# NCRI Prostate Group Priorities 2022 - 2025

# 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 Prostate Group is a multi-disciplinary community of researchers and consumers focused on developing research to improve outcomes for prostate 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 Prostate Group has identified its research priorities working with members of the research community, and NCRI Partners. Full details of the meetings held can be found in Appendix B and a list of participants can be found in Appendix C.

There are multiple areas the NCRI Prostate Group has identified as priorities, an overview of which can be seen below with full details on pages 9-11 of this document. The Group will initially focus on priorities 1-4, 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 Prostate Group structure can be found on page 6.

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 prostate cancer research landscape are addressed over the course of this three-year strategy.

### NCRI Prostate Group strategic priorities at a glance

Priority 1: Engage the wider prostate cancer community to identify the challenges faced in research and propose solutions with a focus on improving collaboration.

Priority 2: Evaluate the role of new screening strategies in reducing the harms of biopsy and over-diagnosis/over-treatment whilst maintaining or improving the improved cancer outcomes associated with population level PSA testing to screen.

Priority 3: Improve early diagnosis of clinically significant prostate cancer.

Priority 4: Develop studies to improve treatment of non-metastatic prostate cancer, with a particular emphasis on surgical and minimally invasive interventions.

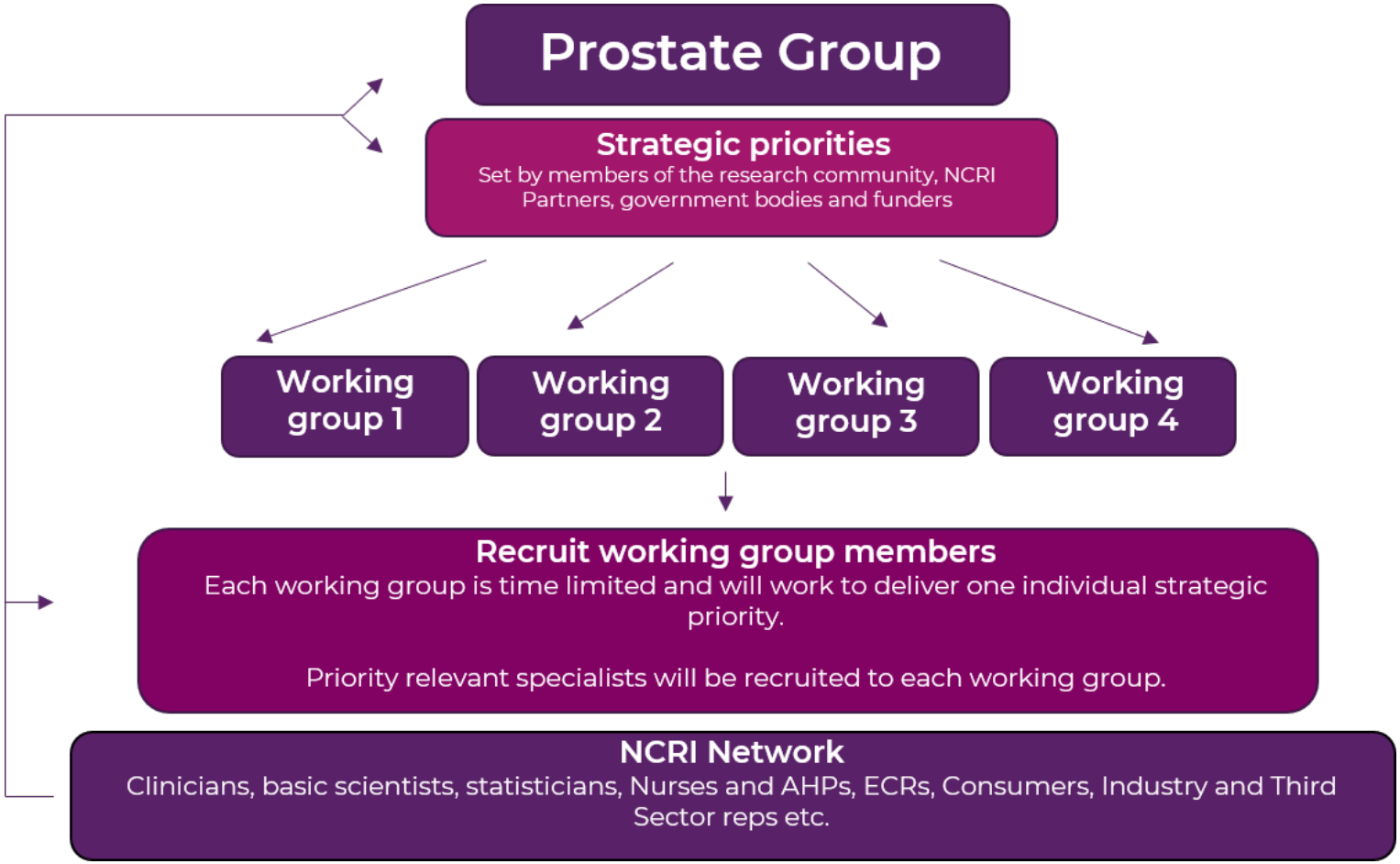
In addition to the priorities listed above, the NCRI Prostate Group will work to build links with international groups and prioritise opening international studies for UK patients with prostate cancer. Through this, the Group aims to expand their network to develop a truly collegiate prostate research consortium, and ultimately help patients with rarer prostate cancers. This will be embedded within the strategy of the Prostate Group, with a focus on proactively building links with international groups, such as the EORTC-GU group and the November Foundation and developing studies that evaluate risk stratified approaches to the treatment of prostate cancer. Further, the Group will ensure we scope out where there are research needs in the metastatic space so that a robust plan for developing and supporting a pipeline of new research questions and trials in the metastatic space can be delivered, alongside the Group's existing role to help in the development of new arms in the STAMPEDE platform trial.

