iPAAC meeting 14 Jan 2021

Cancer screening in Europe – shifting paradigms

International Agency for Research on Cancer
Lyon, France

Partha Basu MD, PhD

Head, Screening Group;

basup@iarc.fr; www.screening.iarc.fr

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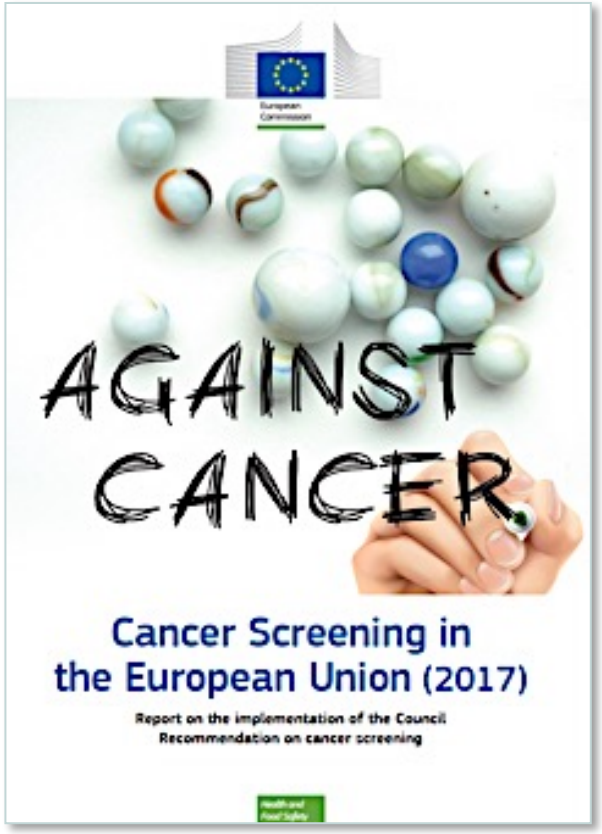
Implementation of recommended breast, cervical and colorectal cancer screening programmes in EU Member States in 2016



	Breast cancer screening	Cervical cancer screening	Colorectal cancer screening
Population-based screening program	25 (95%)	22 (72%)	23 (72%)
Rollout complete	*21 (88%)*	*9 (28%)*	*9 (27%)*
Rollout ongoing	*3 (3%)*	*10 (27%)*	*8 (26%)*
Piloting	*1 (4%)*	*1 (<1%)*	*4 (3%)*
Planning	*0*	*2 (17%)*	*2 (18%)*
Non-population-based screening program	3 (5%)	4 (25%)	2 (4%)
No screening program	0	2 (2%)	3 (24%)

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https://screening.iarc.fr/EUreport.php

- Women with average risk
  - Age 40-44 yrs: No screening
  - Age 45-49 yrs: DM every 2-3 yrs
  - Age 50-69 yrs: DM every 2 yrs
  - Age 70-74 yrs: DM every 3 yrs
- Women with dense breasts
  - Screening with either DM or DBT

https://healthcare-quality.jrc.ec.europa.eu/european-breast-cancer-guidelines

Digital breast tomosynthesis for breast ca detection

- A systematic review & meta-analysis compared DBT and DM in average risked women
- Thirty-eight studies reporting on 488,099 patients (13,923 with breast cancer) were included
- Sensitivity *(higher sensitivity was maintained after adjusting for covariates)*
  - DBT: 88% (83-92)
  - DM: 879% (71-85)
- Specificity
  - DBT: 84% (76-89)
  - DM: 79% (71-85)
- Combination of DBT and DM didn't demonstrate higher accuracy over DBT alone

"For asymptomatic women with an average risk of breast cancer, the ECIBC's Guidelines Development Group (GDG) suggests using either digital breast tomosynthesis (DBT) or digital mammography (DM) in the context of an organised screening programme"

European Radiology (2020) 30:2058–2071

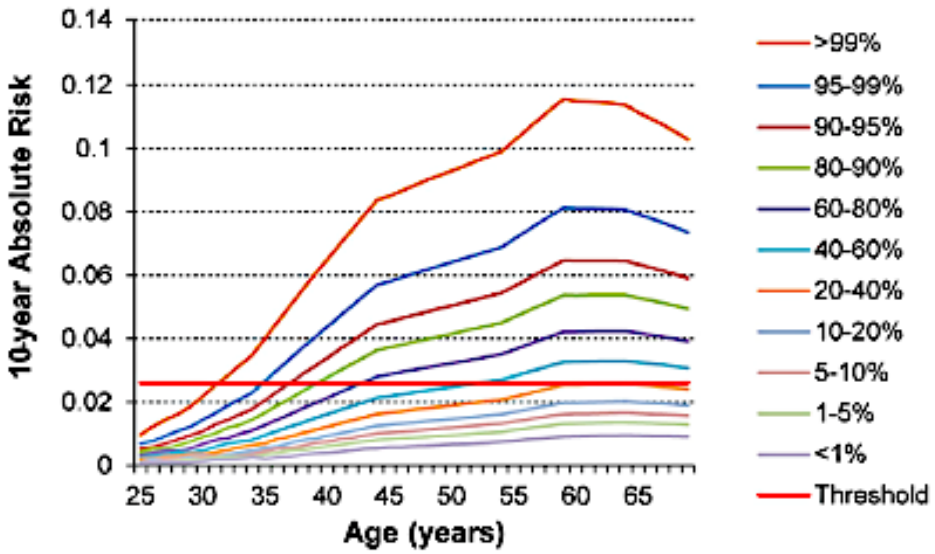
Radiology. 2018 Jun;287(3):787-794

Artificial Intelligence in breast cancer screening

- AI was used to read a large representative dataset from the UK and a large enriched dataset from the USA
- Absolute reduction of 5.7% and 1.2% (USA and UK) in false positives and 9.4% and 2.7% (USA and UK) in false negatives
- The AI system outperformed all of the human readers
- AI system maintained non-inferior performance and reduced the workload of the second reader by 88%

Nature **577,** 89–94 (2020).

