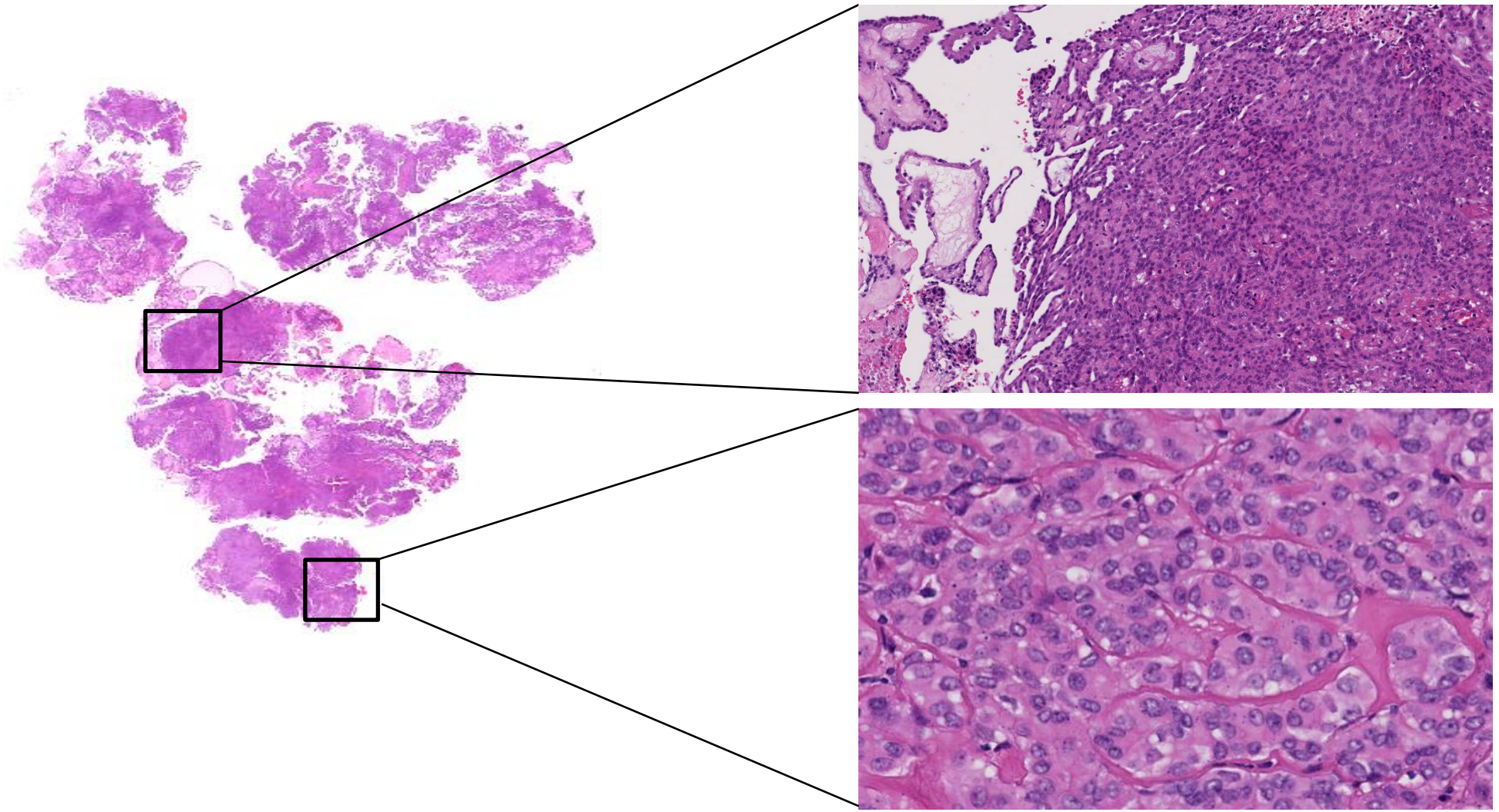
Patient 2: 13 yo female patient

Patient History:
- Abdominal girth for 4 months
- Slightly educed 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

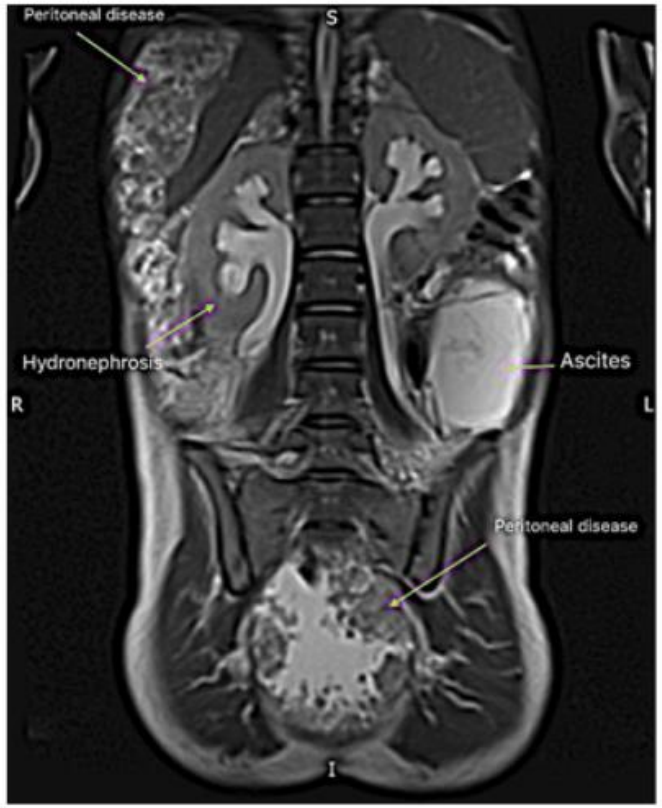
† For a complete list of the genes assayed and performance specifications, please refer to the Appendix

INFORMATION REGARDING PHARMACEUTICAL PRODUCTS AND CLINICAL TRIALS

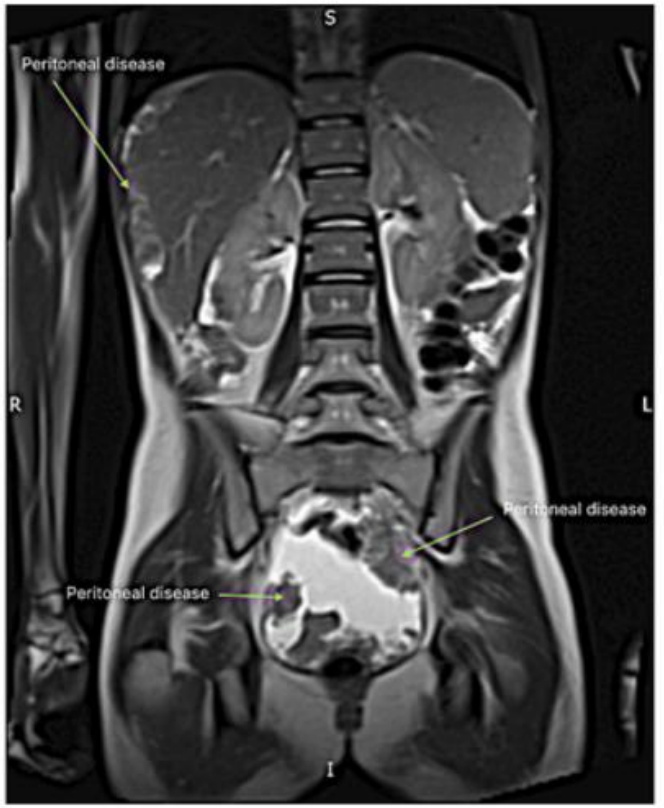
Genomic Findings Detected	Swissmedic-Approved Therapies (in patient's tumor type)	Swissmedic-Approved Therapies (in another tumor type)	Potential Clinical Trials
ALK STRN-ALK fusion	None	Alectinib Ceritinib Crizotinib	Yes, see clinical trials section
Microsatellite status MS-Stable	None	None	None
Tumor Mutational Burden TMB-Low; 3 Muts/Mb	None	None	None

Patient: Treatment and Follow-Up

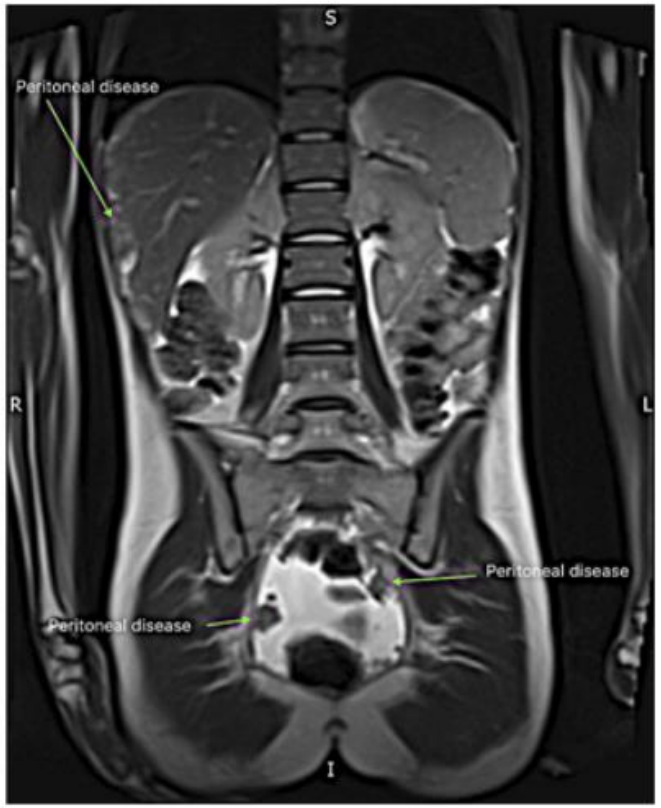
Before treatment



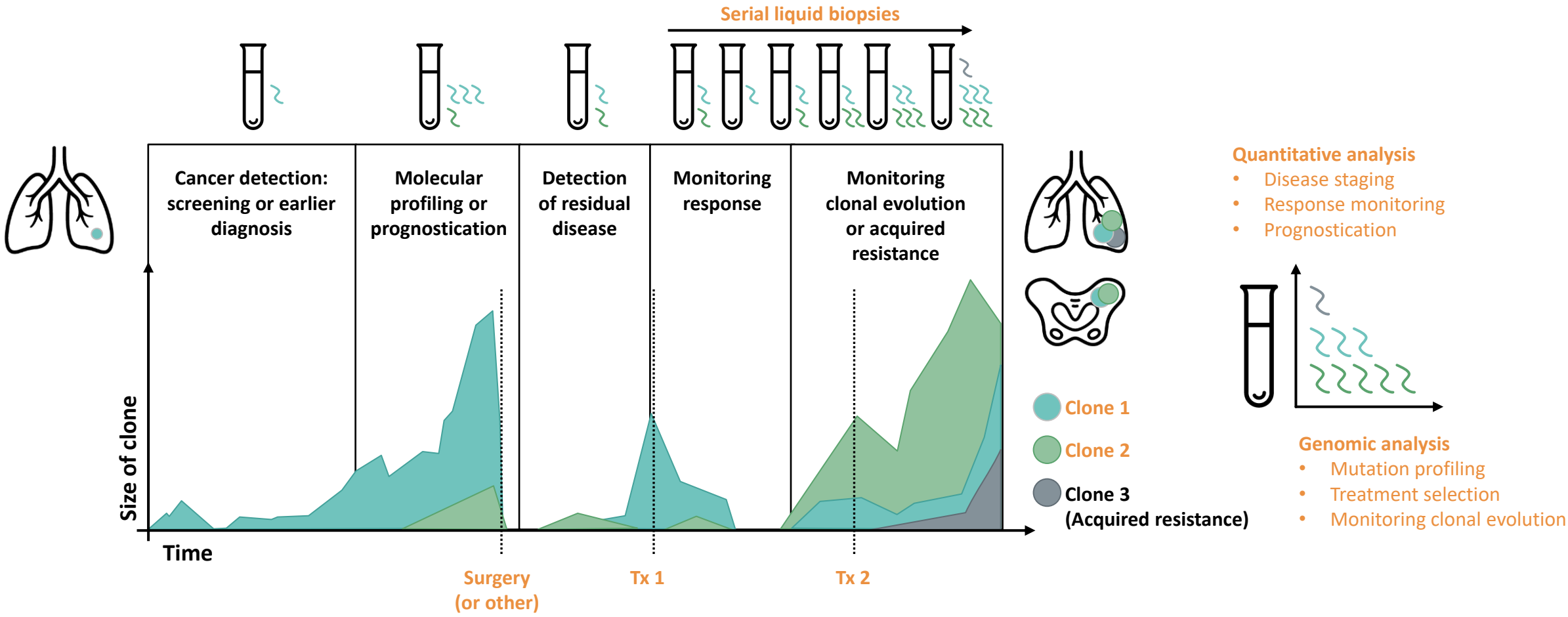
6 weeks of treatment



12 weeks of treatment



Potential applications of liquid biopsies throughout the disease journey



Tx: treatment. Adapted from Wan, J.C.M., et al. (2017) *Nat Rev Cancer* 17:223-38