*"Over the last five years the NCRI Prostate Group has prioritised early diagnosis and the treatment of nonmetastatic localised prostate cancer as key areas for research. As a result, we have increased the number of surgical and interventional studies that aim to improve cancer control and reduced side effects for those men who have clinically significant cancer. Whilst not deprioritizing the treatment of metastatic disease, we recognise greater impact for a greater number of patients can be made by focusing our efforts earlier in the treatment pathway. Over the last two years, we have continued that focus upstream in the cancer pathway by developing, nurturing and mentoring new investigators and new ideas around early diagnosis. We have made huge strides increasing not only the proportion of men being diagnosed with clinically insignificant prostate cancer but also the number of men being biopsied whilst at the same time improving the detection of cancer that is significant and would otherwise progress if either missed or monitored. As we go forward into the next three years, we will build on discussions that have been had over the last two or three years around screening. The NCRI Prostate Group has increasingly recognised the impact that can be made on early diagnosis and early treatment of significant prostate cancer in order to reduce in a substantial and significant way the mortality rate that we are currently seeing in the UK from prostate cancer is through the delivery of a pivotal guideline and policy changing randomised control trials of new and promising screening strategies.*

*We will continue our efforts in early diagnosis and improving the lives of men who have localised prostate cancer while supporting novel treatments for advanced disease, but our greatest impact will be the conception, funding and commencement of the next big screening study. We will continue to support and nurture clinician scientists, especially surgeons and radiation oncologists, to design and deliver innovations in localised treatments such as surgery, minimally invasive interventions and new forms of radiotherapy."*

**Professor Hashim Ahmed, Chair of NCRI Prostate Group**

# NCRI Prostate Group structure at a glance



# NCRI Prostate Working Groups

## Initial working groups in set up

The NCRI Prostate Group has identified four strategic priorities, full details of which can be found on pages 9-11 of this document. Time-limited working groups will be set up to address these four priorities for the NCRI Prostate Group, each of which are outlined below. Once one working group reaches completion, capacity will be transferred to the next priority as they emerge.

