NCRI
National
Cancer
Research
Institute

NCRI Supportive & Palliative Care Clinical Studies Group

Annual Report 2017-18

Partners in cancer research

NCRI Supportive & Palliative Care CSG
Annual Report 2017-18

1. Top 3 achievements in the reporting year

Achievement 1: Successful Quinquennial Review

The CSG had its first Quinquennial Review since the development of its new strategy and change of name in 2015-16 on 8 March 2018. The panel commended the quality of the leadership and congratulated the Group on its successful restructure. The high success rate in grant applications, growth of portfolio of new studies, increase in patient recruitment and completion of studies to time and target were all commended. Recommendations were made regarding the as of yet incomplete strategy for the newest subgroup on Early stage disease and acute treatment toxicities; the under-representation of palliative medicine in the Advanced disease and end of life care Subgroup; the need to work closer with other CSGs; more translational studies; and the need for succession planning with respect to the Subgroup and CSG Chair positions. These issues have been tackled and largely resolved.

Achievement 2: Establishment of all three Subgroups

Both the Early stage disease and acute treatment toxicities and the Survivorship and late consequences Subgroups have recently started since the development of our new strategy in 2015-16. Professor Annie Young has taken the steer on the former and brought to it her important nursing perspective and ability to research patient experience. This has led to a National Institute for Health Research (NIHR) application proceeding to second stage on patient experience of immunotherapy treatment. Several other exciting areas of acute treatment toxicities are being explored in parallel new trial developments. The Survivorship and late consequences Subgroup has, under the leadership of Professor Anthony Maraveyas, progressed in one year from a strategic outline to a detailed thematic programme of work. The most established subgroup on advanced disease, led by Dr Matthew Maddocks, continues to deliver the bulk of the CSG's clinical trial outputs: large multicentre studies recruiting many hundreds of patients in areas such as pain and fatigue management, prognostication, rehabilitation as well as the growing area of health services research. In 2018 each subgroup has recruited new chairs to take their work forward.

Achievement 3: First national conference on hospice and community-based research

Since 2017 we have supported the NIHR Clinical Research Network (CRN): Cancer in establishing the NIHR Charities Consortium. This consists of a dozen large and smaller charities linked with cancer and end of life care, as well as Hospice UK the umbrella organisation for over 200 UK hospices. Members of the CSG have contributed to the formation and remit of the Consortium. The Consortium will hold its first national conference on Hospice and Community-based Research at BMA House in April 2018. It will be opened by Baroness Julia Neuberger and Professor Matt Seymour and involve both current and former members of the CSG. The Consortium is committed to increasing the capacity of hospices to contribute to supportive and palliative care research, and the CSG will play an important part in designing suitable studies for this sector.

2. Structure of the Group

The overall structure of the CSG has not changed in the past year. Anthony Maraveyas filled the position of Chair of the Survivorship & Late Consequences Subgroup.

We have lost three important members, who have been active collaborators and links to other groups for two terms: Dr Vicky Coyle, medical oncologist; Dr Dawn Storey, medical oncologist; and Professor Gareth Griffiths, statistician and Clinical Trials Unit (CTU) lead. We aim to replace these key roles later in 2018.

In their place, the Group welcomed two new members: Dr Catriona Mayland, palliative medicine specialist; and Professor Fliss Murtagh, also palliative medicine specialist. They bring unique methodological skills to strengthen the end of life care work of the Group.

We would also like to acknowledge that during this year, our long-serving coordinator at NCRI Mrs Nanita Dalal, moved to other functions in the office. She will be sorely missed by the CSG; but she has been ably replaced by Miss Aifric Müller.

3. CSG & Subgroup strategies

Main CSG

Development of subgroups

The main CSG strategy for 2017-18 remains the same, having been introduced in 2015-16 with refinements in the subgroups' scope in the following year. All three newly designed subgroups are now in place with their updated strategies (see below), and with strong leaders. The changeover of membership over the past 2 years has eased the process of re-focusing the Group's vision and specific projects. We are striving to involve our consumer members more actively in ensuring their 'patient-centredness' and by identifying potential recruitment and ethical issues.

The most established Subgroup in the past has been the Advanced disease and end of life Subgroup, which in the past year has gained from two new members (Professor Murtagh and Dr Mayland). The newer workstreams of '*Early stage disease and acute treatment toxicities'* and *'Survivorship and late consequences'* were slower in 2016-17 to establish their membership and project development, but through regular face to face and teleconference meetings in 2017-18 they have now produced active workplans.
We aim to take stock of the Group's strategic and membership changes later in 2018 in order to update and amend the overall strategy in early 2019.

Boost engagement with oncologists in other CSGs

An important aim from last year was to boost our engagement with oncologists in other CSGs in order to start designing studies with a more biomedical and translational focus, especially in the areas of acute and delayed treatment toxicities. This priority is now being actively developed in the Early stage disease and acute treatment toxicities and the Survivorship and late consequences Subgroups. The Immunotherapy Toxicities Working Party, which will be initiated during 2018, will continue and strengthen this cross-CSG collaboration.

Increase work with the commercial sector

Another target was to increase our work with the commercial sector: this has proved to be more challenging so far, but the immunotherapy workstream may be more successful in engaging industry.

Early stage disease and acute treatment toxicities Subgroup (Chair, Prof Annie Young)

To be adopted by Multinational Association of Supportive Care in Cancer (MASCC) as its UK 'chapter.

The subgroup chair has recently been appointed to the MASCC Board, which will facilitate this.

To work with site-specific CSGs to develop a portfolio of studies

This encourages the development of studies which focuses on biomarkers and other methods of characterisation of patients to predict and better manage acute treatment toxicities such as venous thromboembolism, chemotherapy-induced nausea and vomiting and chemotherapy-induced peripheral neuropathy.

To have at least two large multicentre portfolio studies approved by Q4 of 2018

Subgroup members are contributing to new trial development in the following two workstreams –

- Acute treatment toxicities – such as patient experience of immunotherapy (proposal shortlisted for NIHR (Young, Griffiths); biomarkers of 5-FU cardiotoxicity (Coyle), prevention of early VTE (Maraveyas, Young).

Prehabilitation and early post-treatment rehabilitation – e.g. PRE-REHAB in multiple myeloma patients undergoing stem cell transplantation (Young) to follow on from the completed PRO-REHAB (Coyle); nutritional advice and support for patients completing treatment and their carers – EAT-CIT (Hopkinson).

The Subgroup's consumer representative, Mrs Jean Gallagher has been involved from the beginning in our development of bids. Working alongside consumers who have had experience of the intervention or disease in question, Jean has shaped and prioritised the patient-centredness of the bids, e.g. in the immunotherapy patient experience HTA bid.

Meetings and TCs held: 14 March 2017; 25 May 2017; 12 February 2018; 18 June 2018.