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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

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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

Report of THE INDEPENDENT REVIEW OF

ADULT SCREENING PROGRAMMES in England, 2019

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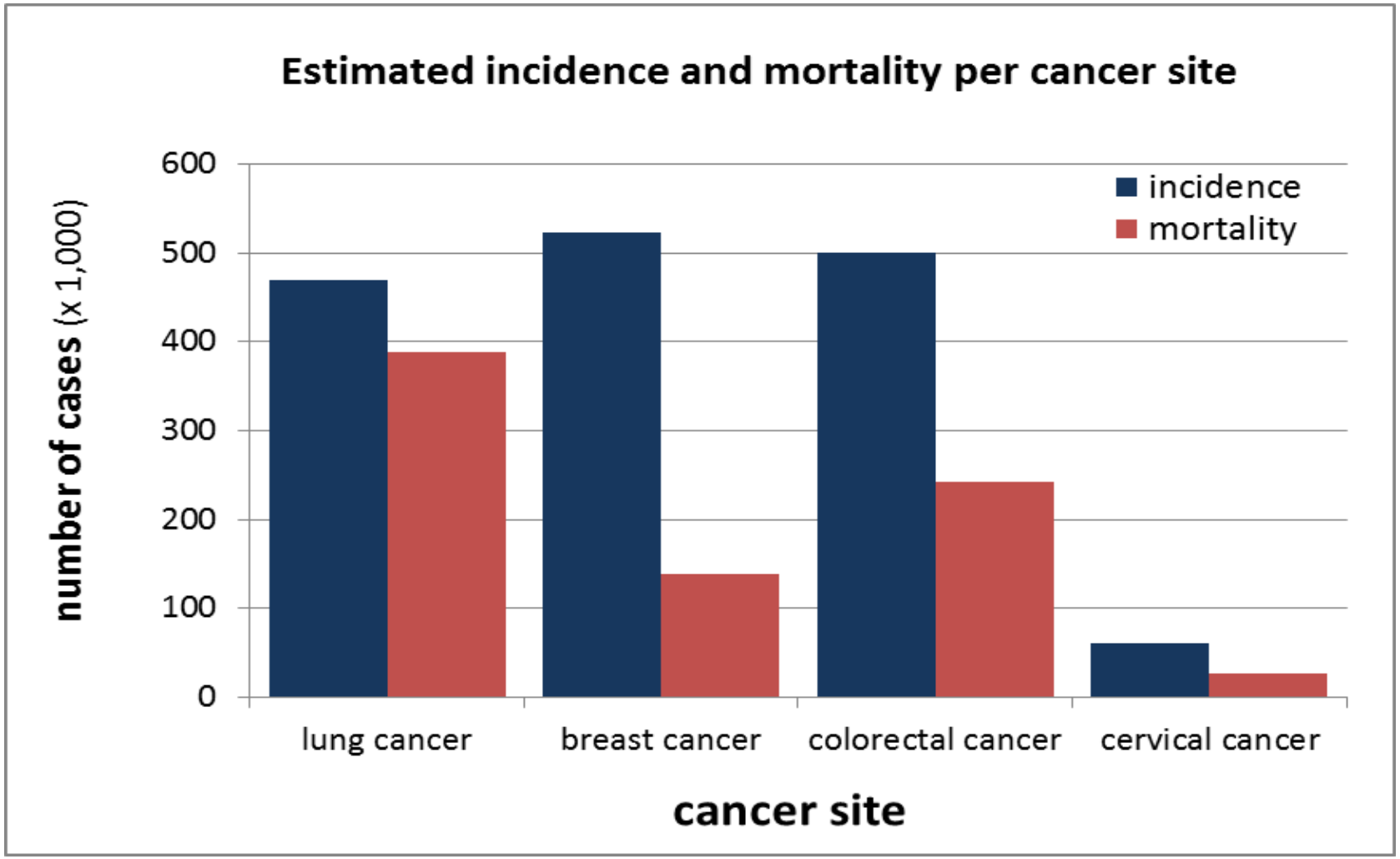
Cancer & cancer screening

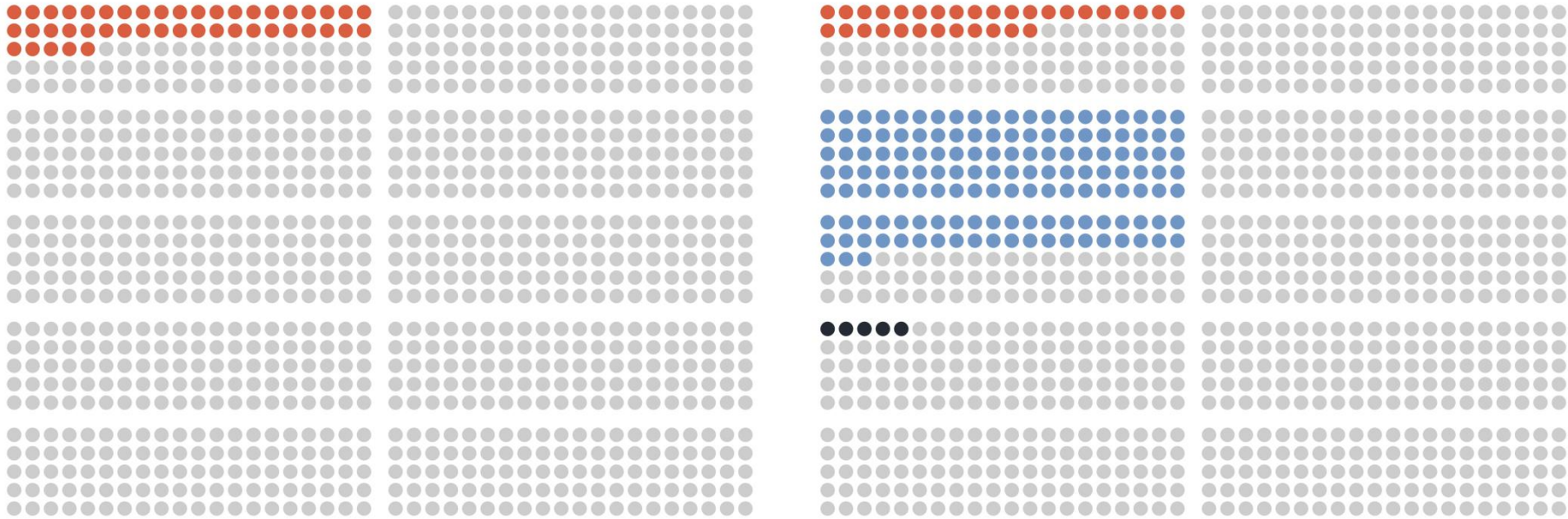


Mammography screening

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%).

1000 women without screening

1000 women with screening



	Without screening	With screening
Women who died from breast cancer	45	32
Women with a false-positive test result	-	143
Women who were unnecessarily diagnosed and treated	-	5
Remaining women	955	820

IJC

The potential of breast cancer screening in Europe

Nadine Zielonke[1] | Lindy M. Kregting[1] | Eveline A. M. Heijnsdijk[1] | Piret Veerus[2] | Sirpa Heinävaara[3] | Martin McKee[4] | Inge M. C. M. de Kok[1] | Harry J. de Koning[1] | Nicolien T. van Ravesteyn[1] | the EU-TOPIA collaborators[5]

[1]Department of Public Health, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands

[2]National Institute for Health Development, Tallinn, Estonia

[3]Finnish Cancer Registry, Helsinki, Finland

[4]London School of Hygiene and Tropical Medicine, London, UK

[5]The EU-TOPIA collaborators are listed in the Appendix

Correspondence
Nadine Zielonke, Department of Public Health, Erasmus MC, University Medical Center Rotterdam, Dr. Molewaterplein 40, Rotterdam 3015 GD, The Netherlands.
Email: n.zielonke@erasmusmc.nl

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Horizon 2020 Framework Programme, Grant/Award Number: 634753

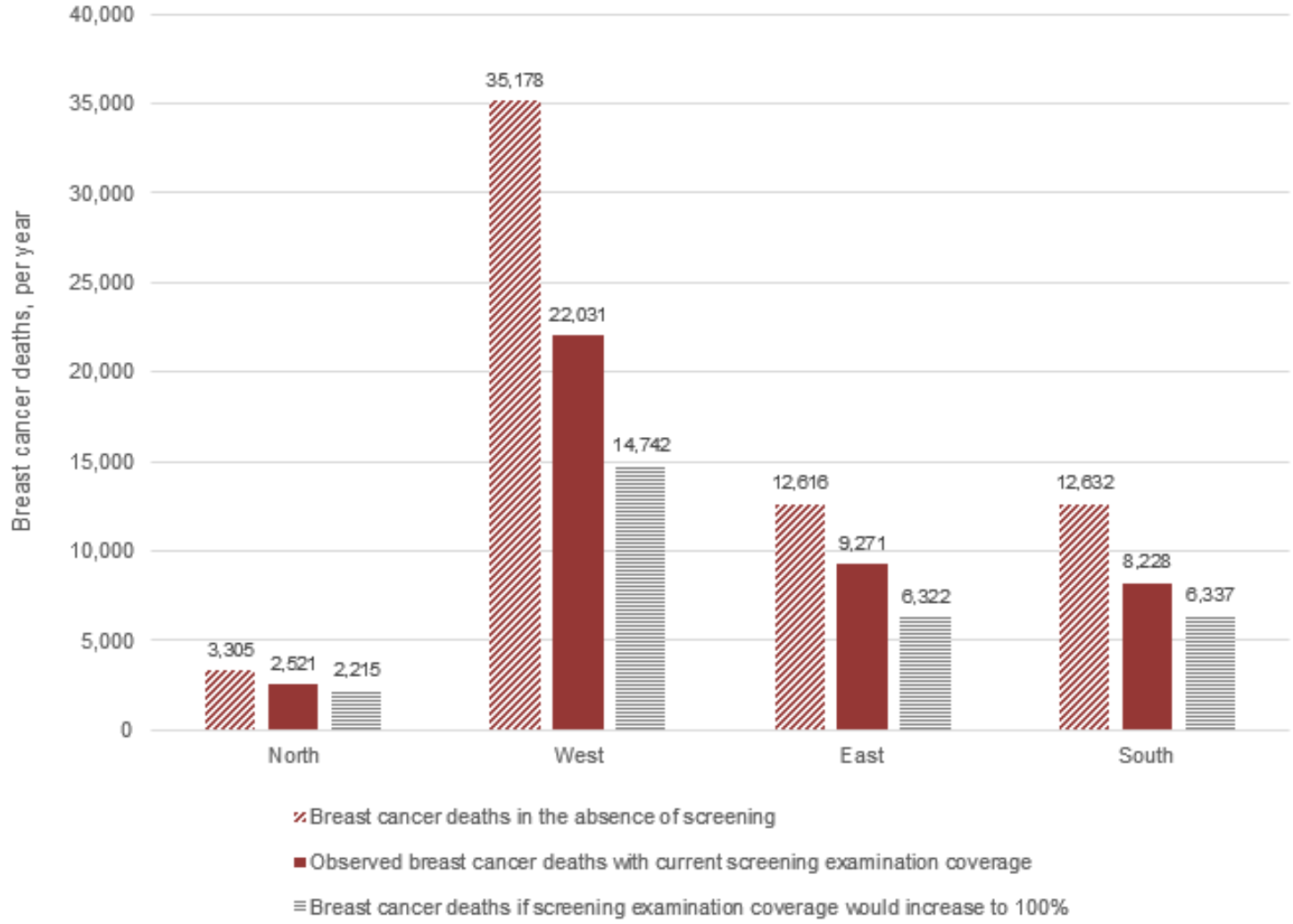
Abstract

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), 64% (North) to 69% (South). Yearly 21 680 breast cancer deaths have already been prevented due to mammography screening. If all countries would reach 100% examination coverage, 12 434 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 15% 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



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**

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DOI: 10.1002/ijc.33126

IJC International Journal of Cancer

CANCER EPIDEMIOLOGY

Risk stratification in breast cancer screening: Cost-effectiveness and harm-benefit ratios for low-risk and high-risk women

Valérie D. V. Sankatsing[1] | Nicolien T. van Ravesteyn[1] | Eveline A. M. Heijnsdijk[1] | Mireille J. M. Broeders[2,3] | Harry J. de Koning[1]

Optimal screening scenario and corresponding outcomes by risk group

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

*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)

Guideline*	Screening strategy	Number of screens	Life years gained	Breast cancer deaths averted	Over-diagnosis	False positives	LYG/ screen
United States Preventive Services Task Force	**Biennial 50-74**	11182	118	**6.7**	14.5	920	**0.0106**
Risk-based	**Family history**	11840	125	**6.9**	14.9	1000	**0.0105**
Risk-based	**Polygenic risk**	12990	141	**7.4**	16.0	1156	**0.0109**
Risk-based	**Family history & polygenic risk**	13089	154	**7.9**	16.6	1169	**0.0117**
Sensitivity analysis							
Risk-based (constrained) †	Polygenic risk	10856	135	**7.1**	14.0	946	**0.0124**