Risk Stratified Screening- MyPeBS study scheme



10-year absolute risk of developing breast cancer by percentiles of the 313 Single Nucleotide Variant polygenic risk scores

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85,000 Women
2.5 years inclusion
4 year-follow-up

40 -70 year-old women
Invitation from organized screening centers or self-volunteering

Dedicated inclusion visit

Exclusion criteria:
Women with prior breast cancer or already identified at very high risk

Eligibility

Randomisation

Group 1
Standard

Group 2
Personalised screening

Standard screening : according to ongoing national recommendation

Risk evaluation
(salivary test needed)

Visit 2 (3 months after):
communication of the risk level and delivery of a personalised schedule

Low risk
→ mammography at 4 years

Very high risk
→ annual mammography + annual MRI (up to 60 years old)

Moderate risk
→ mammography every 2 years

High risk
→ annual mammography

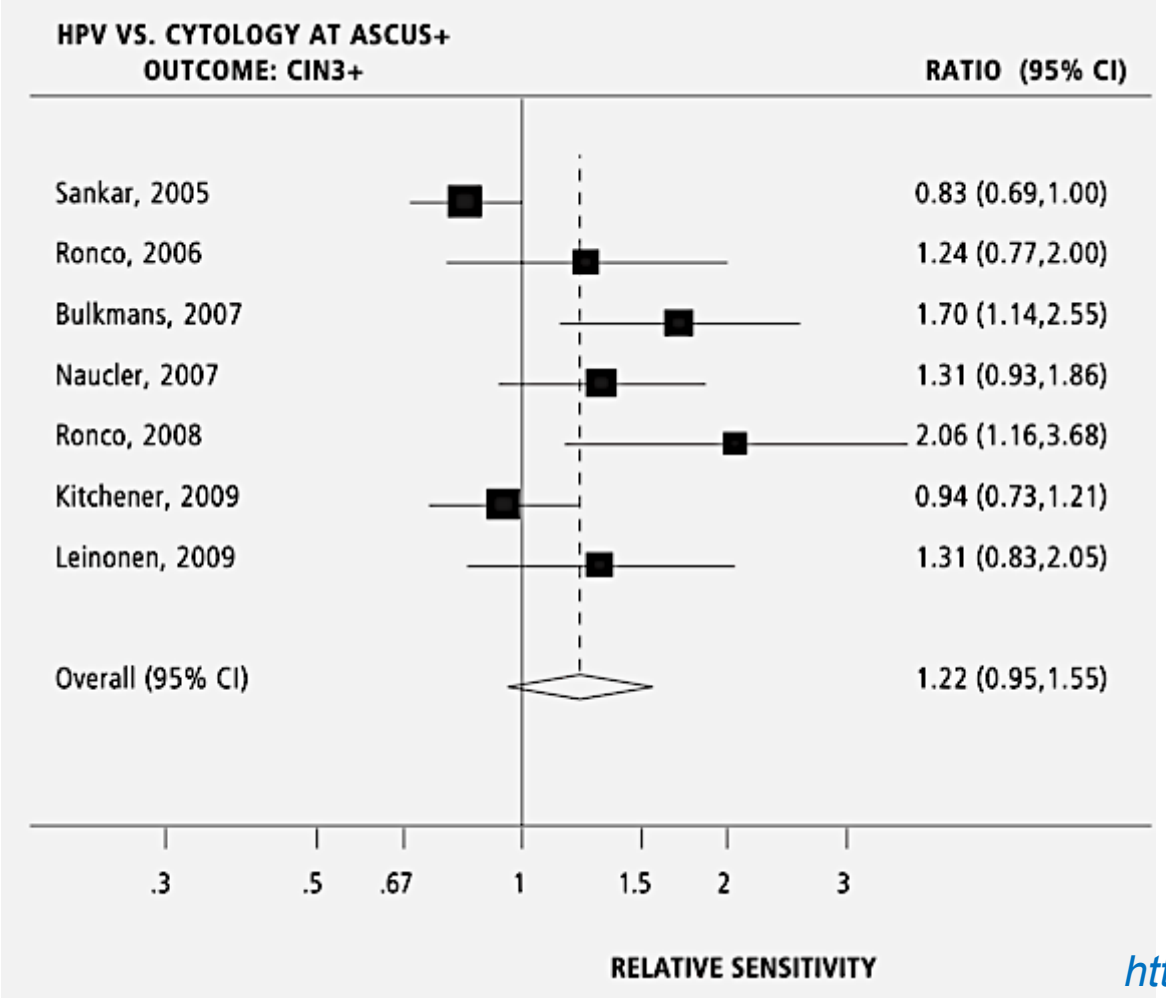
FOLLOW-UP: 4 YEARS PER PARTICIPANT

End-of study mammography at 4 years for all participants
Main evaluation criterion: incidence of stage 2 or higher breast cancer in each group at 4 years