Advanced disease and end of life Subgroup (Chair, Dr Matthew Maddocks)

Symptoms of advancing disease

This Subgroup's remit is to stimulate and develop research concerned with people with advancing disease and towards the end of life. Its strategy is to bolster research in: (i) symptoms of advancing disease, e.g. thrombosis, cord compression, fatigue and breathlessness; (ii) issues near the end of life, e.g. prognostication, management of dying; and (iii) rehabilitation, e.g. optimising independence and therapy decision making.

The current portfolio spans these priorities and includes interventional work (e.g. ACTION and IMPACCT), large scale observational studies (e.g. C-CHANGE and PiPS2), and interventional trials (e.g. MENAC, ENERGY). Subgroup members are encouraged to devise studies targeting recruitment of larger numbers of patients then previously, across many sites, and crucially are open to new sties joining.

Issues towards the end of life

Members have working links with, among others, the European Association of Palliative Care, Multinational Association of Supportive Care in Care, Society on Cachexia and Wasting Disorders and Association of Chartered Physiotherapists in Oncology & Palliative Care.

The subgroup benefits from excellent input from consumer members: Lesley Turner (outgoing member) continues to advisory input into a breathlessness study. Jean Gallagher joined as a co-applicant for the DOSIS trial submitted to RfPB. Jim Elliot works with the Cicely Saunders Institute to help it become a pilot centre for the new HRA questions about PPI and study design changes.

Meetings held: 18 Jan 2917, 12 Sept 2017. Next meeting planned for Q3 2018.

Survivors and late consequences Subgroup (Chair, Dr Anthony Maraveyas)

Overarching key strategic aims:

a) To develop a proposal led by a member or affiliate of this subgroup in each and every section identified to fit the groups strategic remit.

b) To develop at least one proposal that would have the potential to attract industry support partnership

c) To invite key members to join the subgroup that would have key skills to further proposals developed by the subgroup

Peripheral Neuropathy

Proposal being developed. PI Professor Sarah Faithful

Cohort study of the impact of co-morbid conditions on incidence and perpetuation of CIPN.

This follows from the recently published cross sectional study in 512 cancer survivors that showed that the existence of CIPN had detrimental impact on a number of self-reported but also measurable endpoints (such as gait analysis) leading to greater risk of falls. The study interestingly found that major factors playing a role were BMI and lack of physical activity when adjusting for these CIPN existence was less significant. To understand whether these were separate risk factors (e.g. BMI/PA patients were more likely to suffer from chemo induced neuropathy or the damage from CIPN lead to greater inactivity and increase in BMI) a longitudinal study was necessary.

(MobilityLab)- developed by Dr Horak a co-investigator from the states; submission planned for HTA EME funding stream October 2018.

Gastrointestinal Effect of Pelvic Radiotherapy

The EAGLE study (CI Staffurth, co-applicants Nelson, Ahmedzai) has shown the viability of screening for late GI side-effects after radiotherapy for prostate cancer. This needs to be developed into a larger multicentre trial to test the ability of the NHS to roll out the benefits of this screening. No new proposals are in development at this time. The group has strong representation and involvement with EAGLE in prostate cancer, but will seek to extend this to other pelvic disease

Late Consequences after immunotherapy

Proposal being formulated. (PIs) Professor Anthony Maraveyas, Professor Sam H Ahmedzai

Most registration studies of new I-O checkpoint inhibitor therapies stop data collection for adverse events 100 days from the last IMP (investigational medicinal product) administration (though they followed up patients for teratogenesis for 31 weeks). It is becoming apparent that there are either autoimmune side-effects that affected patients in the long term or even permanently or side effects from immunosuppressive agents (such as high dose steroids) that equally leave some patients with chronic problems (e.g. osteoporosis etc.).First draft of proposal

has been circulated and will continue development within the Immunotherapy Toxicities Intergroup Working Party (ITIWP)- 1st meeting expected NCRI meeting in Glasgow (4-6 November 2018). **This proposal offers potential for involvement of Industry partners.**

Lymphedema, chronic vascular and cardiac problems

The subgroup continues to maintain lymphedema as a major area for development though Professor Vaughn Keeley has left the CSG.

Proposal being formulated. (PIs) Professor Sarah Faithful and Dr Alexander Lyon

Sarah Faithful is already collaborating with Dr Andrew Lyons of the Brompton who has an interest in chronic cardiac toxicity from cancer treatments. A systematic review in this area has been done and questions that this review raises could shape the aims around which to develop a collaborative study. If a firm proposal does arise, Dr Lyon should be formally invited to membership of the subgroup

Proposal being developed. (PIs) Professors Anthony Maraveyas and Annie Young

AM&AY are developing a proposal for a randomised study of conventional anticoagulant treatment Vs short course treatment vs observation for distal pulmonary embolism incidentally diagnosed in cancer patients (CLOT-ReSOLVe). The proposal is in development via the Warwick CTU and targeted to the recent **HTA call for incidental pulmonary embolism. Submission date September 2018. This proposal offers potential for involvement of Industry partners.**

Prescribed Exercise, nutrition and rehabilitation

Proposal being developed. (PIs) Dr Gillisn Prue and Professor Anthony Maraveyas

GP leads on a study of prescribed exercise for patients with pancreatic cancer after pancreatectomy that are receiving adjuvant chemotherapy.

The primary objective is to establish the feasibility of delivering an innovative, non-linear exercise training programme to these patients and give an initial indication of its ability to improve QOL and symptoms such as fatigue, psychological distress and sleep disturbance.

The overall aim is to improve cancer-related symptoms, quality of life (QOL) and relapse free and overall survival in patients with pancreatic cancer after pancreatectomy. Working with exercise physiologists, we aim to incorporate biomarkers of functional change in this study.

Suitable call targeted is **pancreatic cancer UK deadline in October 2018.**

4. Task groups/Working parties

Remit of Immuno-oncology Toxicities Working Party (TBC)

In the feedback from the 2016-17 Annual Report review, the panel noted that *"there is a need for supportive care research in the field of immune- oncology and saw this as an opportunity for the CSG to take an international lead. The panel recommended setting up a working party in this area to bring in relevant experts (e.g. the University of Southampton research group)."* The Working Party has taken up this recommendation and after approval of an outline proposal at the Quinquennial Review in March 2018, it has spent several months in developing the full workplan for this task.

Progress to date

Several leading experts in oncology, supportive care, PROMs and quality of life measurement have been recruited to ensure that the Working Party addresses the need to design studies in the acute and late toxicities of immunotherapy in an inclusive and holistic way. The main themes which will be determined at the first meeting, planned for Q3 2018, are likely to include:

- Critical review of existing immunotherapy toxicity management guidelines from ESMO, ASCO, etc
- taking a population-based approach, using cohort designs and registers;
- enhancing acute and late follow-up to existing immunotherapy trials;
- point-of-care data collection using existing databases in NHS treatment sites in order to minimise extra CRF load, working with MIDL facilities in NIHR CRN: Cancer;
- identification of future workforce capacity and training needs to cope with large numbers of immunotherapy-treated survivors and those entering end of life.