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

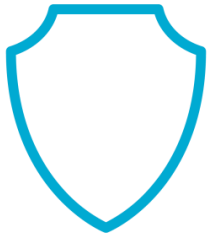
Age extensions to 44 / 74

Screening intervals and test modalities by risk

More equity by (less) diversity

european cancer ORGANISATION

EU Level Screening initiatives: Progress Made on Colorectal Cancer Screening Since 2003



Luigi Ricciardiello
Professor
Chair, Research Committee
United European Gastroenterology

ueg

Scientific umbrella organisation

Aiming to improve digestive health

Uniting 30,000 specialists from every field
In digestive health

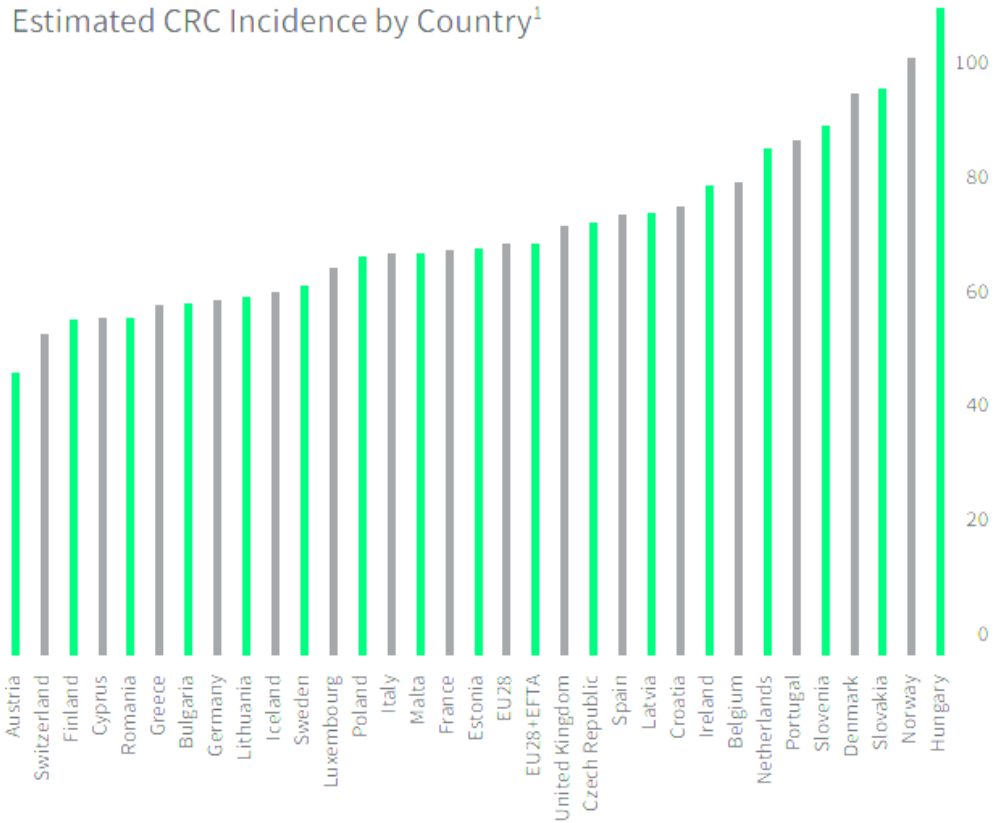
ueg.eu

european cancer ORGANISATION

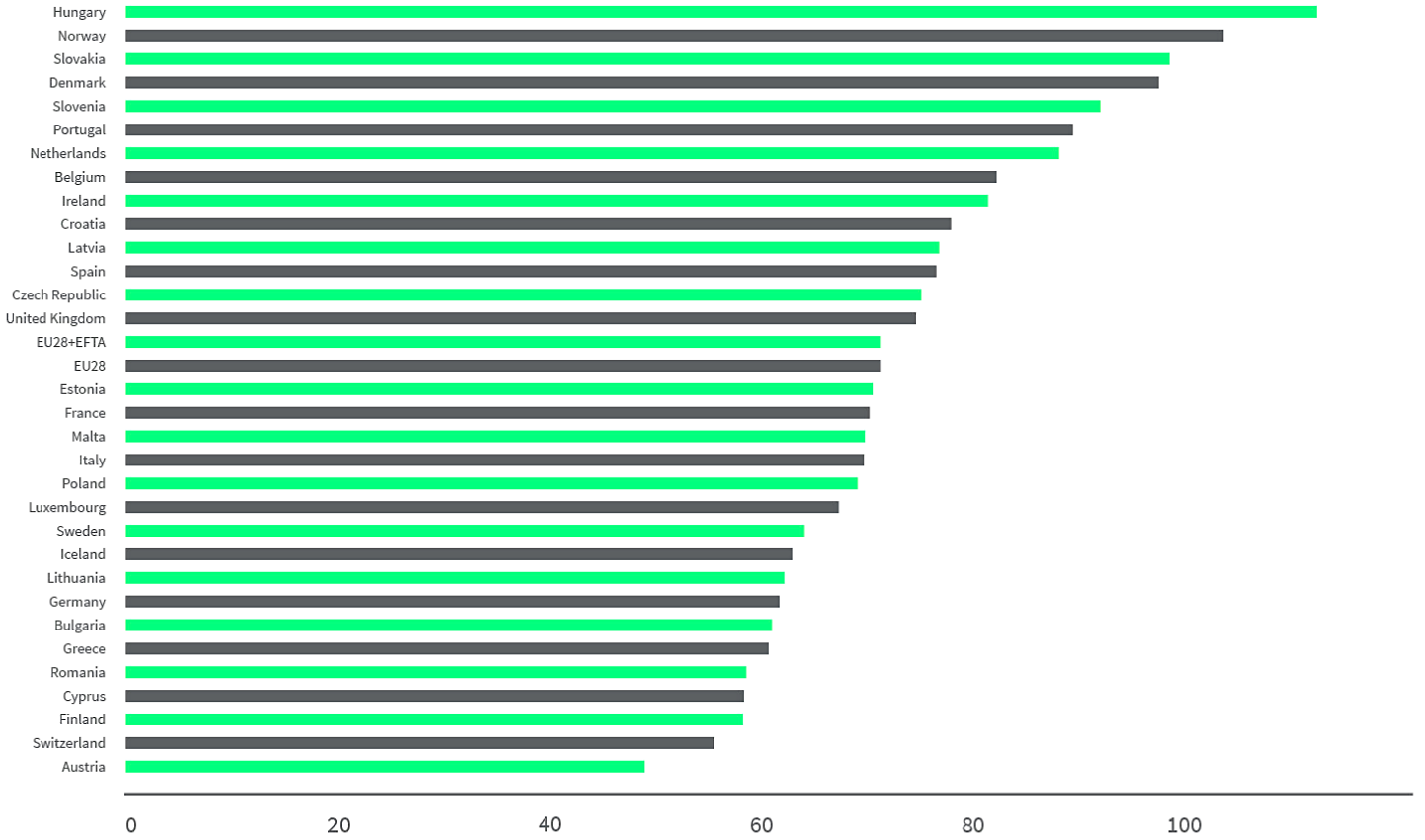
Coordinating European Action against Colorectal Cancer

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.

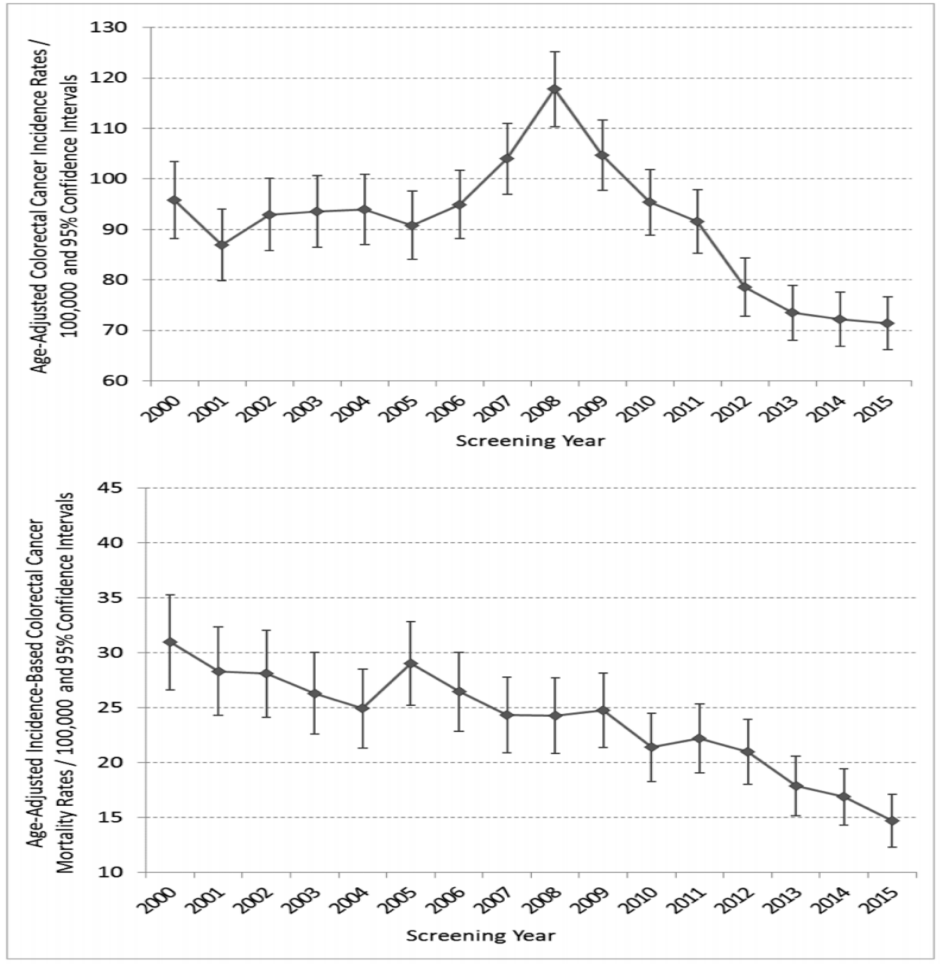


Estimated CRC Incidence by Country



European Parliament. (2010). Written declaration on fighting colorectal cancer in the European Union. Available at: http://www.europarl.europa.eu/sides/getDoc.do?pubRef=-//EP//NONSGML+WDECL+P7-DCL-2010-0068+0+DOC+PDF+V0//EN&language=EN

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

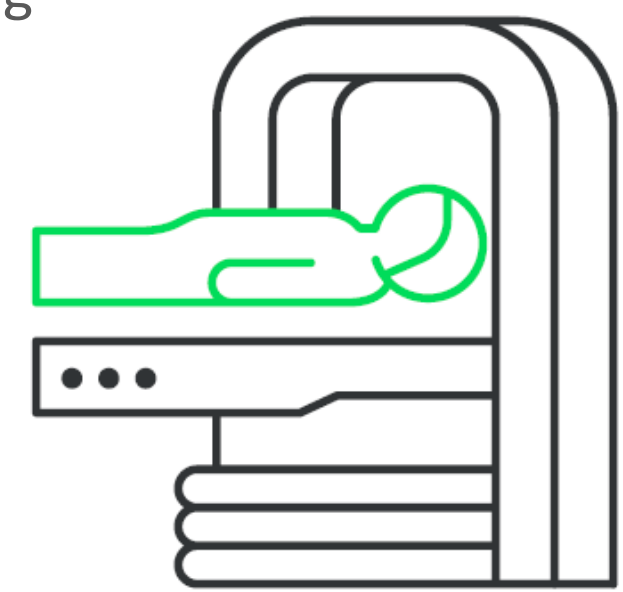
Bulgaria, Greece, Latvia, Romania and the Slovak Republic currently do not have population-based CRC screening programmes[3]

