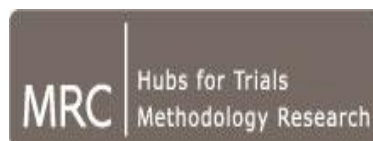


ConDuCT Hub

Newsletter

Autumn 2013



ConDuCT Hub



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Short course programme at the School of Social and Community Medicine, University of Bristol

Our short course programme for the 2013-2014 academic year has started; places are booking up fast, so don't delay in seeing what's on offer at:

<http://www.bristol.ac.uk/social-community-medicine/shortcourse/>

There are several courses on study design, research methodology and statistics which would be of interest to chief investigators of the future!

Updates from our Hub-Affiliated PhD students

Natalie Blencowe: "The overall aims of my PhD research are to explore the complexity of surgical interventions in RCTs, within the literature and in practice, and understand how trial design may need to be adapted to account for this complexity. These aims are accomplished in two components. Firstly, a systematic review of the literature and development of a typology of surgical interventions. This has been completed and some of the results will be presented at the CTMC2013 in Edinburgh. Secondly, establishing the feasibility of undertaking a process evaluation in the operating theatre, using case studies of surgical interventions. This component of the work is ongoing."

Patricia Guyot: "My PhD research aims to improve the use of studies reporting survival outcomes in cost-effectiveness analysis and evidence syntheses. The main objective is to develop a new methodology using RCT and external data to provide unbiased mean survival estimates with an appropriate reflection of the uncertainty. Using one example on head and neck cancer, we succeeded in achieving goodness-of-fit to all sources of evidence (RCT, general population, cancer registries and expert opinion) within one integrated model."

Sean Strong: "I am undertaking a PhD research entitled: Understanding the role of the multidisciplinary team in recruitment to randomised controlled trials: an exploratory qualitative study. My principal aim is to explore how healthcare professionals work together as a team to recruit patients to randomised controlled trials (RCTs). So far I have completed qualitative interviews in three centres, and presently I am analysing the data."

Sia Gravani: "The aim of my PhD project is to investigate methods that could be applied in the design and conduct of RCTs in order to improve the completeness and timeliness of collected trial data so as to enhance trial quality. The objectives of the proposed research will be achieved by three components. I am presently reviewing the effect of staff training on trial data quality. In the next phase I will investigate how web-based tools (e.g. social media, electronic newsletters and reminders) can influence patients' response rates. Finally, I will examine the effect of using incentives in clinical trials."

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From the Statistics Theme

There have been some bemused looks on the faces of my statistical colleagues at other hubs, when they have first seen the new, apparently statistics-free, structure of ConDuCT-II. But hey, worry not! There will be more statisticians than ever involved, with Chris Rogers (Bristol), Jonathan Cook (Oxford), and Julian Higgins (Bristol) joining the Hub. Over the past five years members of the Statistics Theme have spent much of their time on collaborative projects with members of the other themes, such as Sara Brookes and the Outcomes Theme, and myself with the Health Economics Theme. We see the new theme structure as a natural extension of the predominantly multi-disciplinary model of research here in Bristol.

Alan Montgomery left Bristol in the spring to take up a chair in Nottingham University, which also sees him play a leading role in their clinical trials unit. I'm pleased to report he will still be involved with ConDuCT-II, being placed with the Feasibility Design and Trial Conduct Theme. Athene Lane and I have taken on the directorship of the Bristol Randomised Trials Collaboration (BRTC) that Alan vacated, and we will be taking every opportunity to build on the strong links he established with ConDuCT. For example, we will make the case for methodological sub-studies where these can be accommodated within our supported trials.

Finally, the Statistics Theme was well represented at August's International Society of Clinical Biostatistics (www.iscb2013.info; which includes recordings of some talks). For example Patricia Guyot presented her work with Nicky Welton and Tony Ades, "Extrapolation of trial-based survival curves: constraints based on external information". Nicky took to the stage to present her work with Tony, "Prioritising and designing new research when there are multiple competing treatments: how many arms and which treatments?" Julian Higgins continued the network meta-analysis theme with "Addressing consistency of findings in meta-analyses of clinical trials making different comparisons among a set of interventions". This all bodes well for many exciting statistical and statistician-informed developments from ConDuCT-II.

