

# Understanding surrogate outcomes in cancer screening trials: implications for screening policy and practice

Cancer Research UK Early  
Diagnosis Event Series

**Wednesday 17 June 2026**

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# Acknowledgements

We are grateful for the contribution of speakers and participants to the insight session held on Wednesday 17 June 2026.

## Chair and speakers

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# Executive summary

On 17 June 2026, Cancer Research UK convened a session for health system leaders and policymakers to raise awareness of the UK National Screening Committee's (UK NSC) newly published **position statement on surrogate outcomes in cancer screening trials**. The event explored the implications for future screening policy, evidence generation and implementation as new technologies emerge.

A central theme was balancing the desire to accelerate the adoption of promising screening technologies with the need for robust evidence demonstrating that screening delivers more benefit than harm. While cancer-specific mortality remains the gold-standard outcome for evaluating screening programmes, surrogate outcomes such as stage at diagnosis, tumour characteristics and biomarkers may provide earlier indications of effectiveness. However, current evidence is insufficient for surrogate outcomes to replace mortality in determining the overall benefit of new screening programmes.

Discussions highlighted that the relationship between surrogate outcomes and mortality varies by cancer type. Evidence is strongest in cancers such as lung, bowel and breast, but reductions in late-stage disease do not consistently translate into lower mortality across all cancers. These challenges are particularly relevant for emerging technologies such as multi-cancer detection (MCD) tests.

Speakers also explored how health systems can make evidence-informed decisions in the face of uncertainty. Discussions highlighted a growing need for adaptive systems and reversible implementation, or 'screening with an exit strategy'. In-service evaluations (ISEs) are a key approach that enable evidence generation in real-world settings while retaining the flexibility to modify or withdraw programmes as evidence evolves.

Key challenges and opportunities identified included improving data infrastructure and access, strengthening coordination across relevant stakeholders, supporting horizon scanning to inform Ministerial planning, maintaining public trust through clear communication and building readiness for future screening innovations.

Overall, the event reinforced the UK NSC's position that surrogate outcomes can inform screening research, evaluation and policy discussions but cannot currently replace mortality as the definitive measure of screening benefit. Continued methodological development, adaptive evaluation approaches and collaboration across the screening ecosystem will be essential to support safe and effective implementation of future screening innovations.

# Introduction

Rapid advancements in science and technology are leading to the development of many novel cancer tests that have the potential to aid earlier cancer detection. These technologies have the potential to optimise existing cancer screening programmes or enable the creation of new programmes. There is a real appetite across the cancer community – from the public to policymakers – to accelerate the adoption of novel technologies. However, a major barrier to optimising screening programmes and enabling the earlier detection of cancer is our inability to rapidly generate the evidence required to underpin decision-making.

It takes many years to generate enough evidence to demonstrate that a screening programme reduces cancer-specific mortality, which is why there's a growing interest in the use of surrogate outcomes to support earlier decision-making. However, the use of surrogate outcomes in screening has been and remains a highly debated topic.

In May 2026, there was an important development in these discussions. The UK

NSC published a **position statement** on surrogate outcomes in cancer screening trials – a statement which may change how new screening programmes are assessed, recommended, and implemented. In summary, the UK NSC's position is that surrogate outcomes should not replace cancer-specific mortality, but they recognise their potential and provide recommendations to test, implement and assess the feasibility of new outcomes. Policymakers and health system leaders need to understand what the statement means for future decisions, as new screening technology emerges.

Cancer Research UK continues to play a role in convening policymakers, health system leaders, researchers and other stakeholders to build a shared understanding of the evolving cancer screening landscape from evaluation to policy implications. The event on 17 June was organised to provide an overview of the UK NSC's position on surrogate outcomes and explore the implications for health system leaders and policymakers. This included discussions on approaches to evaluation in live services.



# Summary of presentations and reflections from speakers

## Part 1: Overview of UK NSC position statement

### The UK National Screening Committee (UK NSC): role and purpose

**Professor Anne Mackie** outlined the UK NSC's role as an independent scientific advisory body. It provides evidence-based recommendations on screening to the four Chief Medical Officers (CMOs) in the UK and operates outside of direct government influence. The UK NSC is a transparent organisation: they publish outputs publicly and have mechanisms in place to respond to stakeholder queries. The UK NSC follows a structured process to develop recommendations on whether or

not to implement screening, beginning with open calls for topics, followed by rapid and full evidence reviews, which may include systematic reviews and modelling. Throughout this process, the committee seeks to engage expert stakeholders.