### Working group 1

Engage the wider prostate cancer community to identify the challenges faced in research and propose solutions with a focus on improving collaboration.

This working group will produce and publish a position paper addressing challenges such as:

- Methodological issues surrounding the clinical utility and impact on long-term outcomes through the use of more accurate imaging tests in diagnosis and staging.
- Novel trial designs that improve recruitment to challenging research questions on novel interventions especially in the localised disease space.
- The role of numerous fluidic and tissue biomarkers in prediction and prognosis of disease.

### Working group 2

Evaluate the role of new screening strategies in reducing the harms of biopsy and over-diagnosis/over-treatment whilst maintaining or improving the improved cancer outcomes associated with population level PSA testing to screen.

We will, in partnership with funders such as Prostate Cancer UK, convene a steering group of key opinion leaders that guide the approach taken to bring about a successful screening study over the next decade. Once the steering group members have been identified, we will then conduct a consensus group meeting of the wider community through targeted invitation and also through a 'light-touch' application to join. We envisage that some participants of this wider group will then join a consortium to design and submit for funding a phased programme of work in screening. The NCRI will facilitate and manage the consortium through to a funding application.

## Working group 3:

Improve early diagnosis of clinically significant prostate cancer. This working group will improve early diagnosis of clinically significant prostate cancer in a three-fold manner:

- Improve the diagnostic pathway in secondary care using low-cost imaging (MRI / ultrasound) and further reductions in the number of patients requiring a biopsy and the total number of biopsies taken through risk models and nomograms.
- Validate the accuracy and test the utility of novel imaging (biparametric MRI, PSMA PET, multi-parametric ultrasound) and AI tools (for pathology and imaging) in the diagnostic pathway.
- Reduce the burden of repeated invasive biopsy whilst detecting progression of cancer early in patients with non-metastatic prostate cancer that is suitable for active surveillance.

## Working group 4

Develop studies to improve treatment of non-metastatic prostate cancer, with a particular emphasis on surgical and minimally-invasive interventions.

We will achieve this by developing and supporting studies that aim to improve the therapeutic ratio of surgical interventions and radiotherapy through a reduction in side-effects, whilst maintaining effective cancer control, for patients with non-metastatic prostate cancer who require treatment.

# NCRI Prostate Group strategic areas in full

## Priority 1: Engage the wider prostate cancer community to identify the challenges faced in research and propose solutions with a focus on improving collaboration.

By addressing this priority, we aim to engage and enthuse the wider prostate community with a view to enhancing the future of prostate research across the UK, with a focus on collaboration as opposed to competition. Greater collaboration will ultimately result in higher quality multi-centre studies.

This working group will produce and publish a position paper addressing challenges such as:

- Methodological issues surrounding the clinical utility and impact on long-term outcomes through the use of more accurate imaging tests in diagnosis and staging.
- Novel trial designs that improve recruitment to challenging research questions on novel interventions especially in the localised disease space.
- The role of numerous fluidic and tissue biomarkers in prediction and prognosis of disease.

## Priority 2: Evaluate the role of new screening strategies in reducing the harms of biopsy and over-diagnosis/over-treatment whilst maintaining or improving the improved cancer outcomes associated with population level PSA testing to screen.

The changes from biopsying almost all men with an elevated serum PSA level with transrectal systematic biopsy to a pathway that incorporates pre-biopsy MRI triage, targeted transperineal biopsies, active surveillance and focal therapy have led to a significant downward shift in harms in the pathway. These changes mean that the question of screening for prostate cancer becomes very pertinent. However, robust studies with appropriate long-term endpoints such as metastasis-free survival or cancer-specific survival are required in order to convince both screening guidance committees and policymakers that a screening programme for prostate cancer is clinically- and cost-effective. As a result, the NCRI Prostate Group is working with the NCRI Screening, Prevention and Early Diagnosis (SPED) Group alongside Prostate Cancer UK to develop and deliver the next generation screening study.

