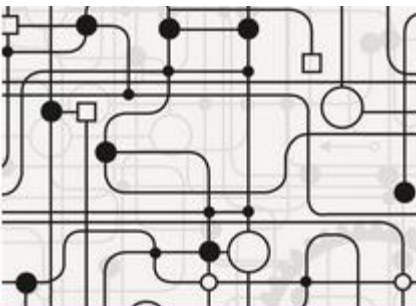




Guidance



Training



Working Groups



Publications



Trials Change Lives



Workshops



Advice

# Improving Health by Improving Trials

Mid-term report  
2014-2016

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## Summary

### Executive Committee

Professor Jane Blazeby (Chair 2016)  
Dr Louise Bowman  
Dr David Crosby  
Professor Will Hollingworth  
Mrs Carol Knott  
Dr Adrian Mander  
Professor Tony Marson  
Mr Matt Sydes  
Professor Jayne Tierney  
Professor Paula Williamson (Chair 2014-2016)  
Dr Ian White

### Network coordinator

Dr Emma Tomlinson (2012-2016)

### International Advisory Group

Professor Isabelle Boutron  
Professor Marion Campbell  
Professor Deborah Ashby  
Professor John Alexander

**Twitter:** @MRCHTMRNetwork

**Website:** [www.methodologyhubs.mrc.ac.uk](http://www.methodologyhubs.mrc.ac.uk)

## Organisation

The Network is a cohort of researchers based in Hubs across the UK undertaking research in trials methodology.

The Network is managed by an Executive Committee. It receives independent oversight from an International Advisory Group (IAG) which first met in June 2015 to advise the Network on objectives and to discuss strategic focus. A further meeting is planned for September 2016.

Each of the Hubs has two senior representatives on the Executive Committee.

Since 2014

**300+ Hub members**

**5 Hubs**

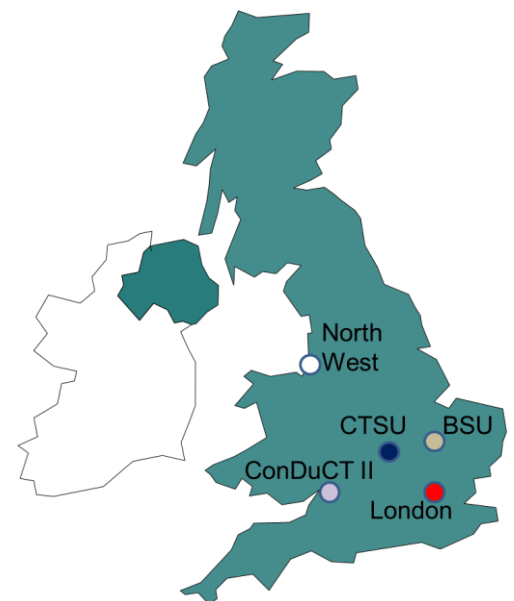
**17 PhD students**

**1 International conference**

**14 new projects**

**£323,000 committed to new research**

**£1,58 million to new studentships**



## Management

The Executive Committee meets quarterly to review the progress of Network activities. This includes strategic discussion with respect to the overall Network objectives, review of capacity building activities, assessment of applications for funding and an update on progress of projects.

The Executive Committee works closely with the Network Coordinator to prioritise budget spending, and the development of new strategic programmes.

## Chair's statement



The Network has changed since its renewal in 2014. There are five core Hubs and the Executive Committee now includes two senior members from each Hub.

We launched and successfully recruited Hub Network PhD students. This cohort has been engaged with their peers from the start. We have a studentship lead. We have expanded the content of the student meeting, to include more opportunities for engagement. Three of the PhD students are clinicians appointed as Research Training Fellows in Methodology in this cohort.

In 2015 we held our 3<sup>rd</sup> International Clinical Trials Methodology Conference (ICTMC) in Glasgow. This was the largest conference we have held so far (over 600 attendees). Over 90% of delegates who completed the feedback survey stated the event met, or exceeded their expectations. We will build on this success.

The Network continues to support strategic investments, important workshops and capacity building through its Project Grant scheme. Projects are available to encourage collaboration between at least two Hubs, and external organisations. Based on the outputs and impacts of projects funded from the initial Network award we launched a 'Guidance Pack' which is available on the Network website. To ensure the Network funding is appropriate to the community, we have recently begun external peer review for all applications.

The Network Working Groups continue to have autonomy to manage their activities. All have external members. For example, the Health Informatics Working Group has strong collaborations with colleagues at the Farr Institute.

In 2016, the Network supported the National Institute for Health Research Evaluation, Trials and Studies Coordinating Centre (NETSCC) in recommending speakers for a Refractory Asthma Trials Workshop. Representatives from the Adaptive Design and Stratified Medicine Working Groups attended the event, and gave presentations on "Dose-finding" and "Using prospective biomarker information in clinical trials", respectively. NETSCC specifically recognise the expertise these groups can offer.