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



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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

european cancer ORGANISATION

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

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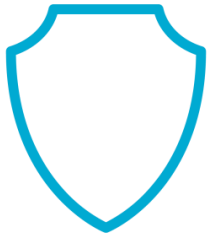
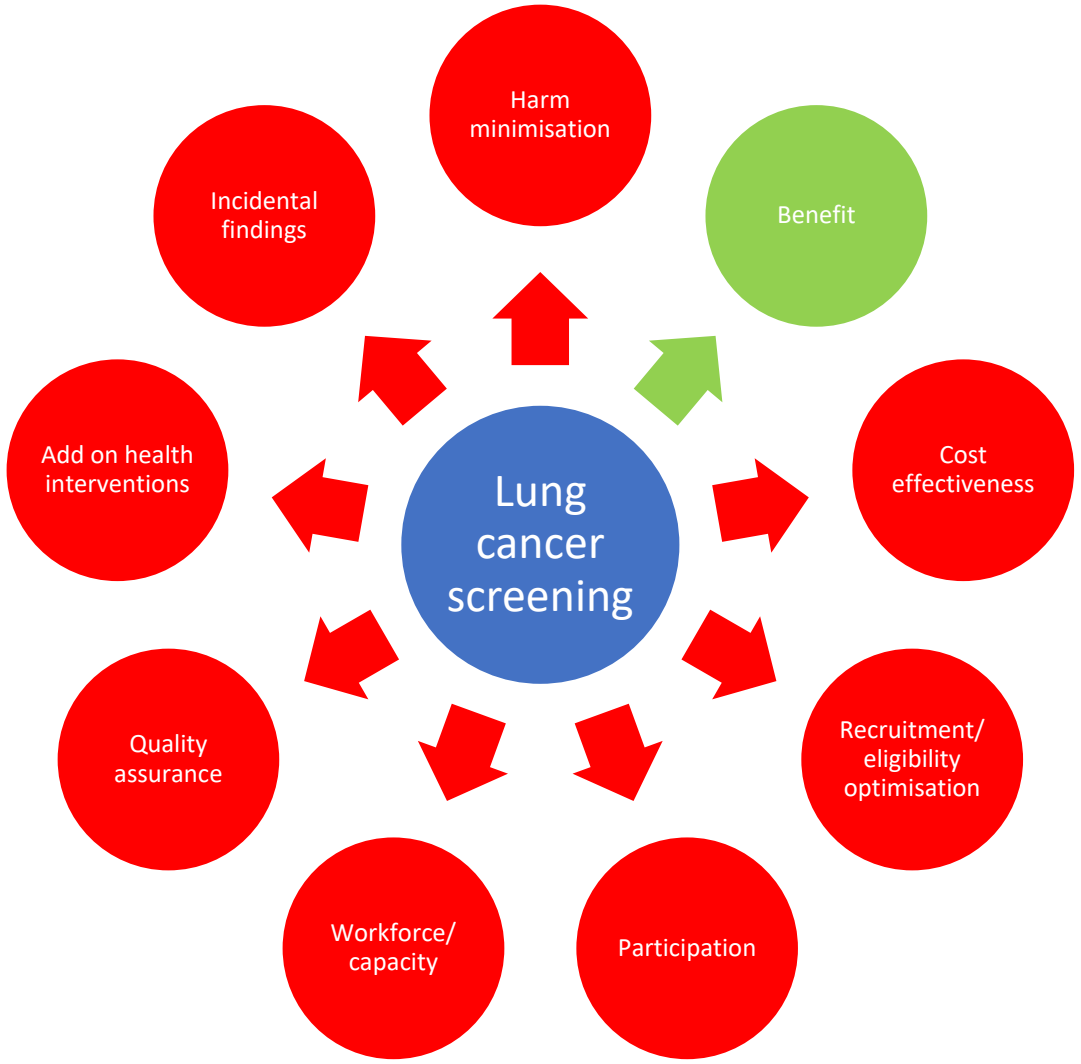
Challenges in the implementation of lung cancer screening



Emma O'Dowed

Consultant Respiratory Physician
Nottingham University Hospitals NHS Trust

Challenges in the implementation of lung cancer screening



False positives

Cervical screening (England 2018)

Negative	Routine screening	≈ 92%	≈ 83%	Negative	Routine screening
Low-grade changes/ inadequate (3%)	Repeat smear	≈ 7%	≈ 13%	Indeterminate	Repeat LDCT at 3 months
Positive	Colposcopy/ surgery	≈ 1%	≈ 5% *	Positive	Lung MDT referral

* 52% lung cancer

NHS Digital Cervical Screening Programme 2017-2018; Crosbie PA, et al. Thorax 2019;**74**:405–409. doi:10.1136/thoraxjnl-2017-211377

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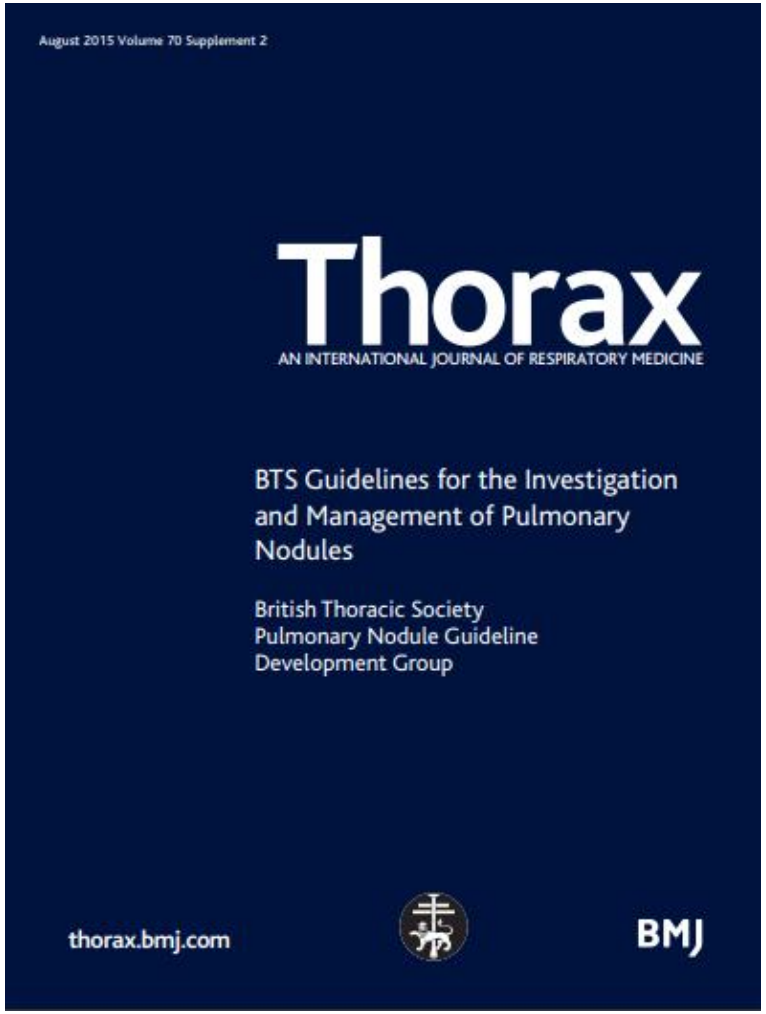
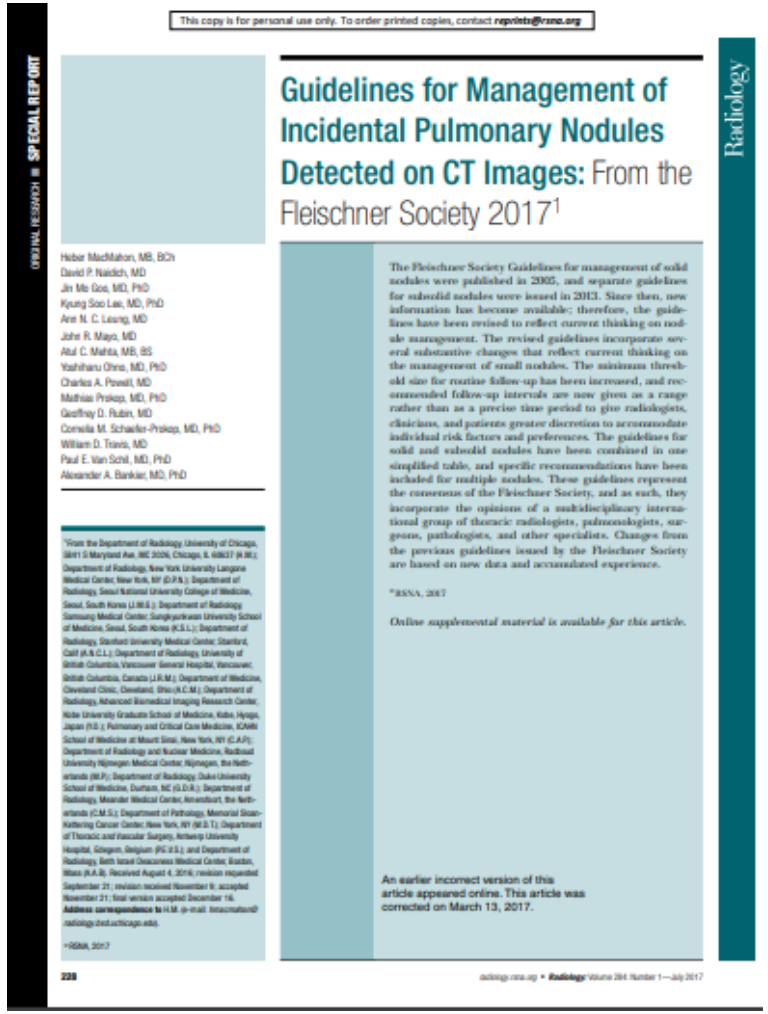
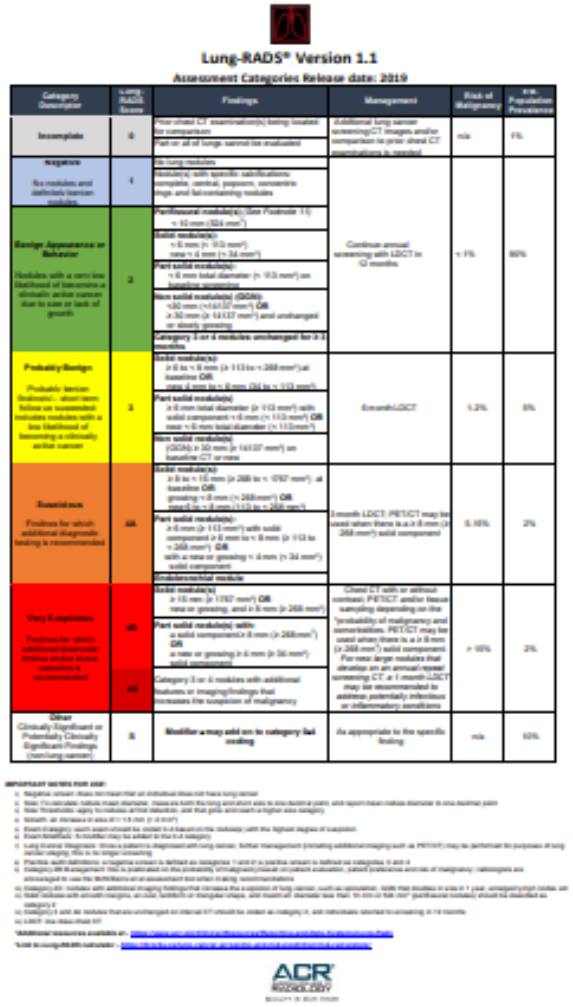
Nodule Guidelines





