NCRI Gynaecological 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 Gynaecological Group is a multi-disciplinary community of researchers and consumers focused on developing research to improve outcomes for gynaecological cancer patients. There is a significant need to improve the wellbeing of women living with gynaecological cancers and addressing this will be at the centre of all work of the NCRI Gynaecological Group.

Each NCRI Group engages in a prioritisation process to identify the strategic priorities 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 Gynaecological Group has identified its research priorities working with members of the research community and NCRI Partners. An overview of those who participated in the strategy-setting process can be found in Appendix B.

There are four key areas the NCRI Gynaecological Group has identified as priorities, an overview of which can be seen below with full details on pages 8-11 of this document. The Group will initially focus on the first priority in each strategic area, forming time-limited working groups to address these priorities. When one working group finishes, capacity will be transferred to address the next priority. An overview of the NCRI Gynaecological Group structure can be found on page 5. A key aim of the NCRI Gynecological Group is to develop trials that incorporate clinical and translational endpoints and the Group will ensure this is embedded in all trials resulting from the priorities outlined in this document.

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

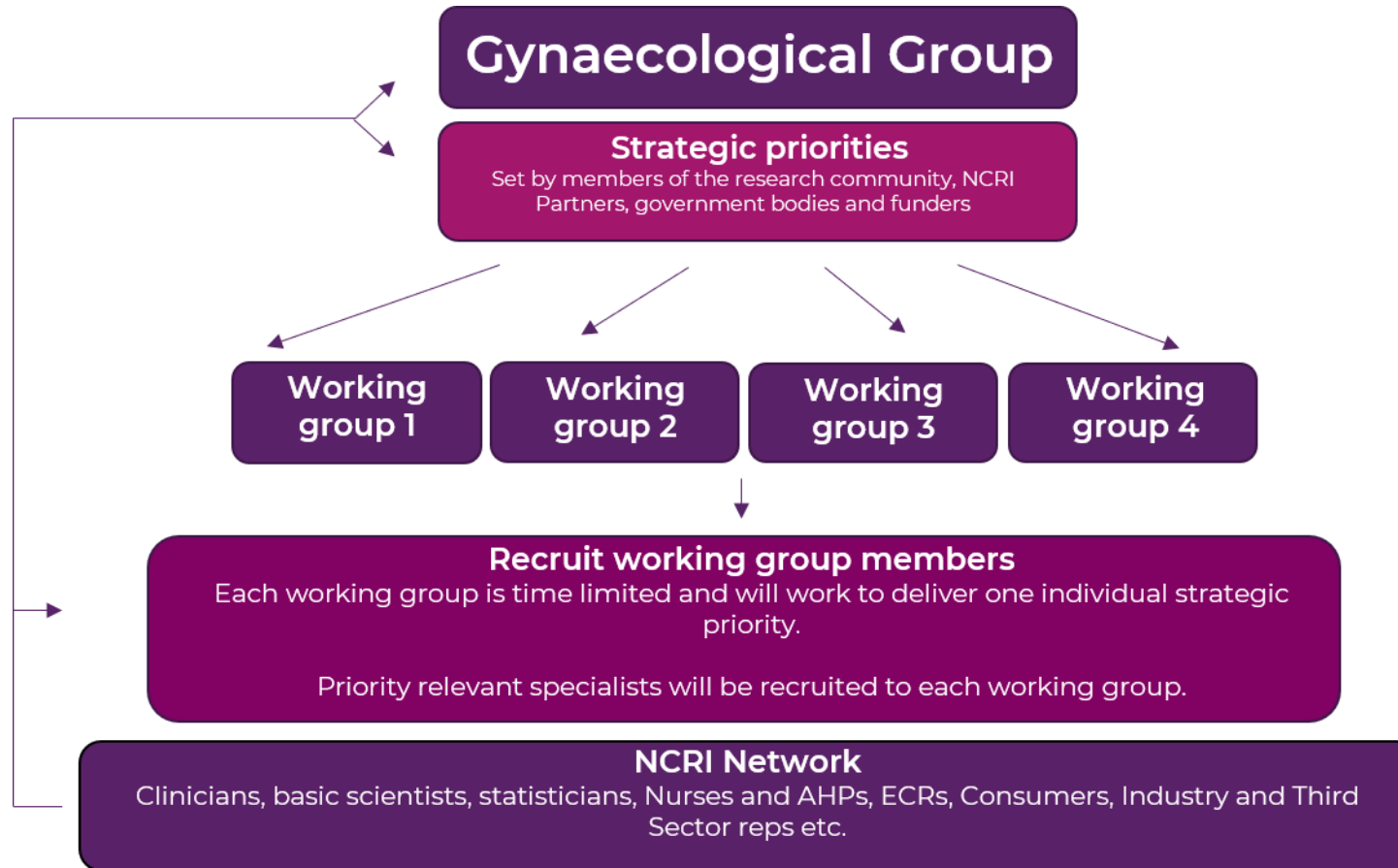## NCRI Gynaecological Group strategic priority areas at a glance

