

ConDuCT Hub Newsletter Spring 2013

MRC | Hubs for Trials
Methodology Research

ConDuCT Hub



ConDuCT Team

Back (L-R): Will Hollingworth, Jonathan Sterne, Lang'o Odondi, Chris Metcalfe, Jane Blazeby, Natalie Blencowe, Robert Whistance, Nicky Welton. Front: (L-R): Ali Heawood, Rhiannon Macefield, Jo Thorn, Sian Noble. Others (not in photo): Tony Ades, Caroline Boulind, Karen Coulman, Alireza Daneshkhah, Jenny Donovan, Patricia Guyot, Athene Lane, Denise McKell-Redwood, Nicola Mills, Sean Strong.

Forthcoming workshop

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ConDuCT Hub



4th July 2013

The Evidence Synthesis and Value of Information theme of the ConDuCT Hub will hold a workshop on

"Value of information methods to inform the prioritisation and design of new research studies"

This workshop will provide an introduction to the concepts behind the value of information analyses methods, and illustrate the methods with recent case studies (see more workshops/conferences on page 5/7).

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Message from ConDuCT Hub Director

Over the past year it has been exciting to see a culmination of outputs from the ConDuCT Hub and a growing vision. Collaborative grants for methodological and applied research in trials have been initiated and new ones funded. Important papers have been published and novel research initiatives started working closely with other Hubs for Trials Methodology Research. I am especially pleased that the Royal College of Surgeons of England have decided to invest in randomised controlled trials in surgery and has appointed five Surgical Trials Centres with Bristol in the first wave. The Bristol Surgical Trials Centre includes members of the registered clinical trials units, the Clinical Trials and Evaluation Unit (Dr Chris Rogers and Prof Barney Reeves), and the Bristol Randomised Trials Collaboration (Dr Alan Montgomery and Prof Jenny Donovan), and academic surgical leaders from both NHS Trusts in Bristol (Prof Gianni Angelini, Professor of Cardiac Surgery and Prof Ashley Blom, Professor of Orthopaedic Surgery). Being led from the Hub the Surgical Trials Centre will provide an unprecedented opportunity to integrate methodological research within trials, to apply new methods to feasibility studies and full RCTs across all types of surgical procedures and to contribute to the cultural change required for surgery to become evidence based in the NHS and worldwide.

Two Hub affiliated students were awarded PhDs in 2012 and both have successfully gained academic clinical lectureships in Bristol. Dr Shelley Potter's PhD focused on feasibility work to inform the design and conduct of future trials in breast reconstruction surgery and Dr Angus McNair completed qualitative research and systematic reviews to inform the development of methods for improved integration of patient reported and clinical outcomes in trials in surgical oncology. The trial conduct theme (led by Dr Athene Lane) published the first ever systematic review of on-site monitoring methods for trials. This review highlights the need for new interventions to improve these processes. The conduct theme together with the qualitative research theme and in collaboration with the North West Hub and MRC CTU are initiating work to evaluate Trial Steering Committees funded by the HTMR Network (led by Drs Ali Heawood and Athene Lane). New trials with integrated qualitative research to optimise recruitment were funded, led by Professor Jenny Donovan. Members of the health economics theme have also had a productive year as evident by the publications.

In 2013 I am looking forward to the new Hub workshop led by Dr Nicky Welton which will introduce "Value of information methods to inform the prioritisation and design of new research studies". This workshop is aimed to educate non-specialists in this field and is the first of its kind in the UK. There will also be a second workshop led by Professor Donovan and her team considering how qualitative research methods can improve the design and conduct of RCTs.

We said goodbye to Jason Madan last summer. Jason has moved to the University of Warwick and we welcome Dr Alireza Daneshkhah within the value of information and evidence synthesis theme. At the end of 2011 we were also joined by Dr Lang'o Odondi within the statistics theme, who has kindly contributed to the creation and writing of this newsletter.