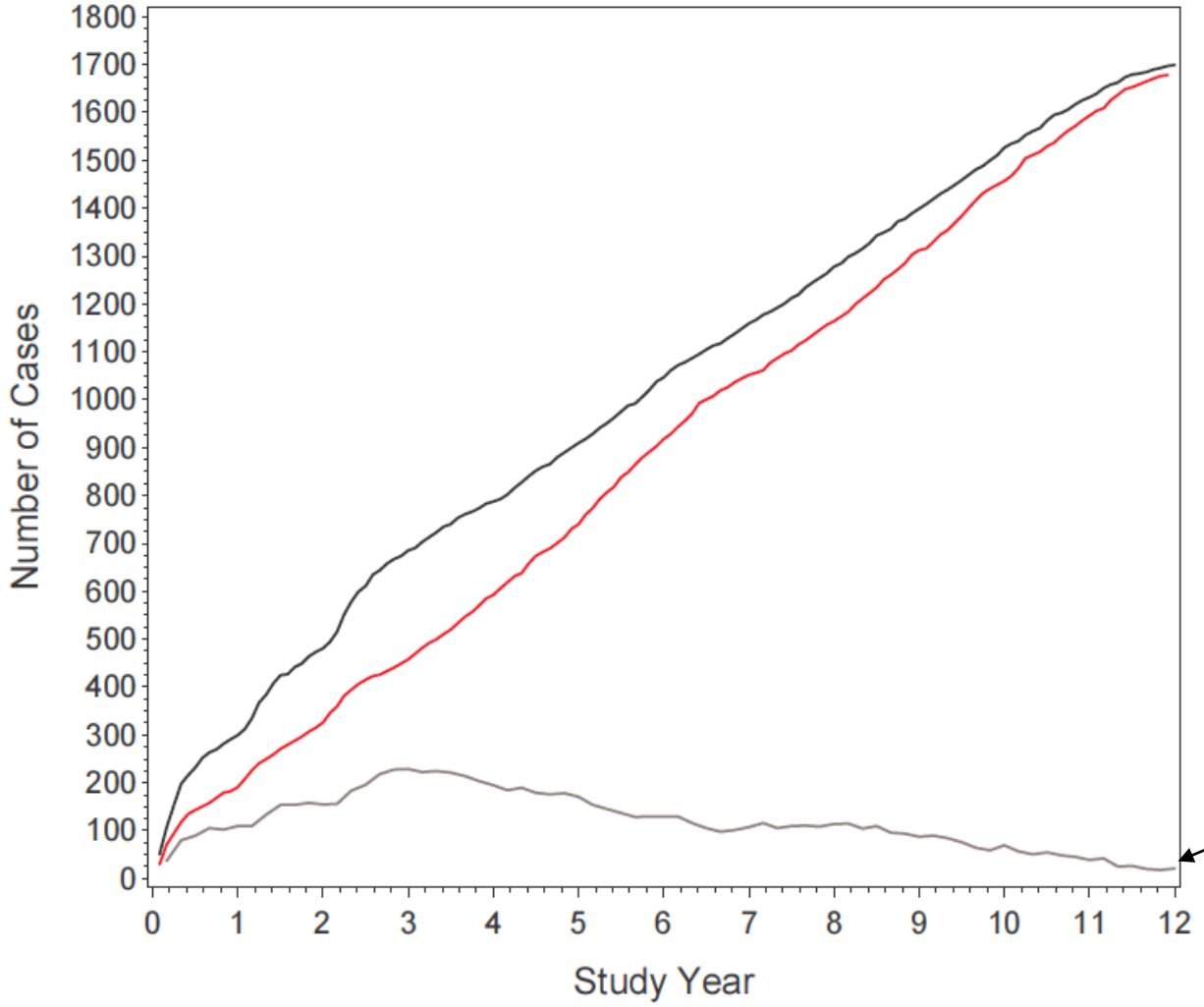


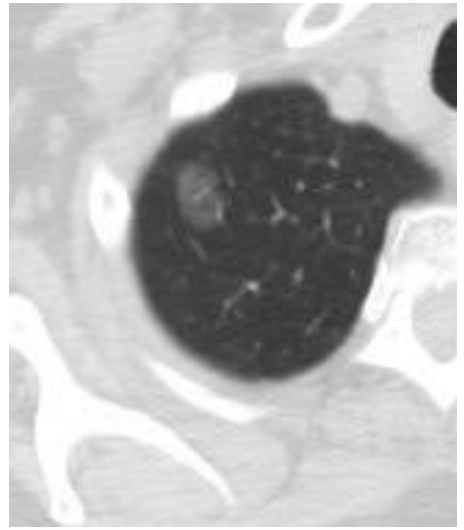
Overdiagnosis

LDCT

CXR

Excess lung cancer





3.3%

Black, W. C., C. Chiles, T. R. Church, I. F. et al. J Thoracic Oncology 2019. DOI 10.1016/j.jtho.2019.05.044

Psychological harm

ORIGINAL ARTICLE

Long-term psychosocial outcomes of low-dose CT screening: results of the UK Lung Cancer Screening randomised controlled trial

Kate Brain,[1] Kate J Lifford,[1] Ben Carter,[1] Olivia Burke,[1] Fiona McRonald,[2] Anand Devaraj,[3] David M Hansell,[3] David Baldwin,[4] Stephen W Duffy,[5] John K Field[6]

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

Brain K et al. Thorax 2016;72:996-1005

Harms associated with referral/ treatment

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

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

* 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 [1]
  - Compared with 3-4% in US [2]

[1] Ruparel M, Quaife SL, Dickson JL, et al. Thorax Epub ahead of print:[Aug 2020]. doi:10.1136/thoraxjnl-2020-214703, [2] Jemal A, Fedewa SA. Lung cancer screening with low-dose computed tomography in the United States-2010 to 2015. JAMA Oncol. 2017;3(9):1278–1281.

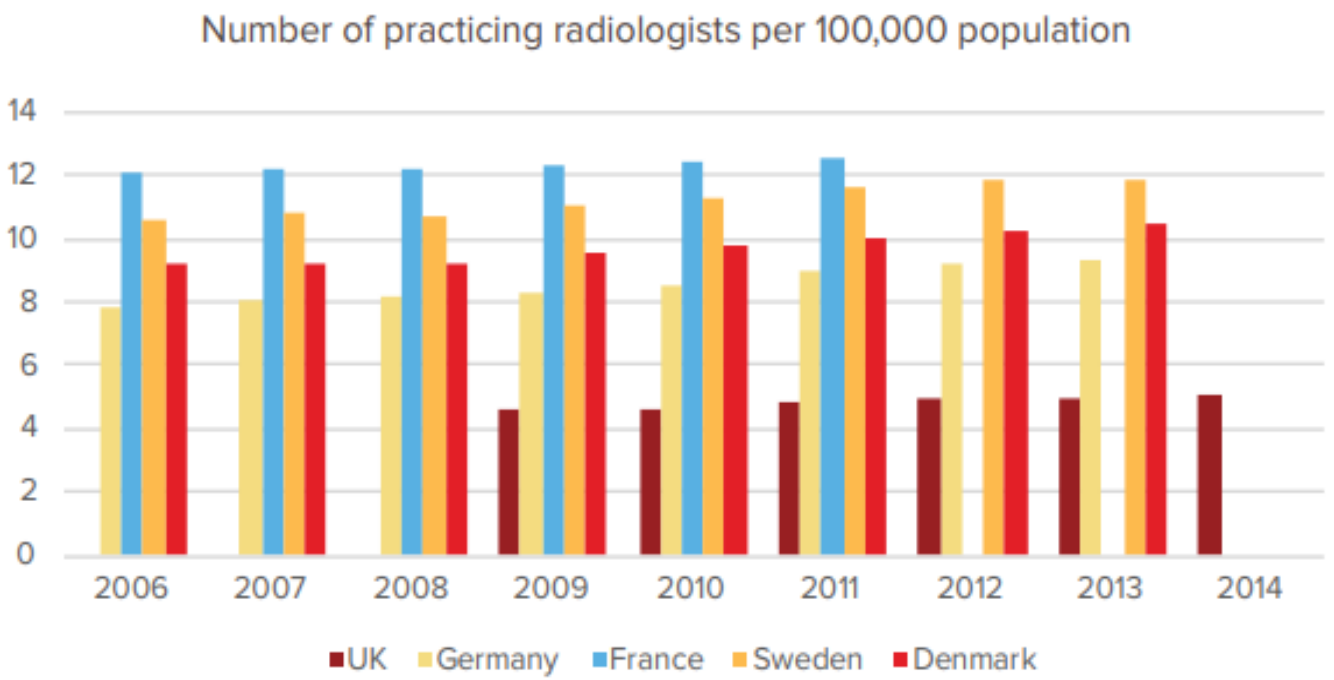
Recruitment

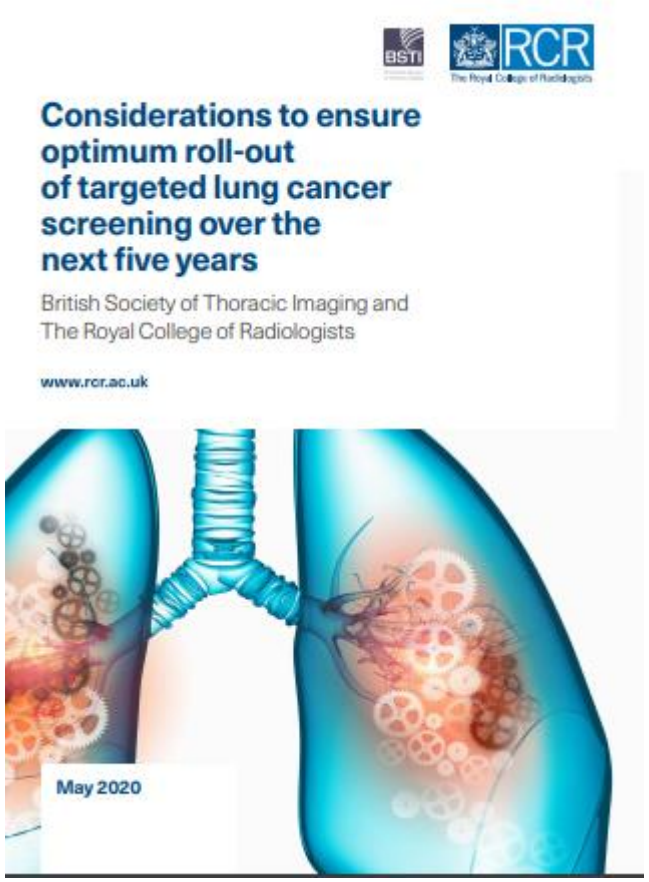
NELSON

YLST

Images courtesy of Carlijn van der Aalst & Mat Callister

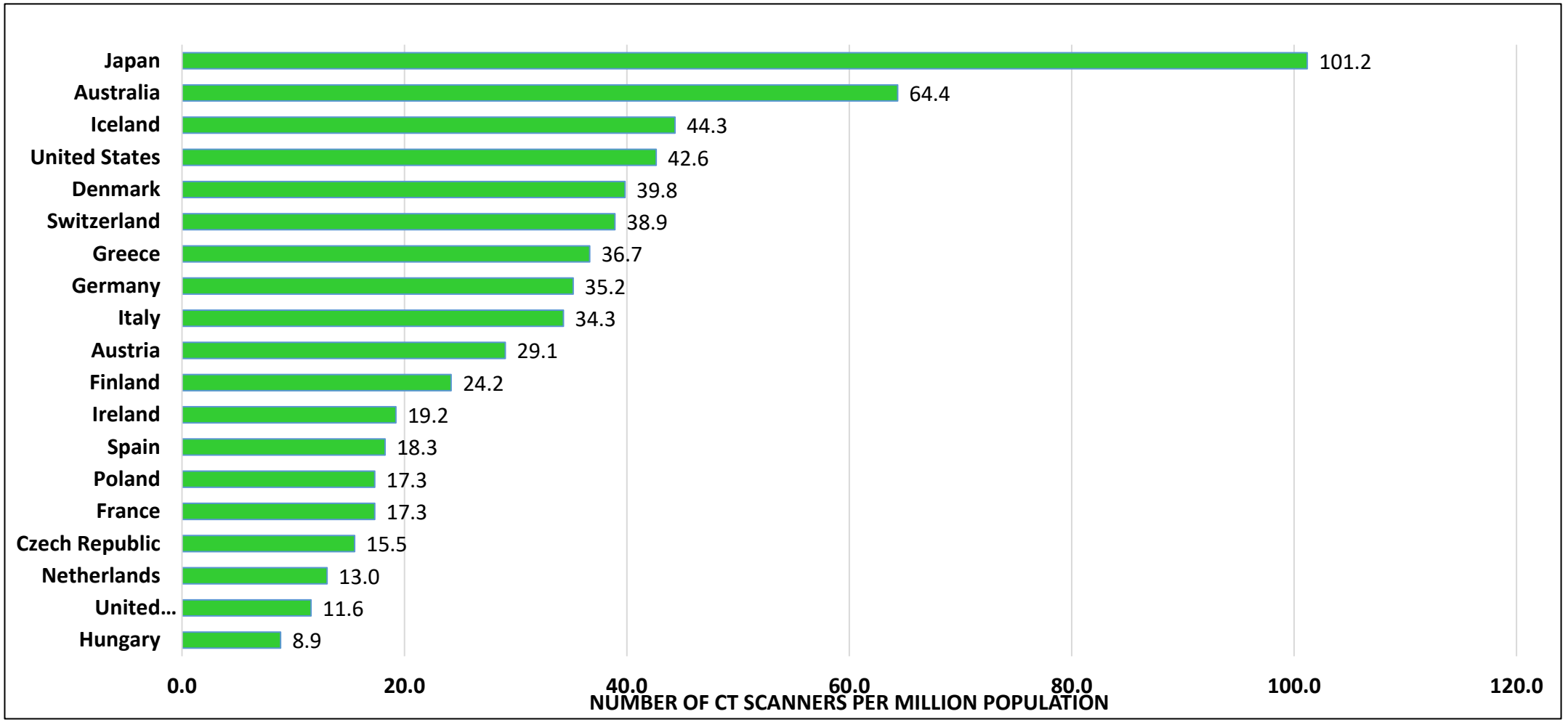
Workforce





Europe's Looming Radiology Capacity Challenge: A Comparative Study. C. Silvestrin. Nov 2016 (Available from https://www.telemedicineclinic.com)

CT scanning capacity



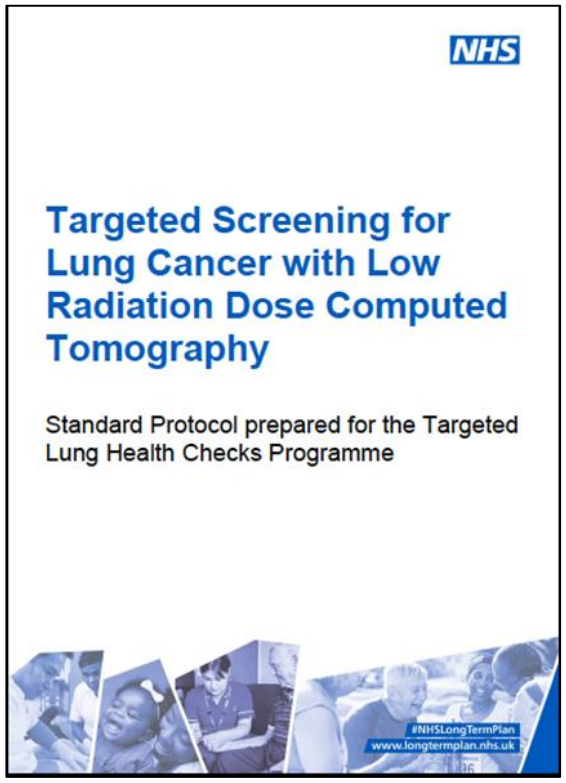
Data from Organisation for Economic Co-operation and Development- available via https://stats.oecd.org