The Network continues to engage with relevant stakeholders, and we have strong relationships with the National Institute of Health Research (NIHR), research funders, the Health Research Board- Trials Methodology Research Network (HRB-TMRN), Ireland, and industry partners including Transcelerate. The 2015 ICTMC conference included an industry/academia session on biomarker trials which was developed with colleagues at Roche. Since 2013, we have been working more closely with the Society for Clinical Trials. The Network presented a well-attended and lively showcase session at their 2016 Annual Meeting in Montreal.

The Network had increased its visibility through redevelopment of its website, and the launch of a Twitter account. There is a fortnightly newsletter collating information and events. We have developed a coherent branding presence across all materials, and initiatives including "Trials Change Lives" our partnership with the Northern Ireland Network for Trials Methodology Research which celebrates the impact of clinical trials on healthcare research and treatment. Two of the podcasts from this project were in the top 5 podcasts accessed from the Cochrane website in 2015.

The Network plans to complete its projects, including the launch of the Recruitment Working Groups online database "ORCCA", and the 4<sup>th</sup> ICTMC, which will be jointly coordinated with the Society for Clinical Trials and held in Liverpool, UK.

The Network has made an important impact on the trials methodology landscape. We aim to continue the Network.

**Jane M Blazeby**, Chair of the Network (August 2016)

## Network Project Grants

The Network projects provide a vital resource to researchers within the Hubs to undertake pilot work or developmental projects which cannot be supported elsewhere. The nature of the scheme also fosters collaborations between Hubs and beyond. The Project Grant scheme provides an opportunity to develop training workshops and events, and to provide complementary funding to support associated projects funded from other sources.

In summer 2015, in consultation with the Working Group leads, the Network reviewed its funding portfolio, and the support available within the scheme. Whilst the Network still reserves the right to support strategic awards, response-mode funding is the main model supported.

- 58% of expected project budget committed to date
- All applications peer reviewed
- Promotion of outputs and impact
- 64 projects funded since 2009 [1]
- 17 projects funded since 2014

### New Project Grants since 2014

Ref	Lead Hub	Title	Type of project
N57	ConDuCT II	Identification of items for inclusion in a standardised resource-use measure	Research project
N61	ConDuCT II	Refinement of and extension to the Cochrane Risk of Bias tool for Randomised trials	Research project
N62	North West	Methods for Patient and Public Involvement (PPI) in Clinical Trials: A Research Priority and Agenda Setting Exercise	Research project
N79	ConDuCT II	Efficient sample schemes for estimation of value of information of future research	Research project
N84	North West	What might a Global Health Trials Methodology Research Agenda look like?	Research project
N86	ConDuCT II	Developing a medical work force to design and conduct trials to improve evidence-based practice: a case study of surgical Trainee Research Collaboratives and a stakeholder workshop	Research project
N67	North West	Development of an interactive website for outcome reporting bias research	Research project/resource development
N78	North West	Development of user-friendly web-based software for conducting Bayesian Phase I dose-escalation studies	Research project/resource development
N85	ConDuCT II	Guidance to optimise pilot study design and conduct: A joint HTMR and NIHR HTA 'Research on Research' proposal	Research project/resource development
N64	North West	Studies Within a Trial and Embedded Trials: Current barriers and facilitators to implementation in funders and clinical trials units	Research project/workshop
N66	MRC CTSU	Developing a patient and public involvement intervention to enhance recruitment and retention in surgical trials	Research project/workshop
N73	North West	Exploring design and use of incentives for recruitment and retention in clinical trials: a workshop and a review.	Research project/workshop
N55	North West	Development of a quality assessment tool for core outcome set development	Workshop
N65	ConDuCT II	Mapping current usage of Health Economic Analysis Plans (HEAPs)'. (HEAPs)'	Workshop
N68	North West	Clinical trials in small populations: methodological challenges and solutions	Workshop
N83	North West	Improving the design and analysis of trials for efficacy and mechanisms evaluation: workshop and training days.	Workshop
N76	North West	Online tool for guidance on designing biomarker-guided randomised controlled trials	Workshop/resource development

Full list of Network projects since 2009 online[1]

## Promoting our research: Guidance Pack

Since the renewal in 2014 the Network has focussed on improving our presence in the community. This has led to the collation and promotion of an online 'Guidance Pack' to highlight key outputs and recommendations for trials methodology[2].

This Guidance Pack and associated projects has been highlighted as part of the NIHR Clinical Trials Toolkit[3], with each of the recommended Guidance Pack articles having individual links to appropriate stations in the Toolkit.

