

NCRI Palliative Care Clinical Studies Group

Introduction

The remit of the Group is in line with the other Clinical Studies Groups with the primary aim being to develop a portfolio of national collaborative studies, which are clinically relevant and likely to have an impact on day-to-day practice. The full committee is concerned with developing a strategy for the Group and identifying priorities for palliative care research. The development of protocols has been devolved to subgroups where the detailed discussion and review of study proposals takes place. The Group was reviewed in May 2009. A summary of the Group's strengths and issues it needs to address can be found in Appendix 1.

Membership and structure

In August 2008, Professor Mike Bennett took over as chair from Professor Henry McQuay who had led the CSG successfully from 2004. The Palliative Care CSG is currently represented by a range of predominantly medical disciplines including palliative medicine, oncology (medical and surgical), primary care, and anaesthesia/pain management. Since August 2008, two nurses and a further two Consumer Liaison Group members (total now is 3) have joined the Group. We have representation also from a clinical trials manager (Gareth Griffiths, Director of Welsh Clinical Trials Unit). A Project Officer (Ms Helen Radford) was appointed in October 2008.

Four subgroups have been formed representing three of the most common symptoms: Pain, Breathlessness and Cachexia, plus an additional Primary Palliative Care Subgroup that spans both the Palliative Care CSG and Primary Care CSDG.

Portfolio and accrual

At May 1st 2009, there are 31 studies on or about to be added to the portfolio. Of these 8 are active, 10 are in set-up, and 13 are closed.

Of the 8 active studies, 5 are interventional (Acufatigue, Phase III BIS, Pregabalin, EPAT, SCORAD) and 3 are observational (Predicting weight loss, PIPS, Spiritual Beliefs). The current studies focus on symptoms (pain, breathlessness, fatigue, and cachexia), prognostication and spirituality. A list of the studies can be found below.

In 2008-2009, accrual to 14 open studies on the palliative care portfolio resulted in 763 patients recruited (the largest annual total to date; similar figure for 2007-2008 was 594).

Table 1: Palliative Care Group Portfolio

Acronym	Title	PI(s)	Status
A pilot psycho-educational intervention for cancer carers	Development and Piloting of a Brief, Short-Term Psycho-Educational Intervention for Informal Carers of Patients at the End of Life	Dr Richard Harding	Open
ACU.FATIGUE	The effectiveness of acupuncture and self-acupuncture in managing cancer-related fatigue in breast cancer patients: a pragmatic randomised trial	Prof Alexander Molassiotis	Open

Advance Care Planning	Advance Care Planning in Advanced Cancer - Can it be achieved? A patient preference trial of a care planning discussion	Dr Louise Jones	Closed
Antifungal Drug Resistance Study	An investigation into the relationship between antifungal drug use, salivary gland dysfunction and antifungal drug resistance in patients with advanced cancer - Phase 1 (Observational Study)	Dr Andrew Davies	Closed
Antifungal Drug Resistance Study 2	An Investigation into the relationship between antifungal drug use, salivary gland dysfunction and antifungal drug resistance in patients with advanced cancer - Phase 2 (Interventional Study).	Dr Andrew Davies	Closed
ASPECTS	Understanding patients and clinicians experiences and views of palliative chemotherapy.	Professor Rona Campbell	Closed
ASyMS-R	Improving the symptom experience of patients with lung cancer receiving radiotherapy: Advance Symptom Management System for Radiotherapy	Prof Yvonne Wengstrom	In set up
Breathlessness in advanced disease: effects on caregivers	Breathlessness in advanced disease: effects on caregivers	Dr Farida Malik	Open
Distress in Palliative Care	Detecting psychological distress in palliative care patients: A research proposal for phase one of a two phase study	Dr Mike Bennett	Closed
EPA nutritional supplement to treat Cancer Cachexia	A pragmatic parallel-randomised single blind controlled trial to investigate the efficacy of an oral nutritional supplementation Prosure™ containing the omega-3 fatty acid, eicosapentaenoic acid or EPA to stabilise weight loss and promote weight gain in	Dr Chris Baughan	Closed
EPAT© -	Edinburgh Pain Assessment Tool - Does the institutionalisation of pain assessment using the EPAT© package reduce pain in cancer unit inpatients more effectively and cost-effectively than usual care and does it have adverse effects?	Professor Marie T Fallon	Open
EPCRC CSA	Computerised symptom assesment for patients with advanced cancer	Prof Stein Kaasa	Open
Exercise Preferences	Physical activity as a therapy for people with incurable cancer: the how, where and when?	Dr Andrew Wilcock	Closed