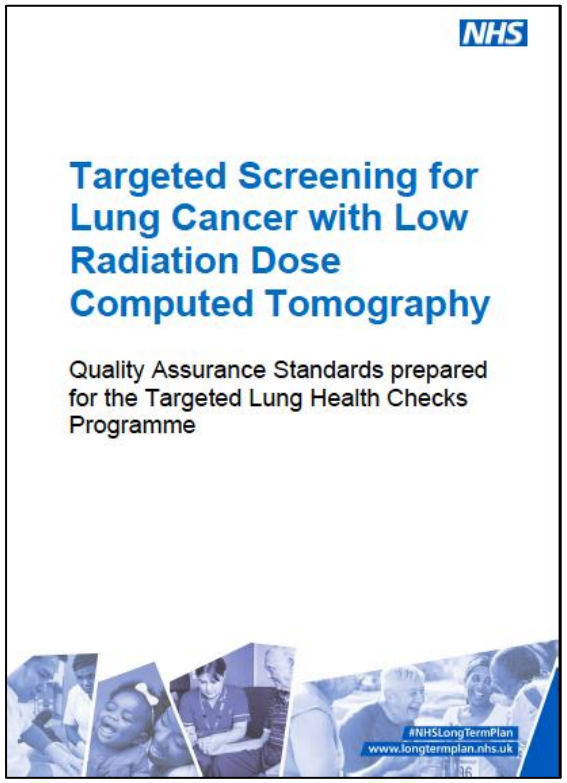
Cost effectiveness

	Method	Result ICER per QALY gained
Villante[1]	Cost-utility model	£22,592
NLST[2]	Cost – model (NLST mortality)	£64,800 (41,000 to 149,000)
UKLS[3]	Cost – stage shift model	£8,466 (5,542 to 12,569)
HTA[4]	Natural history model; discrete event	£28,169
Manchester pilot[5]	Cost – stage shift model	£10,069
Canada[6]	Cost-utility high risk (NLST mortality)	£12,560

1. Villanti, A. C., Y. Jiang, D. B. Abrams and B. S. Pyenson (2013). PLoS One **8**(8): e71379.
2. Black WC, Gareen IF, Soneji SS, et al. N Engl J Med 2014;371:1793-802.
3. Field, JK, Duffy SW, Baldwin DR et al Thorax 2016;71:161–170
4. Snowsill, T., H. Yang, E. Griffin, et al (2018) Health Technol Assess **22**(69): 1-276.
5. Hinde, S., T. Crilly, H. Balata, et al (2018). Lung Cancer **126**: 119-124.
6. Cressman, S., S. J. Peacock, M. C. Tammemagi, et al J Thorac Oncol 2017;**12**(8): 1210-1222.

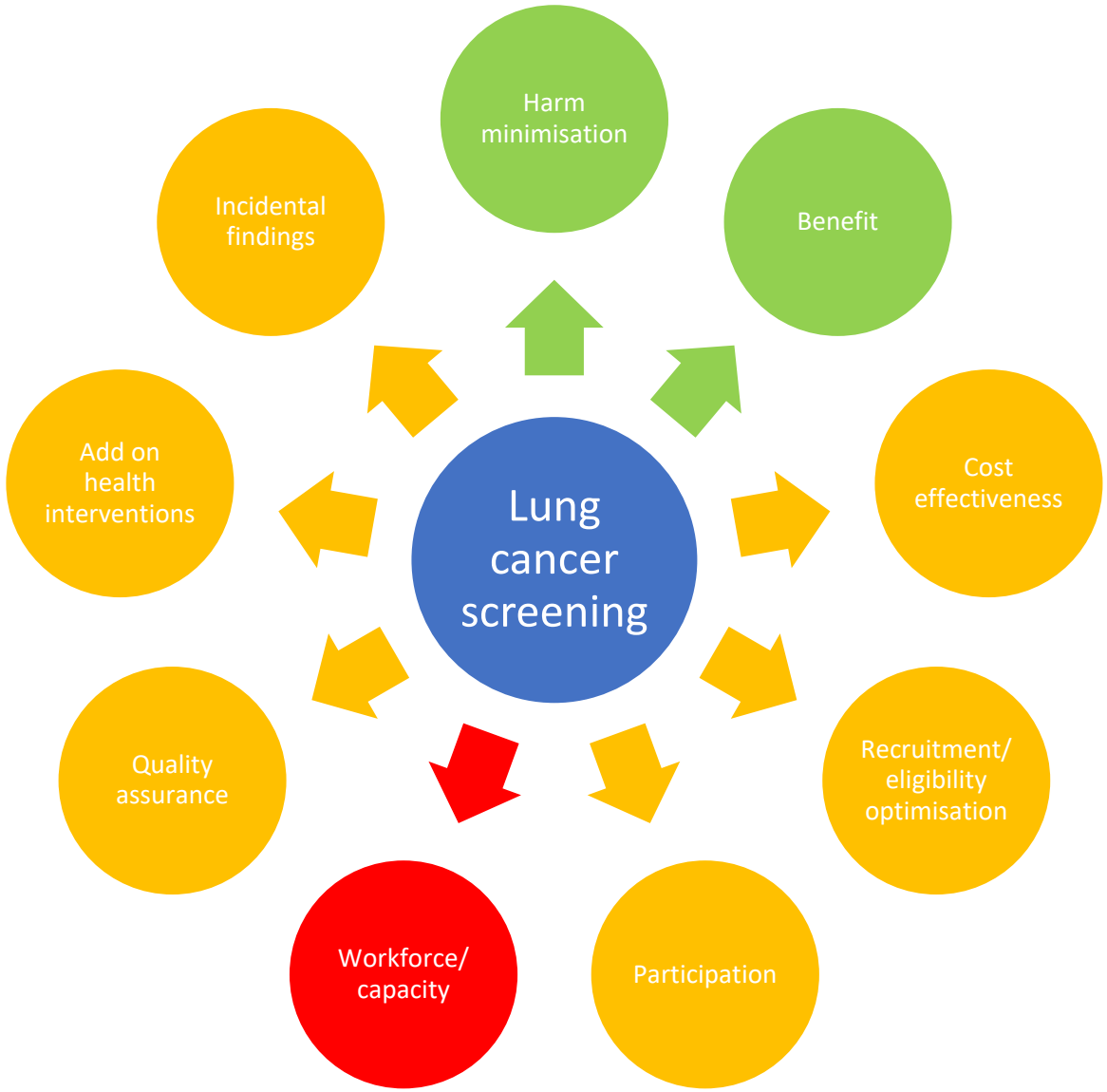
Service implementation and quality assurance





- 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



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Evidence for risk-adapted screening in prostate cancer

Peter Albers, MD

Professor of Urology

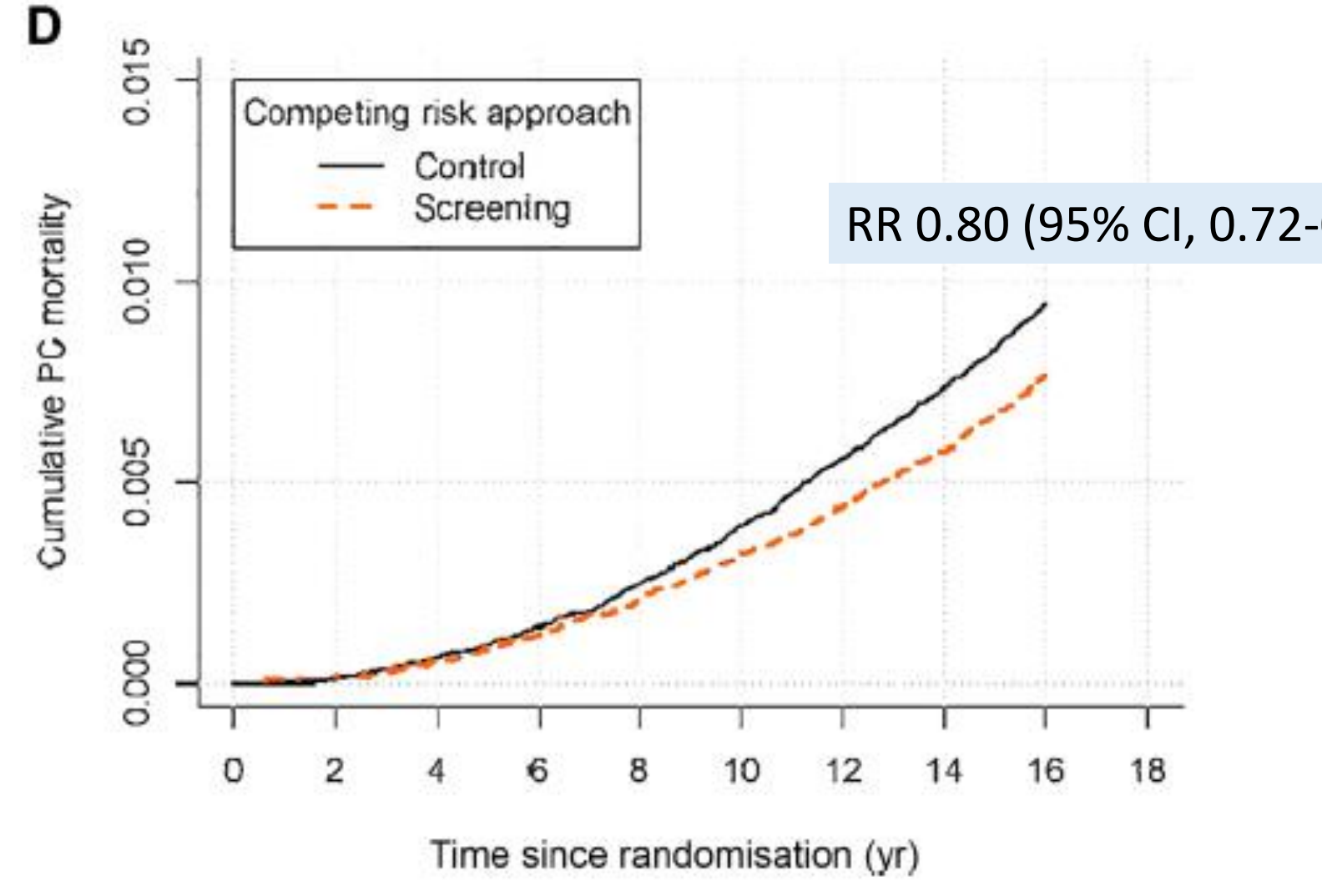
Division Head, C130 Personalized Prevention and Early Detection of Prostate Cancer
German Cancer Research Center (DKFZ) Heidelberg, Germany
Chair, Department of Urology, Düsseldorf University Hospital
Heinrich-Heine-University, Düsseldorf, Germany

Deutsche Krebshilfe
HELFEN. FORSCHEN. INFORMIEREN.

No conflict of interest regarding this talk.

Hugosson J et al. Eur Urol 2019

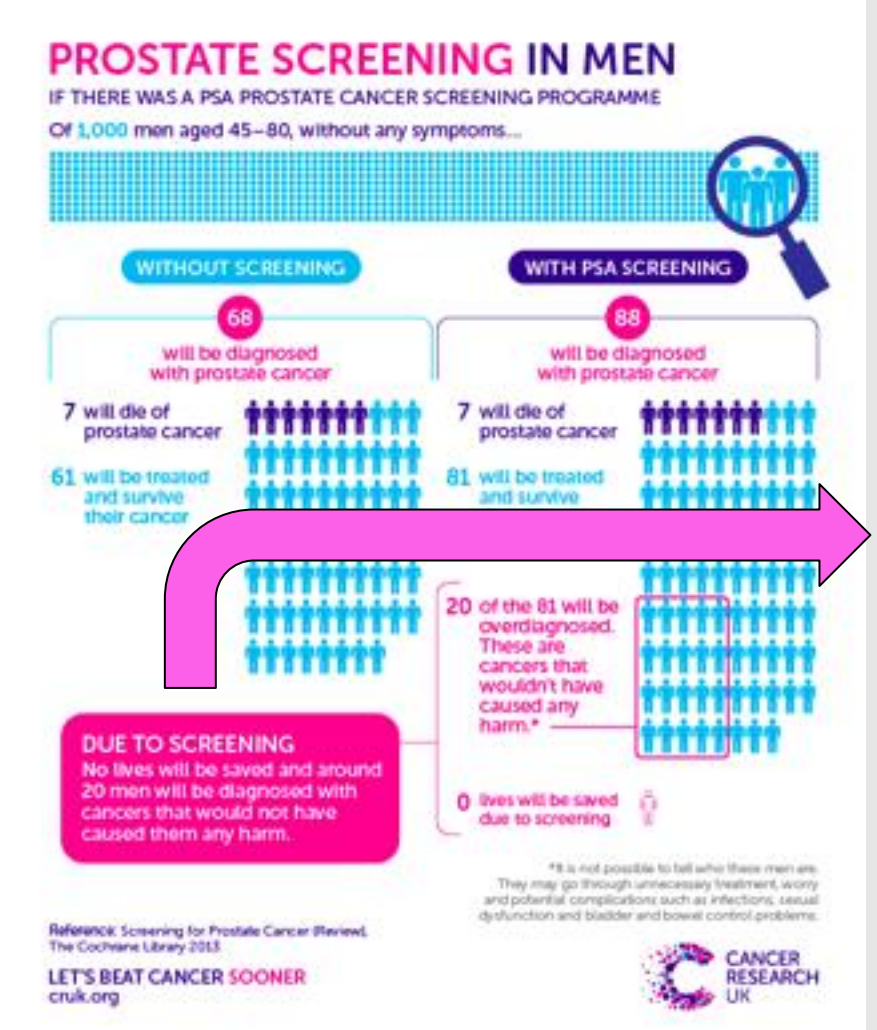
Prostate cancer specific mortality (ERSPC)



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

Hugosson J et al. Eur Urol 2019

Prostate Cancer Screening Patient Information UK



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

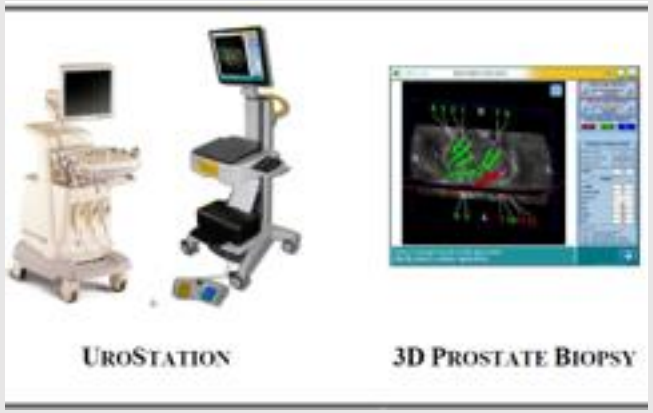
dkfz.