Chris Metcalfe
(Theme lead)

Recent Grant Awards

The Hub has successfully secured renewed funding from MRC for ConDuCT-II: *"COllaboration and iNnovation in DifficUlt and Complex randomised controlled Trials In iNvasive iNterventions"* Blazeby J, Brookes S, Donovan J, Hollingworth W, Lane A, Welton N, Campbell R, Cook J, Heawood A, Hollinghurst S, Hoddinott P, Higgins J, Huxtable R, McNair A, Metcalfe C, Montgomery A, Noble S, O'Cathain A, Peters T, Potter S, Rogers C, Salisbury C, Sterne J, Tilling K, Wiles N. MRC grant (£1,979,499) 2014 - 2019.

A MRC HTMR grant has been awarded to the ConDuCT Hub for:
"An ethnographic study of group decision-making & member roles to understand & improve how Trial Steering Committees & Trial Management Groups contribute to trial conduct" Heawood A, Lane A, Gamble C, McCanns S, Sydes M, Clarke M (co-apps). MRC HTMR (£50,000), Mar 2013 – Feb 2014.

In addition, ConDuCT methodologists have contributed to the following successful grant applications:

- *"A double blind placebo-controlled randomised trial of the addition of the antidepressant mirtazapine for patients with depression in primary care who have not responded to at least 6 weeks of antidepressant treatment"*

Kessler D, Hollingworth W, Lewis G, Davies S, Wiles N, Montgomery AA, Chew-Graham C, Gilbody S, Anderson I, Macleod U, Campbell J, Dickens C. NIHR HTA Programme (£1,858,500) 2013-2016.

- *"Cataract Surgery: Measuring and predicting patient level vision related health benefits and harms"*

Sparrow J, Sterne J, Andrew F, Johnston R, Liu C, Gilbert C, Taylor H, Evans D, Hollingworth W, Tennant A, Nadin S, Elwyn G, Donovan J, Brain K, NIHR Programme Grant (£708,531) 1 Oct 2013 - 30 Sep 2018

- *"A randomised controlled trial to determine the clinical and cost effectiveness of thulium laser transurethral vaporesction of the prostate (ThuVAP) versus transurethral resection of the prostate (TURP) in the National Health Service (NHS)"*

The trial will require methodological inputs to enhance the training and expertise of surgeons at sites and ways to disseminate expertise from the CI centre. Hashim H, Abrams P, Brookes S, Lane A, Noble S, Page T, Cotterill N, Swami K. HTA (£1.2 m) 2013 - 2016.

- *"The effectiveness of Community vs. Hospital Eye Service follow-up for patients with neovascular age-related macular degeneration with quiescent disease: a virtual trial"*

Chakravarthy U, Reeves BC, Harding SP, Rogers C, Wordsworth S, Mills N, O'Reilly D, Peto D, Hogg R. Funded by NIHR HTA (£381,646) Mar 2013 – Sep 2014.

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Welcome ConDuCT-II:



Collaboration and innovation in difficult RCTs in Invasive Interventions

This summer we were delighted to hear that the MRC will fund ConDuCT for a further five years, starting in April 2014. Professor Jane Blazeby will continue as director and is joined by Professor Will Hollingworth as deputy director. With the new funding comes a new name, a re-organisation of our themes (see below), and some new members, all aimed at focusing our work on methodology for RCTs of surgery and other “Invasive Interventions”.

Since the Hubs for Trials Methodology Research first came about in 2009, there has been an increasing awareness, in the media, in the medical literature, and amongst research funders, of the lack of reliable RCT evidence for many surgical procedures. This is a niche ConDuCT has always been well suited to, with practicing surgeons and methodological experts on non-pharmacological trials amongst our number. ConDuCT-II will build on this with our new members including Jonathan Cook (Oxford), Chris Rogers (Clinical Trials and Evaluation Unit, Bristol), Julian Higgins (Bristol), Pat Hodinott (Stirling), and Alicia O’Cathian (Sheffield).

We will maintain our existing collaborations with researchers and trialists at the other hubs, clinical trials units and the research design service, and look forward to building on a new link with the Royal College of Surgeons of England, partly through their funding of a surgical trials centre at Bristol. We have set ourselves ambitious targets for promoting the conduct of surgical trials across the nation, and building capacity amongst budding chief investigators, so expect to hear a lot more from us soon!