I am particularly grateful to Professors Altman, Derbyshire and Sculpher and who attended the ConDuCT Hub mid-term strategy day in November 2011 and provided invaluable feedback and strategic guidance for the Hub's future shape and format. I look forward to 2013 and beyond and wish you all a happy and productive 2013.

Prof Jane Blazeby.

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Recent Grant Awards

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Grants to develop methodology

Members of the Hub have been awarded a grant for a feasibility trial with integrated methodological research. This is in collaboration with the BRTC (Bristol Randomised Trials Collaboration) and with surgeons at the Bristol Royal Infirmary and Plymouth's Derriford Hospital. The ROMIO Trial will include the development of recruitment procedures, methods to standardise surgical interventions in trials and methods for assessing resource use. It will also inform the design and conduct of the main trial.

"Randomised Oesophagectomy: Minimally Invasive or Open (ROMIO), a feasibility study" (Metcalfe C (PI), Blazeby J, Donovan J, Barham P, Berrisford R, Falk S, Goldin R, Hanna G, Hollowood A, Noble S, Sanders G, Wheatley T, Elliot J) NIHR HTA (£408,062). Jan 2013 to Dec 2014.

Members of the ConDuCT Hub were co-applicants for a grant awarded to develop **a method for adjusting trial results for biases in meta-analyses by combining generic empirical evidence of bias with detailed trial assessment**. Turner R(PI), Higgins J, Savović J, Jones H, **Welton N, Sterne J** MRC/NIHR Methodology Project Grant (£283,732) - 36 months.

Two HTMR network grants have been awarded to the ConDuCT Hub:

1. A joint qualitative/trial conduct theme project **"QuANTOC (Qualitative Analysis of Trial Oversight Committees): An ethnographic study of group decision-making and member roles to understand and improve how Trial Steering Committees and Trial Management Groups contribute to trial conduct"**. (Heawood A (co-PI), Lane A (co-PI), Gamble C, McCann S, Sydes M, Clarke M).

- MRC/HTMR network funding (£49,978). In collaboration with the North-West, the All-Ireland and the MRC CTU Hub.

In a related project, the trial conduct theme are also involved in a recently-funded project led by Carrol Gamble (North West Hub) titled

'Trial steering committees for randomised controlled trials: Updating and redeveloping guidance and terms of reference, informed by current practice and experience'.

The QuANTOC study will complement this project and inform the update of the terms of reference.

2. Qualitative research theme funding for a conference in Sheffield on 21 Nov 2012 to discuss **"Maximising the value of combining qualitative research and RCTS"** and a linked workshop to develop **"Guidelines for qualitative research feasibility studies"**. (Donovan J (lead), O'Cathain A, Young B) – MRC/HTMR network funding (£16,000). In collaboration with the North West Hub.

Hub affiliated PhD student Shelley Potter was awarded her PhD in 2012 and has successfully won a grant (£17,510) from the Academy of Medical Sciences to **develop a core outcome set for trials in breast reconstruction surgery**. (Potter S (PI), Blazeby J, Cawthorn S), 24 months.

The Royal College of Surgeons of England have awarded funding (£500,000) for a Surgical Trials Centre in Bristol. This will be led by the Hub, **Blazeby J** (PI), with co-applicants from both CTUs and NHS Trusts in Bristol (Montgomery, Rogers, Angelini, Blom, Donovan and Reeves) - 2013 to 2018.



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ConDuCT Hub and Hub-Affiliated PhD student

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Natalie Blencowe is a NIHR Doctoral Fellow and a surgical trainee. Her PhD is exploring whether the key components of surgical interventions can be identified and standardised within RCTs. Her research will generate methods for developing surgical manuals for RCTs, describing the mandatory, optional and flexible components of interventions, and how fidelity to these standards can be measured. This will be important for the validity of surgical RCTs, so that the results are accepted and accurately implemented in routine clinical practice.

Robert Whistance is a NIHR Doctoral Research Fellow and surgical trainee. His PhD research aims to develop core outcome and information sets for clinical trials and informed consent for colorectal cancer surgery. The project involves systematic reviews, qualitative interviews with patients and clinicians and Delphi consensus methodology. This will be complete by September 2013.



