#### NIHR Statistics Group: Achievements and future plans

Location: HMS Belfast, The Queens Walk, London SE1 2JH

Date: Friday 11 November 2016, 16.00-18.00

#### Chair: Professor Janet Peacock, King's College London

#### Programme

16.00	Registration, Coffee/tea
16.10	Welcome to the event Professor Janet Peacock, NIHR Statistics Group Co-lead; King's College London
16.15	The importance of statistics in medical research Professor Graham Lord, Director of NIHR Comprehensive Biomedical Research Centre, Guy's and St. Thomas' Hospital and King's College London
16.25	The importance of the NIHR Statistics Group Professor Deborah Ashby, Co-Director of Imperial Clinical Trials Unit and Deputy Head of Imperial School of Public Health
16.35	The view of NOCRI <i>Mr Mark Samuels, Managing Director at NIHR Office for Clinical Research</i> <i>Infrastructure (NOCRI)</i>
16.40	History of the NIHR Statistics Group Dr Victoria Cornelius, NIHR Statistics Group Co-lead; Imperial College
16.45	<ul> <li>The NIHR Statistics Group Research Sections: achievements and vision</li> <li>Laboratory studies, Dr Dawn Teare; University of Sheffield</li> <li>Imaging studies, Dr Thomas Fanshawe; University of Oxford</li> <li>Early phase trials, Dr Simon Bond; University of Cambridge Clinical Trials Unit</li> <li>Ophthalmology, Dr Catey Bunce; King's College London</li> </ul>
17.05	<ul> <li>Discussion – Delivering best practice research in the NIHR</li> <li>The NIHR Statistics Group Steering Committee</li> <li>What are the key areas where you have seen successful, productive interactions between statisticians and clinicians/scientists? Any less good? Any examples of value added as a result of such collaboration?</li> <li>What new challenges do you anticipate NIHR statisticians facing in the future?</li> <li>What support is available for statisticians in your organisation/institution?</li> </ul>

17.30 Final words & close

Drinks Reception



NIHR Statistics Group: Achievements and future plans

Friday 11 November 2016



Identifying and promoting best methodological practice in healthcare research for the benefit of patients

Dr Victoria Cornelius, Imperial College London



- Established 2012
- Link statisticians across NIHR infrastructure
- Share knowledge and expertise
- Identify and promote best statistical practice for NIHR studies







#### **Research sections**





- National events for networking, education
- >1000 attendees
- >12 best practice publications
- · Partnerships with industry

### Thanks to...



- NOCRI
- Guy's & St Thomas' BRC
- King's College London
- Moorfields BRC
- Host institutions: Cambridge CTU, Sheffield University, Oxford University, Birmingham
- Volunteers



#### Laboratory Studies

Dawn Teare, University of Sheffield

# Laboratory Studies



- NIHR statisticians felt ill-equipped to support basic scientists seeking statistical advice.
- Experimental processes difficult to understand.
- Scientists frequently reported unsatisfactory exchanges with statisticians.
- Lab scientists not familiar with talking to statisticians at design stage – stark contrast to statistical involvement in clinical research.

# Laboratory Studies



"Experimental biologists, their reviewers and their publishers must grasp basic statistics, urges David L. Vaux, or sloppy science will continue to grow."

Vaux DL, (2012) Nature, 492, 180-181



# The development of RIPOSTE









FEATURE ARTICLE

6

(cc)

SCIENCE FORUM

#### **RIPOSTE:** a framework for improving the design and analysis of laboratory-based research

Abstract Lack of reproducibility is an ongoing problem in some areas of the biomedical sciences. Poor experimental design and a failure to engage with experienced statisticians at key stages in the design and analysis of experiments are two factors that contribute to this problem. The RIPOSTE (Reducing IrreProducibility in labOratory STudiEs) framework has been developed to support early and regular discussions between scientists and statisticians in order to improve the design, conduct and analysis of laboratory studies and, therefore, to reduce irreproducibility. This framework is intended for use during the early stages of a research project, when specific questions or hypotheses are proposed. The essential points within the framework are explained and illustrated using three examples (a medical equipment test, a macrophage study and a gene expression study). Sound study design minimises the possibility of bias being introduced into experiments and leads to higher quality research with more reproducible results. DOI: 10.7554/Life.05517.001