How well do we care for dying patients?	How well do we care for dying patients? The development and validation of a questionnaire assessing relatives' perceptions about the quality of end-of-life care (50 patient, pre-testing study)	Professor John Ellershaw	Closed
KPS	Ketamine in Pain Study - A randomised double-blind controlled trial of s-ketamine versus placebo in conjunction with best pain management in neuropathic pain in cancer patients	Prof Marie T Fallon	In set up
Mechanisms of fatigue in breast cancer survivors	An investigation in to the biological mechanisms and clinical correlates in disease free breast cancer patients following primary treatment	Dr Ollie Minton	Open
MIST-B -	Oral morphine in the symptomatic treatment of breathlessness in cancer patients: a pilot study to determine the optimum dosage regime	Dr Polly Edmonds	In set up
Modafinil for Fatigue in Lung Cancer	Modafinil for the treatment of fatigue in lung cancer: a multicentre, randomised, double-blinded, placebo controlled trial	Dr Bee Wee	Open
NCRN067 - SPRAY STUDY	A double blind, randomized, placebo controlled, parallel group dose-range exploration study of Sativex® in relieving pain in patients with advanced cancer, who experience inadequate analgesia during optimized chronic opioid therapy.	Prof Marie T Fallon	Open
Nebulised Furosemide	Does nebulised furosemide improve severe breathlessness in patients with lung cancer?	Dr Andrew Wilcock	Closed
Pain and pain management in older people.	Pain and pain management strategies in older people with cancer.	Professor Michael Bennett	Closed
Phase III RCT BIS	Phase III randomised controlled trial of a breathlessness intervention service for intractable breathlessness.	Dr Sara Booth	Open
Physical activity level as an outcome measure	Physical activity level as an outcome measure for use in cancer cachexia trials - a feasibility study	Dr Andrew Wilcock	Closed
PiPS	A study to develop a novel prognostic indicator for use in patients with advanced cancer	Dr Patrick Stone	Open
Predicting weight loss	Predicting weight loss in people with cancer: Development of a screening tool.	Vanessa Halliday	Closed
Pregabalin study	Double-blind randomised controlled trial of pregabalin versus placebo in	Professor Marie T Fallon	Open

	conjunction with palliative radiotherapy for malignant bone pain		
QUALYCARE study	Improving the quality of end of life care for patients with cancer and their families	Prof Irene J Higginson	Open
Question Prompt List	Development and pilot testing of the "Question Prompt List (QPL)" intervention to meet information needs of advanced cancer patients	Dr Richard Harding	In set up
SCORAD	A randomised feasibility study of single fraction radiotherapy compared to multi-fraction radiotherapy in patients with metastatic spinal cord compression	Professor Peter Hoskin	Open
Spiritual beliefs study	Study to explore the associations between beliefs and psychological status in patients receiving palliative care	Dr Louise Jones	Open
Supportive Care Intervention for Lung Cancer Patients and Caregivers	A non-pharmacological supportive care intervention for patients with lung cancer and their caregivers in the management of the respiratory distress symptom cluster	Prof Alex Molassiotis	In set up
TENS-CBP	TENS: Transcutaneous electrical nerve stimulation in the management of cancer bone pain	Dr Mike Bennett	Closed
The two-step study	An open, randomised, parallel group study in patients with cancer pain, to compare a two-step analgesic ladder (non-opioid to oxycodone) with conventional management using a three-step approach.	Professor Geoff Hanks	Closed
TIME3	Adjuvant Urokinase in the Treatment of Malignant Pleural Effusion: The Third Therapeutic Intervention in Malignant Effusion Trial (TIME3-UK). (A Randomised Controlled Trial to evaluate whether use of intrapleural Urokinase aids the drainage of multi-septated pleural effusion compared to placebo)	Dr Robert O J Davies	In set up
Transitions to palliative care	Transitions to palliative care in older people in acute hospitals	Dr Merryn Gott	Open

Trials in development

Currently there are several studies at various stages of development including:

