European Commission

Research and Innovation

The **Scientific Advice Mechanism**

How the **Scientific Advice Mechanism (SAM)** works

The Group of Chief Scientific Advisors (GCSA)

SAPEA
Science Advice for Policy by European Academies

Science **A**dvice for Policy by **E**uropean **A**cademies (SAPEA) consortium

A **secretariat** in the European Commission

Three pillars ensure that the advice is based on top science, multidisciplinary and as unbiased as possible

Scientific advice for well-informed policy and better regulation

Transparent and as free from bias as possible

Complementary to other scientific advice bodies in and beyond the EU institutions

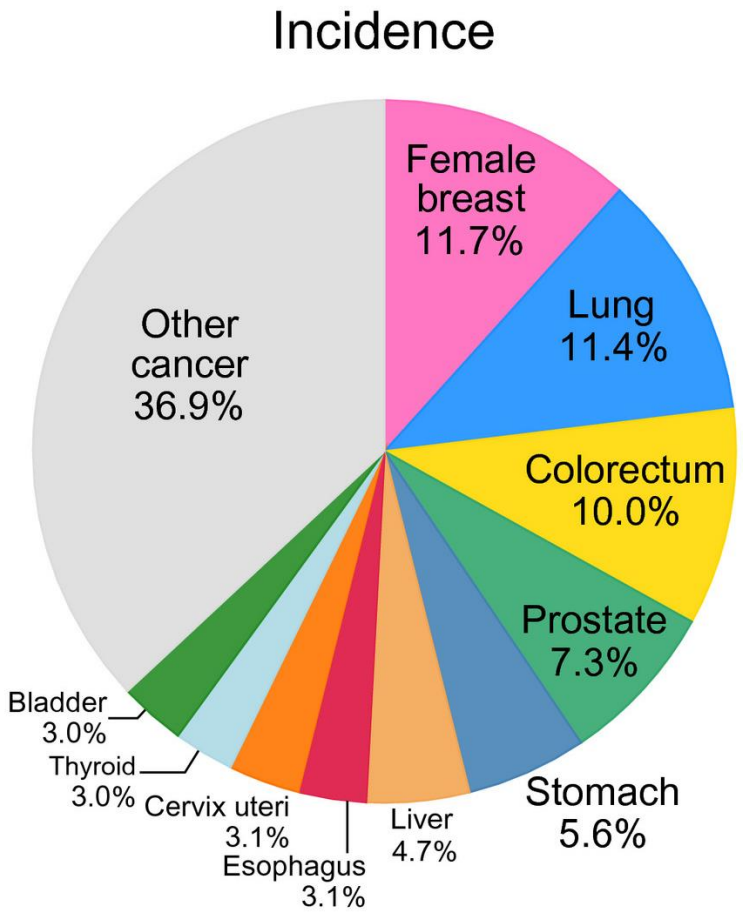
European Commission

Scoping questions to SAM

1 How can cancer screening programmes targeting breast, cervical and colorectal cancers be improved throughout the EU?

2 What is the scientific basis extending such screening programmes to other cancers e.g. lung, prostate and gastric cancers, and ensuring their feasibility throughout the EU?

3 Which are the main scientific elements to consider, and best practices to promote, for optimising risk-based cancer screening and early diagnosis throughout the EU?



