NCRI Screening, Prevention & Early Diagnosis (SPED) Group Priorities 2023 – 2026

NCRI Partners

NCRI is a UK-wide partnership between research funders working together to maximise the value and benefits of cancer research for the benefit of patients and the public. A key strength of NCRI is our broad membership with representation across both charity and government funders as well as across all four nations in the United Kingdom.

Contents

Introduction

The NCRI Groups bring the cancer research community together to develop practice-changing research, from basic to clinical research and across all cancer types, supporting NCRI's strategy. The NCRI SPED Group is a multi-disciplinary community of researchers and consumers focused on developing research to improve outcomes for cancer patients.

Each NCRI Group engages in a prioritisation process to identify the priority areas in its area of research (Appendix A). This process dictates the work of the group as well as providing an assessment of the state of research for the wider research community.

The NCRI SPED Group has identified its research priorities working with members of the research community, NCRI Partners and other funders. Full details of the meetings held can be found in Appendix B and a list of participants can be found in Appendix C.

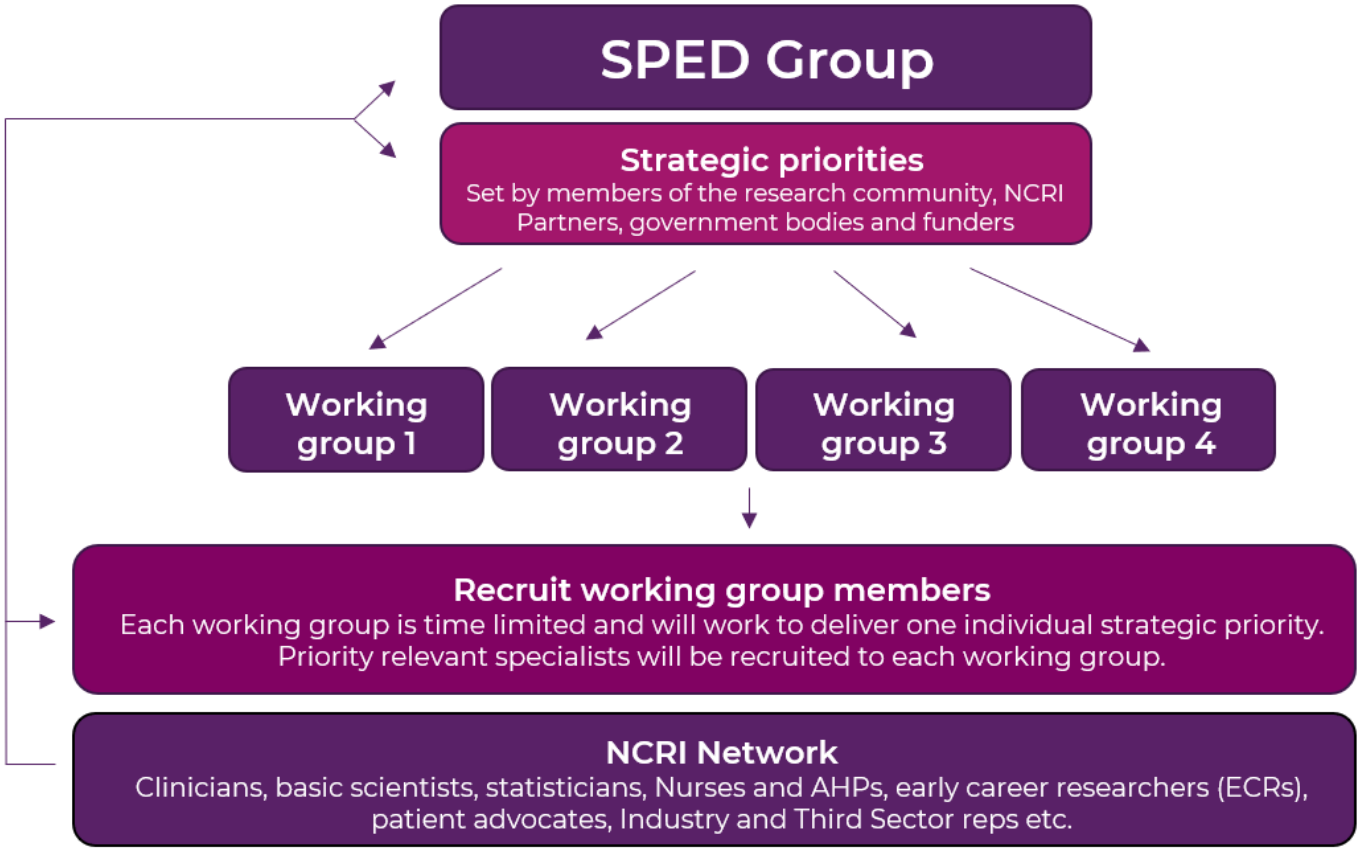
An overview of the areas that the NCRI SPED Group has identified as priorities can be found on pages 6 onwards of this document. Time-limited working groups will address the priorities selected as the first to be addressed. When one working group finishes, capacity will be transferred to address the next priority.