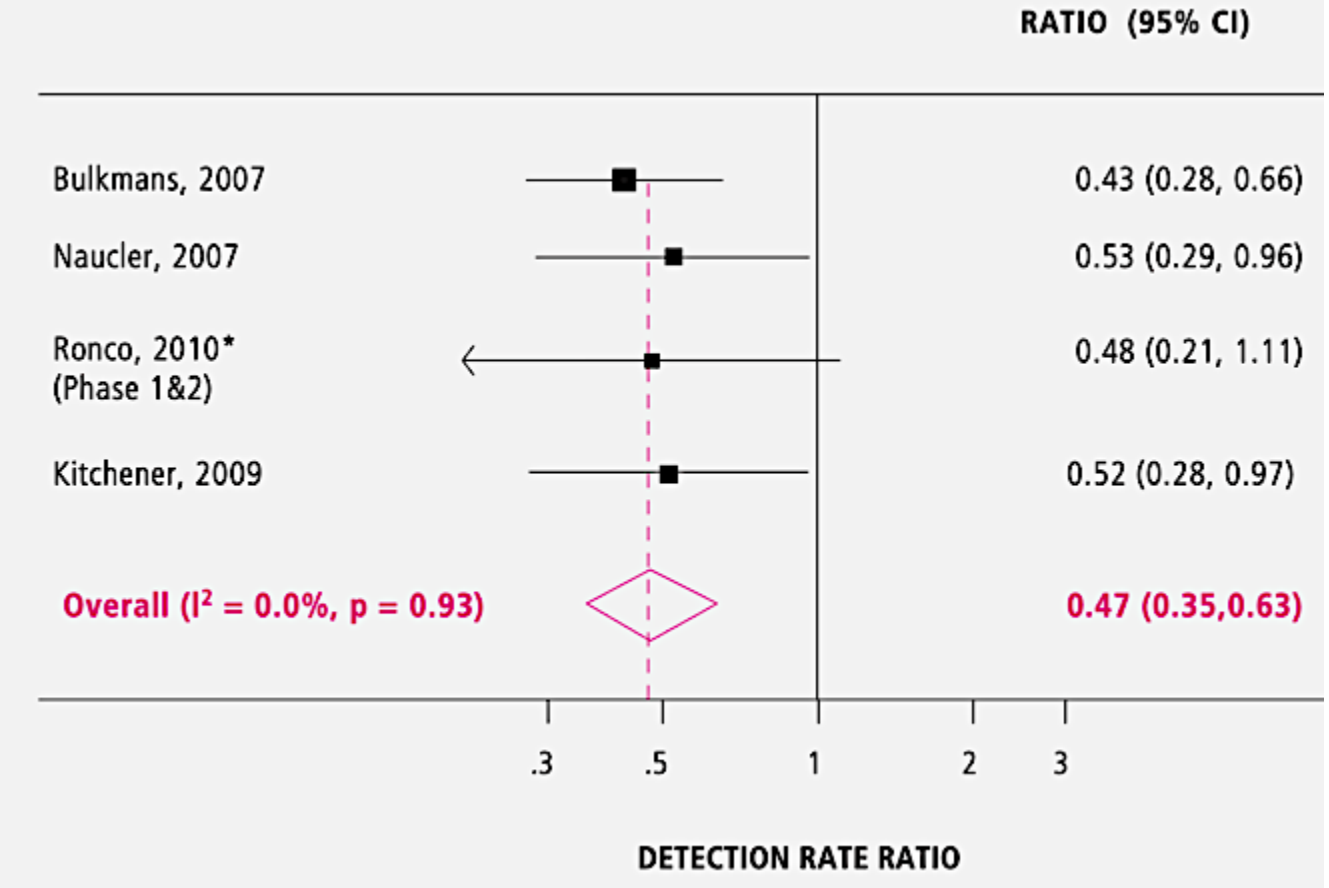
https://clinicaltrials.gov/ct2/show/NCT03672331?term=mypebs&rank=1

Cervical cancer screening – HPV test to replace cytology

DR ratio of HPV testing vs cytology, using CIN3+ as outcome. Meta-analysis of randomised trials.



DR ratio of CIN3+ in HPV Vs cytology group in 2nd screening round, among screen –ve women at baseline.



http://www.epiprev.it/materiali/2012/EP3_4-2012-s/EPv36i3-4suppl1.pdf

Health technology assessment report: HPV DNA based primary screening in Italy

- HPV screening should not be initiated before 30 yrs of age
- Screen +ve women should be triaged with a suitable test before referring to cytology
- Screen -ve women need not be screened before 5 yrs
- Only tests for the DNA of oncogenic HPV, validated according to the European guidelines should be applied
- in the current Italian situation, the overall costs of HPV-based screening are lower than those of conventional cytological screening applied at the current 3-year intervals

Nationwide program: Turkey & the Netherlands; Regional programs: Italy, Sweden, Finland, Denmark

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Epidemiol Prev. May-Aug 2012;36(3-4 Suppl 1):e1-72.

Clinical Microbiology and Infection. Volume 26, Issue 5, May 2020, Pages 579-583

Self-collected samples for HPV test- meta-analysis

Table 1 | Pooled relative sensitivity and specificity of high-risk human papillomavirus (hrHPV) assays based on signal amplification (SA) and polymerase chain reaction (PCR) on self samples versus clinician samples