The Working Party will necessarily work with all the pharmaceutical companies who have an interest in these current products and those in the pipeline. It will need access to several consumer representatives, taken from the pool of patients who have received these treatments and/or their carers. Finally, international 'corresponding members' will be appointed to give advice and feedback, also helping the Working Party to keep abreast of and coordinate with parallel developments abroad.

5. Funding applications in last year

Table 2 Funding submissions in the reporting year

Cancer Research UK Clinical Research Committee (CRUK CRC)				
Study	**Application type**	**CI**	**Outcome**	**Level of CSG input**
May 2017				
None				
November 2017				
None				
Other committees				
Study	**Committee & application type**	**CI**	**Outcome**	**Level of CSG input**
Eat-CIT: an investigation to inform the content of a web based resource to help people with cancer self-manage eating difficulties during Chemotherapy and/or Immunotherapy (systemic anti-cancer) Treatment.	Tenovus Cancer Care iGrant.	Professor Jane Hopkinson	Successful	CSG/Subgroup developed
Oral chemotherapy management in the home: an exploratory case study of treatment adherence in people with cancer living in the Valleys of South East Wales.	KESS2: Knowledge Economy Skills Scholarships, European Social Fund.	Professor Jane Hopkinson	Successful	No CSG involvement
Cancer Carer Capability: an investigation of education, training and skill needed in the home for safe and effective cancer treatment supported by primary care practitioners.	Macmillan Cancer Support. Outline.	Professor Jane Hopkinson	Unsuccessful	No CSG involvement

Coproduction of cancer education for healthcare professionals: a 'how to' toolkit	Tenovus Cancer Care iGrant. Outline	Professor Jane Hopkinson	Unsuccessful	No CSG involvement
Cancer Memory Kit: a feasibility trial of an intervention to help with cancer treatment adherence and management of side effects in people with comorbid cognitive impairment or dementia.	NIHR RfPB. Outline.	Professor Jane Hopkinson	Unsuccessful.	No CSG involvement
GAP4 Exercise and metabolic Health Project.	Movember Foundation Australia.	Dr Gillian Prue	Successful	No CSG involvement
Subsidiary feasibility/pilot trial within the GAP4 Study: Physical Activity with End-State Prostate Cancer Patients	Movember Foundation Australia.	Dr Gillian Prue	Successful	No CSG involvement
Let's get active about waiting.	Cancer Focus Northern Ireland/The Burdett Fund for Nursing.	Dr Gillian Prue	Successful	No CSG involvement
A feasibility trial of a tailored e-web-based psychoeducational intervention for advanced cancer patients and their informal carers.	Marie Curie Cancer Care.	Dr Gillian Prue (Co-I)	Pending	No CSG involvement
Dyadic Psychosocial and Educational Interventions for People with Advanced Cancer and their Informal Caregivers (DIAdIC): An International Randomized Controlled Trial.	EU - H2020 call.	Dr Gillian Prue	Pending	No CSG involvement

SPIN: a Study of Prehabilitation In Non-small cell lung cancer.	Roy Castle Lung Cancer Foundation	Dr Gillian Prue	Unsuccessful	No CSG involvement
The development of a cancer action plan to respond to the health inequities faced by LGBT patients.	Wellcome Trust	Dr Gillian Pruemaya	Unsuccessful	No CSG involvement
Introducing an enhanced model of palliative care to routine oncological care and support for advanced head and neck cancer patients and their families.	Yorkshire Cancer Research 'Connects' scheme – 5-year Senior Research Fellowship	Dr Carolyn Mayland	Successful	CSG/Subgroup supported
The development of a framework to personalise hydration management in cancer care: the use of non-invasive technology to evaluate fluid status and dehydration-related symptoms	Liverpool CCG Research Capability Funding; additional funding from Aintree Head and Neck Patient and Carer Research Forum	Dr Carolyn Mayland (Co-I)	Successful	No CSG involvement
Living well and dying from head and neck cancer an exploratory qualitative study assessing experiences, unmet needs and health service usage.	Liverpool CCG Research Capability Funding; additional funding from	Dr Carolyn Mayland	Successful	No CSG involvement

	Aintree Head and Neck Patient and Carer Research Forum			
International 'Care of the Dying Evaluation' (CODE): quality of care for cancer patients as perceived by bereaved relatives.	Northwest Cancer Research	Dr Carolyn Mayland	Unsuccessful	No CSG involvement
What factors influence how and where people with advanced head and neck cancer die?	Macmillan Research Grants	Dr Carolyn Mayland	Unsuccessful	No CSG involvement
CHRONOS - Comparative Health Research Outcomes of NOvel Surgery in prostate cancer	Prostate Cancer UK	Dr Annmarie Nelson	Successful	No CSG involvement
Attitudes to death and dying survey	Velindre End of Life Board	Dr Annmarie Nelson (Co-CI)	Successful	No CSG involvement
Scope2: A randomised Phase II/III trial to study radiotherapy dose escalation in patients with oesophageal cancer treated with definitive chemo-radiation with an embedded Phase II trial for patients with a poor early response using positron emission tomography (PET	CRUK	Prof Somnath Mukherjee CI; Dr Annmarie Nelson (Co-applicant)	Successful	No CSG involvement
Empower Project	Tenovus	Dr Annmarie Nelson, Professor Simon Noble (Co-CIs)	Successful	No CSG involvement
Research Assessment Outcome Measures for Malignant Bowel Obstruction (RAMBO)	Marie Curie	Dr Annmarie Nelson (Co-applicant)	Successful	No CSG involvement

HIDDen: DVT Hospice Prevalence observational study. Doppler scans of hospice inpatients to establish prevalence of asymptomatic DVT	NIHR HTA	Dr Annmarie Nelson (Co-applicant)	Successful	No CSG involvement
Supporting people bereaved through advanced illness: a systematic review of the evidence and development of a core outcome set for bereaved research in palliative care	Marie Curie	Dr Annmarie Nelson (Co-applicant)	Successful	No CSG involvement
RESOLVE YORKSHIRE: REcognition of Needs and Symptoms in advanced cancer to Improve Outcomes and LiVEs in YORKSHIRE.	Yorkshire Cancer Research	Co-CIs Prof Bennett and Murtagh	Successful	
ImproveCare - The management of clinical uncertainty in end of life care: a feasibility cluster RCT	NIHR HTA	CI Koffamn; Prof Murtagh (co-applicant)	Successful	
Multimodal intervention of nutrition and activity versus usual care for patients with oesophagogastric cancer (MONACO-1)	NIHR HTA	Mr David Bowrey (CI); Professor Sam Ahmedzai (co-applicant)	Pending – in second round	CSG/Subgroup developed
MICA. A phase II trial examining MABp1 (anti-IL1) effects on muscle, physical function and quality of life, in lung, pancreatic or ovarian cancer	MRC	B Lair CI; Professor Sam Ahmedzai (co-applicant)	Pending – second round	CSG/Subgroup developed

6. Consumer involvement

We are very well served in all the Subgroups and at the main CSG level, by our two consumer representatives Mrs Jean Gallagher and Mr Jim Elliott. Jean has specifically been involved in design and co-applicant on DOSIS, Bladder-PATH and the new studies in the Early stage disease and acute treatment toxicities Subgroup.

