Please see below for a link to the webinar recording for the Trials Methodology Research Partnership:

Trial Methodological Research – a little bit extra for big benefits

Dr Frances Shiely, University College Cork

29 May 2020

Please be advised to access the recording via the Adobe Connect app, which you can download when accessing the link below. You may be able to access the recording via a browser, but we are aware that there may be sound issues when doing so.

The slides are also available below.

For any queries, please contact uktmn@nottingham.ac.uk

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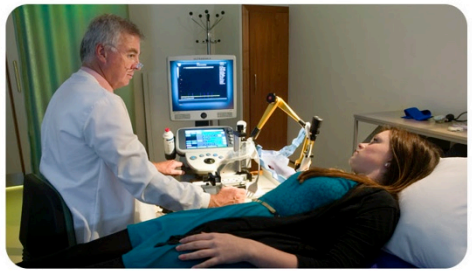
HRB Clinical Research Facility Cork

Trial Methodological Research – a little bit extra for big benefits.

Dr Frances Shiely

HRB CRF-C & School of Public Health

University College Cork, Ireland

https://crfc.ucc.ie

UCC University College Cork, Ireland Coláiste na hOllscoile Corcaigh

HRB Health Research Board

Format

- Brief background
- What is trial methodological research
- Benefits
- Discuss current trial methodological research
- Synergies and collaborations

Background - Educator

- BA Chemistry and Physical Education - Teacher
- PhD Epidemiology
- MA Teaching and Learning in Higher Education
- PG Certificate Clinical Trials

The Day Job(s)

- Senior Lecturer Epidemiology and Public Health, School of Public Health (50%)
- Teaching – BSc Public Health Sciences, MPH
- Research – Population Health Research
- Supervision – PhD, MPH, BSc Public Health Sciences

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- Senior Lecturer Patient Focused Research Education HRB CRF-C (50%)
- Teaching–Founder and Director of MSc Clinical Trials (online)
- UCC PI for the HRB TMRN
- Erasmus + Programmes
- Supervision – PhD, MD, Placement Students

Career Start – Population Health

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- Physical Activity and Behavioural Change
- Lifestyle and obesity
- Community based interventions for overweight and obesity
- Sexually transmitted diseases
- Hazardous alcohol consumption
- Fever in children – parent's knowledge and antipyretic use
- Self-harm and depression
- Anti-microbial resistance and effects of PCT testing
- Needle size for vaccination procedures in children and adolescents. Cochrane Systematic Review

How did I get into trial methodology this 'late' in my career?

- HRB CRF-C 2013
- Wise? In career terms
  - 10 years post PhD
  - Consider your interest areas earlier
  - Difficult to get grants if spread too thin
  - Don't want to be in too narrow a field on the other hand
- Wise? In enjoyment terms
  - YES
  - Catch up – yes, older and wiser!
- Learning for the next generation
  - Mentors: education = opportunity to train the future trialists, but getting on the early grant ladder is vital

What is trial methodology?

- Continuously questioning how and why we "do randomised trials" in a particular way
- Want to make them better and more efficient
- Improve patient health outcomes

TMRP Working Groups

- Stratified Medicine
- Health Informatics
- Adaptive Designs
- Outcomes
- Trial Conduct
- Health Economics
- Statistical Analysis
- Global Health

Priority Methodological Areas

C Tudur Smith, H Hickey, M Clarke, J Blazeby & P Williamson, 2014; Trials

- 'Methods to boost recruitment in trials' were considered the highest priority, closely followed by 'Methods to minimise attrition' and 'Choosing appropriate outcomes to measure'.

PRioRiTy

- https://priorityresearch.ie/priority-one-questions/ (Healy et al. 2018; *Trials)*
- https://priorityresearch.ie/priority-two-questions/ (Brunsdon et al. 2019; *Trials)*

COMET INITIATIVE

+AllTrials

Benefits

- Improved
  - efficiency
  - recruitment
  - retention
  - reporting
  - access
  - Compliance
- Less waste of
  - patient's time
  - researcher's time
  - money
- Less duplication of effort
  - ????
  - ????