**COMET:** Core Outcome Measures in Effectiveness Trials

**DIRUM:** Database of Instruments for Resource Use Measurement

**CONSORT PRO:** Patient-Reported Outcomes

**Monitoring trials efficiently:** The role of central statistical monitoring

**Sharing participant data:** Good practice principles for sharing individual participant data from publicly funded clinical trials

**CONNECT:** Consent methods in paediatric emergency and urgent care trials

**MAMS:** Some recommendations for multi-arm multi-stage trials

**Qualitative research:** Maximising the impact of qualitative research in feasibility studies for randomised controlled trials: guidance for researchers

**Surgical trials:** Interventions in randomised controlled trials in surgery: issues to consider during trial design

**SWATs:** Online database for Studies Within A Trial (SWAT) and Studies Within A Review (SWAR)

**Rheumatoid Arthritis:** Consensus Decision Models for Biologics in Rheumatoid and Psoriatic Arthritis: Recommendations of a Multidisciplinary Working Party

**Trial Steering Committees:** Exploring the role and function of trial steering committees: results of an expert panel meeting.

**Why not to use A+B design:** A discussion of appropriate design for phase I dose escalation studies.

**Optimising Recruitment:** the Quintet Recruitment Intervention

Guidance Pack (August 2016)



# Stories of success: research across the Network

The Network and Hubs invest in a range of various methodology research projects, and we describe just some of the key outputs here.

## Stratified Medicine

### *Designs for trials with multiple biomarkers and treatments*

The MRC BSU Hub, in collaboration with clinical investigators in Cambridge, has developed methodology for designing trials with multiple biomarkers, in the setting where each biomarker can be plausibly linked with a treatment that is likely to be effective in the biomarker-positive group.

- The key idea of the method is to allow randomisation to unlinked treatments if evidence accrues that the linked treatments are ineffective.
- This method is being proposed for use in phase II trials in breast and ovarian cancer that are currently applying for funding.

This is an ongoing project and the methodology will be developed further through a recently funded MRP project grant in collaboration with researchers at the London and North-West Hubs.

### *Multi-arm multi-stage (MAMS) platform trials*

The London Hub developed the method of multi-arm multi-stage trials in which a series of arms could be tested simultaneously (“multi-arm”) with recruitment stopped early to insufficiently active arms based on a series of interim analyses (“multi-stage”). This has been promoted via the Adaptive Designs WG.

- Novel approach for phase II/III trials
- Example trial STAMPEDE (high-risk prostate cancer starting long-term hormone therapy for the first time) [4].
- Provided robust results which NHS England used to revise recommended treatment
- Results have been widely disseminated [5].

This novel approach solves the issue of comparing many different treatment types in a short time space.

## Trial Data

### *Data Sharing*

In 2013, the Network provided funding to support a group to explore good practice for clinical trial data access and sharing.

- A guidance paper was published in 2015 discussing “How should individual participant data (IPD) from

publicly funded clinical trials be shared?”[6] which was endorsed by Cancer Research UK, the MRC Methodology Research Programme Advisory Group, Wellcome Trust and the Executive Group of the UK CRC Registered CTUs Network. The NIHR has also confirmed it is supportive of the application of this guidance.

### *The use of individual participant data (IPD) in systematic reviews: Establishing the state of the art to strengthen the role of evidence synthesis in clinical trials*

The Network funded a workshop of key stakeholders in this area which resulted in a Network/ NIHR funded series of five publications demonstrating various key recommendations including

- Describes examples of IPD meta-analyses having a direct impact on trials, and highlights aspects of the approach that could be better exploited[7]
- Provide step-by-step guidance on the use of IPD meta-analyses of randomised controlled trials, to help stakeholders make better use of them [8]
- Offer practical guidance on the use of IPD meta-analyses of diagnostic and prognostic modelling studies, outlining the key advantages and challenges [9]
- Provides a stand-alone extension to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) covering aspects reporting of IPD meta-analysis[10].

## Qualitative research

The Network, and individual Hubs, recognise the value of investment in qualitative research. A range of projects have been undertaken, and we describe some key outputs here:

- Guidance document produced for feasibility studies in RCT [11]
- QuinteT Recruitment Intervention, produced in collaboration with Recruitment WG[12]
- A systematic review of training programmes for recruiters to RCTs [13]
- Qualitative research within the PIRRIST study which includes engagement and patient and public work across three Hubs.

## Surgical Trials

To date, the Network has directly funded four projects with a direct link to surgical trials, in addition to work ongoing across the Hubs. Two projects are discussed here:

### *Methods to improve trial recruitment and designing and reporting surgical trials to influence practice*

- Follow-up investment from the Royal College of Surgeons of England (RCS) to fund surgical trials centres and surgical speciality leads for trials across the UK.
- A guidance paper published in 2015, “Interventions in randomised controlled trials in surgery: issues to consider during trial design” [14]

### *Developing, delivering and evaluating training courses for recruiters to randomised trials*

- Four workshops to date, reaching over 100 delegates, with content tailored to audience (surgeons or nurses).
- Highlighted by the local Clinical Research Network as a “key element” of providing training to trial recruiters in the South West region.