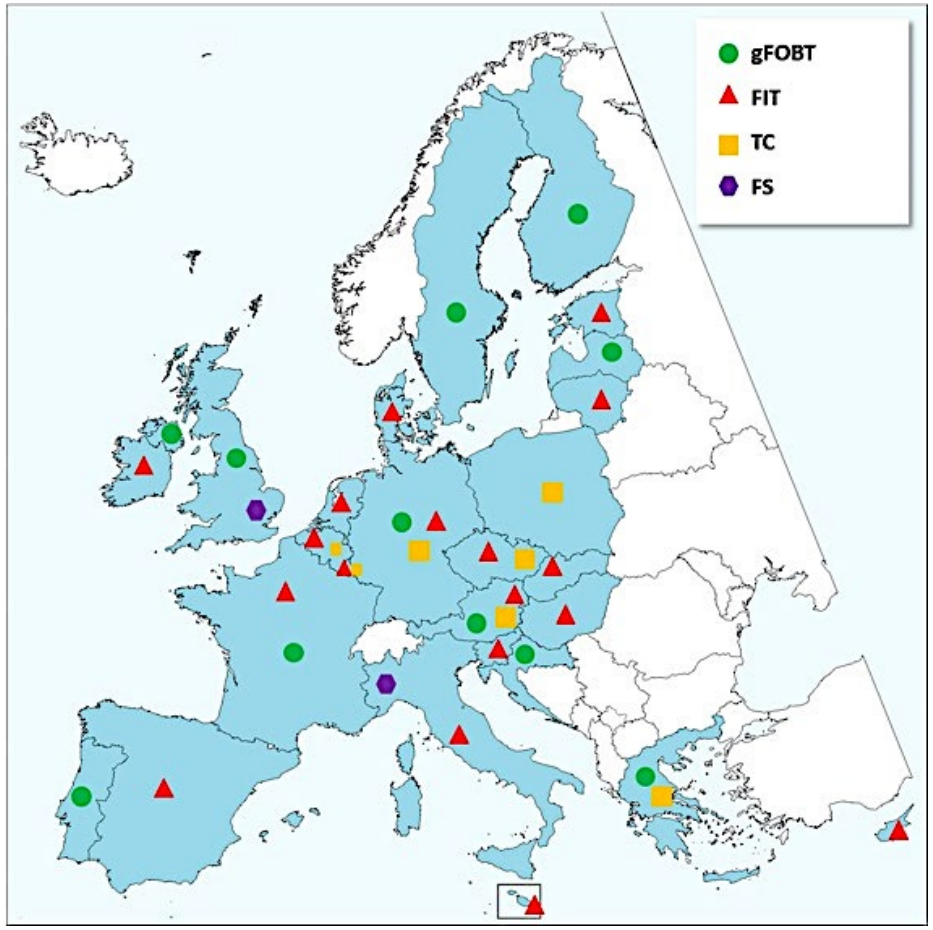
			Ratio (95% CI)			
Assay	Outcome	No of studies	Sensitivity	Specificity	Test positivity	PPV
SA	CIN2+	23	0.85 (0.80 to 0.89)*	0.96 (0.93 to 0.98)*	1.14 (1.05 to 1.24)	0.71 (0.62 to 0.82)
	CIN3+	9	0.86 (0.76 to 0.98)*	0.97 (0.95 to 0.99)*		0.65 (0.57 to 0.78)
PCR	CIN2+	17	0.99 (0.97 to 1.02)	0.98 (0.97 to 0.99)*	1.00 (0.94 to 1.06)	0.97 (0.90 to 1.04)
	CIN3+	8	0.99 (0.96 to 1.02)	0.98 (0.97 to 0.99)*		0.90 (0.78 to 1.05)

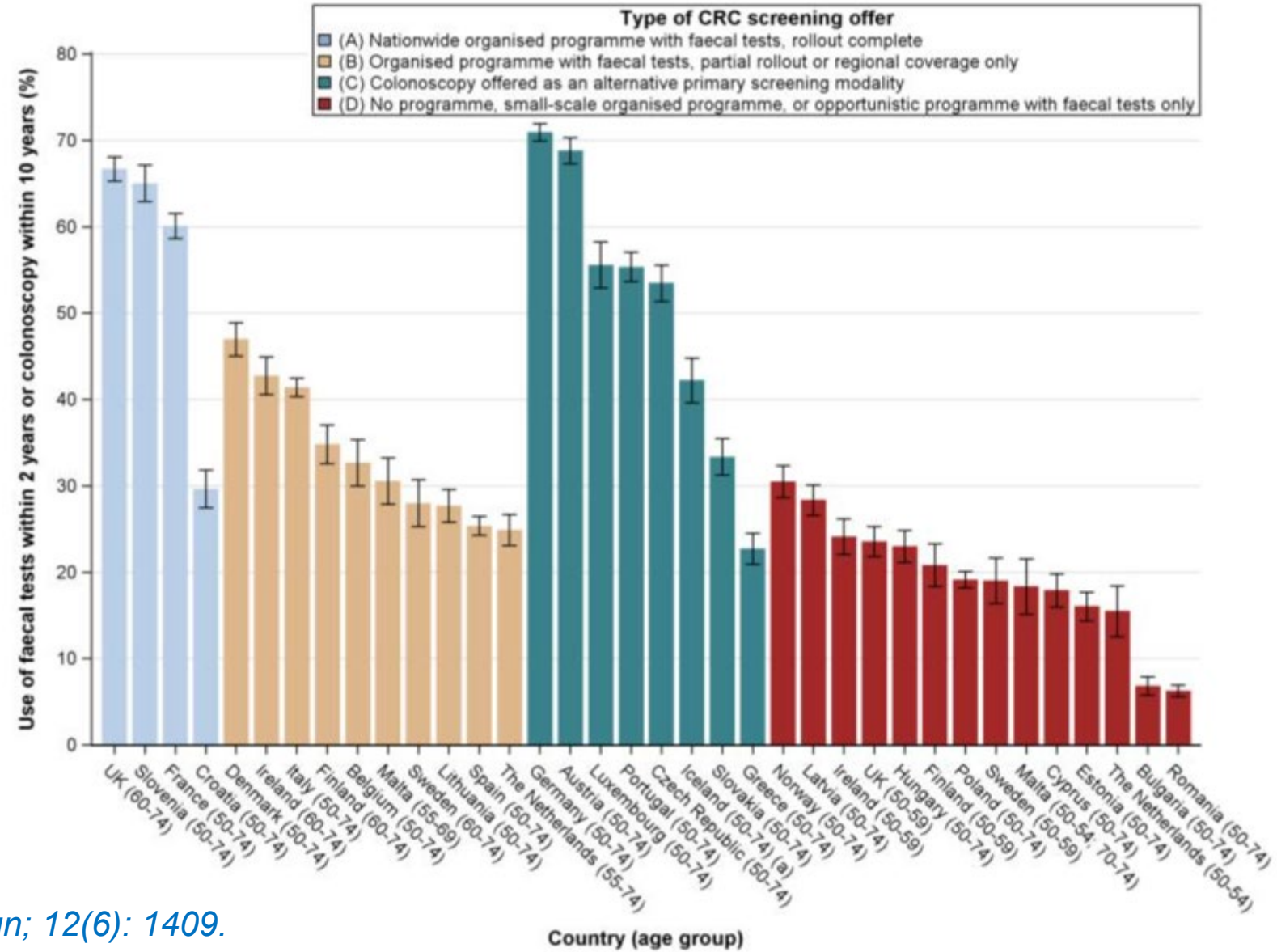
PPV=positive predictive value; CIN2+=cervical intraepithelial neoplasia of grade 2 or worse; CIN3+=cervical intraepithelial neoplasia of grade 3 or worse.
*Statistically significantly different from unity.