The strategies of NCRI Groups will be refreshed every three years. In addition, the research landscape will continue to be routinely assessed by NCRI to ensure the most pressing questions in the research landscape are addressed over the course of this three-year strategy.

"The NCRI SPED Group has played a key role in stimulating and nurturing early- and mid-career researchers to design and conduct studies in cancer screening, prevention, and early diagnosis. Studies that have been through the SPED Group have addressed important clinical, public health, and patient-derived questions and have impacted on health service delivery. Much of the success stems from the multi-disciplinary and collaborative membership of the group. I hope that his document will serve as a road map to stimulate and drive future research into the prevention and detection of cancer."

Professor Peter Sasieni, Chair of the NCRI SPED Group

NCRI SPED Group structure at a glance



NCRI SPED Group strategic priorities

Strategic area 1: Innovative cancer screening and early detection tests

Priority 1: Technology improvement to support screening programmes

The success of national screening programmes is dependent on the technology used to support the programme. This priority is based on the idea of designing a technology platform for one cancer type to begin with (e.g., breast cancer). This platform would have a modular approach for adding in other data such as vaccination and (other) screening programme data, and interface with other information including data on smoking status and family history.

Priority 2: Implementing non-perfect screening tests for methodologists

For cancer types that lack a standard screening test and national screening programme in the UK, there is a hypothesis that use of "non-perfect" tests could be better than having no screening programme. This priority will involve exploration of this theory, for example for prostate cancer.

Priority 3: Implications for the NHS if there was a pan-cancer screening programme

There is significant interest in understanding how the NHS would manage with a pan-cancer screening programme (using a multi-cancer early detection (MCED) test) and the subsequent impacts (e.g., the various impacts on blood sampling, pathology and GP services). There is desire for national multi-disciplinary forums to convene on this subject (including organisations such as Cancer Research UK, who have interest in this field). There are opportunities for research by a Working Group to consider the various aspects of impact.

Priority 4: Using Multi-Cancer Early Detection (MCED) tests for early diagnosis in people at higher risk, with vague symptoms or genetic predispositions (e.g., Lynch syndrome)

There is interest in knowing whether MCEDs could be used in specific segments of the population such as those who are at higher risk, have vague symptoms or have genetic predispositions such as Lynch syndrome. It is accepted that current MCED tests have been developed to test the wider population, as opposed to specific segments of society – resulting in trade-offs. There is however very little cell-free DNA coming from pre-cancerous lesions.

Different forms of test are needed to identify cancers with high sensitivity. If patients have high genetic predisposition for a particular cancer type, specific cancer early detection tests would be recommended above MCEDs.

However, this priority could focus efforts to find out whether the same assay (one MCED test) could be used for the various segments of society, but with different thresholds for different people (i.e., different symptoms, different cancer type predispositions and different diseases), or looking at changes in biomarkers over time in high-risk individuals.