HRB DIFA 2020 – SWAT
Recruitment Methodology

Determine which recruitment channel(s) (Facebook, Twitter, and Quick Response (QR) code) result(s) in the highest response rate and lowest cost-per-recruited sample and which results in greatest proportion of retention.

SWAT

Treweek et al. Trials (2018) 19:139
https://doi.org/10.1186/s13063-018-2535-5

Trials

LETTER Open Access

Trial Forge Guidance 1: what is a Study Within A Trial (SWAT)?

Shaun Treweek[1*], Simon Bevan[2], Peter Bower[3], Marion Campbell[1], Jacquie Christie[4], Mike Clarke[5], Clive Collett[6], Seonaidh Cotton[1], Declan Devane[7], Adel El Feky[1], Ella Flemyng[8], Sandra Galvin[7], Heidi Gardner[1], Katie Gillies[1], Jan Jansen[9], Roberta Littleford[10], Adwoa Parker[11], Craig Ramsay[1], Lynne Restrup[12], Frank Sullivan[13], David Torgerson[11], Liz Tremain[2], Matthew Westmore[2] and Paula R. Williamson[14]

Treweek et al. Trials (2020) 21:33
https://doi.org/10.1186/s13063-019-3980-5

Trials

METHODOLOGY Open Access

Trial Forge Guidance 2: how to decide if a further Study Within A Trial (SWAT) is needed

Shaun Treweek[1*], Simon Bevan[2], Peter Bower[3], Matthias Briel[4], Marion Campbell[1], Jacquie Christie[5], Clive Collett[6], Seonaidh Cotton[1], Declan Devane[7], Adel El Feky[1], Sandra Galvin[7], Heidi Gardner[1], Katie Gillies[1], Kerenza Hood[8], Jan Jansen[9], Roberta Littleford[10], Adwoa Parker[11], Craig Ramsay[1], Lynne Restrup[12], Frank Sullivan[13], David Torgerson[11], Liz Tremain[2], Erik von Elm[14], Matthew Westmore[2], Hywel Williams[15], Paula R. Williamson[16] and Mike Clarke[17]

HRB DIFA 2020 – SWAT
Recruitment Methodology

Enhancing Men's Awareness of Testicular Diseases (E-MAT): A Feasibility Study

SWAT

Determine which recruitment channel(s) (Facebook, Twitter, and Quick Response (QR) code) result(s) in the highest response rate and lowest cost-per-recruited sample and which results in greatest proportion of retention

- 6 community GAA clubs
- 2 randomly selected to each recruitment method
- *Primary outcomes:* proportion of participants who consent to participate relative to those received the link; proportion of those randomised who remain in the study to conclusion;
- *Secondary outcomes:* no. of hits on platforms; cost per strategy

Pharmacovigilance

O'Riordan D, M Kinane, KA Walsh, **F Shiely**, J Eustace, M Bermingham. Stakeholders' knowledge, attitudes and practices to pharmacovigilance and adverse drug reaction reporting in clinical trials: a mixed methods study. *European Journal of Clinical Pharmacology. Accepted for publication.*

- Follow on methodological study – education intervention on ADR training

Development of Methodological Tools

Risk Based Monitoring

- Hurley C, F Shiely, J Power, M Clarke, JA Eustace, E Flanagan, PM Kearney. Risk based monitoring (RBM) tools for clinical trials: A systematic review. *Contemporary Clinical Trials*, 2016; 51:15-27.
- Hurley C, CM Sinnott, M Clarke, PM Kearney, E Racine, JE Eustace, F Shiely. Perceived barriers and facilitators to Risk Based Monitoring in academic-led clinical trials: a mixed methods study. *Trials,* 2017; 18(1)*:1-11. DOI 10.1186/s13063-017-2148-4*

- Trialling different methods could be a potential SWAT

Recruitment Methodology: Case Study

The challenges of recruitment to a randomised trial registry – what information matters to the patient?