## Studies within a Trial

Studies within a trial, or “SWATs”, are a growing area of interest. The Network has supported projects to establish a database of these studies in collaboration with the Northern Ireland Network for Trials Methodology Research, and has provided funding to explore how to make studies within trials routine[15].

This project surveyed UK clinical trial units leads, senior trialists, trial managers and funders to explore what the barriers to include embedded research were and included the creation of database of studies with the Northern Ireland Network for Trials Methodology Research[15] and workshops at ICTMC2015.

## Outcomes

### *COMET: Core Outcome Measures in Effectiveness Trials*

The COMET Initiative [16] brings together people interested in the development and application of agreed standardised sets of outcomes, known as ‘core outcome sets’ (COS). These sets represent the minimum that should be measured and reported in all clinical trials of a specific condition, and are also suitable for use in clinical audit or research other than randomised trials. The Network provided initial funding of this resource, subsequently supported by EU funding.

- COMET resource recommended by NIHR

- Annual meetings and events

### *CONSORT PRO: Patient-Reported Outcomes*

The Network funded a project to develop guidance for reporting patient-reported outcomes (PROs) in RCTs.

- Extension to CONSORT (CONsolidated Standards of Reporting Trials) to facilitate optimal reporting of RCTs in which PRO's are primary or secondary end points. (*JAMA* 2013 – highly cited)[17]
- CONSORT-PRO extension provides guidance for authors of trials describing patient-reported outcomes[18]
- Recommended by trial funders including NIHR

## CONNECT- paediatric emergency care trials

We supported a small project aligned with a Wellcome Trust biomedical ethics post-doctoral fellowship to undertake a study which aimed to enhance consent processes when families are approached about clinical trials in paediatric urgent and emergency care.

- Development of web resource and guidance on “Consent methods in paediatric emergency and urgent care trials” [19]

## Resource Use Questionnaires

### *DIRUM: Database of Instruments for Resource Use Measurement*

The Network supported investment in the DIRUM resource over three separate grants[20]. DIRUM is a repository of resource use measures and related methodological papers that allows economists to share questionnaires, identify best practice and collaborate on resource use methodology projects.

- Since its launch DIRUM has been visited more than 8600 times with over 2300 downloads.

Another related project involves the identification of items for inclusion in a standardised resource-use measure.





## Capacity building- PhD students

One of the main objectives within the renewal of the Network was to support capacity building in clinical trials methodology. From 2014 we directly invested in developing a cohort of PhD students, undertaking specific projects in trials methodology research. 19 new awards were made, and 17 studentships accepted, supporting the largest cohort of students undertaking methodology research in the UK. Our cohort includes three Clinical Research Training Fellowships in Methodology to support clinical PhD research.

### Network-funded PhD studentships

Student	Hub	Title
Rachel Nash	ConDuCT II	E1- Development of an objective measure of clinical recovery after cardiac surgery for use in RCTs
Ceri Rowlands*	ConDuCT II	E4- Optimising recruitment into randomised controlled trials in unplanned general surgery
Rachael Watson	North West	P15- Participation in clinical trials: analysis of organisational and site team factors that impact on site performance.
Graham Powell*	North West	P16- Using routine data in large multicentre clinical trials
Lydia Emerson	All-Ireland	P21- Designing a process evaluation framework for understanding factors that impact on successful delivery of trials investigating complex critical care interventions
Jennifer Thompson	London	P27- Statistical design and analysis of cluster-randomised stepped wedge / phased implementation trials
Lucy Beasant	ConDuCT II	P5- Treatment preference in paediatric randomised controlled trials.
Annabel Allison	MRC BSU	Q1- Identifying and estimating treatment effects in cancer trials with dynamic treatment regimes
Gemma Clayton	ConDuCT II	Q10- Incorporating external evidence syntheses in the analysis of a clinical trial
Daniel Hill-McManus	North West	Q25- Development and application of linked pharmacometric-pharmacoeconomic analyses in clinical drug development
Heather Catt	North West	Q28- Cost-effective modelling for benefit-risk assessment
Ashma Krishan	North West	Q29- The analysis and reporting of time to event data in randomised controlled trials: impact on evidence synthesis and cost effectiveness
Karen Barnes	North West	Q30- Methods to assess and improve the uptake of core outcome sets
Danielle Edwards	MRC CTSU	Q34- Exploring the use of routine datasets for recruitment and follow-up in large randomised trials
Diasmer Panna Bloe	MRC CTSU	Q38 - Evaluating electronic data capture systems for the collection of patient reported outcomes and related data.
Christopher Jarvis	London	Q42-Spatial Analysis of Cluster-Randomised Trials
Katherine Fairhurst*	ConDuCT II	Q7- Optimising the design and evaluation of pilot work to inform efficient randomised controlled trials in surgery- Kerry Avery.