Priority 5: Patient information related to Multi-Cancer Early Detection (MCED) tests

This priority is focused on risk and evidence communication to members of the public and patients. There is recognition that research into MCEDs has been heavily publicised and tests are now being advertised to the public. Issues include how to provide a clear explanation of the difficulties of interpretation, and communicating that further tests would still be necessary following positive MCED test results.

For this priority, a working group would form for the purpose of qualitative research into educating and protecting the public, have social policy researcher involvement and involvement from those with regulatory experience from other healthcare products.

Priority 6: Increase the uptake of screening (and screening research) for those people willing to participate

There is interest in research to understand how to increase the uptake of screening for those people potentially willing to participate. This working group will inform the community of the number of people willing to participate but not entering into research. Such data could then be used as a benchmark figure to compare screening uptake with. We must note that MCED tests are currently exploring this, and this working group should build on existing evidence.

Priority 7: Applicability of risk models for ethnic minorities for targeted screening

This working group will investigate the applicability of risk models for ethnic minorities in the UK. This will involve risk stratification to encompass different ethnic groups; and reaching underserved populations in terms of geography, educational attainment and acceptability of the screening test being used. As an example focal area, this work could start in lung cancer.

Priority 8: Creating the infrastructure to look at targeted screening programmes

There is great interest in improving the efficiency of cancer screening though risk stratification. Such a risk classifier might be based on demographics, lifestyle and medical records, or it might be based on a polygenic risk score, or on a combination of both approaches. Either way, there is a need to be able to ascertain the basic data to estimate risk in a large study cohort without costly study-specific testing and data acquisition. Work is needed on how to best exploit cohorts (such as Our Future Health) that have already collected such data and to embed trials of targeted screening within them.

Strategic area 2: Enhancing trial methodology in screening, prevention and early diagnosis research

Priority 1: Drugs repurposing for precision prevention

There is ultimate futility at the end of the road for precision prevention if NICE do not recommend drugs or MHRA do not license drugs that could be used to prescribe a repurposed medication for high-risk conditions e.g., aspirin for Lynch syndrome. The aim of this priority is for the group to explore how they could support licencing decisions including the insurance or liability aspect to it.

Notably, the Department of Health and Social Care held a roundtable discussion with Medical Research Council (MRC) and Breast Cancer Now. The group should consider linking in with these organisations and with the multi-agency Medicines Repurposing Programme (hosted by NHS England) to explore this further, not just for cancer prevention but all repurposed drugs.

Priority 2: Optimising sequential interventions for behavioural research

This priority aims to look at improving efficiency of trial designs for sequential interventions i.e. Sequential, Multiple Assignment, Randomised Trial (SMART) in behavioural research for cancers across screening, prevention and early diagnosis.

Priority 3: Literature review of surrogate endpoints

Surrogate endpoints in clinical trials can play a significant role for patient care as it allows results to be measured sooner and therefore has the potential to allow patients to access new treatments earlier. However, there is a lack of research on surrogate endpoints across cancer research. The aim of this priority is to conduct a literature review on surrogate endpoints across several cancers in screening, prevention and early diagnosis (that is complimentary to existing and ongoing reviews) and liaise with a UK funding body to commission a funding call for guidelines on the development, validation, and application of surrogate endpoints.

Priority 4: Evaluate the effectiveness of several Multi-Cancer Early Detection (MCED) tests

Currently there are several MCED tests for cancer available in the UK. The field is progressing rapidly, and assays derived today have greater analytic sensitivity than those developed 5 years ago. There is a challenge of how to compare different assays and how to assess whether a new assay has greater clinical utility than an earlier assay that has been shown to be beneficial in an early randomised controlled trial. A key aim will be to evaluate (or compare) the effectiveness of a few (3-6) MCED tests through a Multi-Arm Multi-Stage (MAMS) trial. Another aim will be to create a living review to track the evolving landscape and to serve as a resource to independent researchers.