Screening programmes are resource-intensive public health interventions. Therefore, they need to demonstrate a justifiable use of limited healthcare resources in addition to clear health benefits.



# Surrogate outcomes: UK NSC position and current evidence

**Surrogate outcomes can inform discussions and evaluations of new screening programmes, but they cannot yet replace mortality as the definitive trial outcome for benefit.**

**Dr Sarah Batson** provided an overview of existing evidence for surrogate outcomes in screening, the UK NSC's position statement on **surrogate outcomes** and the evidence required for **MCD tests**.

## The case for surrogate outcomes

Surrogate outcomes can enable earlier assessment of screening interventions, allowing trials to be smaller and faster. The value of surrogate outcomes depends on whether they reliably predict the outcome of ultimate interest – target cancer-specific mortality. Surrogate outcomes such as stage at diagnosis, tumour characteristics, and biomarkers are only meaningful if changes in these measures translate into real reductions in mortality for the specific cancer under investigation.

## Challenges in using stage-based surrogate outcomes

Screening can influence outcomes in multiple ways, some beneficial and others potentially harmful, including overdiagnosis. Stage-based measures are currently the most practical surrogates in screening but have important limitations. For example, staging is typically recorded at diagnosis and does not give information on the potential rate of progression. This is an important limitation because cancers diagnosed at the same stage can have different biology and prognoses. A shift

towards earlier-stage diagnosis may therefore not necessarily translate into reductions in advanced disease or mortality if the additional cancers detected are slow-growing or indolent tumours that would never have caused harm.

Furthermore, evidence suggests that the relationship between stage shift and mortality reduction varies by cancer type. There are strong associations between stage and survival in cancers such as lung cancer, but there are weaker or no associations in others, including liver cancer. Therefore, where prognosis remains poor regardless of stage at diagnosis, screening may reduce the incidence of late-stage disease without translating into reductions in mortality. Current evidence suggests that a shift from stage 4 to an earlier stage may not be an optimal measure.

While a reduction in late-stage disease is encouraging, it is not sufficient on its own to demonstrate benefit, particularly as definitions of “late stage” can vary between cancer types and reductions do not always lead to improved outcomes. As noted in the UK NSC position statement on the evidence required for MCD tests, these considerations are particularly important. While reductions in late-stage disease may be observed when evaluating MCD tests, this may not translate into lower mortality. MCD tests may preferentially detect aggressive or micro-metastatic cancers, weakening the link between stage shift and mortality reduction.

## Principles for the use of surrogate outcomes

Considering the above, surrogate outcomes cannot yet reliably replace cancer-specific mortality as the gold-standard measure of effectiveness of new screening programmes.

There is a need for more adaptive approaches to screening implementation, such as phased or reversible implementation models that allow programmes to be modified, expanded or withdrawn as evidence emerges. These approaches could also provide opportunities to assess and validate candidate surrogate outcomes in parallel with implementation, while long-term follow-up continues to confirm impacts on mortality and the overall balance of benefits and harms.

## Key messages from the position statement

- ✓ Interest is growing in surrogate outcomes in cancer screening as they can provide data to inform decisions before mortality outcomes become available and require smaller less expensive trials.
- ✓ We lack reliable screening-specific methods and sufficient data to judge whether surrogate outcomes can replace mortality as the primary outcome in trials of new cancer screening programmes.
- ✓ Surrogate outcomes can inform discussions and evaluations of new screening programmes as part of the standard multicriteria considerations assessments of benefits and harms. They cannot yet replace mortality as the definitive outcome for benefit.
- ✓ If a randomised controlled trial shows a significant reduction in late-stage disease, and mortality meaningfully differs by stage, this may be sufficient to initiate supporting research and start building implementation infrastructure while awaiting longer term mortality data.
- ✓ Methodological advances, together with adaptive and reversible implementation strategies, may enable earlier evidence informed decision making while ensuring that screening delivers net benefit.

# Part 2: Reflections for health systems and policy makers

**Future approaches to screening need to have clear thresholds for the adoption and progression of appropriate in-service evaluations (ISEs), given their significant system-wide implications.**

**Dr Tasmin Sommerfield** offered reflections from a Scottish health system perspective on the UK NSC surrogate outcomes position statement and on the implications of a potential increase in UK NSC ISE recommendations. Tasmin highlighted that effective screening consists of a whole pathway, from eligible cohort identification right through to referral for assessment and treatment. Delivery of the actual screening test is simply one component in this pathway. This means that the introduction of a new screening programme, even on a purely evaluative basis, has a long lead in time with significant implications for infrastructure and resources.