Mailing self sampling kits to women's home address is more effective in reaching populations that are under-screened compared with sending invitation or reminder letters for clinician sampling

doi: 10.1136/bmj.k4823 | BMJ 2018;363:k4823

CRC Screening in Europe – Prevalence of faecal test use within previous 2 yrs or colonoscopy use within previous 10 yrs among population aged 50–74 years





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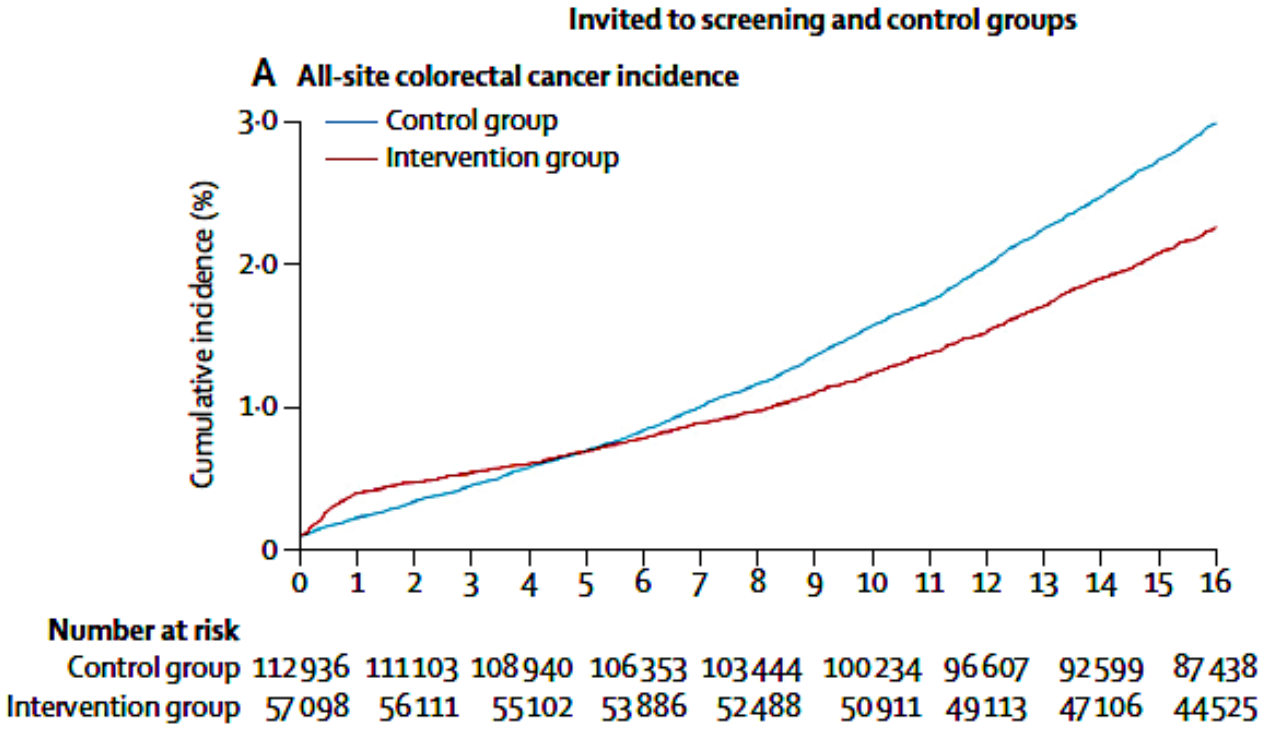
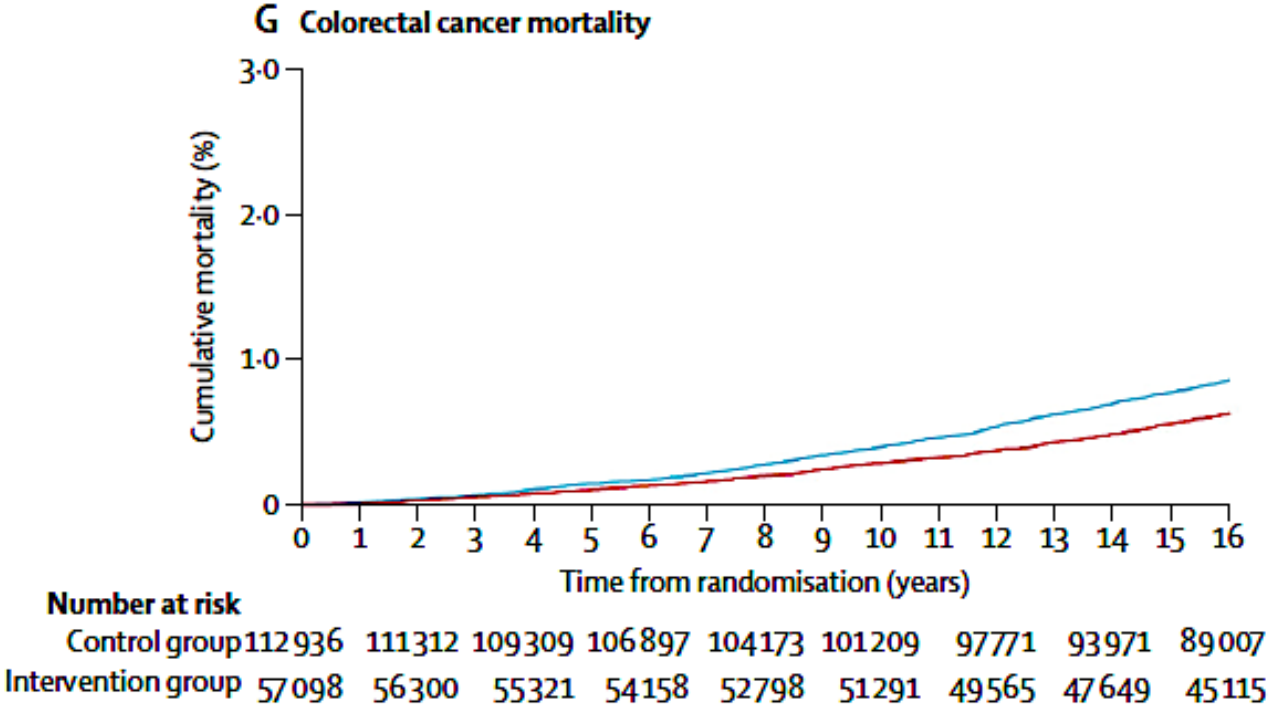
Cancers (Basel). 2020 Jun; 12(6): 1409.