We will, in partnership with funders such as Prostate Cancer UK, convene a steering group of key opinion leaders that guide the approach taken to bring about a successful screening study over the next decade. Once the steering group members have been identified, we will then conduct a consensus group meeting of the wider community through targeted invitation and also through a 'light-touch' application to join. We envisage that some participants of this wider group will then join a consortium to design and submit for funding a phased programme of work in screening. The NCRI will facilitate and manage the consortium through to a funding application.

## Priority 3: Improve early diagnosis of clinically significant prostate cancer.

The UK has led improvements in reducing the number of men requiring biopsy, over-diagnosis of low-risk cancer and improved diagnosis of higher-grade cancer through its strategic role in supporting robust studies in MRI before biopsy. However, further improvements can be made using risk models and new imaging tests. In addition, addressing workforce challenges in radiology and pathology as well as reducing inter-observer variability in interpretation of imaging and pathology are necessary through potential use of novel AI tools. Finally, further improvements to standardise and improve active surveillance for low- and intermediate-risk cancers using imaging and fluidic/tissue-based biomarkers are required. We will address these issues in a three-fold manner:

- Improve the diagnostic pathway in secondary care using low-cost imaging (MRI / ultrasound) and further reductions in the number of patients requiring a biopsy and the total number of biopsies taken through risk models and nomograms.

Building on the work of the prostate group in the conception and development of the funded IP7-PACIFIC study, we will work on the need and approach to evaluating new risk calculators and fluidic biomarkers to further increase the number of men who might avoid an immediate biopsy through robust prospective studies ideally in comparative fashion.

- Validate the accuracy and test the utility of novel imaging (biparametric MRI, PSMA PET, multi-parametric ultrasound) and AI tools (for pathology and imaging) in the diagnostic pathway.

The NCRI Prostate Group will support a randomised control trial evaluating the role of PSMA PET imaging in the staging of high-risk prostate cancer to test the true utility of this new imaging technology. A working group will be set up in conjunction with representation from NHS England and other stake-holders to develop a randomised controlled study in this area. Other studies evaluating the role of PSMA PET imaging in men who have rising PSA but either a negative MRI or an equivocal MRI and negative biopsies are needed in order to further improve the diagnostic pathway. Micro-ultrasound has recently been shown to have accuracy for cancers in some men and we will determine whether there might be a role for this in the UK and how we might test its effectiveness in a comparative setting. A number of AI tools have already been developed both for the evaluation of MRI and histology. There is a need to determine how accurate these are and whether they impact the diagnostic pathway in a positive manner to improve outcomes for patients. So, whether these tools sit as triage tools to identify suspicious cases that expert radiologists or pathologists then focus their time on or whether these tools are adjuncts which helps with the reporting of MRI and histology in order to reduce inter-observer variability and generally increase the early identification of significant prostate cancer are going to be critical decisions over the next five years. Not only will clinical validation studies be required in order to prove the accuracy of these AI tools but once accuracy is established the clinical utility i.e. how these tools make a difference to clinical outcomes in the medium to long term, are necessary.

- Reduce the burden of repeated invasive biopsy whilst detecting progression of cancer early in patients with non-metastatic prostate cancer that is suitable for active surveillance.

Finally, once diagnosed with low-risk or medium risk prostate cancer which is suitable for active surveillance there is a need to evaluate new surveillance strategies that incorporate fewer biopsies and potentially detect progression earlier than PSA and clinical examination or biopsies. MR-imaging is again likely to play an important role in this space. We will set up a working group to develop a comparative study so that it is competitive for funding applications.

## Priority 4: Develop studies to improve treatment of non-metastatic prostate cancer, with a particular emphasis on surgical and minimally-invasive interventions.