1. Early detection
2. Personalised medicine
3. Rare cancer: vulval cancer
4. Improve wellbeing in women undergoing treatment for gynaecological cancers

"The NCRI Gynaecological group is focused on the clinical and translational issues relating to the early detection and treatment of gynaecological malignancies, encompassing ovarian, endometrial, cervical and vulval cancer. Over the last decade, in collaboration with our international groups and charitable partnerships, we have developed and delivered practice changing trials that have significantly improved gynaecological cancer care. The priorities outlined below address the key challenges the community faces to ensure that we continue to improve outcomes and move towards our goal of tailored/personalised treatment options for women. The new NCRI Network and focused working groups will facilitate these important advances."

Dr Shibani Nicum, Chair of NCRI Gynaecological Group

NCRI Gynaecological Group structure at a glance

Gynaecological Group

Strategic priorities
Set by members of the research community, NCRI Partners, government bodies and funders

Working group 1 | **Working group 2** | **Working group 3** | **Working group 4**

Recruit working group members
Each working group is time limited and will work to deliver one individual strategic priority.

Priority relevant specialists will be recruited to each working group.

NCRI Network
Clinicians, basic scientists, statisticians, Nurses and AHPs, ECRs, Consumers, Industry and Third Sector reps etc.

NCRI Gynaecological Working Groups
Initial working groups in set up

The NCRI Gynaecological Group has identified eight strategic priorities that fall in to four areas of research, full details of which can be found on pages 8-11 of this document. Four time-limited working groups will be set up to address the first priority in each strategic priority area for the NCRI Gynaecological Group, each of which are outlined below. Once one working group reaches completion, capacity will be transferred to the next priority.

Working group 1

Identify the challenges faced in early detection of gynaecological cancers and establish a joint consensus on the future of research into early detection of these cancers in the UK

This priority will address the unique challenges faced in early detection of endometrial, ovarian, vulval and cervical cancers and aim to establish a joint consensus on the future of research into early detection of gynaecological cancers across the UK, as well as outline areas which should be the focus of multidisciplinary research over the coming years. This working group will produce and publish a paper and will consider the following:
- The role of Multi-Cancer Early Detection (MCED) tests in gynaecological cancers diagnosis.
- How machine learning and artificial intelligence can play a role in diagnostics and early detection of gynaecological cancers.
- Novel tests/strategies for improved detection of gynaecological cancers.
- Ways in which uptake of vaccination and screening for cervical cancer could be optimised in diverse socio-economic groups.

Working group 2

Identify effective biomarkers for primary and recurrent ovarian cancer

This priority aims to develop a trial for ovarian cancer. The following areas of need should be considered by the working group to define the area of focus:
- Improving understanding of the tumour microenvironment and role of immunotherapy following the limited benefit to date with immune checkpoint inhibitors.
- Treatment options for patients with poorer outcomes, for example those who are less likely to respond to PARP inhibitors/those with homologous recombination proficient tumours.
- Therapy options for patients who have had prior PARP inhibitor therapy.
- Development of biomarkers to determine who will respond to PARP inhibitor rechallenge.
- Treatments for those that are resistant to/intolerant of platinum-based therapy.

Working group 3

Develop recommendations of standard practice in vulval cancer and explore the potential for development of an observational trial

This working group will build on the findings from the national vulval audit and link with the Royal College of Radiologists (RCR) vulval group to develop a position paper outlining the recommendations of standard practice and areas of need in vulval cancer. This group will then consider the potential for a multicentre observational trial in vulval cancer similar to the atomCAT2 observational trial in anal cancer (a multicentre study of overall survival, locoregional control and distant metastasis in anal cancer utilising distributed learning). The group will engage with national and international groups to ensure collaboration.