(CiSA CoMH Interdisciplinary Seed Award 2019)

- National dialysis database
- Registries provides an ideal platform for the conduct of RCTs due to the ready availability of case records, participant randomisation and follow-up data
- Literature on patient consent to registries is scant. Explore the challenges to recruitment
- PhD in the same area. Planned to do a CONSORT extension
- A quantitative survey of renal dialysis patients. 140 in one centre. 87 participated. Some open ended questions.
- Median 67 yrs; 69% male; 24.1% <55 yrs old, 21.8% 56 to 66 yrs, 28.7% 67 to 74yrs, 25.3% >75

Findings

Research phrase (n = 87)	Percentage				
	Excellent	Very Good	Good	Fair	Poor
"Healthcare Registry"	6.9	20.7	34.5	19.5	18.4

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"Kidney Research Registry"	4.6	23.0	37.9	19.5	14.9
"Clinical Trial"	9.2	27.6	32.2	14.9	16.1

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"Clinical Trial"	9.2	27.6	32.2	14.9	16.1
"Randomisation"	4.6	14.9	23.0	23.0	34.5

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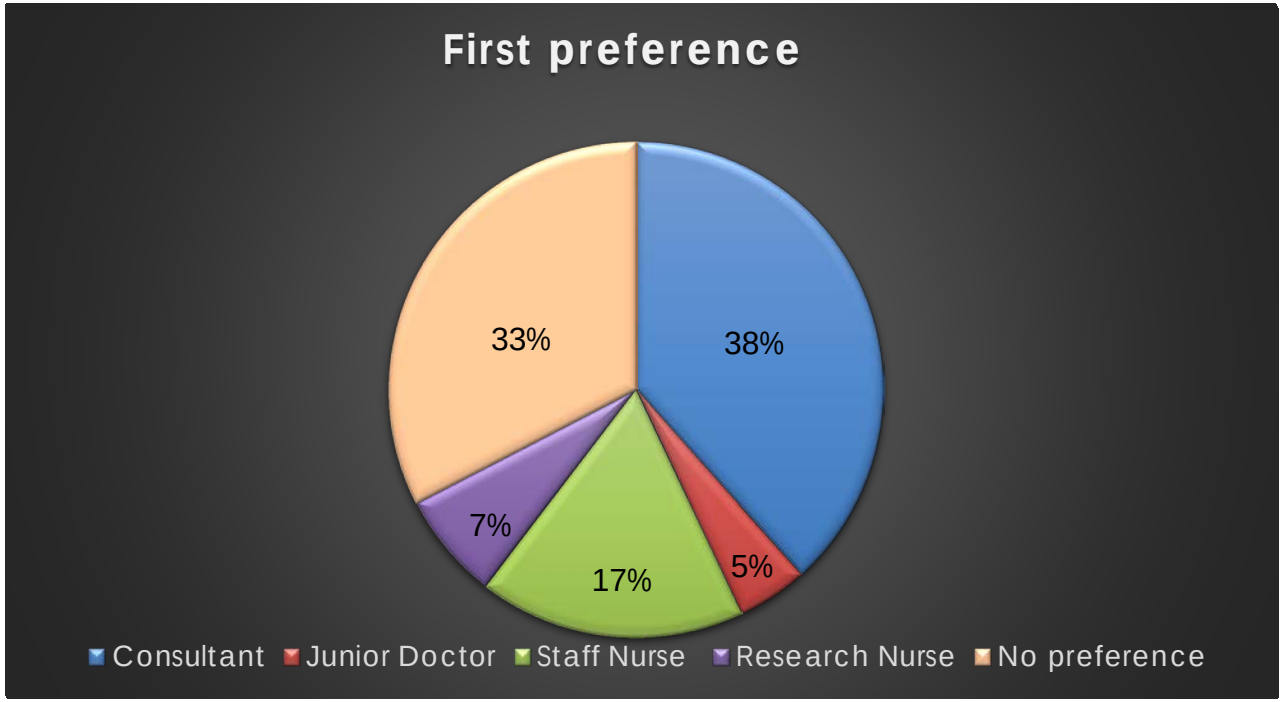
"Clinical Trial"	9.2	27.6	32.2	14.9	16.1
"Randomisation"	4.6	14.9	23.0	23.0	34.5
"Informed Consent"	14.9	31.0	36.8	10.3	6.9

Findings

- How would participants like to receive the information? 54.1% orally. 28.2% by post, 9.4% email and 8.2% telephone (discuss and consent at next dialysis)

Who?