Jean Gallagher

This section has been added on behalf of Mrs Jean Gallagher

Jean is an important and active member of the Group, giving both patient and carer perspectives on all aspects of the CSG discussions, bringing her prior and long experience in nursing. She has particularly focused on new studies coming through the Early stage disease and the Advanced stage disease subgroups.

Jean's work with local universities on generic studies (e.g. Patient Safety and Information Technology at Leeds University) strengthen her understanding of health research. Her end of life experience is aided by volunteering at her local hospice – card-making as distraction therapy – in which she speaks with patients.

She has a long track record of involvement in cancer studies. The studies relevant to the CSG are outlined below:

- DOSIS Co-applicant in this UK arm of an international study of palliative radiotherapy
- 'STEP' Co-author with Prof Mike Bennett on this study, which is a follow on from time for Palliative 'Time for Pall'
- GO2 Member of steering group
- VTE studies Her training as a nurse as well as a consumer has been helpful in these anticoagulant studies

Jim Elliott

Jim joined the Group during 2017-18 and has been involved with the following.

Engagement with CSG activities and members since the last report:

- Attending meetings to assist in planning the Annual Trials Meeting: contributions to teleconferences to help plan the agenda and identify speakers; questions to presenters and feedback on proposals.
- Attended the Survivorship and Late Consequences Subgroup meeting, 8th November at NCRI Conference, Liverpool: contributed to discussions of plans

Proposed future working with the CSG:

- Jim is interested in looking at recruitment to and retention in portfolio studies and for factors that influence the rates of recruitment, including time to recruit first patient and time to target and how patients are retained. There is widespread variation with only a small

proportion recruiting well and to targets. Are there characteristics of those studies that could be described and applied to other studies that are not recruiting well? This could fit with one or more of the priorities identified from the PRioRiTy project and its successor, which Jim is involved with along with the STEER project.

- From his role at the Health Research Authority (HRA) (his part time “day job”) Jim has developed an approach that consumers can take to help researchers with whom they are working to design studies to better present this involvement in their research ethics applications and improve their chances of outright approval or reduce the number of conditions and time to final approval. This was shared at the last meeting and has received widespread support but needs to be taken forward in a systematic way. The HRA is now looking to set up “Test Beds”, or pilot sites, to do this, which could be done through some of the institutions that CSG members are part of and or and across the CSG’s portfolio of studies.

7. Priorities and challenges for the forthcoming year

Priority 1

Collaboration with site-specific CSGs

Work with site-specific CSGs to develop supportive and palliative care studies, or sub-studies within their existing portfolio, to advance our understanding of symptom burden, early and late toxicities and experience in end of life care. We plan to do this by engaging with other CSGs through their own strategy days, annual trials meetings and at specific requests for our assistance. Examples of requests for our advice and collaboration on these issues include the Upper Gastrointestinal CSG, Brain Tumour CSG, Teenage & Young Adults and Germ Cell Tumour (TYA & GCT) CSG.

Priority 2

Collaboration with cross-cutting CSGs

Work with cross-cutting CSGs such as Psychosocial Oncology & Survivorship (POS), Primary Care, TYA & GCT. We had invited POS presentations at our 2017 Annual Trials Meeting and a specific study (HORIZONS) presentation by Dr Lynn Calman at a main CSG meeting. A meeting is planned for July 2018 with POS and Primary Care CSGs to explore opportunities for cross-working and to clarify areas of overlap. We also work with CTRad – a second round proposal is being submitted by Dr Paula Mulvenna on our translational study in elucidating mechanisms and treatment targets for radiation-induced pain flare. There is possibility of collaboration for this study with Dr E Chow in Sunnybrook Hospital Toronto. Professor Maraveyas recently presented a study idea to the SPED Advisory Group on early detection of in situ bladder cancer using NextGen sequencing on bladder sediment, and obtained very helpful feedback.

[This was a recommendation from the Quinquennial review.]

Priority 3

Engage with industry more effectively to launch pharma and device manufacturer supported research

We have a track record of industry-led studies (novel opioid analgesic CORAL and CORAL XT trials from Grunenthal; opioid-naloxone combination TARGIN from Mundipharma; opioid-induced constipation study OIC from Astra Zeneca). However, we wish to develop more trials from the CSG itself in which industry can provide drug or similar support, such as our Select-d qualitative sub-study on thrombosis which was part supported by Bayer. Similarly, the recently closed trial SARCABON using the novel Src inhibitor Saracatanib for bone-cancer pain was Medical Research Council funded with drug supplied by Pfizer (Andrew, Ahmedzai). However, our attempts to engage with the medical device industry for research with injection and infusion devices for symptom management have so far been unsuccessful (Dickman).

[This was identified as an area of need in the 2016-17 annual review feedback.]

Challenge 1

Development of translational studies

To develop more studies with a planned translational hypothesis, rather than as an 'add-on' to an existing trial with a 'backward translational' exploratory study. Opportunities for these can arise from our cross-referencing with other site-specific CSGs, and also through the planned Immunotherapy Toxicities Working Party. Examples include the EXERTION study in preparation for exercise and rehabilitation in adjuvant pancreatic cancer patients (Prue); and neuropathy and cardiotoxicity studies in development (Faithful).

[This was identified as a challenge at the March 2018 Quinquennial Review.]

Challenge 2

Engage other CSGs, industry and international partners in the Immunotherapy Toxicities Working Party

The CSG is aware that there are already emerging guidelines from European Society for Medical Oncology (ESMO), American Society of Clinical Oncology (ASCO) and other groups on managing these toxicities. However, on close examination their evidence base is often weak. We need to identify the areas where our Working Party can make most significant progress by designing short and long-term studies to fill the evidence gaps for the next round of guideline updates. Moreover, it is important that the studies we design are responding to patients' experience and priorities. We are also mindful that pharmaceutical companies may be initially reluctant to extend toxicity data collection beyond the current minimum period required for drug registration. We also need to design studies that can be adapted to include new diagnostic groups in the future as the indications for these drugs expand; this needs engagement with a wide pool of CSGs.

[This was identified as a recommendation in the 2016-17 annual review feedback.]