Long term effects of once-only flexible sigmoidoscopy screening after 17 years of follow-up: the UK RCT

26% reduced risk; p<0.0001



30% reduced risk; p<0.0001)



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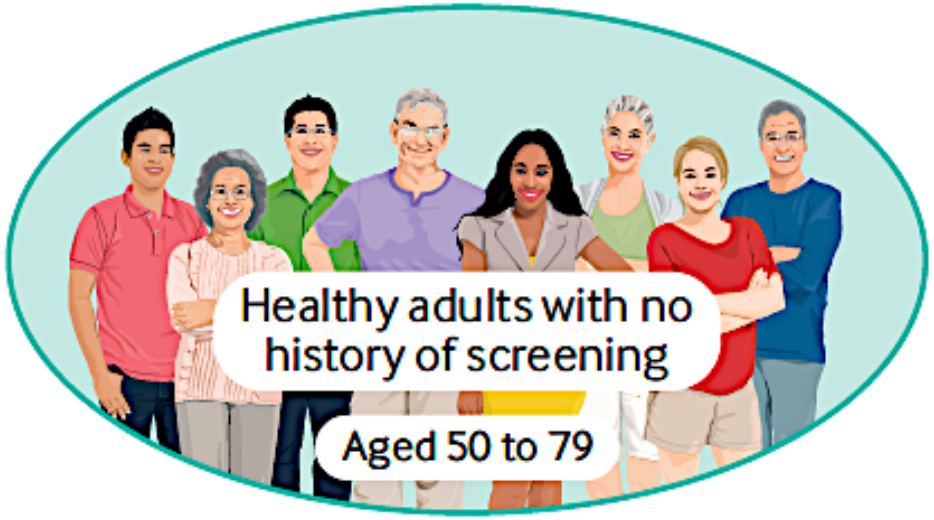
Lancet http://dx.doi.org/10.1016/S0140-6736(17)30396-3

Risk-stratification for CRC Screening

Population



Estimating risk

Understanding a person's risk of cancer can help to determine the benefits and harms of different screening tests for their individual situation.

We suggest using a tool such as the QCancer® calculator to estimate the risk of colorectal cancer for each person in the next 15 years. This calculates risk, based on:

Age | Sex | Ethnicity | BMI | Smoking status | Medical and family history

Link to QCancer® calculator qcancer.org/15yr/colorectal/

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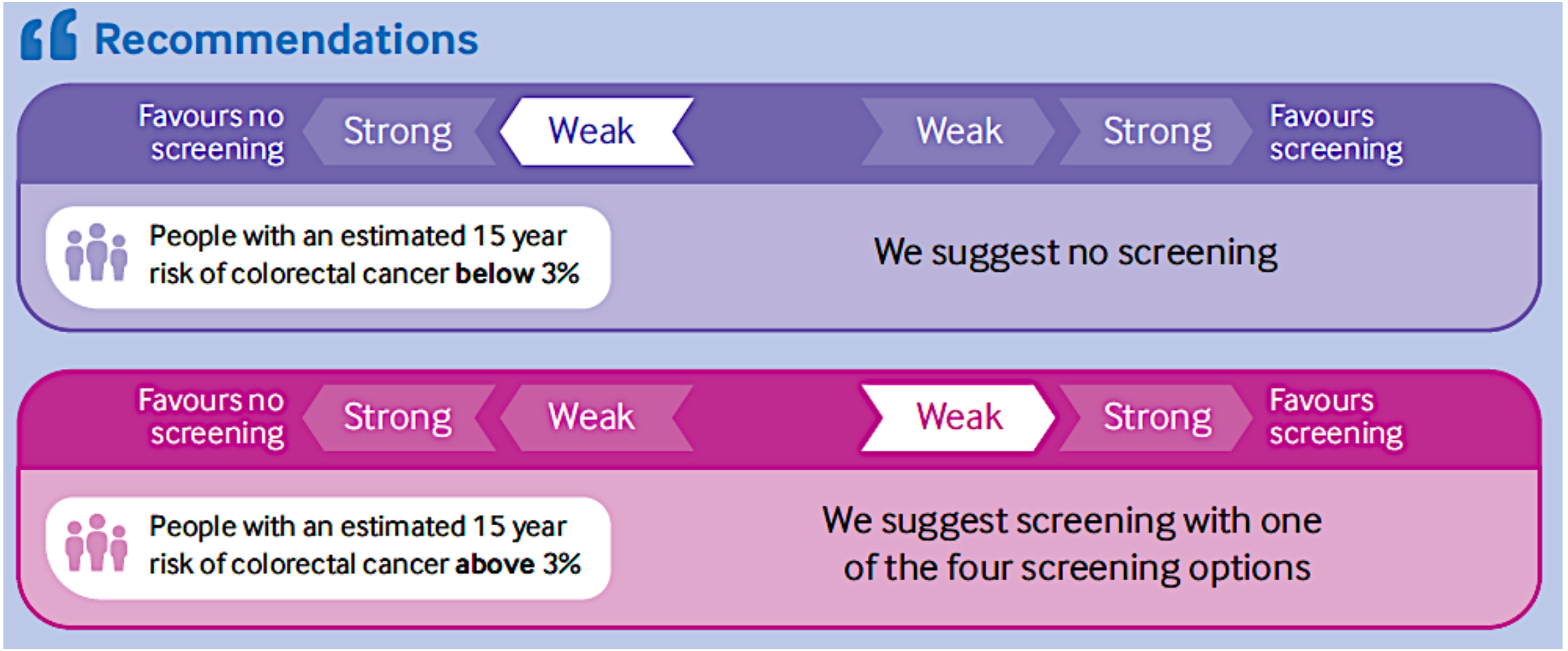
BMJ 2019;367:l5515 doi: 10.1136/bmj.l5515

Risk-stratification for CRC Screening



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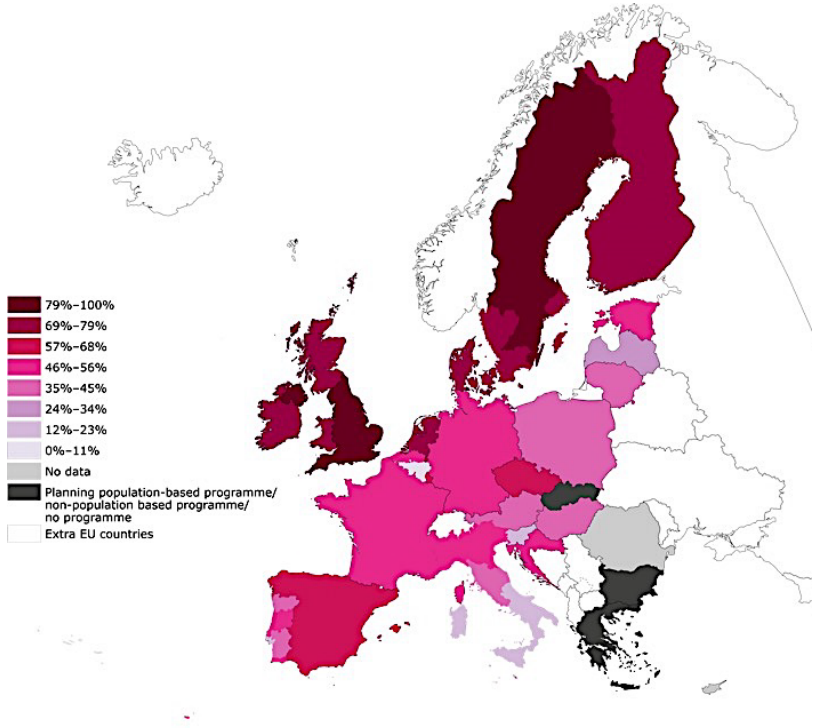
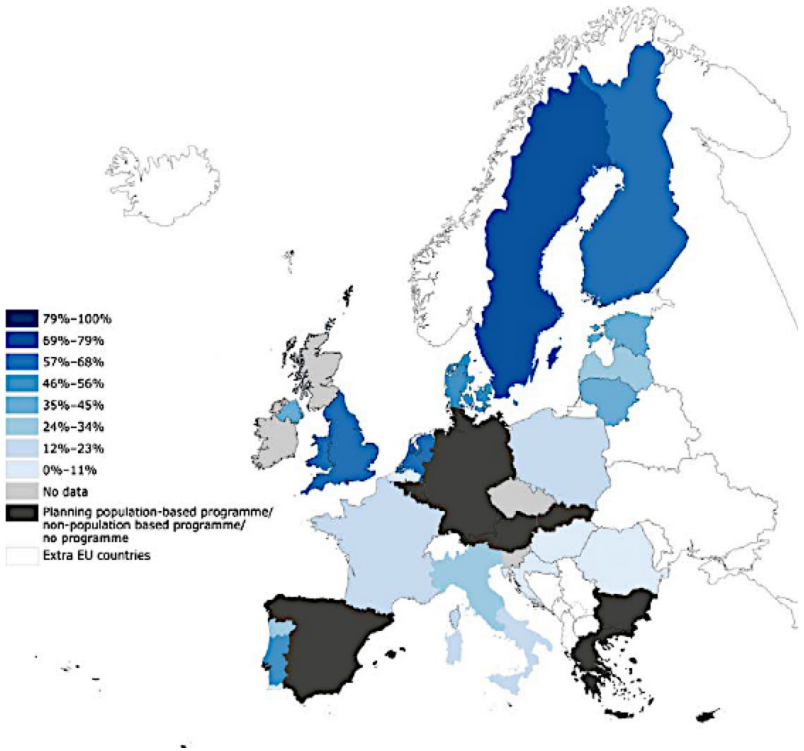
BMJ 2019;367:l5515 *doi: 10.1136/bmj.l5515*