Priority 5: Precision prevention for high-risk population

This priority aims to develop a precision prevention study for individuals at high-risk of cancer. Areas to consider include:

- Interventions for patients with an inherited cancer predisposing mutation (e.g., Lynch Syndrome, Li-Fraumeni Syndrome, BRCA1 and BRCA2 mutation carriers).
- Studying cancer vaccines to prevent recurrence in cancer patients with no detectable disease post primary treatment.
- The use of MCED screening in other clinics i.e. diabetes clinic and the identification of other risk factors e.g. strong smoking history, positive MCED test but nothing else picked up through other complementary screening tests.
- How accessible are MCED tests for the under-served patient population
- How to improve the uptake of MCED tests for people who come from an ethnic minority or low socio-economic status backgrounds

Priority 6: Psychological harms of MCED screening

It is known that cancer screening tests can cause anxiety. There is interest in the research community on assessing the acceptability of psychological harms caused by MCED screening tests, for example, from a false positive or negative result. The aim of this priority is to explore the benefits and harms caused by MCED tests. Areas to consider:

- Are recommendations on thresholds of harms needed or should qualitative flexible assessments be developed instead?
- How are MCED tests being presented to patients?
- Could the group compare psychological harm of MCED tests with other screening programmes to see if anxiety levels are higher with MCED test or the same as they are in breast, cervical or bowel screening programmes.

Strategic area 3: How to make the most of national cohorts and data in cancer research

Priority 1: How to engage participants to take part in research involving their data

This priority will focus on how to engage participants in routinely collected data that could be used by researchers. Areas to consider:

- Challenges around perception among participants of how their data will be used i.e. people think their data is being sold to commercial companies.
- How to improve uptake from invitations? Do people open letters? Do they perceive text messaging as a scam? Could NHS invitations come from GPs or through an app?
- Patient perspective - what is acceptable to patients?