Findings

- 29.8% of patients have concerns about their data being stored in a registry
- 24.1% consider their information to be private and don't want it uploaded and stored in a registry.
- Despite that, only 10.3% of patients said they would be very unlikely/not likely to consent to their medical information being uploaded to a registry. 79.3% were very likely/likely to give their consent.

- 58.8% of patients felt their doctors should conduct trials while 41.2% felt that their doctors should just get on with patient treatment and let somebody else conduct the clinical trials.

Findings

- **If you were considering signing up to participate in a kidney randomised trial registry would you discuss it with somebody?** Yes =67.8%

- Spouse/Partner = 35%
- GP = 15%
- Child = 13.3%
- Parent = 6.7%
- Friend = 1.7%)
- Other = 28.3% – Consultant

- **Should patients be involved in other aspects of the study process, such as the design or conduct of the study, for example?**

- Very important =21.2%
- Important = 41.2%
- Moderately important = 11.8%
- Of little importance = 25.9%

Qualitative Findings

Motivators (n = 61). 3 Reasons Why?

25 patients provided one reason

24 patients provided two reasons

12 patients provided three reasons

Themes

- *Help research, Science and Medical Advancement (31 cited this).* "beneficial for research", "to help research" or "bettering research"
- *Self-benefit (n = 32)* "to help myself", "beneficial for myself", "personal benefit". Learning/education: "to learn more about my condition", "to understand my condition", "like to know more about it", "to learn better/improve quality of life"
- *Help Others (n = 18)* to help others on dialysis", "to improve someone else's situation", "to improve others health"
- *Why not? (n=5) no harm in it*

Qualitative Findings

Key Pieces of information of concern they would most like to discuss (n = 66)

- Time and commitment (n = 18)
- Risk and side effects (n = 18). Side effect of drugs, safety of information, who will access data, if the trial was open to review, are there other similar trials with existing results. If a trial went wrong, am I a guinea pig.
- Personal benefit (n = 15). Would participation be of personal benefit.
- Effect on current treatment (n = 10)

HRB TMRN SWAT 2019

Development and testing of a novel multi-trial programmable animation platform: An education intervention to improve the efficiency and success rate of pre-screening and subsequent recruitment.

- **Shiely, F**. Effects of a multi-trial programmable animation platform on the efficiency and success of pre-screening and subsequent recruitment to a randomised trial. Protocol for a Study within a Trial (SWAT). *Northern Ireland SWAT Repository, 2019; SWAT 107: 1-3.* *https://www.qub.ac.uk/sites/TheNorthernIrelandNetworkforTrialsMethodologyResearch/SWATSWARInformation/Repositories/SWATStore/*

- PRioRiTy 4: What are the best approaches for designing and delivering information?"
- MRC-NIHR-TMRP Partner: Professor Shaun Treweek

Method

Intervention

AV programmable animation lasts 5-6 minutes

- 1) Rationale for trials and key concepts (e.g, importance of trials, randomisation, placebo control, blinding)
- 2) Participant selection (main entry criteria, voluntary basis, ability to withdraw)
- 3) Calendar of events and explanation of typical activities at each visit
- 4) Visual illustration of risk probabilities (e.g. common versus rare events)

Interventions and comparators

Intervention 1: Audio visual programmable animation (n = 60)

Intervention 2: Usual care (n = 60)

Method

Outcomes Evaluation

Questionnaire on trial knowledge and confidence in participation

Primary Outcome

1. Host trial recruitment: Proportion of screened participants who meet the eligibility criteria who consent to participate in the host trial.
2. Self-reported visual analog scale (VAS) of participant's confidence in their ability to make the right decision regarding trial participation independent of the clinician's recommendation

Secondary Outcomes

1. Pre-screening success.
2. Self-reported assessment on VAS of adequacy of understanding of trials
3. Effectiveness of the animation
4. Proportion of participants recruited to the host trial who are retained

Does patients' guided self-reflection on their illness increase engagement with and recruitment to clinical trials: a mixed-methods study within a trial (SWAT).