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\* Clinical student

## Current students

The Network supports 17 current PhD students directly. Here are two of their stories

### Jennifer Thompson



#### *London Hub*

#### *Statistical design and analysis of cluster-randomised stepped wedge / phased implementation trials*

Jennifer Thompson is coming to the end of the second year of her

PhD. She is studying design and analysis issues with the use of stepped wedge trial designs, a trial design where clusters switch from the control condition to the intervention condition at randomly allocated time points during the trial.

One criticism of these designs is that the intervention effect is confounded with changes in the outcome over time and this is the focus of this PhD. So far she has been focusing on raising awareness of this issue as it is widely disregarded in practice. In the final year of the PhD, Jennifer hopes to provide analysis methods that are less sensitive to this confounding and enable use of these methods in statistical software. This will lead to trials with more robust results and better informed policy decisions as a result.

### Danielle Edwards



#### *MRC CTSU Hub*

#### *Exploring the use of routine datasets for recruitment and follow-up in large randomised trials*

Recruitment into clinical trials is difficult with many trials not recruiting to target. This can cause many problems including financial, ethical and practical issues that

can severely undermine the quality of the research. Using the Heart Protection Study centralized recruitment data, I have explored the differences in recruitment between male and female invitees along with other demographic factors (age, ethnicity, socioeconomic status). A significant difference in the proportion of men and women agreeing to continue with the study was observed at each stage of the recruitment process (response to invitation, screening, entering run-in, randomisation) which was also observed in the REVEAL dataset nearly 20 years later. I am now exploring how HES data and registries can be used to follow-up patients in randomised trials to avoid the need for intensive event adjudication. If successful, this will provide a more efficient and cost-effective method to follow-up trial participants.

## Student Symposia

Since 2011, the Network has hosted annual symposia for methodology students based within the Network. This has previously also included students who are Hub members funded by various sources.

- 5 student symposia to date
- 6<sup>th</sup> planned autumn 2016
- Studentship lead post created 2014 (Louise Bowman)
- Engagement with Network and Hub students

The 2015 student symposia afforded the opportunity for informal networking and a commissioned workshop on the second day focussed on “Building Research Networks”, run by an independent trainer. We plan to include a similar opportunity to engage with an external trainer at future meetings.

Students directly funded by the Network also receive free registration at the ICTMC as a part of their studentship award, providing an ideal opportunity to network with colleagues working in all disciplines of clinical trials methodology, in addition to the student cohort.

## PhD studentships across the Network

Prior to the Network supporting a directly-funded cohort of students, the individual Hubs supported training and development of a cohort of students funded by various sources. The value of being part of a Network is recognised by the development of these students, and we discuss some case studies here.

We believe that the experience of being based within a Hub, which is part of a thriving Network of peers, has contributed to both their success in their studies, and provided unique experience for developing their current careers. We discuss some of the Network students who have completed since 2014 here.

### ConDuCT II Hub: Natalie Blencowe



*Understanding the complexity of surgical interventions: an exploratory study with implications for RCTs in surgery*

**PhD awarded: January 2015**

**NIHR Doctoral Fellowship**

Natalie's PhD explored how qualitative research methods can be applied in the operating theatre to standardise surgical interventions in RCTs.

Natalie notes that *"My involvement with the Hub has immersed me into a research methodology environment and provided first-hand insight into research infrastructure and leadership."*

She has currently becoming a co-applicant on two HTA studies, and established the SPARCS (Severn and Peninsula Audit and Research Collaborative for Surgeons, <http://www.sparcs.org.uk/>) initiative for surgical trainees to contribute to multicentre studies and learn trials methodology.

**Current role:** NIHR Clinical Lecturer, member of ConDuCT II Hub

### North West Hub: Amy Cotterill



*Novel Methods for Early Phase Clinical Trials*

**PhD awarded: September 2015**

**Funder: NIHR**

Identifying the right dose to use is one of the big challenges in drug development. During Phase I of development the challenges are enhanced further by extremely small sample sizes.

Amy Cotterill's PhD, undertaken at the MRC NWHTMR (Lancaster University), investigated different methods that aim to maximise the information included in the decision making.

Amy's research contributed to dose-escalation methods that utilize Pharmacokinetic data and biomarkers in addition to toxicity data in dose-escalation studies and developed Bayesian phase II designs.