Prioritisation & Trial Design	Trial Recruitment	Feasibility Design & Trial Conduct	Clinical & Patient Reported Outcomes
To develop methods to ensure that RCT funding is targeted at the most urgent clinical questions and that RCTs, once funded, are designed to collect complete and unbiased evidence on cost-effectiveness.	To extend the integrative research methods developed in ConDuCT to ensure the rapid implementation of findings that will improve recruitment to RCTs tackling 'difficult' research questions	To develop methodology for feasibility and pilot studies, to ensure main trials are efficient, evaluating relevant and deliverable treatments, and are completed on time.	To develop methods to include clinical and patient reported outcomes in RCTs, and to design methods to communicate data from RCTs into practice to inform decision-making.
Will Hollingworth Nicky Welton	Jenny Donovan	Athene Lane Jane Blazeby	Sara Brookes Jane Blazeby

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Jenny awarded OBE

The Hub was thrilled to congratulate Professor Jenny Donovan of the Qualitative Research Theme, who was awarded an OBE in the Queen's honours in recognition of her services to social medicine, outstanding contributions to health research and advancement of medical science.



Credit: Anthony Devlin/PA Images

New team members

The Hub welcomed Dr Anne Daykin who joined us in March 2013 to work on QuANTOC (Qualitative Analysis of Trial Oversight Committees) with Ali Heawood and Athene Lane. Anne will be conducting qualitative work (non participant observation, interviews and analysis of documents) to examine decision making of Trial Steering Committees and Trial Management Groups and how this shapes trial conduct. QuANTOC will contribute to updates to the MRC Terms of Reference for Trial Steering Committees. The study is a joint Qualitative/Trial Conduct Theme project, with collaborators from three other HTMRs, and funded by MRC HTMR network funding.

We also welcome two new members to the Hub's Evidence synthesis Theme. Peter Bryden joined the EVI theme as health economic modeller in October 2013, and will work on two applied projects that will involve value of information analyses: (i) interventions for children exposed to domestic violence; (ii) anticoagulants for primary and secondary prevention of venous thromboembolism. Also Dr. Howard Thom joined the university in September 2013, having completing a PhD developing methods for cost-effectiveness and value of information analyses in the face of structural uncertainty. Howard will be an affiliate member of the EVI theme, and work on three applied projects that will involve value of information analyses: (i) antidepressants by baseline severity of

symptoms; (ii) treatments for obsessive compulsive disorder; (iii) anticoagulants for atrial fibrillation.

Qualitative methods in trials

18 June 2013 and 20 March 2014

The Qualitative Methods Theme successfully conducted, for the second time, a workshop on "How qualitative methods can contribute to the design and conduct of randomised trials".

This one-day short course illustrated how qualitative methods can be integrated at various stages of a randomised trial, from the development and feasibility stages to the running of the main trial, to enhance trial design and conduct. It focused on the use of common and more novel qualitative methods within challenging-to-conduct pragmatic trials, undertaken within a health service context. The course proved very popular, yet again, and was extremely well received – "Really useful to hear first-hand experience from actual trials"; "All the talks were very relevant and interesting – doesn't happen on a course very often!".

The workshop will run again on 20 March 2014 and bookings can be made through the University of Bristol School of Social and Community Medicine Short Course website:

<http://www.bristol.ac.uk/social-community-medicine/shortcourse/>

Internal pilot trials

London: 24 March 2014

The Outcomes Theme, led by Dr Kerry Avery together with co-applicants Professor Jane Blazeby, Elaine O'Connell Francischetto and Dr Chris Metcalfe, in collaboration with the North West Hub, have been granted MRC HTMR network funding for a one-day workshop scheduled for 24 March 2014:

"Optimising the design and evaluation of pilot work to inform efficient RCTs: a workshop to consider the key issues and areas for future research"

The workshop will focus on internal pilot trials and aims to bring together key stakeholders, including research methodologists, medical statisticians, clinicians, trialists and funding body representatives. The aim is to develop guidance for funding bodies when evaluating the use and success of pilot work, and when considering progression to a main trial.

The guidance will also be of relevance to researchers involved in the design and conduct of pilot trials. The workshop will identify an agenda for further research in this area.

This one day workshop on pilot work will largely be by invitation only. It will take place at the Royal College of Surgeons of England, Lincoln's Inn Fields, in London.