MRC-NIHR-TMRP Partner: Professor Shaun Treweek

Hypothesis

- We hypothesise that enhanced self-awareness of disease and how research/trials can benefit the individual patient biologically, psychologically and socially, will increase recruitment rates.

Method

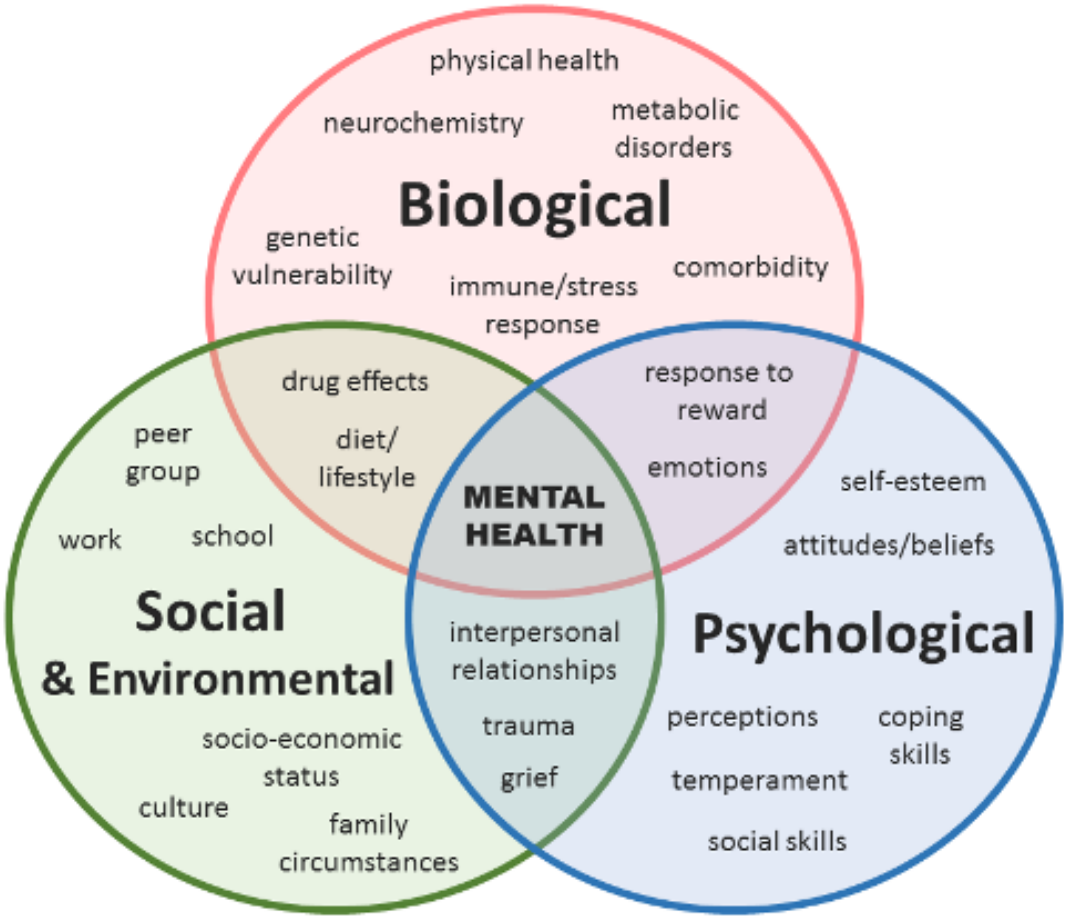
Intervention (n = 15); Control – usual care (n = 15)

-Patient self-reflection led by researcher

-Will reference the primary trial

-Will provide probing questions to encourage self-reflection, engagement

-Empower patients to better understand the consent process, as well as how the trial could impact on their specific illness



A post-intervention questionnaire on trial specific knowledge, benefits and risks and confidence in participation

Method

Qualitative Study (N = 5)

- Random selection, 15% from both arms.
- Semi-structured interview after the primary trial consent visit.