Patricia Guyot's PhD research aims to improve the use of studies reporting survival outcomes in cost-effectiveness analysis and evidence syntheses. A literature review has highlighted that, in numerous health technology assessments, survival outcomes were not analysed in the framework of a single and coherent analysis but instead by two separate models. To improve transparency and to facilitate secondary analyses of results from RCTs, a reliable algorithm permitting the reconstruction of data based on Kaplan-Meier curves reported in the literature was developed. Her current project is exploring alternative models for extrapolation of trial-based survival curves using external information.

Karen Coulman is a PhD student undertaking research which aims to: 1) Develop a core outcome set for obesity surgery from the patient perspective and, 2) Investigate patients' experiences of living with the results of obesity surgery including ways to improve post-operative follow-up care. She has undertaken a systematic literature review of patient-reported outcomes in obesity surgery and is preparing for publication a synthesis of published qualitative research. These will be followed by qualitative interviews and a Delphi process (3 questionnaire rounds) with obesity surgery patients.



Caroline Boulind is a core surgical trainee in Wessex with a career interest in ENT. Her MD research thesis is exploring blinding, and the assessment of its success in randomised controlled trials of surgical interventions. This research aims to improve the understanding of surgeons regarding blinding and how novel techniques can be successfully used to blind complex surgical trials.



Sean Strong is a NIHR Academic Clinical Fellow and specialist registrar in general surgery. His PhD research title is

"Understanding the role of the multidisciplinary team in recruitment to randomised controlled trials: an exploratory qualitative study." This qualitative research aims to study how teamwork between healthcare professionals influences the process of recruitment to an RCT and understand the role of cancer multidisciplinary team meetings in trial recruitment, using semi-structured interviews.

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ConDuCT News/Workshops

New team member

We are delighted to welcome Dr Alireza Daneshkhah to the ConDuCT team (Value of Information theme) from January 2013. Ali has a wealth of experience working with Gaussian Process Emulators, which will bring valuable new skills to the theme. Ali replaced Dr Jason Madan who left ConDuCT to take up a position as Assistant Professor in Health Economics at the University of Warwick. We wish Jason all the best in his new job, and hope to continue to work with him in the future.

Recruit and retain

16 January 2013

Members of the qualitative research theme contributed to a one day workshop led by Paula Williamson of the North West Hub:

"Recruitment and retention in clinical trials: current knowledge and future directions for research".

This work originated from the Recruitment to Trials Methodology Working Group (co-ordinated by Nicola Mills of ConDuCT's qualitative research theme). The meeting, held in Manchester on 16 January 2013, was funded by the MRC/HTMR network in conjunction with North West Hub (lead), ConDuCT Hub, Oxford Hub, All Ireland Hub, Edinburgh Hub, Leeds CTU, York CTU and Newcastle CTU. It was a very stimulating day, bringing together 48 participants from the HTMR network and the registered CTU network to learn about and discuss current and future initiatives to improve trial recruitment and retention. Discussion is already underway on how to take ideas forward..

21 November 2012

The qualitative research theme, in conjunction with the North West Hub and other experts in the field, held a very successful one-day conference in Sheffield on 21st November 2012 on

'Maximising the value of combining qualitative research and randomised controlled trials'.

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The conference brought together researchers who have undertaken a wide range of qualitative research within RCTs with a view to establishing and sharing good practice, facilitating networking and considering ways to strengthen the use of qualitative research in RCTs.

Findings presented at the conference included a report from the eagerly-awaited QUART systematic review of published articles of qualitative research undertaken within trials. There were productive parallel discussion sessions on a range of related topics which provided an opportunity for networking.

27 March 2012

The qualitative research theme led a workshop at the University of Bristol on

"How qualitative methods can contribute to the design and conduct of randomised trials".

The aim of this ConDuCT Hub workshop was to:

- Illustrate 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
- Enhance trial design and conduct
- Focus on the use of common and more novel qualitative methods within challenging-to-conduct pragmatic trials, undertaken within a health service context.