**Current role:** Baxalta methodology group with close links to Lancaster University.

### MRC BSU Hub: Finbarr Leacy

*Multiple imputation under missing not at random assumptions via fully conditional specification*

**PhD awarded: March 2016**

**Funder: MRC**

Multiple imputation methods have become very popular for handling missing data under a "missing at random" assumption that missing data are comparable to observed data. Often, however, researchers want to perform sensitivity analyses to explore the impact of departures from the "missing at random" assumption. Finbarr Leacy's PhD studied methods for doing this and included a case study of imputing HIV status in the ZAMSTAR trial as well as theoretical demonstration of methods within the popular MICE (multiple imputation by chained equations) framework.

Following this project, the MRC BSU Hub received a MRP grant to study the application of the methods to longitudinal randomised trials, together with researchers in Bristol and the London Hub and Finbarr himself from his new post.

**Current role:** Research Lecturer in Biostatistics at the Royal College of Surgeons in Ireland.



## Capacity building –other support

We recognise that building a strong community of trials methodologists should not be limited to supporting PhD research projects. The Network therefore included training workshops as part of ICTMC2015, and also hosts a training resource online highlighting courses across the UK[21].

### Supporting clinicians

#### **Key issues for successful study design and conduct: A focussed workshop for Academic Clinical Trainees**

- 2 day workshop
- Introduction to trials methodology
- Collaboration with the Academy of Medical Sciences
- Plenary speaker: Tom Walley (NIHR)

Following the workshop, delegates were contacted after 12 months to discuss the value and impact of the event.

All respondents would recommend the workshop to colleagues at this career stage, with three delegates presently applying to be a Chief Investigator on a trial.

#### **How to be a good CI**

- 2 one day workshops to date
- Key issues for new Chief Investigators
- Discussion sessions
- Plenary speaker: Rory Collins (workshop 1), Ian Roberts (workshop 2)
- Presentations from CTU and NETSCC colleagues
- 2 further workshops planned 2016/2017

Delegate feedback included:

*“I am a new CI and I found the talks invaluable” and “This was a really enjoyable and extremely useful day. It was inspiring to hear from people who had successfully run trials. It was also comforting to talk to other CIs who were experiencing the same difficulties.”*

The Network also supports a clinical capacity building panel, who meet regularly to discuss the future support available to supporting clinicians in trials. They have lobbied the Academy of Medical Sciences and the Wellcome Trust and actively engaged in developing appropriate Network workshops, with the NIHR, to support this group.

### Training and workshops

Through its project grant scheme, the Network provides funding to support a range of methodological training opportunities, in addition to supporting clinicians. We include some examples here.

#### **Clinical trials in small populations**

- Two day intensive workshop, winter 2015- fully subscribed with 45 delegates
- Website hosting training resource and meeting outputs[22]
- Workshop led to Network engagement with PSI and the University of Sheffield CTU

#### **Meta-Modelling for Value of Information Calculations**

- One day workshop to explore meta-modelling, autumn 2014- fully subscribed 31 delegates
- Presentation of new software packages using a common example
- Positive feedback
- Further workshop planned autumn 2016- 2 day technical workshop



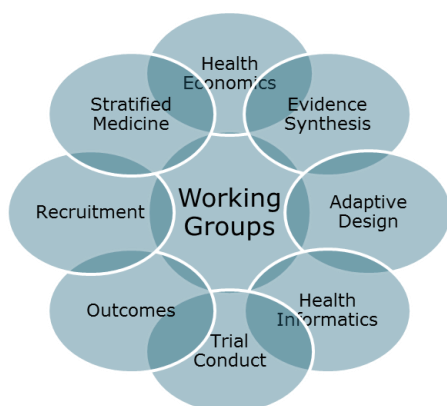
## Our place in the community

The Network supports both internal and external stakeholders through a portfolio of engagements. By building strategic partnerships we ensure that our work is at the forefront of clinical trials methodology.

By ensuring internal Hub members are supported, and their development encouraged, the Network has formed strong links across the community. The Network supports and engages both internally and externally, in the UK and internationally.

### Engagement activities

#### Working Groups



There are 8 active Network Working Groups (WG) in areas of strategic importance to methodology research[23]. WG are managed by at least two co-leads from within the Network.

- Autonomy to manage activities
- Responsible to the Network Executive Committee
- Members from across the community
- Presence at ICTMC2015
- Host webinars and events
- Support Network PhD students
- Produce guidance documents

The Working Groups also provide responses to queries from stakeholders in the community, and engage in discussions on key issues. Some examples are included here.

#### *Refractory Asthma workshop*

**Working Group:** Adaptive Design, Stratified Medicine

#### **Contribution to work of external organisation:**

Working Group experts attended a workshop, contributing both to presentations and to open discussion with the NIHR Efficacy and Mechanisms Evaluation Programme on new methodological approaches to trials in refractory asthma.