Challenge 3

Respond to the key priorities from the NCRI 'Living With and Beyond Cancer' (LWBC) initiative

This important priority-setting partnership with James Lind Alliance (JLA), in which members of the CSG contributed through privileged access to draft topics thanks to its leader Dr Feng Li, will be announced at the NCRI Conference in November 2018. This CSG should be prepared to launch several new trial proposals based on the top 10 priorities, as it most likely these will be subject of commissioned calls by NIHR, Marie Curie and Macmillan in the coming years. As it likely that most of the priorities will be 'generic' across cancer types, and across age groups, we need to be prepared to engage quickly with a wide range of CSGs and cross-cutting CSGs, in particular Primary Care, POS and TYA & GCT.

8. Appendices

Appendix 1 - Membership of main CSG and subgroups
Appendix 2 – CSG and Subgroup strategies
- A – Main CSG Strategy
- B – Early stage disease and acute treatment toxicities Subgroup Strategy
- C – Advanced disease and end of life Subgroup Strategy
- D – Survivorship and late consequences Subgroup Strategy

Appendix 3 - Portfolio Maps

Appendix 4 – Top 5 publications in reporting year

Appendix 5 – Recruitment to the NIHR portfolio in the reporting year

Appendix 6 – QQR feedback

Professor Sam H Ahmedzai (Supportive & Palliative Care CSG Chair)

Appendix 1

Membership of the Supportive & Palliative Care CSG

Name	Specialism	Location
Dr Gillian Prue	Physiotherapy	Belfast
Dr Paula Mulvenna	Clinical Oncologist	Newcastle upon Tyne
Mrs Jean Gallagher	Consumer	Bingley
Mr Jim Elliott	Consumer	Newport
Dr Teresa Young	Health Service Researcher	Middlesex
Dr Sabine Best	Marie Curie representative	London
Dr Caroline Forde*	Medical Oncologist	Belfast
Professor Anthony Maraveyas	Medical Oncologist	Hull
Dr Dawn Storey	Medical Oncologist	Paisley
Professor Jane Hopkinson	Nurse	Cardiff
Professor Annie Young	Nurse	Warwick
Professor Sam Ahmedzai (Chair)	Palliative Medicine	Sheffield
Professor Christina Faull	Palliative Medicine	Leicester
Dr Catriona Mayland	Palliative Medicine	Liverpool
Professor Fliss Murtagh	Palliative Medicine	Hull
Dr Andrew Dickman	Pharmacist	Blackpool
Dr Matthew Maddocks	Physiotherapist	London
Dr Annmarie Nelson	Scientific Director, Marie Curie Palliative Care Research Centre	Cardiff
Professor Gareth Griffiths	Statistician	Southampton

* denotes trainee member

Membership of the Subgroups

Advanced disease and end of life Subgroup		
Name	**Specialism**	**Location**
Mrs Jean Gallagher	Consumer	Bassett
Dr Vicky Coyle	Medical Oncologist	Belfast
Professor Sam Ahmedzai	Palliative Medicine	Sheffield
Professor Christina Faull	Palliative Medicine	Leicester
Professor Fliss Murtagh	Palliative Medicine	Hull
Dr Carolyn Mayland	Palliative Medicine	Sheffield
Dr Andrew Dickman	Pharmacist	Blackpool
Dr Matthew Maddocks (Chair)	Physiotherapist	London
Professor Jane Hopkinson	Nurse	Cardiff

Early stage disease and acute treatment toxicities Subgroup		
Name	**Specialism**	**Location**
Mrs Jean Gallagher	Consumer	Bingley
Dr Gillian Prue	Physiotherapist	Belfast
Dr Teresa Young	Health Service Researcher	Middlesex
Dr Vicky Coyle	Medical Oncologist	Belfast
Prof Anthony Maraveyas	Medical Oncologist	Hull
Dr Dawn Storey	Medical Oncologist	Paisley
Professor Annie Young (Chair)	Nurse	Warwick
Dr Rebecca Hale **	Oncology and Haematology	Lothian
Professor Sam Ahmedzai	Palliative Medicine	Sheffield
Professor Gareth Griffiths	Statistician	Southampton

Survivors and late consequences Subgroup		
Name	**Name**	**Name**
Mr Jim Elliott	Consumer	Newport
Dr Gillian Prue	Physiotherapist	Belfast
Dr Teresa Young	Health Services Researcher	Middlesex
Dr Anthony Maraveyas (Chair)	Medical Oncologist	Hull
Dr Dawn Storey	Medical Oncologist	Paisley
Dr Sara Faithful **	Nurse	Guildford
Professor Sam Ahmedzai	Palliative Medicine	Sheffield
Dr Richard Wagland **	Senior Research Fellow	Southampton

**denotes non-core member

Appendix 2

CSG & Subgroup Strategies

A – Main CSG Strategy

Since 2015-16, the CSG's strategy has been to reflect the current scope of supportive and palliative care in cancer across the whole continuum of cancer from diagnosis, through treatment, through remission/survivorship and into end of life. Five main areas of focus have emerged.

1. **Problems facing patients with early stage disease and who are undergoing acute curative and adjuvant treatments:** Some of the symptoms this group of patients experience arise from the cancer disease itself but the CSG has prioritised targeting the symptoms of adverse effects that arise from therapies such as surgery, radiotherapy, chemotherapy and biological treatments. An important new area is the growing number and range of toxicities from immunotherapies as these could ultimately reach a very large group of patients.

Progress: Studies developed by the Group include – detection and prevention of venous thromboembolism; 5-FU related cardiotoxicity; chemotherapy-induced peripheral neuropathy; prehabilitation prior to stem cell transplant and in lung cancer; patient experience of immunotherapy trials. We have given feedback and contributed to study development in other CSGs, eg antimicrobial therapy in children during treatment (TYA), geriatric and frailty assessment (Upper GI). The new Immunotherapy Toxicities Working Party will have an important contribution to this workstream.

2. **Symptoms and problems with functioning in patients with advanced, progressive disease and those who are at the end of life:** Hitherto, the CSG has enjoyed a very good track record in trials in advanced disease covering pain management, breathlessness, cachexia and fatigue. We continue to build on this but are also expanding to other key problems such as those research recommendations from the 2015 NICE guideline on care of the dying adult. This highlighted recognising when a person is entering the last days of life, management of agitation and delirium, of noisy respiratory secretions and of anticipatory prescribing. In addition, we will focus on the largely unrecognised or ignored side-effects of traditional palliative medical treatments, e.g. opioid-induced constipation, immunomodulation and hyperalgesia.

Progress in 2017-18*:* Studies from the Group have covered prognostication in advancing disease, cachexia and fatigue management, pain management, complications of opioid therapy, novel molecule (saracatanib) for pain arising from bone-metastases, anticipatory prescribing, rehabilitation. Another workstream that will become more important is health services research in end of life care, especially in settings outside the acute hospital and beyond cancer.