Cancer Screening in the EU – Exam Coverage in 2013/14



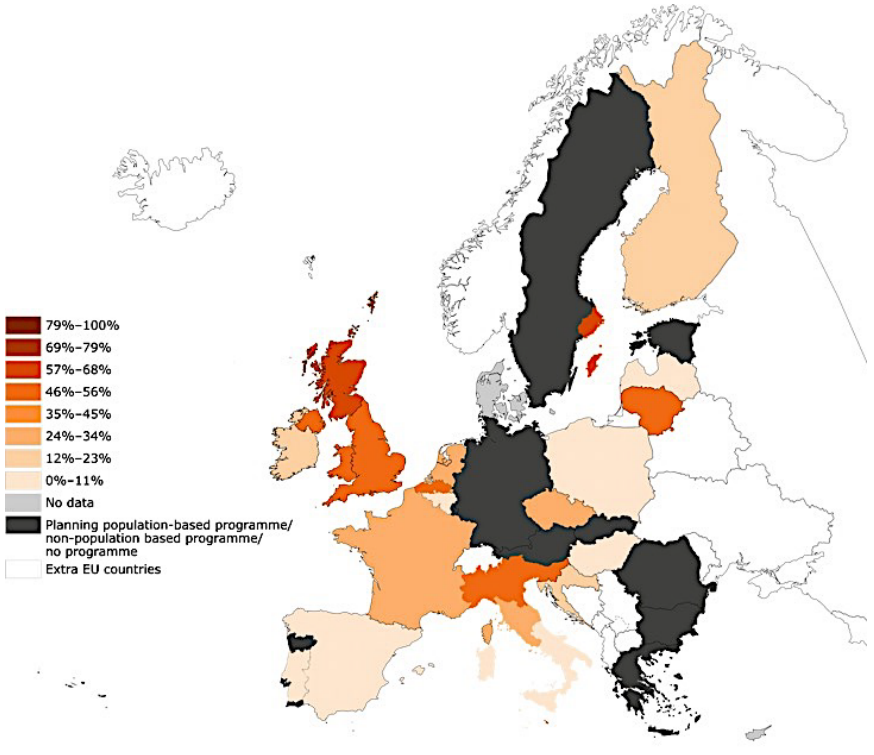
Breast ca screening (50-69 y)

Average: 49%



Cervix ca screening (program age)

Average: 30%



CRC screening (program age)

Average: 14%

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https://screening.iarc.fr/EUreport.php

Population-based programmes in the EU- Quality of data collected to evaluate performance

	Breast cancer screening	Cervical cancer screening	CRC screening
No. of MS with Pop-based programmes	**25**	**22**	**23**
No. (%) of MS having a screening registry linked to cancer registry	**20 (80%)**	**17 (77%)**	**15 (65%)**
No. (%) of MS having further assessment results >90% complete	**15 (60%)**	**10 (45%)**	**13 (56%)**

https://screening.iarc.fr/EUreport.php

efpia
European Federation of Pharmaceutical Industries and Associations

The principles of a European Cancer Dashboard: Cancer policy stakeholders converge

What gets measured gets done

World Health Organization

Key issues that need to be considered while revising the current annex of the European Council Recommendation (2003) on cancer screening

Int J Cancer 2020 Jul 1;147(1):9-13.

Antonio Ponti[1], Partha Basu[2], David Ritchie[3], Ahti Anttila[4], Andre L. Carvalho[2], Carlo Senore[1], Meritxell Mallafré-Larrosa[3],

Cancer site	European Council recommendations 2003 on cancer screening	Issues to be considered in revised recommendation
Cervical cancer	Screening with Pap smear starting at age 20–30 years	Adopt HPV-based cervical cancer screening with appropriate interval and age range
		Adopt appropriate management strategies for screen-positive women
		Define appropriate screening policies following the introduction of HPV vaccine in immunization programs
Breast cancer	Mammography screening in women aged 50–69 years	Mammography screening in women aged 45–74 years
		Wait for more conclusive evidence on the use of tomosynthesis for breast cancer screening
Colorectal cancer	Screening with fecal occult blood test in men and women aged 50–74 years	FIT for age 50–74 once every 2 years or flexible sigmoidoscopy once in a lifetime for colorectal cancer screening
		Wait for more conclusive evidence on screening once in a lifetime with colonoscopy
Lung cancer	No recommendation	Wait for more conclusive evidence on lung cancer screening with LDCT for heavy smokers aged between 55 and 74 years, taking into consideration resource implications, cost-effectiveness and harms
Prostate cancer	No recommendation	Wait for more conclusive evidence on prostate cancer screening taking into consideration harms to benefits ratio
		Monitor opportunistic testing

Interr