We will achieve this by developing and supporting studies that aim to improve the therapeutic ratio of surgical interventions and radiotherapy through a reduction in side-effects, whilst maintaining effective cancer control, for patients with non-metastatic prostate cancer who require treatment.

New approaches to delivery of surgery using frozen sections, for instance in the Neurosafe randomised control trial, was supported by the NCRI Prostate Group and over the next five years further innovations in surgery, such as the evaluation of Retzius sparing radical prostatectomy and precision prostatectomy, will be supported through evaluation in comparative studies ideally using novel trial designs to ensure recruitment is efficient.

Over the last three to four years the NCRI Prostate Group has supported the evaluation of minimally invasive approaches such as focal therapy which early studies have shown a 5 to 10 fold decrease in genital urinary and rectal toxicity compared to radical therapy with five year iso-effectiveness. The Prostate Cancer UK funded IP4-CHRONOS RCT pilot was the culmination of this and the NCRI Prostate Group will now work with the Trial Management Group as well as key partners such as the EORTC GU group and funders to determine the strategy for the main RCT going forward, through a platform trial not only in the UK but potentially across Europe. This will be a key priority for the group.

Finally, technological advancements in radiotherapy using stereotactic delivery, MRI guidance and proton radiation may lead to reductions in patient burden and reduced genitourinary and gastrointestinal toxicity whilst maintaining efficacy of the treatment itself. These as well as dose escalation and ultra-hypo-fractionated radiotherapy paradigms will need robust comparative studies designed in conjunction with the NCRI Radiotherapy Group. We will form a radiotherapy led working group to scope out what studies are required.