Delivering a new screening programme requires investment in IT systems, specialised equipment, workforce and diagnostics. Therefore, strong business cases are required to ensure optimal use of limited health system resources. Programmes fully endorsed by the UK NSC have a clear rationale for implementation, while those that still have evidence gaps and are being introduced on a time-limited, in-service evaluation basis face greater challenges.

Implementation timelines are often long and complex, particularly due to IT constraints, and challenges can vary across different parts of the NHS. It's becoming increasingly difficult

to identify eligible populations as screening moves beyond simple age/sex-based criteria towards more targeted approaches based on behaviours and/or genetics, which require more advanced data collection and digital recording systems.

There is undoubtedly value in the ISE process as it generates additional evidence in a real-world setting and accelerates the full implementation process once UK NSC formally recommends the new screening programme. However, if the evaluation shows that the proposed new programme is not effective then it needs to be withdrawn. This brings challenges in managing expectations among the eligible population, health professionals, the media, the public, and policymakers – particularly given resistance to withdrawing or changing services.

**Professor Sir Mike Richards** echoed key takeaways from the presentations and reflections, including the valuable role of UK NSC and how current evidence highlights important gaps in interpreting stage shift as an outcome. While reversible implementation offers a way to act and make progress in the face of emerging evidence, it must be undertaken cautiously, with careful consideration of the risks and uncertainties involved – a segue into the next part of the event.

# Part 3: When evidence evolves: reversible implementation and the role of in-service evaluation

**Reversible implementation, including ISEs, enables evidence generation within real-world screening programmes when there is uncertainty about the potential benefits and harms. As a tool for informing screening policy, successful ISEs depend on strong partnerships, robust evaluation, and a clear focus on addressing evidence gaps relevant to future decision-making.**

## **‘Screening with an exit-strategy’**

**Anne** and **Dr Lisa Douet** highlighted the growing role of reversible implementation, or ‘screening with an exit-strategy’. This represents a shift from the traditional approach of waiting for definitive evidence before introducing a screening intervention. It enables evidence to be generated within real-world services while retaining the flexibility to modify or discontinue programmes if emerging evidence shows that benefits do not outweigh harms. This is particularly important given that some screening programmes have been shown to cause more harm than benefit (e.g. neuroblastoma screening).

## **The role of ISEs**

ISEs are a key mechanism for reversible implementation. They are designed to address evidence gaps that can only be answered by evaluating interventions within a live screening programme. Unlike pilots, ISEs are explicitly evaluative, with a clear understanding from the outset that programmes may be adapted or stopped based on the findings. Typically, ISEs are introduced in selected areas and compared with areas where the intervention has not been implemented. By evaluating the entire screening pathway within routine services, they provide valuable evidence on

real-world delivery, feasibility, and operational impacts that may not be captured in traditional randomised controlled trials.



## Characteristics of successful ISEs

- ✓ Clearly defined, policy-relevant research questions that address specific evidence gaps.
- ✓ Robust and adequately powered study designs capable of generating reliable evidence.
- ✓ Independently evaluated, often delivered through NIHR-funded academic partners.
- ✓ Strong partnership between the UK NSC, NHS and NIHR throughout design and delivery.
- ✓ Clear positioning as research and evaluation activities to maintain public trust.
- ✓ Transparent communication and management of public expectations, recognising that programmes may change or stop.
- ✓ Potential to inform both policy decisions and programme implementation, including optimal delivery models.



## Delivery challenges and opportunities

ISEs are complex to design and deliver, requiring substantial public investment and careful selection of interventions with the potential to deliver long-term value. Services continue while evidence is collected, enabling the UK NSC to make informed recommendations. If ISEs are conducted more frequently, there may be a requirement for ministerial approval before proceeding, noting their resource intensity. Findings may sometimes demonstrate that benefits are smaller than anticipated (for example, where the positive predictive value is lower than expected) but they can also generate important learnings about how programmes can be delivered most effectively, as seen in lung screening.