3. **Problems facing patients who are long-term survivors of cancer, or those living with cancer as a chronic illness:** This is ultimately one of the greatest challenges as more people are living for longer after cancer treatment. There is need to delineate and differentiate our Group's interests in 'survivorship', from those in other CSGs, eg Psychosocial Oncology and

Survivorship and Primary Care. Thus we are focusing on the medical barriers they face to returning to a "normal" lifestyle after treatment (including return to work) and especially on the clinical issues which arise as late consequences of anti-cancer treatments. These may be structural, e.g. loss of limbs or organ function, e.g. late GI malfunction after pelvic radiotherapy; or lifestyle-related, e.g. nutrition and exercise programmes for survivors. Strategically we are collaborating with the NCRI Living With and Beyond Cancer (LWBC) initiative and also with the Psychosocial Oncology and Survivorship and the Primary Care CSGs.

***Progress*:** Although this workstream only started in November 2017, it has already generated studies in late effects of chemotherapy-induced peripheral neuropathy, cardiotoxicity of novel anti-cancer agents, surveillance for VTE risk, management of persistent fatigue and breathlessness. We anticipate the new Immunotherapy Working Party will generate new research themes and topics in this workstream.

4. Translational research

An important part of our overall strategy is to incorporate fundamental biomedical questions wherever possible and to add research questions relating to mechanisms. This was discussed at our Quinquennial Review in March 2018. The QR panel gave this feedback: *"Focus on doing "forward-looking" translational research questions as well "reverse" treatment questions. For example, research questions currently generated by the Group involve looking at symptoms of a drug. The Group should focus on developing trials involving new treatment methods.*

"It was felt the Group should do more translational research work and recommended appointing a basic scientist to the Group."

Progress: We are therefore working with other CSGs and basic scientists to add translational aspects to our studies where relevant, e.g. biomarkers and genomics of symptom expression, pharmacogenetics of drug usage and adverse effects. This will also be key to the membership of the Immunotherapy Working Party. For this area, we will also need to engage more effectively with the pharmaceutical industry for both anti-cancer drugs and also new symptom palliation treatments, eg antibodies to pain neuronal targets.

5. Complementary therapies

We also have a remit for researching the use of specific complementary therapies in order to increase their evidence base. This workstream is partly a 'legacy' of the interests of the CSG from over 5 years ago. However, there has been a growth of interest in pursuing non-pharmacological methods for management of adverse effects of anti-cancer treatments, eg myalgia and arthralgia as well as hot flushes from endocrine manipulation in breast cancer; and non-medical approaches for breathlessness.

Progress: We will continue to review this area which is important to patients but often overlooked by clinicians. Our Group has expertise in acupuncture (Teresa Young) and we are considering options for clinical studies using this modality in modulating adverse effects from immunotherapy and other therapies.

Strategic Review

The Group's current strategy was started in 2015-16. We plan to review this strategy in the light of the Quinquennial Review and its feedback, and in consequence of our achievements and less successful areas. The new strategy will also reflect the changes in membership of the CSG. A high priority will be to set up mechanisms to increase collaborations between CSG members, especially those with unusual or unique skills, to speed up protocol development and grant writing in between as well as during Subgroup meetings. This work will start at the autumn 2018 meeting and will be complete by spring 2018.

B – Early stage disease and acute treatment toxicities Subgroup Strategy

Stemming from a needs assessment study of cancer patients who had been potentially cured1, carried out by members of our CSG, this new subgroup is utilising the results as the foundation of our strategy. One third of people were found to have a moderate or severe 'unmet' need, arising from their cancer - in living their 'new normal' lives. Research for people with early stage disease and research on treatment toxicities have markedly progressed since then, alongside the patient voice.

1. We aim to be the UK arm of MASCC – Multinational Association of Supportive Care in Cancer, the international group that many of our CSG members contribute to – and for this CSG subgroup, to take our UK studies of toxicities of treatment, globally. We now have the opportunity to work closer with MASCC with one of our subgroup members (AY) being elected on the MASCC Board.

2. Our priority strategic actions are to develop our own portfolio studies e.g. patient experience of immunotherapy; and to work with other CSGs in integrating the science of supportive care with mainstream oncological treatments. For example, in our venous thromboembolism (VTE) prevention and treatment studies, we are joining with international groups in identifying blood biomarkers of VTE, ultimately to predict risk of VTE or recurrence of VTE; we wish to incorporate translational elements into the majority of our toxicity studies.

3. The Early Stage Disease and Acute Treatment Toxicities Subgroup strives to have two large portfolio studies approved by Q4 of 2018.

Progress in 2017-18:

In line with our strategic plan, the subgroup has taken on a new stream of work, focusing on the experience of patients in the early phase of disease and their treatments into survivorship and is collaborating with the survivorship subgroup group on this work.

The Early stage disease and acute treatment toxicities Subgroup currently has 16 open studies, 6 of which are multi-centre.

The subgroup has had two face to face meetings and 3 teleconferences, forming proposals around symptoms and complications of cancer and toxicities from the therapies used. We have also reached out to other CSGs to collaborate in specific supportive and palliative areas of care. Each member of the subgroup is responsible for the development of one bid:

1. Acute treatment toxicities

    - *Immunotherapy (IO)* – Patient Experience (GP, AY, GG), Quality of Life (GP, AY, GG), initially taken through existing IO studies at Southampton University. *With our CSG as leads for the bid, we have been shortlisted for the final stage of an NIHR bid on gastrointestinal toxicities from IO drugs (May 2018)*

    - Chemotherapy-induced nausea and vomiting in multi-day chemotherapy regimens (AY, SA)

    - 5-FU cardiotoxicity biomarkers (VC)

- Prevention of Venous Thromboembolism [VTE] (AM, AY)

2. Prehabilitation and rehabilitation for patients with early stage disease (GP)

- Having just completed PRO-REHAB (patients who have had treatment for adjuvant and advanced disease, we have worked alongside the Supportive Care, Transfusion & Late Effects subgroup of the Haematological Oncology CSG, to design a PREHAB study (to follow on from PRE-EMPT) in patients with multiple myeloma undergoing autologous transplantation.

- Also following on the PRO-REHAB study findings and subgroup involvement (VC) in the CHALLENGE study, GP (physiotherapist) is leading on a multi-site prehabilitation and rehabilitation exercise study in patients with lung cancer.

C – Advanced disease and end of life Subgroup Strategy

This Subgroup's remit is to stimulate and develop research concerned with people with advancing disease and towards the end of life. Members have working links with, among others, the European Association of Palliative Care, Multinational Association of Supportive Care in Care, Society on Cachexia and Wasting Disorders and Association of Chartered Physiotherapists in Oncology & Palliative Care.