Up-coming short course

The above workshop proved very popular and was extremely well received. The workshop will run as a short course on **18 June 2013**, in conjunction with the ConDuCT Hub (see <http://www.bristol.ac.uk/social-community-medicine/shortcourse/>).

The recruitment to trials methodology Network group, led by Nicola Mills, has written a document on '**Tips for recruitment to trials**' which outlines some steps that might help trial teams to plan a successful recruitment strategy or address recruitment difficulties if they arise.





Recent Presentations

Nicola Mills (Qualitative methods theme): "The role of patient treatment preferences in improving trial recruitment: evidence from the ProtecT trial", invited speaker at the International Meeting of the British Thoracic Oncology Group, Dublin, January 2012

Chris Metcalfe (Statistics theme): "Estimating the optimal treatment effect when the randomised controlled trial design incorporates variable exposure to active intervention", an oral presentation at the Annual Conference of the International Society of Clinical Biostatistics (ISCB) in Bergen, Norway, August 2012

Jo Thorn (Health economics theme): "Comparison of costing methodologies applied to cost profiles at the end of life", a presentation at the Health Economists' Study Group meeting, Exeter, January 2013

Jane Blazeby (Patient reported outcomes and Hub Director): "Methods for successful surgical trials", West Midlands Research Collaborative Annual Meeting, Birmingham, November 2012

Rhiannon Macefield (Improving trial conduct, PRO theme): "Improving the Reporting of Patient Reported Outcomes", a pre-conference workshop contribution at the 19th International Society for Quality of Life Research (ISOQOL) in Budapest, Hungary, October 2012.

Nicky Welton (Evidence synthesis and value of information theme): "Value of information analysis", invited speaker at the Clinical Trials Unit (CTU) Statisticians meeting in Bristol, December 2012.

Chris Metcalfe (Statistics theme): "The challenges for the design and analysis of surgical trials", invited speaker at the Clinical Trials Unit (CTU) statisticians meeting in Bristol, December 2012

Patricia Guyot (Hub affiliated PhD student): "Methods for extrapolation from clinical trials data to inform economic evaluation", to present at the HTMR funded workshop in, Oxford, January 2013.

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ISOQOL 2012 Conference

ConDuCT Hub members and affiliates Natalie Blencowe, Rhiannon Macefield, Robert Whistance and Sean Strong all attended the International Society for Quality of Life Research (ISOQOL) 19th annual conference in Budapest, Hungary, in October 2012.

This year's conference was entitled '**The journey of quality of life research: A path towards personalised medicine**' and was attended by clinicians, policy makers, industry representatives and patients from all over the world being held in the Marriott hotel on the banks of the river Danube. The first day of the main conference focused on the role PROs can play in clinical effectiveness research, and in particular looked at the importance of PRO data in informing treatment decisions and healthcare policy.

and described how it will oversee major improvements in outcome reporting for clinical trials. Sean's poster considered whether patients in the UK are receiving written information about HRQL after surgery for oesophageal cancer. Rob presented a poster on a systematic review of PRO measures used in prospective studies of colorectal cancer surgery.

ISOQOL awarded its first ever Emerging Leader Award to Dr Melanie Calvert (Midlands Hub) for her 'exceptional leadership and potential'. Dr Calvert has published widely on HRQL in a range of diseases including neurological disorders, heart failure and surgical site infection and has collaborated with Professor Jane Blazeby in developing the CONSORT PRO extension.



Abstract submissions now open for ISOQOL 2013

Both Natalie and Rhiannon presented their posters. Natalie's was entitled 'Developing a core outcome set for oesophageal cancer surgery: the role of patient-reported outcomes', which comprised a systematic review and synthesis of PRO measures. Rhiannon's poster reported early results for a Delphi survey that will determine the core information to provide patients with prior to undergoing surgery for oesophageal cancer. Rhiannon also presented work on behalf of the **Core Outcome Measures in Effectiveness Trials (COMET) initiative**, which summarised the success of the COMET cross-Hub collaboration

There was a mentor/mentee reception on the evening of the first day, which provided an opportunity for career researchers to meet more 'long-standing' ISOQOL members. This was a great way to learn about PRO research in an informal environment.