- An early intervention with breathlessness training for patients with lung cancer: a comparison of two programmes, high intensity and low intensity (Dr M Johnson) submission to HTA.
- Melatonin impact on Cancer Anorexia Cachexia Syndrome: Randomised Phase II study (Dr M Watson)
- Evaluation of an Assessment Tool and Treatment Guidelines for the Management of Cancer Cachexia (Professor K Fearon)
- IMPACCT (Improving the Management of Pain from Advanced Cancer in the Community) – programme grant application (Professor M Bennett)
- Phase III RCT of TENS for cancer bone pain (Professor M Bennett)

Meetings

There have been no national meetings held by the Palliative Care CSG though the Group is hosting a parallel session at the 2009 NCRI Cancer Conference.

Collaborations

Several members and subgroups have developed research collaborations with international researchers. For example, with Dr Abernathy in USA (Breathlessness Subgroup); with Professor Strasser in St Gallen, Switzerland (Cachexia Subgroup); with Professor Hagen in Calgary, Canada (Pain Subgroup). The CSG is not formally part of the European Palliative Care Research Collaboration (EPCRC) though Professor Fallon, Dr Forbes, and Professor Fearon are collaborators within the research programmes.

Links have been established with the Primary Care CSDG (via a shared subgroup) and with the Radiotherapy CSG (via a research project). There are no formal links with ECMCs or NICE and HTA. Representation from the two UK Supportive and Palliative Care Research Collaboratives has been more successful with COMPASS than with CECo. This probably reflects the dominance of medical disciplines within COMPASS in contrast to CECo.

Relationships with Clinical Trials Units are mostly established at investigator level rather than CSG. However, the Welsh Trials Unit (represented by Gareth Griffiths) has a direct connection with the Palliative Care CSG. A number of CSG members have established links with industry and this has led to the imminent adoption of at least one industry sponsored study onto the portfolio with another undergoing consideration.

Other activities

A review of the 13 closed studies shows that 9 (69%) closed before reaching recruitment target, and 5 (38%) only reached 50% or less. Of 21 studies that are either closed or active, 9 (43%) had extended their study closure dates. Smaller, single centre, mainly observational, studies have been more successful in reaching target recruitment than larger multicentre RCTs. Problems clearly exist for palliative care research capacity.

There are several well rehearsed reasons for poor recruitment and attrition within palliative care research (e.g. frail population, lack of research 'mind-set',) but perhaps the most significant and least discussed is research infrastructure and capacity. Many, but not all, of the studies on the portfolio are single centre studies and this probably reflects the perception that there is insufficient capacity to plan and deliver multicentre studies. In contrast, the most obvious solution for poor recruitment (particularly to intervention studies) is to engage several centres.

An analysis of recruitment to the palliative care portfolio across the NCRN from 2003 to 2008, demonstrates that 19 (58%) of the 33 networks in England, and 4 (66%) of the 6 networks within Wales, Scotland and Northern Ireland, have never recruited to the portfolio in the 5 years that the Palliative care CSG existed. The most active research networks (in order of activity) have been: Yorkshire; Avon, Somerset and Wiltshire; Peninsula; South West London; Greater Manchester; Mid Trent; South East London; and North London, which have recruited 1188 (87%), of the total 1362 patients during this period. These centres are characterised by the presence of enthusiastic research champions in palliative care, many of whom are or have been members of the CSG. Furthermore, this analysis demonstrates that recruited patients are from England and that recruitment in the devolved nations has been negligible to March 2008.

This portfolio analysis has prompted a national survey of all CLRN and Cancer Research Network managers to better understand reasons for poor recruitment and examples of good practice. This information will be used to model the formation of a National Specialty Group for palliative care studies.

3-year strategy and Priorities for next year

Since taking up the CSG chair in August 2008, I have focused on the following strategic aims for 2008 – 2010 [with timescales in parentheses]:

CSG governance

- I secured funds for a project officer (Helen Radford) and have worked with them to audit the accuracy of all open studies and made contact with every chief investigator [March 2009]. This has enabled us to evaluate the portfolio in more detail and we will repeat this exercise every 6 months.
- Representatives from important constituencies have been / will be encouraged to apply for membership to ensure that the CSG reflects the UK palliative care research community as much as possible [March 2009].