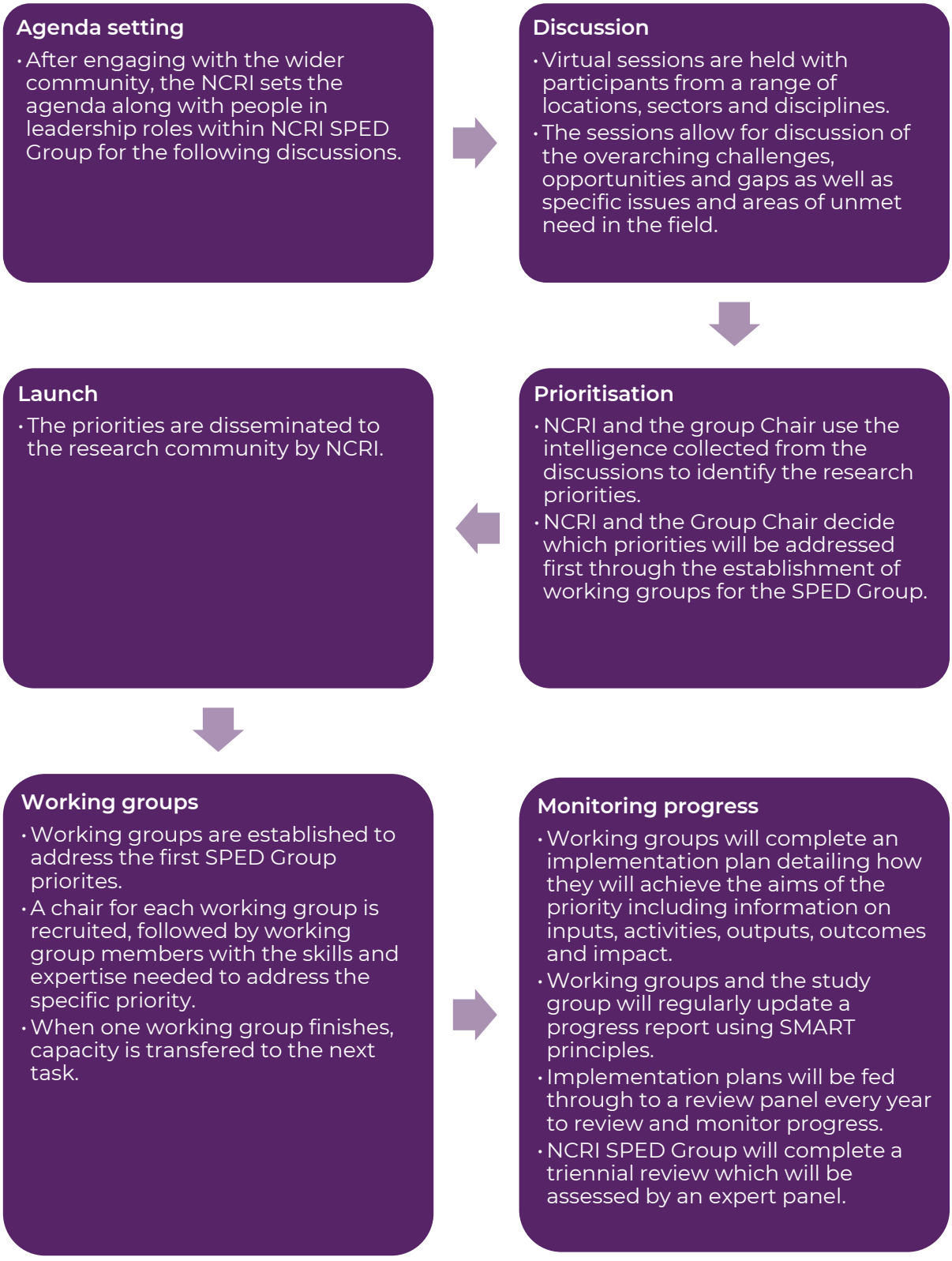
NCRI Cross-cutting priority

Identify barriers resulting in a lack of diversity in clinical trials and propose solutions to improve equality, diversity, and inclusion.

Barriers resulting in a lack of diversity in clinical trials across cancer types has been raised as an issue in many of NCRI's discussions with researchers. For this reason, this priority will be addressed collaboratively in a working group comprising experts from across NCRI Groups. This priority aims to establish the reasons behind a lack of diversity in clinical trials and provide solutions to increase participation of a diverse cohort of patients in future studies. A working group will address the common issues across the board, as well as identifying cancer-type specific barriers, and produce guidelines on the steps to take to improve the inclusion of patients from a range of backgrounds into clinical trials from their inception. More details on this working group will be decided in due course.

Appendix A

NCRI SPED Group priority setting process



Appendix B

NCRI SPED Group strategy sessions 2023

The NCRI SPED strategy sessions, held in February-March 2023, attracted over 80 participants from a range of sectors and disciplines, including NCRI Consumer Forum members, early career researchers and NCRI Partners. The introductory presentations allowed for discussion of the current landscape and the overarching challenges, opportunities, and gaps in research in SPED, whilst the subsequent breakout sessions gave experts the opportunity to exchange ideas on priorities areas of future research in this field, with each group involving researchers from wide ranging disciples encouraging cross-cutting collaboration to meet the most pressing needs in research into SPED today.

Session 1: Innovative cancer screening and early detection tests

Date: 28 February 2023
Chair: Prof Emma Crosbie

Session 2: Enhancing trial methodology in screening, prevention and early diagnosis research

Date: 8 March 2023
Chair: Prof Peter Sasieni

Session 3: How to make the most of national cohorts and data in cancer research

Date: 14 March 2023
Chair: Prof Emma Crosbie

Appendix C

Strategy sessions and NCRI SPED Group contributors

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Advancing Cancer Research Together

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