## 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.

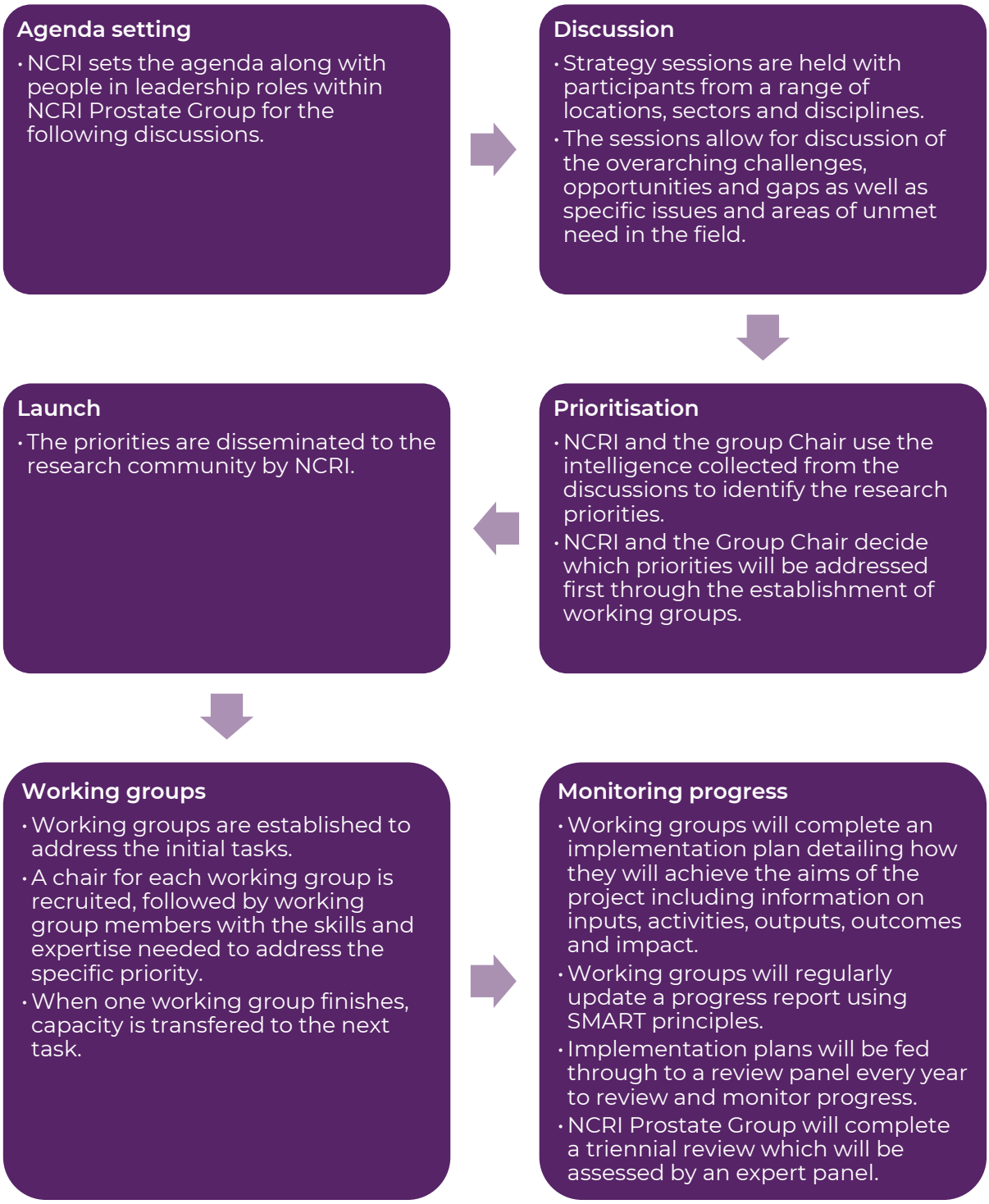
# Next steps

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 Prostate Network. The progress of these working groups will be published in the annual reports and triennial review of NCRI Prostate Group. These can be found on the NCRI website. Members of the NCRI Prostate 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 Prostate Group priority setting process



# Appendix B

### NCRI Prostate Group priority discussion sessions 2019

The NCRI Prostate Group strategy day, held in March 2019, attracted 45 participants from a range of sectors and disciplines, including NCRI Consumer Forum members, early career researchers and NCRI Partners. The introductory presentation allowed for discussion of where the Group have come from, their achievements from the previous strategy and feedback from their most recent annual and quinquennial reviews. Subsequent sessions focussed on known key gaps in prostate cancer research in imaging, surgery, radiotherapy and systemic therapies which set the scene to inform discussions in the breakout sessions where experts exchanged ideas on what the future direction of the Group should be.

## NCRI Prostate Cancer Clinical Studies Group Strategy Day Agenda

**Thistle City Barbican, Central St, London EC1V 8DS**
**Tuesday 26 March 2019**

| | | |
|---|---|---|
| 12:30 | **Arrival and lunch** | |
| 13:00 | **Welcome & Introductions**<br>Review of Last Strategy, Annual Report, QQR Report | Hashim Ahmed |
| 13:30 | **Living with and Beyond Cancer** | Sue Duncombe |
| 13:45 | **Key gaps in knowledge** | |
| | Imaging | Tristan Barrett |
| | Surgery | Greg Shaw |
| | Radiotherapy | Alison Tree |
| | Systemic Therapy | Gert Attard |
| 14:30 | **Tea & Coffee break** | |
| 15:00 | **Breakout Sessions: Where are we going** | All |
| 16:00 | **Strategy setting** | All |
| 17:00 | Close | |