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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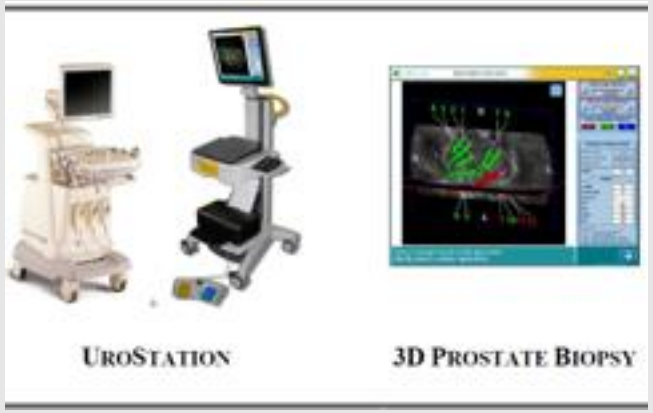
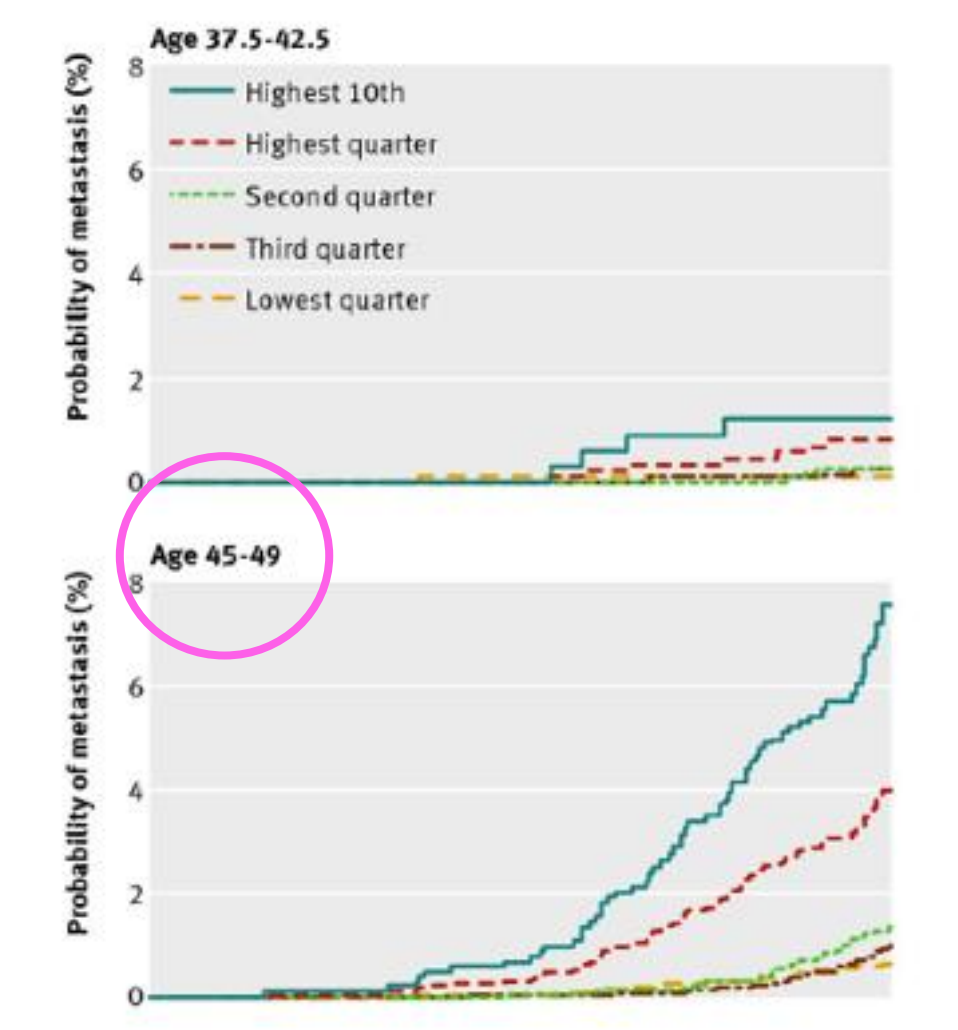


Prediction of PCA metastasis by „baseline“ PSA



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

dkfz.

PROBASE

Die Deutsche Prostatakrebs Screening Studie

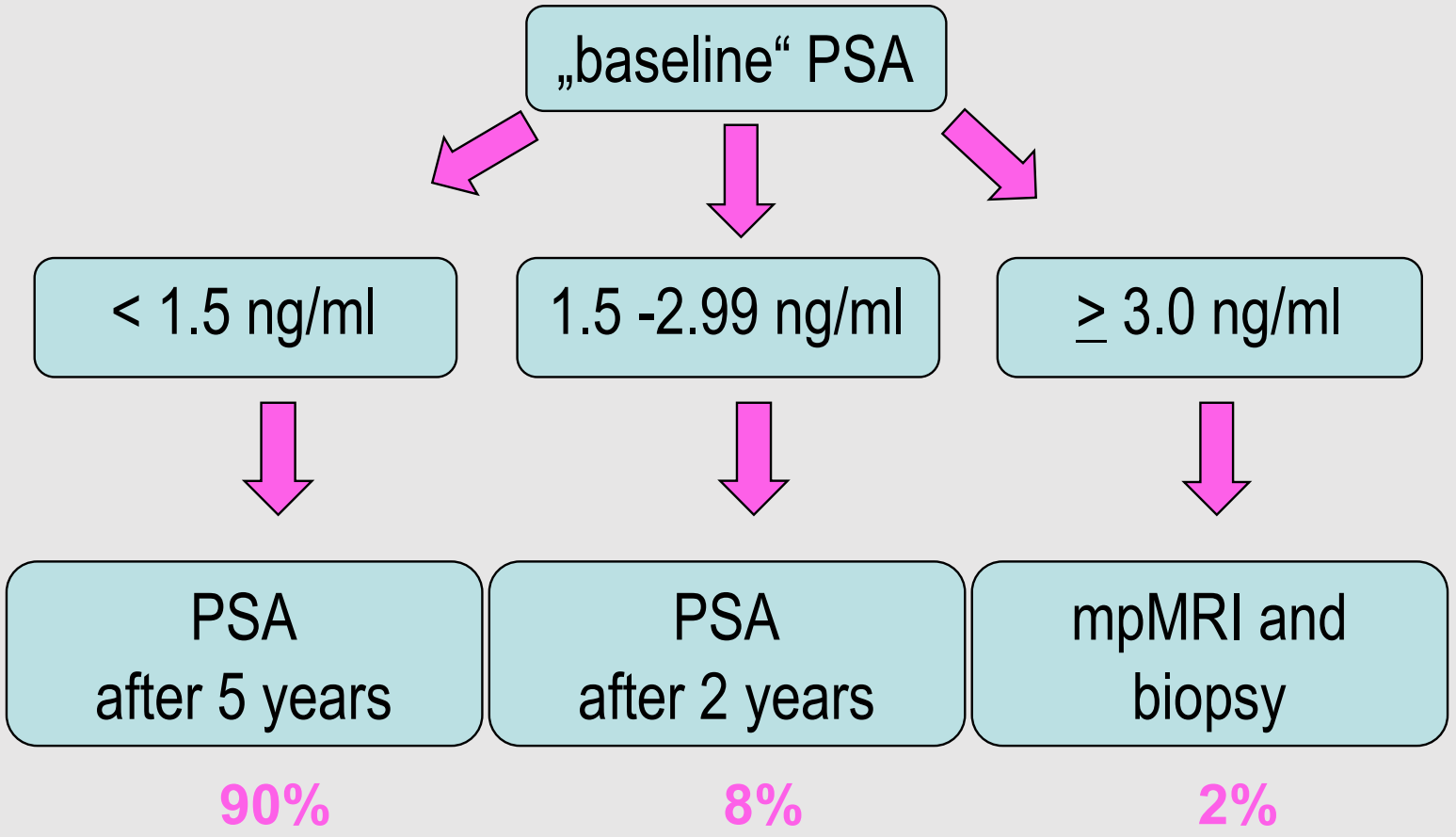
Risk-adapted **pro**state cancer (PCa) early detection study based on a "**base**line" PSA value in young men – a prospective multicenter randomized trial (**PROBASE**)

dkfz.