## Current and future applications of ISEs

ISEs can support both early decision-making and implementation planning by generating evidence in real-world settings. For example, they have informed decisions in newborn screening for spinal muscular atrophy (SMA) and are being used to evaluate innovations such as AI in breast screening (EDITH) and HPV self-sampling in cervical screening. Looking ahead, both speakers emphasised that reversible implementation and ISEs will play an increasingly important role in assessing emerging technologies where important evidence gaps remain. This includes MCD tests, which have generated considerable interest but require careful consideration of their impact on existing screening programmes, as well as the substantial workforce and service capacity potentially needed. By testing interventions within routine practice, ISEs can provide valuable evidence on effectiveness, delivery, and scalability, helping to inform future screening policy and programme design.

# Key themes across questions and discussion

## The use of surrogate outcomes in cancer screening

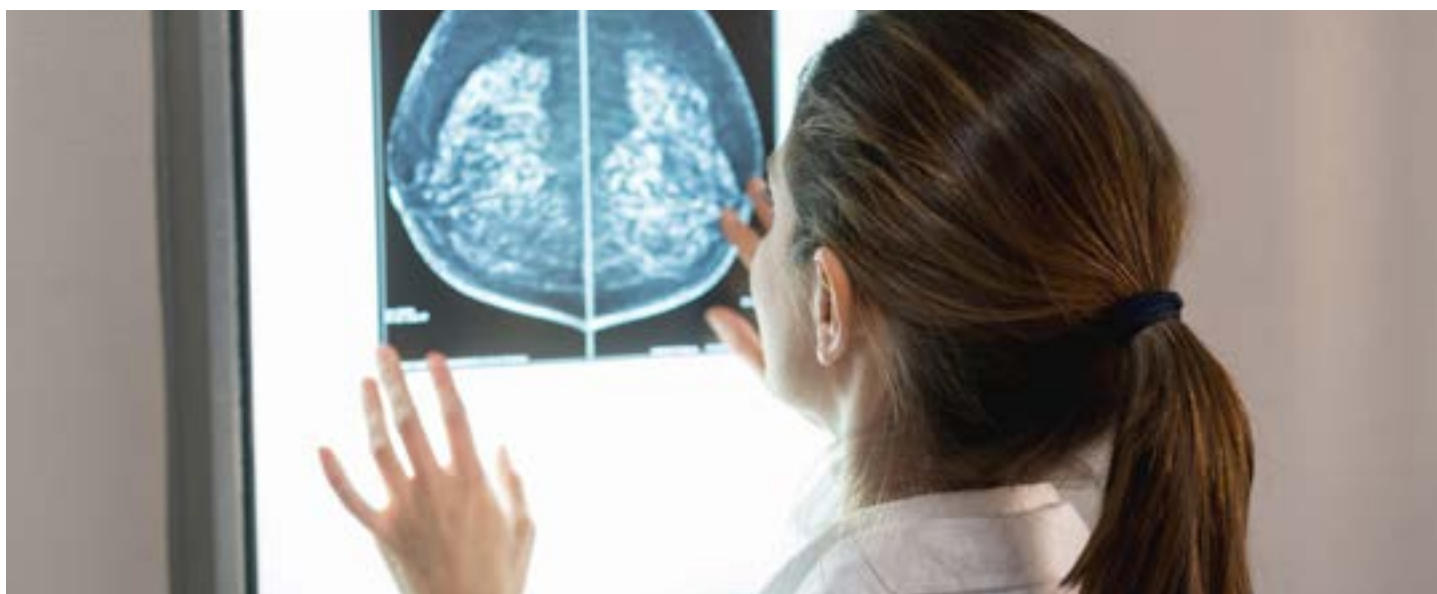
The discussion reinforced that cancer-specific mortality remains the most appropriate outcome for most screening evaluations. All-cause mortality is often too broad and unlikely to detect the modest effects of screening, particularly given the influence of comorbidities. It's important to note this nuanced distinction – cancer screening programmes should seek to reduce deaths from cancer, rather than 'save lives' from any condition.

Discussion highlighted that the reliability of surrogate outcomes varies significantly by cancer type. Evidence is strongest in cancers such as lung, breast, and bowel, where correlations between stage shift and mortality have been observed. In contrast, cancers such as liver show weaker or inconsistent relationships. Suitability also depends on therapeutic options which evolve over time as treatments improve.

## Considerations for ISEs

There was strong support for ISEs, but acknowledgement that they can be complex, time-consuming, and resource intensive. Suggestions included focusing initial evaluations on a smaller scope before expansion, and ensuring studies remain relevant as evidence evolves. Discussions emphasised the importance of generating real-world learning—particularly on acceptability, behaviour, and delivery.