Working group 4

Develop recommendations for improving wellbeing of women undergoing treatment for gynaecological cancers

This working group will write a position paper detailing recommendations for improving the wellbeing of women undergoing treatment for gynaecological cancers and define the areas for further development. Key areas to be considered include:

- Elderly/geriatric gynaecological cancer patients
    - Use of Frailty Index to guide treatment decisions.
    - Role of pre-habilitation.
    - Survivorship in elderly cohorts.
- Menopause support
    - The need for improved treatment of menopausal symptoms for patients who have undergone treatment, as highlighted by patient groups and charities.
    - Improved survivorship/mental health after all gynaecological cancers, building on the success of the OvPsych 2 trial (conducted by the NCRI Gynaecological Group) which demonstrated the impact of early psychological support for women with ovarian cancer.

NCRI Gynaecological Group strategic areas in full

Strategic area 1: Early Detection

Earlier detection of cancer is vital to improving overall survival and an integrated multidisciplinary approach is essential to ensure that research is rapidly translated into patient benefit. This strategic area aims to identify the key areas of need and improve the outcomes of gynaecological cancer patients.

Priority 1: Identify the challenges faced in early detection of gynaecological cancers and establish a joint consensus on the future of research into early detection of these cancers in the UK

This priority will address the unique challenges faced in early detection of endometrial, ovarian, vulval and cervical cancers and aim to establish a joint consensus on the future of research into early detection of gynaecological cancers across the UK, as well as outline areas which should be the focus of multidisciplinary research over the coming years. This working group will produce and publish a paper and will consider the following:
- The role of Multi-Cancer Early Detection (MCED) tests in gynaecological cancers diagnosis.
- How machine learning and artificial intelligence can play a role in diagnostics and early detection of gynaecological cancers
- Novel tests/strategies for improved detection of gynaecological cancers.
- Ways in which uptake of vaccination and screening for cervical cancer could be optimised in diverse socio-economic groups.

Priority 2: Develop a protocol/trial for early detection and faster diagnosis of ovarian cancer

Outcomes for women with advanced ovarian cancer remain poor and there is currently no effective screening programme for its detection. This working group will build on the work and outcomes of priority 1 and hold a workshop to brainstorm early detection of ovarian cancer. Following this, the group will aim to develop a pilot feasibility study for the earlier detection and faster diagnosis of ovarian cancer. To achieve the aims of this priority, the group will consider the following:
- Novel biomarkers/tests in early detection.
- Potential of non-invasive screening tools, for example, urine tests.
- Role of MCED tests in diagnostic pathways for faster diagnosis.
- Diversity of participants in any resulting trials.
- The role of Pathology/AI.

Priority 3: Produce practice-changing protocols for treatment of endometrial cancer

Endometrial cancer diagnosed at its earliest stage has a 5-year survival of more than 90% compared to around 15% when the disease is diagnosed at the latest stage. However, there is currently no screening programme available for endometrial cancer. Work on this priority will aim to improve outcomes of endometrial cancer from early diagnosis. Areas of consideration when addressing this priority include:
- Real-world data to inform practice-changing protocols for treatment of endometrial cancer.
- Role of early detection tools/MCED tests.
- Prospective evaluation of outcomes of high-risk patients with Lynch Syndrome.

Strategic area 2: Personalised Medicine

A key aim of the NCRI Gynecological Group is to develop trials that incorporate clinical and translational endpoints to facilitate the development of predictive biomarkers/companion diagnostic tests that can identify those patients who are most likely to benefit and spare others the toxicity of treatment. When developing such tests, the following areas should be considered:

- Study design including window, neoadjuvant trials and umbrella designs.
- Improved understanding of tumour microenvironment.
- Role of combination therapy/multi-modality treatment approach.
- Predictive biomarkers development.
- Use of Imaging endpoints.
- Role of AI.
- Ensure equitable access to clinical trials for diverse social and ethnic groups.
- Consider the role of real-world treatment evaluations/comparisons with phase III trial outcomes.

Priority 1: Identify effective biomarkers for primary and recurrent ovarian cancer

This priority aims to develop a trial as outlined above for ovarian cancer. The following areas of need should be considered by the working group to define the area of focus:
- Improving understanding of the tumour microenvironment and role of immunotherapy following the limited benefit to date with immune checkpoint inhibitors.
- Treatment options for patients with poorer outcomes, for example those who are less likely to respond to PARP inhibitors/those with homologous recombination proficient tumours.
- Therapy options for patients who have had prior PARP inhibitor therapy.
- Development of biomarkers to determine who will respond to PARP inhibitor rechallenge.
- Treatments for those that are resistant to/intolerant of platinum-based therapy.