Our strategy is to bolster research in: (i) symptoms of advancing disease, e.g. thrombosis, cord compression, fatigue and breathlessness; (ii) issues near the end of life, e.g. prognostication, management of dying; and (iii) rehabilitation, e.g. optimising independence and therapy decision making.

Progress in 2017-18: The current portfolio spans these priorities and includes interventional work (e.g. ACTION and IMPACCT), large scale observational studies (e.g. C-CHANGE and PiPS2), and interventional trials (e.g. MENAC, ENERGY). Subgroup members are encouraged to devise studies targeting recruitment of larger numbers of patients than previously, across many sites, and crucially are open to new sites joining.

D – Survivors and late consequences Subgroup Strategy

This Subgroup's remit was revisited on 8 November 2017 when Professor Maraveyas stepped in as short term chair (one year appointment).

The overall direction and strategy was not altered substantially, though it was recognised that within each of the three main themes a different emphasis on study direction would be modified. These themes are:

1. Medical problems faced by longterm survivors as a consequence of treatment

2. Cardiovascular, including thromboembolism and lymphoedema

3. Exercise, nutrition and rehabilitation

The specific topics that emerged from these themes are as follows:

i. Peripheral neuropathy

ii. Gastrointestinal effects of pelvic radiotherapy

iii. Late consequences after immunotherapy

iv. Lymphoedema, chronic vascular and cardiac problems

v. Prescribed exercise, and rehabilitation for fatigue, pain, breathlessness and recurrence reduction.

The subgroup aims to develop at least 3 or more projects from these themes during 2018 and is looking for closer collaboration with industry, eg there is potential with the nutrition industry, e.g. with fish oil or neutraceuticals.

Progress in 2018-19:

1. Medical problems faced by longterm survivors as a consequence of treatment modalities

Examples of studies currently in progress or development include lower GI consequences of pelvic radiotherapy – EAGLE (Nelson, Ahmedzai); CIPN Cohort longitudinal Study In late development seeking submission to HTA EME possibly Q3 2018 (Faithful); prolonged effects of immunotherapy - Beyond 100 Days Immunotherapy Toxicity Register (Maraveyas).

2. Cardiovascular, including thromboembolism and lymphoedema

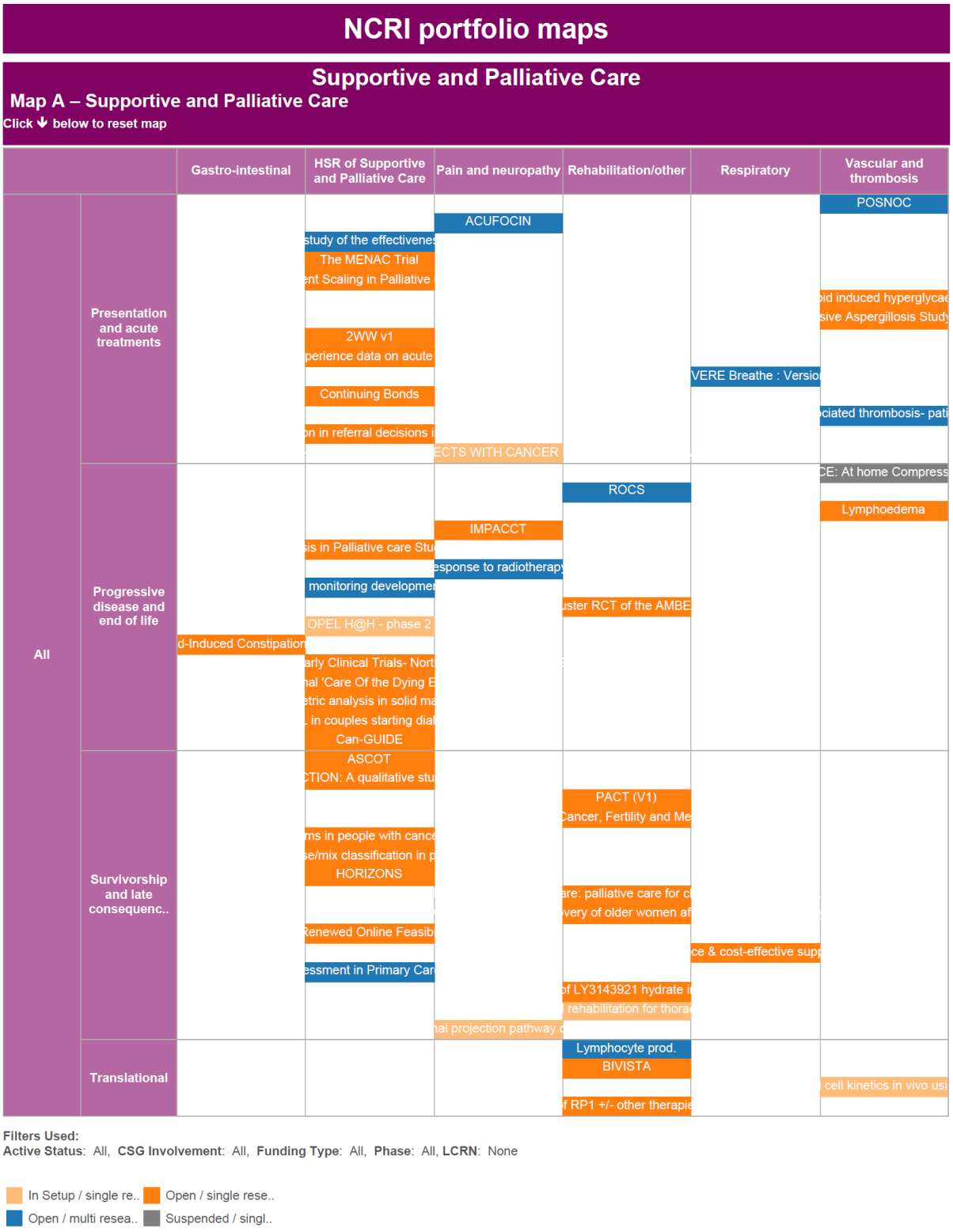
Studies include cardiotoxicity of novel anti-cancer agent (Faithful with Lyon, Brompton), detection of incidental PE - CLOT-ReSOLVe (Maraveyas, Young), novel treatments for lymphoedema management (Keeley).