PROBASE

Die Deutsche Prostatakrebs-„Screening" Studie

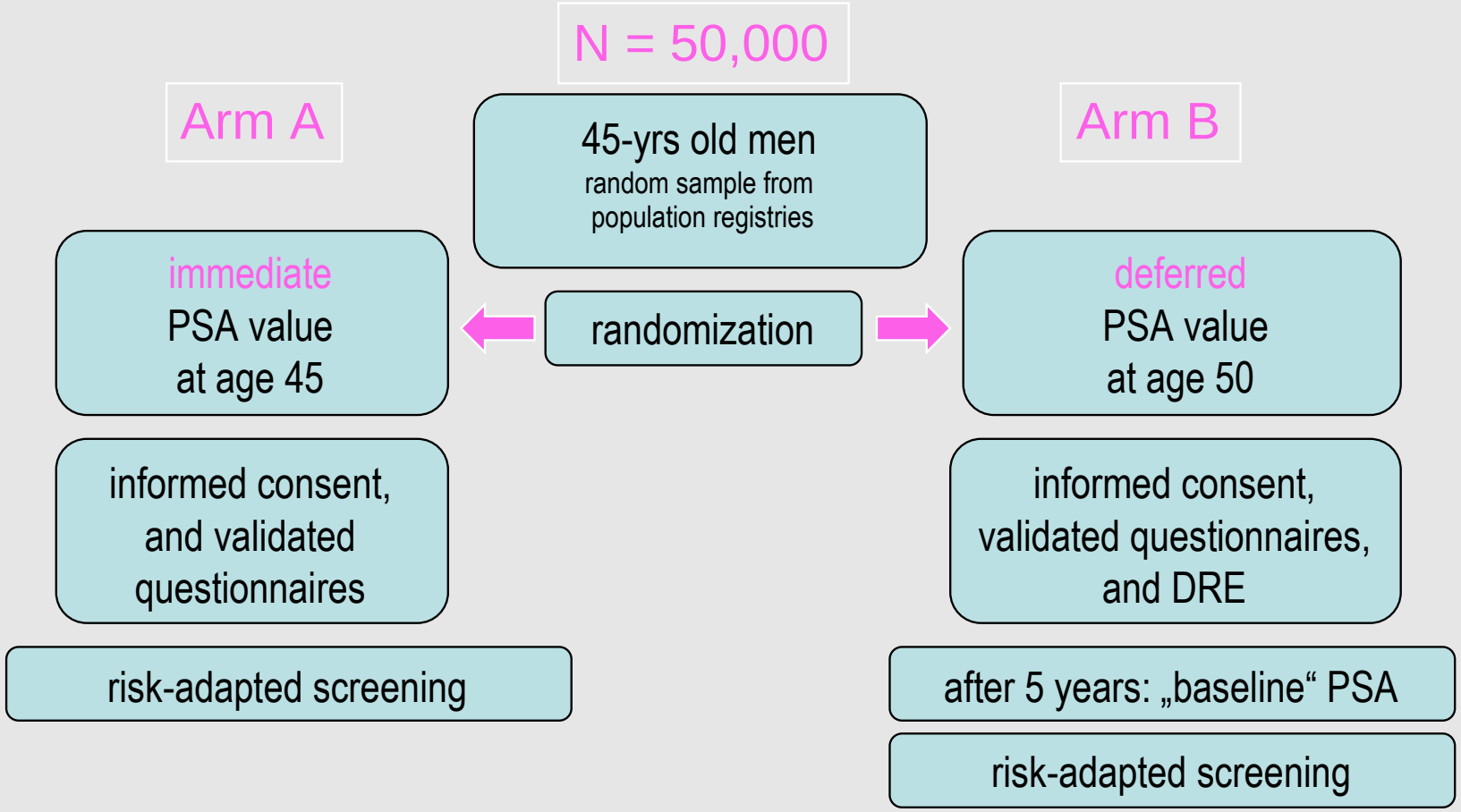
Study Design



PROBASE

Die Deutsche Prostatakrebs-„Screening" Studie

Study Design

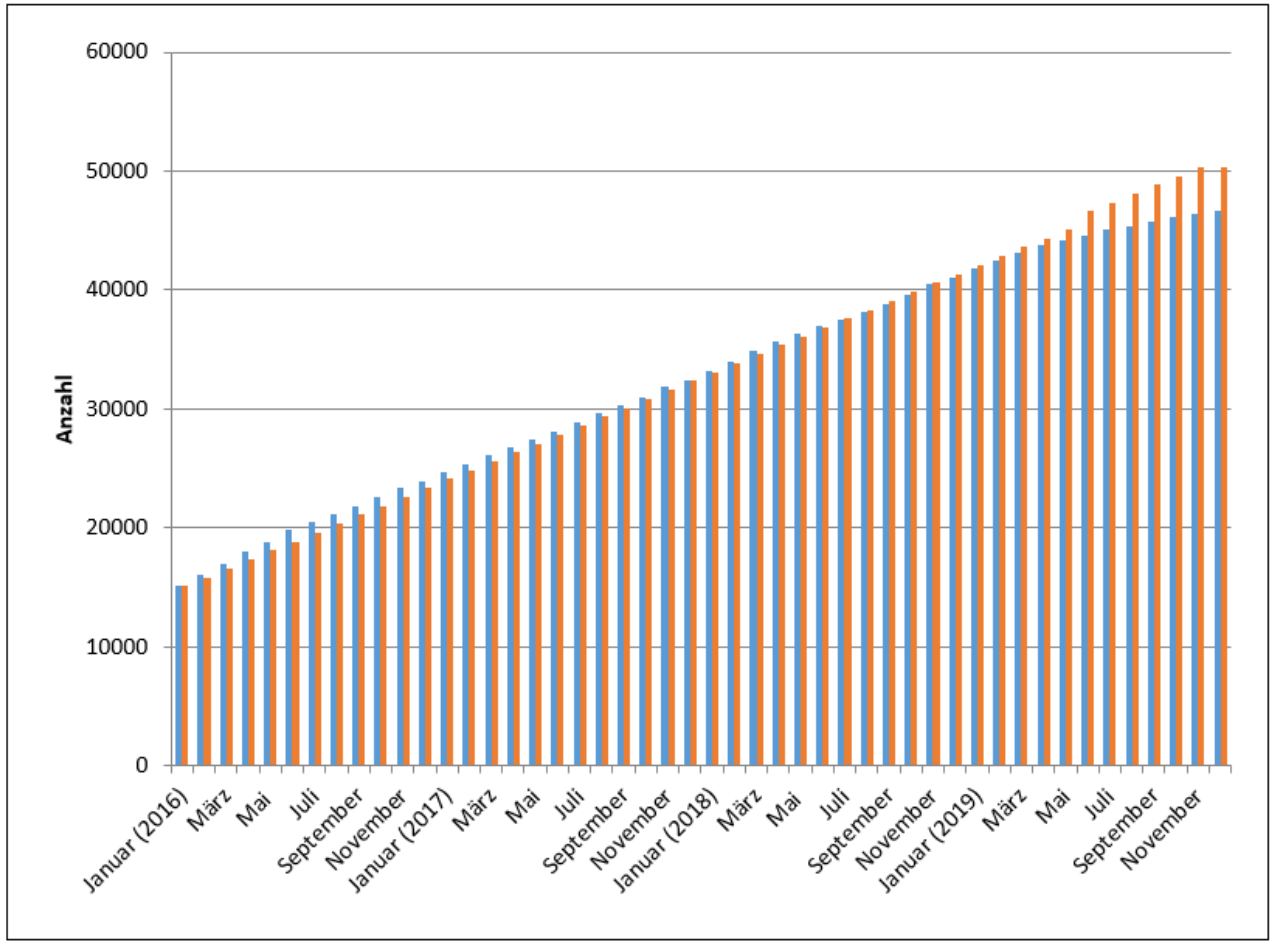


dkfz.

PROBASE
Die Deutsche Prostatakrebs Screening Studie

Deutsche Krebshilfe
HELFEN. FORSCHEN. INFORMIEREN.

Accrual Feb 2014 – Dec 2019: 46,642 participants



expected
observed

ueg.eu

data cut-off Dec 31, 2019

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

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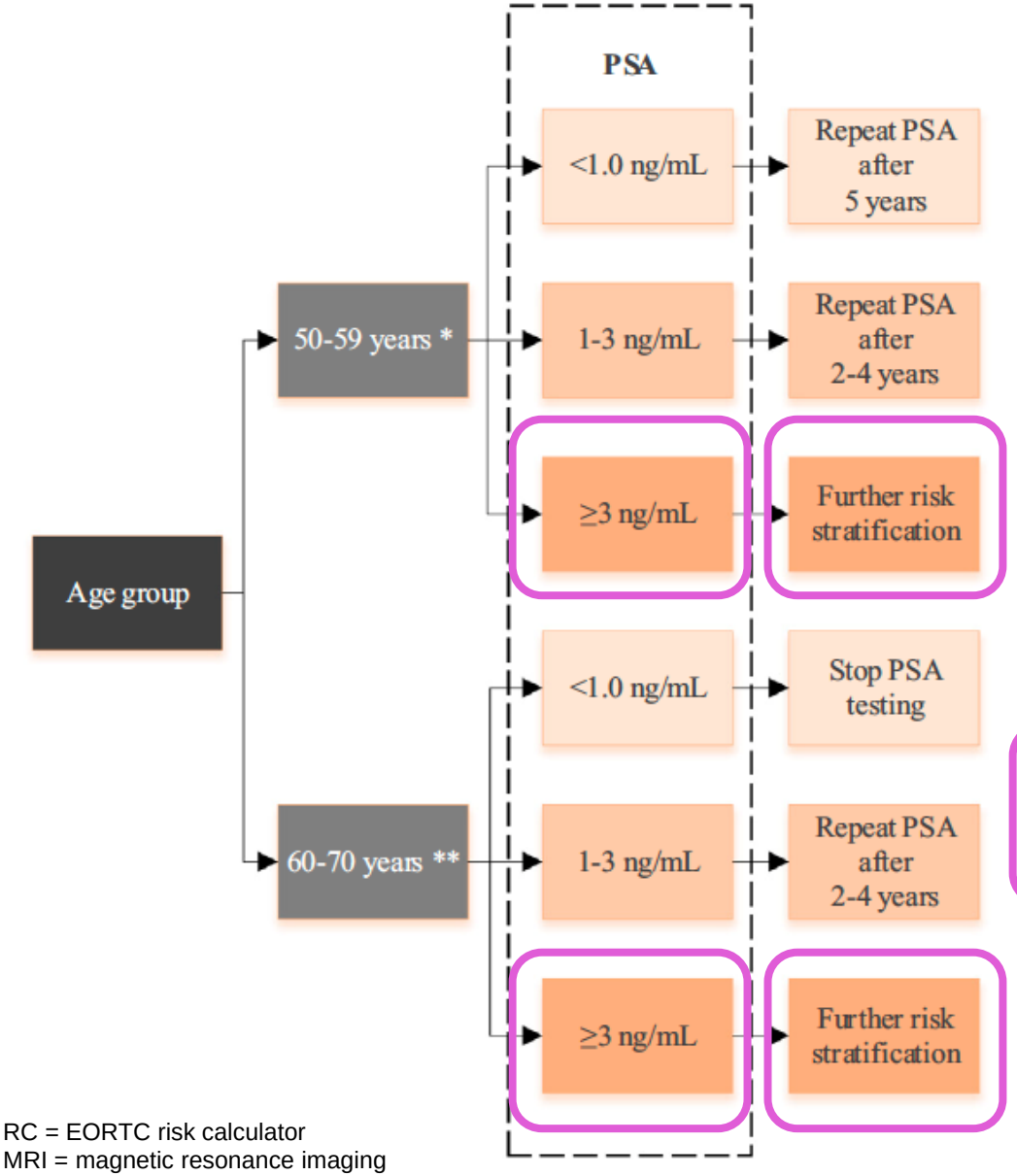
available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Platinum Opinion

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

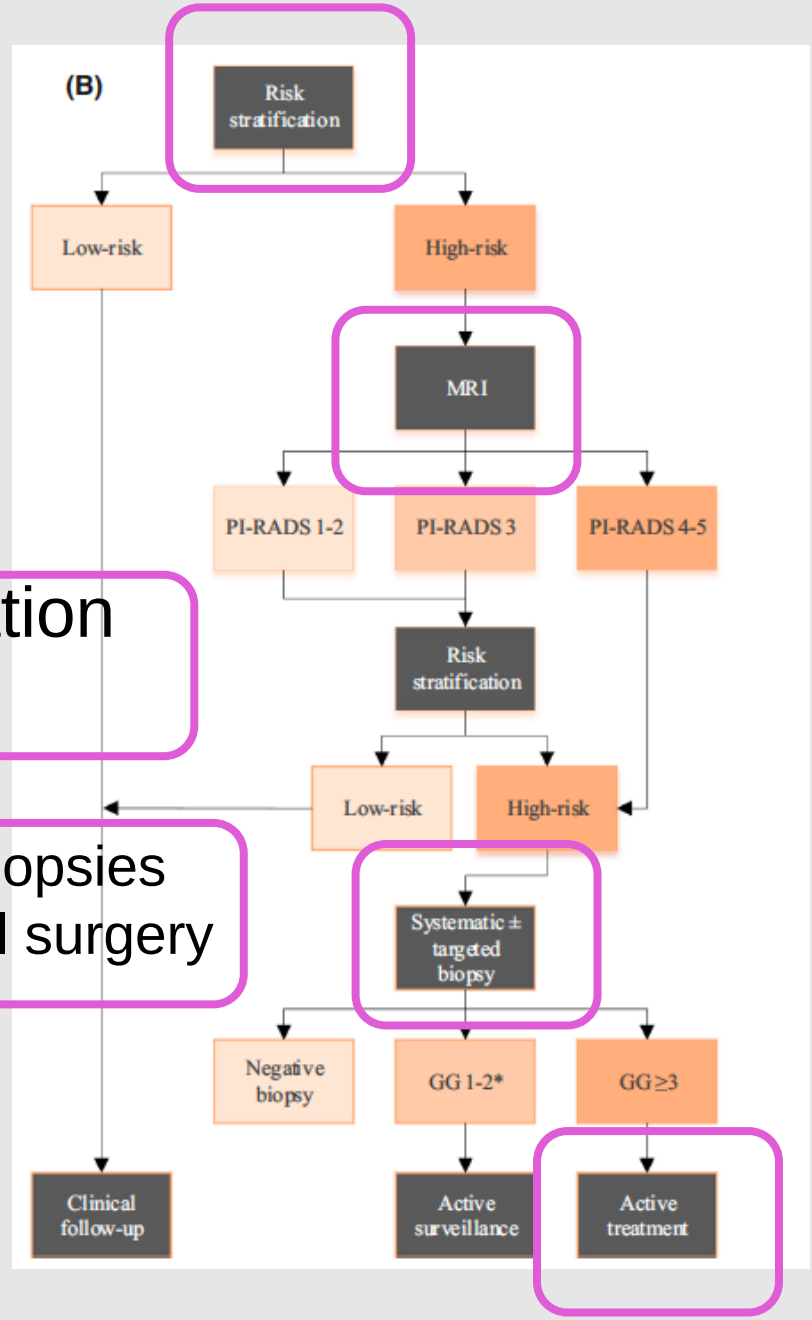
Hendrik Van Poppel[a,†,*], *Renée Hogenhout*[b,†], *Peter Albers*[c,d], *Roderick C.N. van den Bergh*[e], *Jelle O. Barentsz*[f,‡], *Monique J. Roobol*[b,‡]



RC = EORTC risk calculator
MRI = magnetic resonance imaging

Risk Stratification (RC, MRI)

avoids > 50% of biopsies and > 50% of radical surgery



Van Poppel H Eur Urol 2021

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

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. **Please contact our CEO, Mike Morrissey, if you would like to join the Prevention, Early Detection and Screening Network (free-of-charge).**

Member Societies

Patient Organisations

Invited Stakeholders