Priority 2: Identify effective biomarkers for primary and recurrent cervical cancer and develop a trial with translational endpoints

This priority aims to develop a trial that incorporates clinical and translational endpoints developing personalised treatment options. Trials in this area may be undertaken in collaboration with commercial partners due to the current landscape of large investment in research and development of, for example, immunotherapy treatments by pharmaceutical companies. When developing this trial, the following should be considered:
- Combinations of therapy including immune checkpoint inhibition and radiotherapy.
- Improved understanding of tumour microenvironment.

Priority 3: Identify effective biomarkers for primary and recurrent endometrial cancer and develop a trial with translational endpoints

Work on this priority will follow a similar course as priorities 1 and 2 above to develop a trial with translational outputs with a focus on endometrial cancer. When developing this trial, the points listed in the overview to this personalised medicine strategic area should be considered. In the current landscape potential areas of focus could include the following:

- Defining additional biomarkers of response to immunotherapy beyond mismatch repair (MMR) deficiency.
- Combinations of therapy beyond immune checkpoint inhibition and antiangiogenic agents.

Strategic area 3: Rare Cancer: Vulval Cancer

Vulval cancer is a relatively rare disease and historically there have been limited academic/commercial interventional trials conducted. Vulval cancer remains an area of significant need, which this priority will seek to address.

Priority 1: Develop recommendations of standard practice in vulval cancer and explore the potential for development of an observational trial

This working group will build on the findings from the national vulval audit and link with the Royal College of Radiologists (RCR) vulval group to develop a position paper outlining the recommendations of standard practice and areas of need in vulval cancer. This group will then consider the potential for a multicentre observational trial in vulval cancer similar to the atomCAT2 observational trial in anal cancer (a multicentre study of overall survival, locoregional control and distant metastasis in anal cancer utilising distributed learning). The group will engage with national and international groups to ensure collaboration.

Strategic area 4: Improve wellbeing in women undergoing treatment for gynaecological cancers

Patient centred research to improve symptom management and well-being following treatment for a gynaecological cancer is a key focus. This working group will review the outcomes from the Living With and Beyond (LWBC) James Lind Alliance (JLA) Priority Setting Partnership (PSP), as well as opinions of NCRI Consumers and NCRI Partners and set priorities for improving living with and beyond gynaecological cancers.

Priority 1: Develop recommendations for improving wellbeing of women undergoing treatment for gynaecological cancers

This working group will write a position paper detailing recommendations for improving the wellbeing of women undergoing treatment for gynaecological cancers and define the areas for further development. Key areas to be considered include:
- Elderly/geriatric gynaecological cancer patients
  - Use of Frailty Index to guide treatment decisions.
  - Role of pre-habilitation.
  - Survivorship in elderly cohorts.
- Menopause support
  - The need for improved treatment of menopausal symptoms for patients who have undergone treatment, as highlighted by patient groups and charities.
  - Improved survivorship/mental health after all gynaecological cancers, building on the success of the OvPsych 2 trial (conducted by the NCRI Gynaecological Group) which demonstrated the impact of early psychological support for women with ovarian cancer.

NCRI Cross-cutting priority

Identify barriers in clinical trials participation and propose solutions to improve equality, diversity, and inclusion.