Evidence gathering and synthesis

Scoping paper

May ‘21

Sept

Oct

Nov

Three SAPEA workshops

Sounding board

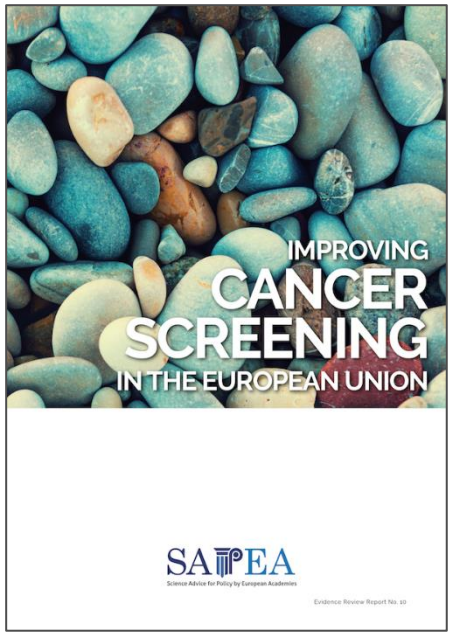
Jan ‘22

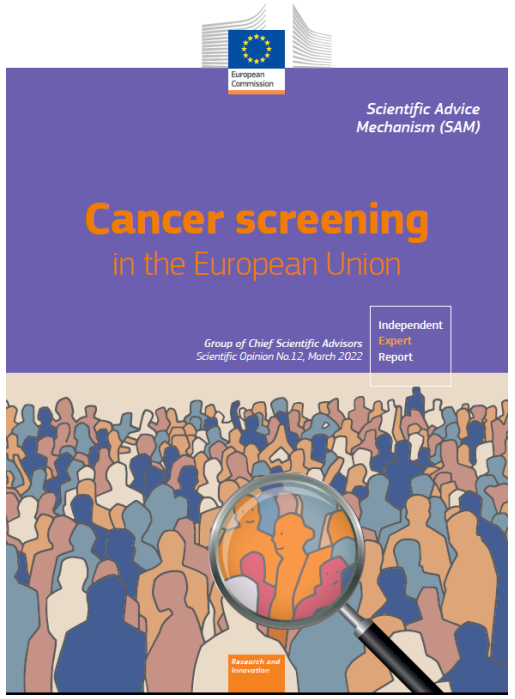
Stakeholder

Jan ‘22

2 March ‘22

publication of the SAPEA report and Scientific Opinion





SAPEA brief summary on evidence presented in the 3 Cancer Screening Workshops

Working Group Chair, University of Cambridge
Working Group Co-Chair, Erasmus MC, Rotterdam

SAPEA
Science Advice for Policy by European Academies

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement 737432.

Methodology

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

Evidence was explored in 3 workshops and each addressed a question raised in the scoping paper:

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?

Workshop 1

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 cancer types should be kept under consideration for the future.

Workshop 1: 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

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

Workshop 1: 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) 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

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.

Workshop 1: 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

Workshop 1: 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

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.

Workshop 2: 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 consider introducing screening at 45 years
- Modelling suggests more risk adapted screening could improve outcomes (high and low risk) and be cost-effective. Randomised trials are underway to test this.
- Trial evidence supports supplemental regimens for high-risk women could include MRI for women with dense breasts

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

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

Workshop 2: 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

Workshop 2: 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
- HPV testing is changing the paradigm
- 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
- ***We have an unprecedented opportunity to eliminate cervical cancer***
- 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

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 bottle-necks 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

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

Recommendation 1: Improve existing screening programmes for cervical, colorectal, and breast cancer

1.1 Improve the participation of citizens in existing cancer screening programmes by **making access to screening easy** (e.g. through self-sampling, home-based testing), by providing information through decision-making aids and through shared decision-making between citizens and clinicians.

1.2 **Ensure that best practices and standards are developed and applied** in screening, along with staff training and continuous monitoring and evaluation for quality assurance.

1.3 Extend **breast cancer screening for women below the age of 50** with mammography or digital breast tomosynthesis and for women with dense breasts with magnetic resonance imaging (MRI).

1.4 For cervical cancer, **prioritise screening by testing for human papilloma virus (HPV)** and support its eradication through the uptake of vaccination against HPV below 15 years of age.

1.5 For colorectal cancer, **use faecal immunochemical testing (FIT)** as the preferred triage test for referring individuals for follow-up colonoscopy.

Recommendation 2: Extend population-screening programmes to additional cancers

2.1 **Extend screening programmes to lung cancer using low-dose computed tomography** for current and ex-smokers, particularly in the light of the high numbers of deaths caused by this disease and the strength of the evidence.

2.2 **Extend screening programmes to prostate specific antigen (PSA)-based prostate cancer screening**, in combination with additional MRI scanning as a follow-up test, as there is good evidence that screening with PSA testing can reduce deaths from prostate cancer.

2.3 For gastric cancer, population-based **screen and treat programmes for *Helicobacter pylori*** are only recommended in regions with intermediate to high gastric cancer incidence.

2.4 At present, neither the experts nor the literature review finds scientific grounds for recommending population-based endoscopic screening for oesophageal cancer and ultrasound and CA125 screening for ovarian cancer.

Recommendation 3: Take advantage of the rapidly developing science and technology to optimise early diagnosis and risk-based cancer screening

3.1 Develop a system of "**living guidelines**" that can be rapidly modified and updated in response to scientific findings.

3.2 **Further develop and implement risk-stratified screening** in order to improve the harm-benefit ratio of screening programmes.

3.3 Ensure **preparedness for the introduction of new screening methods**, in particular for less invasive and blood-based cancer screening where large-scale clinical trials are expected to yield results for multiple cancer screenings in the coming years.

3.4 Support the establishment of **biobanks** appropriate for biomarker-based cancer screening research.

3.5 Support **the harmonisation of protocols and quality assurance** within and between countries