#### *How does society use evidence to judge the risks and benefits of medicines?*

**Working Group:** Health Economics, in collaboration with the Northern Ireland Network for Trials Methodology.

#### **Contribution to work of external organisation:**

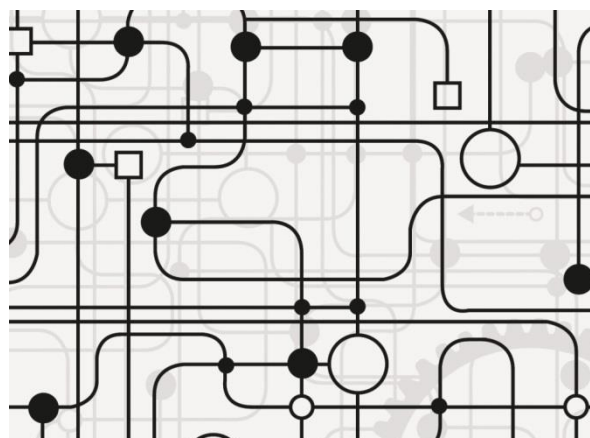
Provided formal written response as part of an open call from the Academy of Medical Sciences for evidence on “How does society use evidence to judge the risks and benefits of medicines?”

#### *Springer Nature: Guideline for data sharing*

**Working Group:** Evidence Synthesis

#### **Contribution to work of external organisation:**

Working Group provided comment to the Springer Nature publishers on draft guideline for data sharing. Following this consultation, Springer Nature made several changes to draft, resulting in publication of descriptions of non-public clinical datasets.



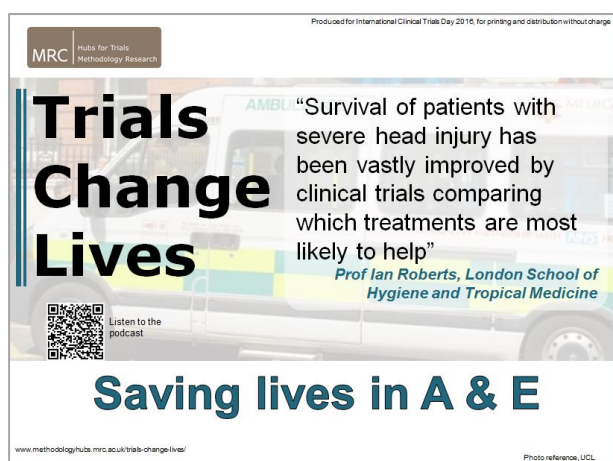


# Trials Change Lives

## Trials Change Lives

Since 2014, the Network has developed an online resource with colleagues from the Northern Ireland Network for Trials Methodology Research linked to International Clinical Trials Day.

The Trials Change Lives initiative includes a free collection of podcasts and posters showing how trials have really made a difference. Speakers describe how trials have changed lives for themselves, their patients, their research, or their community[24]. Two of our podcasts were listed in the top 5 podcasts from the Cochrane website for 2015.



## Webinars

The Trial Conduct WG has been producing regular webinars since 2014, covering a wide range of subjects in trials methodology. New speakers for 2016 include Prof Julia Brown (CTU Network) and Prof Hywel Williams (NIHR)[24].

Topics in 2016 have included; “*You have to keep your nerve on a DMC*”, and “*Clinical trials safety and regulation: application of risk-based methodological approaches*”.

Live webinars are well-attended, with opportunities for questions to the speaker and lively discussion of the topic. All webinars are recorded and available online[25].

## Methodology advice

Together with our publications and Guidance Pack[2], the individual Hubs provide extensive support and advice to researchers with questions about the use of non-standard methods in trials, both individually and collectively through the Network and its WG.

The Network receives more niche queries, where exploration and discussion with experts can be highly beneficial[26]. For example, we recently assisted the Oxford Centre for Statistical Medicine, regarding covariance adaptive response adaptive (CARA) randomisation. The Network was able to facilitate discussion with three statisticians with adaptive experience and agreed details within the patient information sheet (PIS).

## International engagement

### International Clinical Trials Methodology Conference

The Network has established a biannual conference focussed on trial methodology. Since the first meeting in 2011, this has subsequently become the largest clinical trials conference in Europe.

- ICTMC2015- Glasgow November 2015
- Over 600 delegates from 9 countries attended
- 93% of feedback respondents noted the conference met, or exceeded, expectations
- Keynote speakers: Prof Sheena McCormack, Prof Peter Sandercock
- Plenary discussion session: biomarkers and industry trials
- 6 workshops
- Exhibition and poster session
- Abstracts published in the journal *Trials* [27]



To strengthen engagement with industry, the biomarkers session included consultation with colleagues from Roche, and the final Panel presenting also drew expertise from Astra Zeneca, various UK academic partners, and the Network's own Stratified Medicine Working Group.