Increasing portfolio

- The CSG will facilitate the adoption of emerging studies (e.g. by writing to academic departments, SuPaC Collaboratives), and identify studies elsewhere in the NCRN portfolio that could be dual badged under palliative care. [Oct 2009]
- I will develop plans with sub-group chairs that identify activity and objectives within the 4 subgroups; this could be part of an away day. [Dec 2009]

Building capacity

- The baseline audit of activity has highlighted a potential problem of inadequate research capacity. The Group will explore the role of a National Specialty Group in palliative care, and how this might work alongside the CSG (or whether both functions can be merged into one committee). This will examine the issue of palliative care research that is focused on non-cancer conditions, and how this activity can be captured for the portfolio. [March 2010]
- The project manager and I will write to CLRN directors and cancer research network managers to identify scope for increasing resources to support palliative care studies, and barriers to undertaking them. The CSG will work to promote the adoption of relevant industry studies. [March 2010]

Responding to the DoH End of Life Care Strategy

- In response to the DoH End of Life Care Strategy, the CSG will examine the research elements in the strategy, and set up a meeting with representatives of other CSGs to identify formal and informal links that may promote the development of studies, and report on how the NCRI can support the strategy's objectives. [Dec 2009]

Professor Mike Bennett, Chair

Appendix 1

Key strengths and issues from the Progress Review, 1st May 2009

The key strengths of the Group identified at the May review were:

- *Comprehensive Progress Review Report*
- *The Group's activity, energy and ideas flowing from the Group*
- *Addressing the issues identified at the last review*
- *The positive trajectory that the Group are on*
- *Strong leadership by both the current and previous chairs*
- *A clear understanding of the environment in which the Group works*
- *Well lead subgroups with clearly defined roles*
- *Successful development of studies through the subgroups*
- *Project officer role has been positive and productive providing the Group with information that they are clearly using*
- *Varied, broad and appropriate membership*
- *Nurse membership*
- *A clear strategy*

The Panel identified the following issues which the Palliative Care CSG needs to consider:

- *Increasing recruitment*
- *Completing recruitment to open studies*
- *Being creative in harnessing both NCRN and CLRN resources to improve recruitment*
- *The Group's high impact studies and how they might be best supported and results from these disseminated*
- *Developing international collaborations with Europe and North America*
- *Holding a regular meeting to showcase the work of the Group*
- *Encouraging a greater number of individuals to contribute to discussions about the Group's work*

Appendix 2.

2008/09 Publications and abstracts

Farquhar M, Higginson IJ, Booth S. Repeated measurement of quality of life in palliative care research: the experience of using the SEIQoL-DW in a pilot phase II RCT of a complex intervention for breathlessness (PCC conference abstract) *Palliative Medicine* 2008 22: 30.

Farquhar M, Higginson IJ, Booth S. Referring to a complex intervention for breathlessness, the 'Breathlessness Intervention Service' (BIS): expectations and experiences of referrers of COPD patients (EAPC conference abstract) *Palliative Medicine* 2008; 22: 459

Bausewein C, Higginson IJH, Gysels, M, Booth S. Non-Pharmacological Interventions for Breathlessness in Advanced Cancer. *Cochrane Review February 2008 John Wiley & sons Ltd.*

Booth S, Moosavi S H, et al. (2008). "The aetiology and management of intractable breathlessness in patients with advanced cancer: with a systematic review of pharmacological and inhaled therapy." *Natural Clinical Practice Oncology* 5(2): 90 - 100.

Bausewein C, Booth S, Higginson IJ. Measurement of dyspnoea in the clinical rather than the research setting. *Current Opinion in Palliative and Supportive Care* 2008, 2:95–99

Bausewein C, Kühnbach R, Booth S, Gysels M, Higginson IJ. Recruitment and follow-up in a longitudinal study contrasting COPD and cancer. EAPC Research Forum 2008 Trondheim. *Palliative Medicine* 2008; 22 (4): 550

Bausewein C, Booth S, Gysels M, Higginson IJ. Dilemma of RCTs in palliative care: evaluating a hand-held for relief of breathlessness. EAPC Research Forum 2008 Trondheim. *Palliative Medicine* 2008; 22 (4): 458

Simon S, Higginson IJ, Harding R, Booth S, Bausewein C. Effectiveness of Benzodiazepines for the Relief of Breathlessness – a Systematic Review. *Palliative Medicine* 2008; 22 (4): 461

Simon S, Bausewein C. The Pathophysiology of Dyspnoea in End-Stage Chronic Heart Failure (CHF) - Implications for Symptom Management. *Palliative Medicine* 2008; 22 (4): 461

Glare P, Downing M, Maltoni M, Sinclair C, Stone P and Vigano A. Predicting survival in advanced disease. *European Journal of Cancer* 2008; 44(8): 1146-1156.