Barriers resulting in a lack of diversity, in terms of ethnicity, social deprivation, age and language spoken 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.
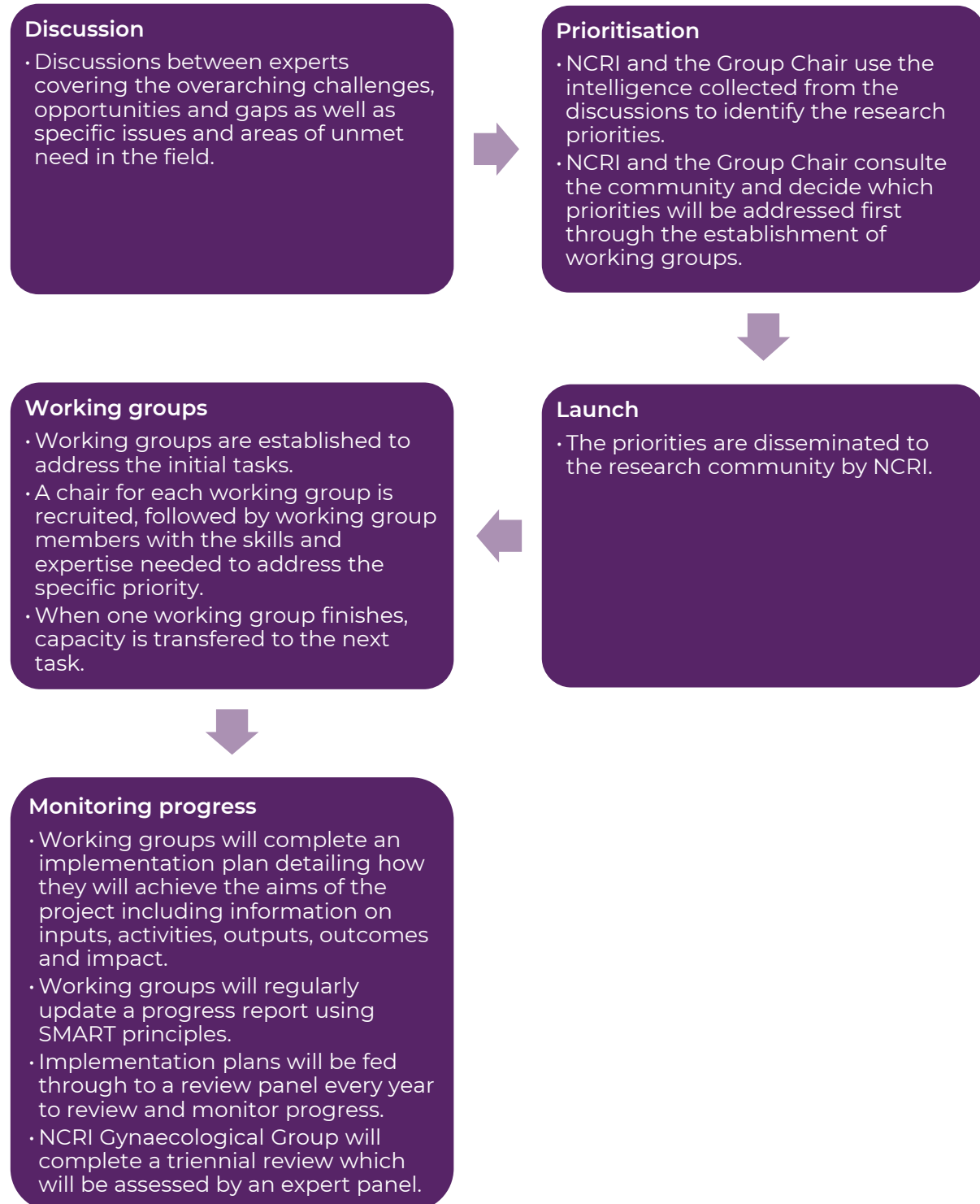
An area of consideration for gynaecological cancers in particular is the evaluation of real-world data sets, for example, comparing real-world outcomes with clinical trial outcomes, which has the potential to highlight the benefits/toxicities of new treatments in patients who do not routinely take part in clinical trials.

Next steps

Working groups addressing the highlighted tasks are currently being formed. These groups will be made up of the experts needed to address each research question. To be the first to hear about opportunities to join these working groups please sign up to the NCRI Gynaecological Network. The progress of these working groups will be published in the annual reports and triennial review of NCRI Gynaecological Group. These can be found on the NCRI website. Members of the NCRI Gynaecological Network will also be updated periodically on the progress of the group.

Please get in touch if you have any questions or comments regarding this report or if you are interested in joining one of the NCRI Networks, the NCRI Consumer Forum or our NCRI Early Career Researcher Forum.

Appendix A
NCRI Gynaecological Group priority setting process

Discussion
- Discussions between experts covering the overarching challenges, opportunities and gaps as well as specific issues and areas of unmet need in the field.

Prioritisation
- NCRI and the Group Chair use the intelligence collected from the discussions to identify the research priorities.
- NCRI and the Group Chair consulte the community and decide which priorities will be addressed first through the establishment of working groups.

Working groups
- Working groups are established to address the initial tasks.
- A chair for each working group is recruited, followed by working group members with the skills and expertise needed to address the specific priority.
- When one working group finishes, capacity is transfered to the next task.

Launch
- The priorities are disseminated to the research community by NCRI.