# Appendix C

## Strategy discussion and NCRI Prostate Group contributors:

**Dr Mehran Afshar**
King's College London (KCL)

**Prof. Hashim Ahmed**
Imperial College London

**Prof. Gerhardt Attard**
University College London (UCL)

**Dr Tristan Barrett**
University of Cambridge

**Hazera Begum**
University College London (UCL)

**Prof. Dan Berney,**
Barts Health NHS Trust

**Prof Rob Bristow**
Manchester Cancer Research Centre

**Prof. Janet Brown**
University of Sheffield

**Prof. Richard Bryant**
University of Oxford

**Dr Fay Cafferty**
Institute of Cancer Research (ICR)

**Mr Paul Cathcart**
Guy's and St Thomas' NHS Foundation Trust

**Prof. Francis Chinegwundoh**,
Barts and The London School of Medicine and Dentistry

**Dr Simon Crabb**
University of Southampton

**Mrs. Kristina Duggleby**
Cancer Research Network

**Prof. Silke Gillessen**
The Christie NHS Foundation Trust

**Prof. Emma Hall**
Institute of Cancer Research (ICR)

**Dr Athar Haroon**
Barts Health NHS Trust

**Mr Rakesh Heer**
Newcastle University

**Dr Ann Henry**
Leeds Teaching Hospitals NHS Trust - Leeds Cancer Centre

**Dr Matt Hobbs**
Prostate Cancer UK

**Mr. Alex Hoyle**
University of Manchester

**Dr Satinder Jagdev**
Leeds Teaching Hospitals NHS Trust

**Prof. Suneil Jain**
Queen's University Belfast - The Patrick G Johnston Centre for Cancer Research

**Prof. Rob Jones**
University of Glasgow

**Mr Christof Kastner**
Addenbrooke's Hospital NHS Foundation Trust

**Prof. Athene Lane**
University of Bristol

**Mr Tom Leslie**
Nuffield Department of Surgical Sciences

**Dr Zafar Malik**
Clatterbridge Cancer Centre NHS Foundation Trust

**Dr Anita Mitra**
University College London Hospitals NHS Foundation Trust (UCLH)

**Dr Reena Morjaria**
Prostate Cancer UK

**Prof. Joe O'Sullivan**
Northern Ireland Cancer Centre

**Dr Simon Pacey**
University of Cambridge

**Dr Nuria Porta**
Institute of Cancer Research (ICR)

**Dr Shonit Punwani**
University College London Hospitals NHS Foundation Trust (UCLH)

**Dr Prabhakar Rajan**
Barts Cancer Institute

**Mr Greg Shaw**
University College London (UCL)

**Mr Prasanna Sooriakumaran**
University of Oxford

**Prof. John Staffurth**
Cardiff University

**Dr Aravindhan Sundaramurthy**
NHS Lothian

**Dr Matthew Sydes**
University College London (UCL)

**Dr Hannah Tharmalingam**
Mount Vernon Cancer Centre

**Ms. Tara Thorneycroft**
Institute of Cancer Research (ICR)

**Dr Alison Tree**
Royal Marsden NHS Foundation Trust

**Dr Nicholas van**
Royal Marsden NHS Foundation Trust

**Dr Mohini Varughese**
Royal Devon and Exeter NHS Foundation Trust

**Prof. Sobhan Vinjamuri**
Royal Liverpool and Broadgreen University Hospitals NHS Trust

**Dr Richard Wagland**
University of Southampton

**Dr Hayley Whitaker**
University College London (UCL)

**Dr Abbie Fearon**
National Cancer Research Institute

**Ms Nicola Keat**
National Cancer Research Institute

**Ms Frankie Parody**
National Cancer Research Institute

**Ms Laura Chambers**
National Cancer Research Institute

**Ms Rachel Lawrence**
National Cancer Research Institute

**Miss Iris Vera Utrilla**
National Cancer Research Institute

Advancing Cancer Research Together

**Report produced by:**

Abbie Fearon, Senior Programme Manager (Strategic Projects), NCRI
Laura Chambers, Senior Programme Manager (Groups), NCRI
Rachel Laurence, Communications Manager, NCRI
Nicola Keat, Head of Groups, NCRI

National Cancer Research Institute
2 Redman Place,
London, E20 1JQ

T: +44 (0)20 3469 8798
F: +44 (0)20 3014 7658

info@ncri.org.uk
www.ncri.org.uk