3. Exercise, nutrition and rehabilitation

These focus on patients in remission and returning to work, but there has been an overlap with exercise and rehabilitation research led by the Advanced disease subgroup. An example of a new study is exercise in adjuvant pancreatic cancer – EXERTION (Prue),

Appendix 3

Portfolio maps



Appendix 4

Top 5 publications in the reporting year

Trial name & publication reference	Impact of the trial	CSG involvement in the trial
1. Cancer cachexia: rationale for the MENAC (Multimodal-Exercise, Nutrition and Anti-inflammatory medication for Cachexia) trial. Solheim TS et al BMJ Support Palliat Care. 2018 Feb 9. pii: bmjspcare-2017-001440	Following the failure of several trials to slow down or reverse cancer cachexia by use of pharmacological means alone, the MENAC trial was designed as a multimodal intervention incorporated exercise and nutritional support to two tested anti-inflammatory agents (NSAID and EPA). The feasibility study has been completed successfully and we are now engaged on designing larger follow-up trials to test the principle in larger populations. This is likely to be the most fruitful approach to cachexia management so far.	This international study was designed with input from three CSG members (the late Professor Ken Fearon, Prof Marie Fallon and Dr Matthew Maddocks). A new trial is being developed for the UK (MONACO-2) that will use the lessons learnt from the MENAC feasibility study in upper GI cancer patients (CI Dr Barry Laird + M Maddocks, M Fallon, SH Ahmedzai).
2. Supporting carers to manage pain medication in cancer patients at the end of life: A feasibility trial. CCMM (Cancer Carers Medicines Management) Latter S et al. Palliat Med. 2018 Jan;32(1):246-256	This study showed that it is feasible to inform and support carers to play an active role in giving medicines to patients dying at home. This could have important consequences for the NHS in terms of quality and costs of care at the end life. It identified areas of problematic recruitment and will be used to inform future studies in this area.	This study was developed with the help of the old Pain Subgroup of the CSG, by two members (Professor Mike Bennett, former chair, and Professor Jane Hopkinson, current member).
3. How well do we currently care for our dying patients in acute hospitals. The	This study used a questionnaire (CODE) to evaluate the perceptions of bereaved relatives	The CI Dr Mayland is a new member to the CSG and will play an important role in the Advanced

views of bereaved relatives? (CODE) CR Mayland at al, Supportive and Palliative Care 2017 Sep;7(3):316-325.	of people who had died in hospital. It was incorporated into the large National Care of the Dying Audit led by Royal College of Physicians. It demonstrated for the first time that post-bereavement evaluation of care in the last days of life is feasible and acceptable.	disease and end of life care Subgroup, pursuing this and other related lines of research.
4. Phase of Illness in palliative care: Cross-sectional analysis of clinical data from community, hospital and hospice patients. Mather H, Murtagh FE at al. Palliat Med. 2018;32(2):404-12.	This is a key paper from the NIHR C-CHANGE trial which has clarified how end of life care for cancer and other longterm conditions is being mainstreamed into NHS services and in non-NHS hospice and care home sectors.	The CI Prof Fliss Murtagh has recently joined the Group and will play an increasingly important role in helping the CSG to address the methodological challenges of undertaking rigorous research in end of life care.
5. How many people will need palliative care in 2040? Past trends, future projections and implications for services. S. N. Etkind et al, BMC Medicine (2017) 15:102.	The NHS needs better data to make predictions about future capacity and workforce issues with regard to the demographic expansion of elderly people and their related life-limiting condition including cancer and dementia. The PI for the study (Dr Etkind) is an NIHR ACF and will likely develop a career pathway in this area.	The CI Prof Fliss Murtagh has recently joined the Group.

Appendix 5

Recruitment to the NIHR portfolio in the reporting year

In the Supportive & Palliative Care CSG portfolio, 14 trials closed to recruitment and 11 opened.

Summary of patient recruitment by Interventional/Non-interventional

Year	All participants		Cancer patients only		% of cancer patients relative to incidence	
	Non-interventional	Interventional	Non-interventional	Interventional	Non-interventional	Interventional
2013/2014	1473	393	524	324	-	-
2014/2015	1336	498	1290	473	-	-
2015/2016	869	2261	706	2244	-	-
2016/2017	2510	1923	2250	1747	-	-
2017/2018	2132	3798	1875	3573	-	-

Appendix 6

Feedback from the Quinquennial Review Panel*

The Panel thanked the Supportive & Palliative Care CSG for the documentation provided and the openness with which they had engaged in discussions.

The Panel identified a number of strengths of the Group and issues that the CSG need to consider:

Strengths

- The Panel commended the strong and active leadership.
- The Panel congratulated the Group on their successful restructure.
- The CSG's portfolio of studies has had clear international impact and changed practice.
- High success rate with funding applications despite the challenges in the research funding landscape over the past two years.
- Successful recruitment to time and target.
- The Panel was impressed by the increase in the number of patients going into interventional trials over the past few years.
- Exemplary Group in terms of interacting with the NIHR Supportive & Palliative Research Delivery Manager to actively resolve trial delivery issues.

Issues for the CSG to consider

- The Early Stage Disease & Acute Treatment Toxicities Subgroup seems to be lacking a clear strategy, particularly with regards to acute treatment toxicities. An important step for the Subgroup will be to liaise with the wider acute oncology community and refine the goals of the Subgroup, with respect to this area.
- The Panel noted inadequate representation from palliative medicine on the Advanced Disease & End of Life Care Subgroup and encouraged the Subgroup to focus on this area when refreshing recruitment. In addition to this, it was recommended the Subgroup fostered collaboration with hospices by appointing a Hospice UK representative.
- Setting up a time limited NCRI Working Party with the Primary Care CSG to explore co-morbidities and personalised medicine, given that in the next 30 years most cancer patients will be over 65.
- Focus on doing "forward-looking" translational research questions as well as "reverse" treatment questions. For example, research questions currently generated by the Group involve looking at symptoms of a drug. The Group should focus on developing trials involving new treatment methods.
- It was felt the Group should do more translational research work and recommended appointing a basic scientist to the Group.
- The Panel noted that the Chair is highly involved and committed to the Group, which was commended, but they felt this was largely possible because the Chair is retired and that it would be difficult for a future Chair to maintain the same level of commitment. The Panel felt that for the Group to continue to function well after the current Chair stands down, there needs to be a plan in place to delegate tasks to members/Subgroup Chairs and ensure any external links current members have are formalised with the CSG before they step down.

- Start succession planning of Subgroup Chairs roles now, to allow smooth handover in the summer when the Subgroup Chairs are rotated off.

Issues for the NCRI/NIHR CRN to consider

- The NCRI CRG team will assist the Supportive & Palliative Care CSG Chair in the recruitment of the trainees, including asking members to circulate the advert to junior researchers and approaching relevant organisations to assist with advertising.
- The NCRI Head of CRGs and NCRI Clinical Director will discuss how to take forward outcomes of the recent Acute Oncology Workshop before the next Strategy Advisory Group meeting, to establish how the S&PC CSG will be involved in this work.
- The NCRI Executive Team will arrange an annual meeting between all the cross-cutting CSG Chairs and Subgroup Chairs, to promote better collaboration.

In concluding the Review, Professor Seymour thanked everybody for participating and the NCRI CSG Team for preparing the paperwork and organising the Review. The business of the meeting took four hours. ***The Group will be reviewed in five years' time.***

**Please note that the above feedback is awaiting final sign off from the Quinquennial Review Panel.*