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Designing and reporting of surgical trials



On 27-28 June 2013, the Outcomes Theme, in collaboration with the Cambridge Biostatistics Hub, held a two-day specialist workshop the Royal College of Surgeons of England in London:

“Designing and reporting surgical trials to influence practice: Developing guidance to recognise the complexity of surgical interventions in RCTs”

The workshop's aim was to consider the complexity of surgical interventions and the challenges this creates in the design, conduct and analysis of surgical RCTs. Among the 38 attendees were surgeons, clinical trials methodologists, statisticians, qualitative researchers, and representatives from funding bodies and medical journals.

The sessions consisted of a mixture of presentations, vignettes of current surgical RCTs, and small group work. There were lively discussions which will be captured in a report for publication, highlighting important issues which need to be addressed when designing and seeking funding for surgical trials.

It is anticipated that use of this guidance will improve RCTs by helping surgeons and chief investigators design and describe surgical trial proposals with a better chance of obtaining funding, of being successfully completed, and of having an impact on clinical practice. The workshop received excellent feedback from participants and, due to its success, further work in this methodological area is being planned.

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A selection of presentations at recent conferences

Core Outcome Measures in Effectiveness Trials (COMET) 3rd Meeting, Manchester, June 2013:

- Blazeby J: "Methods for inclusion and integration of stakeholders in the development of core outcome sets" (invited talk)
- Macefield RC, Blencowe NS, Jacobs M, Strong S, McNair AGK, Avery KNL, MacKichan F, Nicklin J, Sprangers MA, Brookes ST, Blazeby JM: "Methods for selecting core clinical and PRO domains: an example from oesophageal cancer" (poster)
- Howes N, Hopkins J, Whistance RN, Byrne J, Mahon D, Welbourne R, Blazeby JM: "Development of a core outcomes set for adverse event reporting after bariatric surgery" (poster)
- Potter S, Brookes S, Blazeby J (and others): "Initial results of the BRAVO (Breast Reconstruction and Valid Outcomes) Study, a multicentre consensus process to develop a core outcome set for research and audit in reconstructive breast surgery" (oral)

Health Economists' Study Group (HESG), Warwick, June 2013:

- Edwards RT, Lloyd-Williams H, Charles JM, McIntosh E, Craig N, Hollingworth W, Lawson K, Donaldson C: "Health economics and population health: emerging methodological and policy issues for the health economics community" (oral).
- Hollinghurst S, Banks J, Bigwood L, Walters F, Hamilton W, Peters T: "Using willingness-to-pay to establish patient preferences for cancer testing in primary care" (oral).

Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland (AUGIS) Annual Scientific Meeting, Newcastle, September 2013:

- Strong S, Brookes S, Donovan J, Wilson C, Crosby T, Griffin M, Blazeby J: "Oesophageal squamous cell cancer: induction chemotherapy versus induction chemotherapy and chemoradiotherapy – a randomised feasibility study" (Oral)
- Berrisford RG, Blencowe N, Donovan JL, Elliott J, Goldin R, Hanna G, Noble S, Avery KNL, Metcalfe C, Blazeby JM (and others): "Randomised Oesophagectomy: Minimally Invasive or Open. The ROMIO feasibility trial" (Poster)
- Blencowe NS, Macefield RC, Jacobs M, Strong S, Blazeby JM: "Which outcomes are important to patients and surgeons? Core information prior to oesophageal cancer surgery" (Poster)
- Blazeby J, Welbourn R, Byrne J, Rogers C, Paramasivan S, Donovan J: "Recruiting patients into RCTs in bariatric

surgery is possible: on-going progress in the By-Band study" (oral)

International Society of Quality of Life (ISOQOL) Research Annual Conference, Miami, USA, October 2013:

- Macefield RC, McNair AGK, Blencowe NS, Brookes ST, Blazeby JM: "Implementing the CONSORT patient-reported outcome extension in RCTs in oncology: understanding the items that influence clinical decision-making" (Poster)
- Julie Rouette, Jane Blazeby, Melanie Calvert, Madeline King, Ralph Meyer, Paul Peng, Jolie Ringash, Melanie Walker, Michael Brundage: "Evaluation of the CONSORT extension recommendations for PRO reporting in clinical trials: an international survey of oncologists" (Poster)

Some oral presentations to look out for at the 2nd Clinical Trials Methodology Conference, Edinburgh, November 2013:

- O'Connell E: "Optimising the design and evaluation of pilot work to inform the main trial: a review of current evidence and considerations of future practices"
- Turner N: "A comparison of four different approaches to measuring health utility in depressed patients"
- Paramasivan S: "Keep an open mind: Using qualitative research to make recruitment easier in the B-Band randomized controlled trial"
- Mills N: "Recruiters to randomized trials can be trained to facilitate recruitment and informed consent by exploring patients' treatment preferences"
- Wade J: "Evaluating best practice in informed consent discussions: a new method of evaluating information provision and patient understanding during trial recruitment consultations"
- Daykin, A: "An ethnographic study of group decision making to understand and improve how Trial Steering Committees contribute to trial conduct"
- Lane JA: "Evaluation of source data verification in a multicentre cancer trial (Protect)"
- Blencowe N: "Accounting for intervention complexity in RCTs in surgery: new approaches to intervention definition and methods for monitoring fidelity"
- Odondi L: "Design, analysis and reporting of active-control randomised trials: a systematic review"

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Selected publications

Welton NJ, Madan J, Caldwell DM, Peters TJ, Ades AE. Expected Value of Sample Information for cluster randomised trials with binary outcomes. *Medical Decision Making* (in press) doi:10.1177/0272989X13501229

Redmond N, **Hollinghurst S**, Costelloe C, **Montgomery A**, Fletcher M, **Peters T**, Hay A. An evaluation of the impact and costs of three recruitment strategies used to recruit young children to a primary care randomised controlled trial. *Clinical Trials* 2013;10:593-603 doi:10.1177/1740774513494503

Hamilton DW, de Salis I, **Donovan JL**, Birchall M. The recruitment of patients to trials in head and neck cancer: a qualitative study of the EaStER trial of treatments for early laryngeal cancer. *European Archives of Oto-Rhino-Laryngology and Head & Neck* 2013;270:2333-2337 doi:10.1007/s00405-013-2349-8

Hollingworth W, Metcalfe C, Mancero S, Harris S, **Campbell R**, Biddle L, **McKell-Redwood D**. Are Needs Assessments Cost Effective in Reducing Distress Among Patients With Cancer? A Randomized Controlled Trial Using the Distress Thermometer and Problem List. *Journal of Clinical Oncology* 2013;31(29):3631-3638 doi:10.1200/JCO.2012.48.3040

Wiles N, Thomas L, Abel A, Ridgway N, Turner N, Campbell J, Garland A, **Hollinghurst S**, Jerrom B, Kessler D, Kuyken W, Morrison J, Turner K, Williams C, **Peters T**, Lewis G (2013). Cognitive behavioural therapy as an adjunct to pharmacotherapy for primary care based patients with treatment resistant depression: results of the CoBaLT randomised controlled trial. *The Lancet*;381:375-384 doi:10.1016/S0140-6736(12)61552-9

Cook JA, McCulloch P, **Blazeby JM**, Beard DJ, Marinac-Dabic D, Sedrakyan A; IDEAL Group. IDEAL framework for surgical innovation 3: randomised controlled trials in the assessment stage and evaluations in the long term study stage. *BMJ* 2013;346:f2820 doi:10.1136/bmj.f2820

Salisbury C, **Montgomery A, Hollinghurst S**, Hopper C, Bishop A, Franchini A, Kaur S, Coast J, Hall J, Grove S, Foster N. A pragmatic randomised controlled trial of the effectiveness and cost-effectiveness of 'PhysioDirect' telephone assessment and advice services for patients with musculoskeletal problems. *BMJ* 2013;346:f43 doi:10.1136/bmj.f43

Turner N, Campbell J, **Peters TJ, Wiles N, Hollinghurst S**. A comparison of four different approaches to measuring health utility in depressed patients. *Health and Quality of Life Outcomes* 2013;11:81 doi:10.1186/1477-7525-11-81

Burns A, O'Mahen H, Baxter H, Bennert K, **Wiles N**, Ramchandani P, Sharp D, Turner K, **Thorn J, Noble S**, Evans J. A pilot randomised controlled trial of cognitive behavioural therapy for antenatal depression. *BMC Psychiatry* 2013;13:33 doi:10.1186/1471-244X-13-33

Avery KN, Barham CP, Berrisford R, **Blazeby JM, Blencowe NS, Donovan J**, Elliott J, Falk SJ, Goldin R, Hanna G, Hollowood AD, **Metcalfe C, Noble S**, Sanders G, Streets CG, Titcomb DR, Wheatley T. Understanding surgical interventions in RCTs: the need for better methodology. *The Lancet* 2013;381:27-8 doi:10.1016/S0140-6736(13)60015-X

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