Participants noted the tension between ensuring robust, inclusive evaluation and keeping pace with rapidly emerging evidence. Suggested approaches included more adaptive and iterative research designs, starting with smaller evaluations that could scale up, and developing flexible research platforms that can evolve over time. There was also recognition of the risk that traditional evaluation timelines may be overtaken by technological change.



## Engagement with the public, policymakers and systems

Maintaining public trust was identified as a major challenge. **Research** has suggested that the public may continue to favour screening even where benefits are limited. Clear communication about benefits and harms is essential, alongside careful handling of changes or withdrawals, informed by research and behavioural science. Trust relies on alignment between robust evidence (UK NSC), effective delivery (NHS), and high-quality research (NIHR/third sector). A question was also raised as to whether there are any lessons from withdrawal of Bowelscope and age extension in managing public trust and confidence.

Participants highlighted the need for a more coordinated, forward-looking approach to horizon scanning to inform policy and system planning. To support informed, timely decision-making, policymakers and Ministers require a “whole system” view of upcoming innovations, including any resource implications which may overlap between programmes and new technologies. The UK NSC actively undertakes horizon scanning to anticipate future developments and has a forward-looking pipeline and workplan. Currently, this is particularly tailored to the needs of the NHS in England where the relationships with the English policymaking system are clearer than

those in Wales, Scotland and Northern Ireland. Screening policy decisions are ultimately devolved, with each of the four UK nations independently determining if and how to implement recommendations. While there is information exchange and collaboration across all nations, this could be improved for Northern Ireland, Scotland, and Wales.

There is a need to actively create momentum through lobbying and external pressure to support innovation in screening and accelerate the shift towards more preventive and predictive approaches. Achieving this will require the development of adaptive platforms and alignment with the right political context, recognising that enabling this broader system change extends beyond the remit of the UK NSC.

## Data improvements required

Significant challenges were raised around data availability, access, and fragmentation within NHS systems, as well as variation across the UK. There is a need for more integrated, system-wide data platforms that capture the full screening pathway and support both service delivery, monitoring and research. Improved national datasets (e.g. staging data) were noted as an important step forward, particularly for nations where this is not yet fully available. It was noted that the new Health Data Research Service should consider this going forwards.

# Key next steps

## Next steps from the UK NSC position statement

- ✓ Conduct research to characterise, quantify and validate the relationship between different surrogate outcomes and mortality.
- ✓ UK NSC and NIHR to develop methods to assess when surrogates are sufficient, using metrics that can be applied in decision-making.
- ✓ Evaluate the acceptability, accuracy, and generalisability of surrogate outcomes across different population subgroups.
- ✓ Develop adaptive or reversible implementation approaches (e.g. phased implementation with clear stop/go/modification criteria).
- ✓ UK NSC and NIHR to determine whether decision-analytic modelling of overall effectiveness and cost-effectiveness can assist interpretation of surrogate outcomes in screening.

## Next steps identified through discussion

Discussions following presentations identified several actions for stakeholders across the screening ecosystem to consider:

- ✓ **Strengthen and expand the use of ISEs** to generate real-world evidence, with clear criteria for when they are appropriate and how they should be designed, funded, and implemented.
- ✓ **Adopt more agile and adaptive evaluation approaches with clear thresholds.** The system should move towards more flexible, adaptive platforms to keep pace with rapidly evolving technologies such as AI and MCD tests.
- ✓ **Improve data infrastructure and access.** Investment is needed in integrated, system-wide data platforms that capture the full screening pathway and support both service delivery and research.
- ✓ **Optimise coordination across the screening ecosystem.** Further alignment is needed between the UK NSC, NHS, NIHR, policymakers, third sector and researchers in areas such as horizon scanning, research prioritisation, and data sharing.

- ✓ **Support forward planning and horizon scanning for policymakers.** Policymakers across all UK nations should be supported with a clear view of upcoming screening innovations and their resource implications. This needs strengthening in Northern Ireland, Scotland and Wales in particular.
- ✓ **Prioritise communication and public engagement to maintain public trust.** Stronger use of behavioural science and communication strategies is needed to clearly convey the benefits and harms of screening, and manage expectations, especially when programmes are modified or withdrawn.
- ✓ **Build system readiness for preventive and predictive screening approaches.** There is a need to create momentum for innovation, including supporting a shift towards prevention and prediction, underpinned by political alignment and system leadership.

If you have any questions or wish to discuss this topic further, please email the Strategic Evidence team via [SEInbox@cancer.org.uk](mailto:SEInbox@cancer.org.uk).

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