Primary Outcome

- Primary trial recruitment: Proportion of subjects meeting eligibility criteria and who consent to participate in the primary trial.

Secondary Outcomes

- Confidence in ability to consent to a trial
- Factors influencing agreed participation or refusal from the primary trial.

HRB TMRN Summer Student Scholarship 2019

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Patients' perspectives on what trialists should communicate to them when being invited to participate in a randomised trial.

Purpose

Our principal aim is to establish what information the patient might expect to be given, when being recruited to a randomised trial.

Method

- Semi -structured interviews with 30-35 patients in 8-10 randomised trials currently running in Cork University Hospital.
- Interviews will be transcribed and analysed using NVivo software.
- We will use thematic analysis to identify the priority patient seeking information.
- We will rank the identified themes/areas, according to the greatest number of times mentioned by patients

Outcomes Methodology Research

CRF-C
HRB Clinical Research Facility Cork

The relevance of clinical trial outcomes regarding clinical decision making in (i) Breast Cancer and (ii) Nephrology

Method

- N = 25 trials from each specialty; randomly selected.
- The project presents trial outcomes to (i)a panel of health professionals and (ii) patients
- Seek to establish
  - a) whether the primary outcome was considered most important
  - b) how other outcomes were ranked.
- The panel are not be told which outcome is the primary one, and the order of outcomes is randomised.

TRIAL FORGE

Role of the trial manager in effecting trial conduct

Purpose

- To ascertain the current training level of clinical trial managers, their approaches to clinical trial management and in their view, the important factors that successfully deliver a clinical trial.

Method

- A mixed-methods study will be conducted: a cross-sectional survey of clinical trial managers working in Clinical Research Facilities in Ireland and the UK or those in positions managing clinical trials;
- A follow-up telephone interview with a 10% subset of the respondents for more indepth discussion.
- Quantitative data will be analysed in SPSS. Quantitative data will be transcribed, and analysed thematically in NVivo.

Involving the research nurse in the design phase of clinical trials: should it be compulsory?

Purpose

- To ascertain if research nurses can predict the status of the trial, i.e, terminated, withdrawn or successful and the reasons for the status.

Method

- Randomly select 20 Phase III clinical trial protocols from clinicaltrials.gov.
- Five research nurses in the HRB CRF-C will be given four protocols, each, in a room with no access to the internet. They will be asked to predict the status of the trial and any problems they forsee.
- These will be compared to the information available on the trial from clinicaltrials.gov and any trial publications on the 20 trials.

Summary

- You do have to give a little extra but we do that to……
  - Maximise clinical trial efficiency
  - Ultimately change practice for the better
  - Improve people's outcomes/quality of lives

- Why else would we do what we do?

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MSc CLINICAL TRIALS

CKU17 PART TIME (ONLINE)

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Health Research Board
TMRN
Trials Methodology Research Network

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6th TRIAL METHODOLOGY SYMPOSIUM

Improved trials for better health decisions for an informed public

14-15 OCTOBER **2020**

OCT 14 — 14:00 – 16:00

OCT 15 — 10:00 – 12:00

OCT 15 — 14:00 – 16:00

UCC University College Cork, Ireland Coláiste na hOllscoile Corcaigh

CRF-C HRB Clinical Research Facility Cork

Health Research Board TMRN Trials Methodology Research Network

https://www.hrb-tmrn.ie/training-education/upcoming-events/

Find us on twitter and linkedin

#trialmethodology

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