The conference concluded on a high with a dinner cruise down the Danube. The next ISOQOL conference will be held in 2013 in Miami and all are encouraged to submit work to what is promising to be a very enjoyable and engaging meeting.

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Selected publications



Hollingworth W, McKell-Redwood D, Hampson L, Metcalfe C. Cost utility analysis conducted alongside RCTs: Are economic endpoints considered in sample size calculations and does it matter? *Clinical Trials* 2012.
doi: 10.1177/1740774512465358.

Thorn JC, Noble SM, Hollingworth W. Timely and complete publication of economic evaluations alongside randomised controlled trials. *Pharmacoeconomics* 2012, ISBN: 11707690.

Jacobs M, **Macefield RC, Blazeby JM,** Korfage IJ, van Berge Henegouwen MI, de Haes HC, Smets EM, Sprangers MA. Systematic review reveals limitations of studies evaluating health-related quality of life after potentially curative treatment for esophageal cancer. *Quality of Life Research* 2012. doi: 10.1007/s11136-012-0290-8.

Macefield RC, Avery KNL, **Blazeby, JM.** Integration of clinical and patient-reported outcomes in surgical oncology. *British Journal of Surgery* 2013, 100(1):28-37.

Dias S, **Ades AE,** Sutton AJ, **Welton NJ.** A generalised linear modelling framework for pairwise and network meta-analysis of randomised controlled trials. *Medical Decision Making* 2012.
doi: 10.1177/0272989X12458724.

Macefield RC, Beswick A, **Blazeby JM, Lane JA.** A systematic review of on-site monitoring methods for healthcare randomised controlled trials. *Clinical Trials* 2013, 10(1):104-124.

Guyot P, Ades AE, Ouwens MJ, **Welton NJ.** Enhanced secondary analysis of survival data: reconstructing the data from published Kaplan-Meier survival curves. *BMC Medical Research Methodology* 2012, 12:9.

Welton N, Ades AE. Research decisions in the face of heterogeneity: what can a new study tell us?. *Health Economics*. 21: 1196-1200.

Tomlin Z, deSalis I, Toerien M, **Donovan JL.** Patient advocacy and patient centredness in participant recruitment to randomized-controlled trials: implications for informed consent. *Health Expectations* 2012. doi: 10.1111/j.1369-7625.2012.00792.x.

Savovic J, Jones HE, Altman DG, Harris RJ, Juni P, Pildal J, Als-Nielsen B, Balk EM, Gluud C, Gluud LL, Ioannidis JPA, Schultz KF, Beynon R, Welton NJ, Wood L, Moher D, Deeks JJ, **Sterne JAC.** Influence of reported study design characteristics on intervention effect estimates from randomized, controlled trials. *Annals of Internal Medicine* 2012, 157:429-438.

Hampson L, Metcalfe C. Incorporating prognostic factors into causal estimators: A comparison of methods for randomised trials with a time-to-event outcome. *Statistics in Medicine* 2012, 31:3073-3088.

Brundage M, **Blazeby J,** Revicki D, Bass B, de Vet H, Duffy H, Efficace F, King M, Lam CL, Moher D, Scott J, Sloan J, Snyder C, Yount S, Calvert M. Patient-reported outcomes in randomized clinical trials: development of ISOQOL reporting standards. *Quality of Life Research* 2012. doi: 10.1007/s11136-012-0252-1.

Price MJ, **Ades AE,** Angelis DD, **Welton NJ,** Macleod J, Soldan K, Turner K, Simms I, Horner PJ. Mixture-of-exponentials models to explain heterogeneity in studies of the duration of *Chlamydia trachomatis* infection. *Statistics in Medicine* 2012. doi: 10.1002/sim.5603.

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