### Network presence at international conferences

The Network has presented invited sessions at several conferences including:

- Society for Clinical Trials, Annual Meeting Montreal May 2016: Invited session attended by over 60 delegates
- International Society for Clinical Biostatistics, Birmingham August 2016: Invited session focussed on biomarker identification and novel trial design
- HRB-TMRN 1<sup>st</sup> clinical trials symposium, Dublin September 2015- Presentation from Paula Williamson (North West Hub) on trial outcomes and COMET.

### Working with CTTI (US): Tackling obstacles to high quality clinical trials caused by inappropriate regulation

- Active collaboration with the US-led Clinical Trials Transformation Initiative (CTTI).
- Engagement with FDA and EMA in CTTI's ongoing Quality by Design project to actively promote high quality approaches to clinical trial streamlining.
- Collaboration with China Oxford Centre for International Health Research in Beijing to create the environment for tackling obstacles to high-quality clinical trials in China.
- Launch of the MoreTrials campaign in collaboration with Sense About Science in order to engage actively with the public and policy makers about the need for trials [28].

### Global Health

In summer 2016, the Network invested in a collaborative project to support exploration in a global health research agenda. The collaboration supports engagement with the Global Health Network, and researchers in low and middle income countries.



## Raising our profile

By ensuring we have a clear and consistent message in all our communications we ensure the Network is a professional organisation with international presence in the community.

Some recent activities are discussed here:

- Brand refresh 2015- new website and newsletter relaunch[29]
- Continued promotion of Network fortnightly newsletter. Over 600 subscribers (July 2016)
- Engagement with International Clinical Trials Day through a range of posters and podcasts in collaboration with Cochrane
- New twitter account launched in spring 2016 @MRCHTMNetwork. The twitter is an ideal platform to promote the Network's activities and events.
  - The feed attained over 200 followers within two months
  - The Network uses this as a platform to highlight research, guidance and workshops
  - Pivotal in promoting the Trials Change Lives initiative with colleagues
  - Ideal platform for dissemination to stakeholders

### Your Tweet activity

Your Tweets earned **2,849 impressions** over the last week



- Continued support of regular meetings of Hub members- next Members Meeting planned for autumn 2016
- Continued consultation with our stakeholders through discussion, and International Advisory Group meetings
- Submitting a publication to "Clinical Trials" on the Network's story, summer 2016
- Implementation of Guidance Pack- an ongoing activity undertaken by the Executive Committee.

## The future of the Network

The Network is presently funded until 2019. This funding provides a valuable resource to the trials community by leadership and support of research in clinical trials methodology.

The Network's mission is Improving Health by Improving Trials, and the Network is now in a position to see the strong foundations it has built and how they can underpin further research and collaborations.

Over the next two years we will continue to work on the implementation of the Guidance Pack, and we will develop new outputs including the publication of the "Online resource for recruitment research in clinical trials" (ORCCA) recruitment resource in 2016.

We will continue to review the impact of our research projects, working with stakeholders in the UK and internationally to ensure that new Network outputs and research are taken into consideration when reviewing Clinical Trial funding applications.

We'll also see the completion of the first directly funded Network PhD students and we will continue to lobby partners in the UK about the value and importance of trials methodology training.

## Supporting MRC investments

The MRC delivery plan 2016-2020 includes methodology as an underpinning process essential to all that it does. We consider that trials methodology is one part of the related methodological work. There are enormously important potential collaborations between trials methodology and informatics, computation, stratified medicine and academic relationships with industry.

We provide a conduit for the community to engage in trials methodology research, and provide invaluable support to key stakeholders in the community providing capacity and leadership in this area. We are developing our interests in Global Health and have recently invested in a new project to explore a global health trials methodology research agenda, with collaborations including the Global Health Network, and colleagues from Low and Middle Income Countries.

Our Stratified Medicine, and Health Informatics Working Groups are open to colleagues from all areas, and are not restricted to Network members. They hold active collaborations with industry partners, and other national networks including the Farr Institute. We are also developing engagements in the area of Public Health, particularly led by the MRC CTSU Hub.

We will continue to support the development and uptake of novel methods in clinical trials methodology, we will invest in future clinical and non-clinical leaders in trials methodology and we plan to continue to influence the standards of trials nationally and worldwide.

## The next 5 years 2019-2024

The Network will be applying to the MRC in 2017 to discuss opportunities for further funding for a Network of trials methodologists. It is recognised that the model will need to evolve, as the Hubs become independent. Proposals for this work will be presented and discussed with the International Advisory Committee in September 2016.



**May 7-10 2017, Liverpool, England**



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## *Improving Health by Improving Trials*

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[www.methodologyhubs.mrc.ac.uk](http://www.methodologyhubs.mrc.ac.uk)

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