Minton O and Stone P. How common is fatigue in disease-free breast cancer survivors? A systematic review of the literature. *Breast Cancer Research and Treatment* 2008 Nov;112(1):5-13 .

Stone P and Minton O. Fatigue in Patients with cancer. *European Journal of Cancer* 2008; 44(8): 1097-1104

Radbruch L, Strasser F, Elsner F, Goncalves JF, Loge J, Kaasa S, Nauck F and Stone P. Fatigue in Palliative Care Patients – an EAPC approach. *Palliative Medicine* 2008; 22: 13 – 32.

Minton O, Stone P, Richardson A, Sharpe M and Hotopf M. Drug therapy for the management of cancer related fatigue. *The Cochrane Library Issue 1 2008*

Eley HL, Skipworth RJ, Deans DA, Fearon KC, Tisdale MJ. Increased expression of phosphorylated forms of RNA-dependent protein kinase and eukaryotic initiation factor 2alpha may signal skeletal muscle atrophy in weight-losing cancer patients. *Br J Cancer.* 2008;98:443-9.

Wilcock A, Maddocks M, Lewis M, England R, Manderson C (2008) Symptoms limiting activity in cancer patients with breathlessness on exertion: ask about muscle fatigue. *Thorax.* 63:91-2.

Robb K, Bennett MI, Johnson MI, Simpson KH, Oxberry SG. Transcutaneous Electrical Nerve Stimulation for cancer pain in adults. Cochrane systematic review. *Cochrane Database Syst Rev* 2008 Jul 16;(3):CD006276

Robb K, Oxberry SG, Bennett MI, Johnson MI, Simpson KH, Searle RD. A Cochrane systematic review of Transcutaneous Electrical Nerve Stimulation for cancer pain. *Journal of Pain and Symptom Management* 2008; 37(4):746-53

Thekkumpurath P, Venkateswaran C, Kumar M, Bennett MI. Screening for psychological distress in palliative care: a systematic review. *Journal of Pain and Symptom Management* 2008; 36(5): 520-528.

Murray SA, Barclay S, Bennett MI, Kendall M, Amir Z, Lloyd-Williams M. Palliative Care Research in the Community: it's time to progress this emerging field (editorial). *Palliative Medicine* 2008 22(5): 609-11.

Searle RD, Bennett MI, Johnson MI, Callin S, Radford H. Transcutaneous Electrical Nerve Stimulation for cancer bone pain. *Journal of Pain and Symptom Management* 2009;37(3):424-8.

Chatwin J, Closs SJ, Bennett MI. Pain in older people with cancer: attitudes and self-management strategies. *European Journal of Cancer Care* 2009;18(2):124-30.

Searle RD, Bennett M. The management of neuropathic pain in cancer. *Progress in Palliative Care* 2008; 16(1): 7-13.

Venkateswaran C, Thekkumpurath P, Kumar M, Bennett MI. Making sense of end-of-life distress. *European Journal of Palliative Care* 2008; 15(1): 15-21.

Wilcock A, Walton A, Manderson C, Feathers L, El Khoury B, Lewis M, Chauhan A, Howard P, Bell S, Frisby J, Tattersfield A. Randomised, Placebo-Controlled Trial Of Nebulised Furosemide For Breathlessness In Patients With Cancer. *Thorax.* 2008 Apr 11. [Epub ahead of print]

Wilcock A, Maddocks M, Lewis M, England R, Manderson C. Symptoms limiting activity in cancer patients with breathlessness on exertion: ask about muscle fatigue. *Thorax*. 2008 Jan;63(1):91-2.

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Kelly L, White S and Stone P. The B12 / CRP index (BCI) as a simple prognostic indicator in patients with advanced cancer: a confirmatory study. *Annals of Oncology (in press)*.