Monitoring progress
- Working groups will complete an implementation plan detailing how they will achieve the aims of the project including information on inputs, activities, outputs, outcomes and impact.
- Working groups will regularly update a progress report using SMART principles.
- Implementation plans will be fed through to a review panel every year to review and monitor progress.
- NCRI Gynaecological Group will complete a triennial review which will be assessed by an expert panel.

NCRI Gynaecological Group priority discussion contributors

The NCRI Gynaecological Group developed their strategic priorities through discussions with professionals from a range of sectors and disciplines, including NCRI Consumer Forum members, early career researchers and NCRI Partners. Chairs and members of the previous Gynaecological Group subgroups, listed below, contributed to the priorities.

Cervix/Vulva Workstream
Dr Emma Hudson, Velindre NHS Trust (Subgroup Chair)

Dr Susana Banerjee, Royal Marsden NHS Foundation Trust

Dr Tara Barwick, Imperial College Healthcare NHS Trust – St Mary's Hospital

Dr Emma Cattell, Somerset NHS Foundation Trust

Dr Emma de Winton, Royal United Hospitals Bath NHS Foundation Trust

Dr Asma Faruqi, Barts Health NHS Trust

Dr Jenny Forrest, King's College London (KCL)

Dr Lynn Hirschowitz, Birmingham Women's and Children's NHS Foundation Trust

Dr Susan Lalondrelle, Royal Marsden NHS Foundation Trust

Dr Rosemary Lord, Clatterbridge Cancer Centre NHS Foundation Trust

Ms Jackie Martin, Sheffield Teaching Hospitals NHS Foundation Trust

Dr Jess Mason, Somerset NHS Foundation Trust

Dr Pinias Mukonoweshuro, Royal United Hospitals Bath NHS Foundation Trust

Prof Nick Reed, Beatson West of Scotland Cancer Centre

Dr Vanitha Sivalingam, University of Manchester

Dr Alexandra Taylor, Royal Marsden NHS Foundation Trust

Prof John Tidy, Sheffield Teaching Hospitals NHS Foundation Trust

Mr Jeremy Twigg, King's College London (KCL)

Endometrial Workstream
Prof Emma Crosbie, University of Manchester (Subgroup chair)

Prof Kinta Beaver, University of Central Lancashire

Dr Andrew Clamp, Christie NHS Foundation Trust

Dr Emma de Winton, Royal United Hospitals Bath NHS Foundation Trust

Dr Yvette Drew, Newcastle upon Tyne Hospitals NHS Foundation Trust

Dr Gemma Eminowicz, University College London Hospitals NHS Foundation Trust (UCLH)

Dr Maria Kyrgiou, Imperial College

Healthcare NHS Trust – St Mary's Hospital

Dr Rosemary Lord, Clatterbridge Cancer Centre NHS Foundation Trust

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Dr Esther Moss, University Hospitals of Leicester NHS Trust

Dr Pinias Mukonoweshuro, Royal United Hospitals Bath NHS Foundation Trust

Dr Jaya Nautiyal, Imperial College London

Dr Christine Parkinson, Addenbrooke's Hospital NHS Foundation Trust

Dr Melanie E B Powell, Barts Health NHS Trust

Dr Azmat Sadozye, Beatson West of Scotland Cancer Centre

Prof Naveena Singh, Barts Health NHS Trust

Dr Axel Walther, University of Bristol

Dr Karen Whitmarsh, Clatterbridge Cancer Centre NHS Foundation Trust

Dr Dennis Yiannakis, Lancashire Teaching Hospitals NHS Foundation Trust

Ovarian Workstream

Dr Rebecca Bowen, Royal United Hospitals Bath NHS Foundation Trust (Subgroup chair)

Dr Susana Banerjee, Royal Marsden NHS Foundation Trust

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Dr Mona El-Bahrawy, Imperial College London

Prof Christina Fotopoulou, Imperial College Healthcare NHS Trust – St Mary's Hospital

Dr Sadaf Ghaem-Maghami, Imperial College London

Rosalind Glasspool, University of Glasgow

Dr Rebecca Kristeleit, Guy's and St Thomas' NHS Foundation Trust

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Prof Sundha Sundar, University Hospitals Birmingham NHS Foundation Trust

Dr Axel Walther, University of Bristol

Dr Nafisa Wilkinson, Leeds Teaching Hospitals NHS Trust – Leeds General Infirmary

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