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### Next Steps



- Illustrate how using the RIPOSTE framework can lead to optimal designs through worked up examples/ scenarios.
- repeated measures.
- missing data
- sample size and statistical power
- multiple hypothesis testing
- data display

### **Future Plans**



• Two publications drafted

'unit of analysis/repeated measurements' and

'handling missing data due to limit of detection'.

 Applying for up to three NIHR Research Methods Fellows with Senior Investigators at distinct Institutions.



## **Imaging Studies**

Tom Fanshawe, University of Oxford Sue Mallett, University of Birmingham



- Studies using imaging are often interdisciplinary, have complex designs and cut across different clinical areas
- Methods developed in one area of research are likely to inform and benefit studies in other areas

#### Imaging studies section – Main objective

# To promote good design and statistical practice through

 providing a networking group for statistical researchers involved in imaging studies

## **Current activities**



- Launch meeting, Oxford 2013 (Imaging in Translation Research)
- Twice-yearly meetings (since 2014), including
  - Statistical Issues in designing a large-scale reliability exercise in ultrasonography of the joint synovium
  - Statistical issues in clinical trials of inflammatory bowel disease
  - Sample size and power in imaging studies
- Meeting reports available online
- Maintaining a JISC-MAIL mailing list
- Presentation and dissemination of group at relevant conferences



Organising committee of 7 members, from the Universities of Oxford, Birmingham, Cambridge, Leeds & Warwick Meetings in Oxford, Birmingham & Warwick have attracted more than 120 attendees, geographically spread across the UK

"Nice balance of clinical background & presentation of statistical challenges"

"There is little opportunity for me to discuss stats issues in my job, so this was very useful"

"Scenarios very interesting & provocative"



#### **Future Plans**



- Continue the programme of meetings while expanding our membership
- Promote and disseminate group and its aims at relevant conferences
- Publications (overview of designing reliability studies in imaging in preparation)



## Early Phase Clinical Trials

Simon Bond, Cambridge CTU

## Background



- What dose of a new drug causes serious effects dose limiting toxicity
- Very common design used by clinicians : 3+3
- Statistical community has identified for decades serious issues with the design
- Impasse reached in changing practice.

#### **Rule-Based** approach



# NHS National Institute for Continueal Reassessment Design Health Research Estimate Dose-Response Curve using cumulative data Identify Dose Nearest to Target **Probability**

### **Traditional Design**





# Example: Continual Reassessment Method









- Statisticians and trialists across academia, government and industry
- Talks:
  - Examples where change is achieved
  - Experts in methodology
- Workshop:
  - Scope the problem
  - Identify stakeholders
  - Action plan

#### Output so far



- Papers
  - Identification of barriers. Survey results.
  - How to implement main alternative method
- ICTMC conference
  - Use of pre-prepared analysis tool
  - Posters
- Identification of clinical leaders willing to change unilaterally



#### **Ophthalmic section**

Catey Bunce, Kings College London

#### **Ophthalmic Section**



- In 2011, 7 letters were published in the British Journal of Ophthalmology entitled "Incorrect Statistical Analysis" reporting on statistical or design errors in papers which had been published in the BJO
- In 2012, two papers were published in leading US Ophthalmic Journals raising concern with regards to the statistical validity of research published in the ophthalmic domain <sup>1,2</sup>

 Lee CF, Cheng ACO, Fong DYT, Ophthalmology. 2012 Apr;119(4):869-72 Eyes or Subjects : Are Ophthalmic Randomized Controlled Trials Properly Designed and Analysed?
 Karakosta A, Vassilaki M, Plainis S, Elfadl NH, Tsilimbaris M, Moschandreas J. Am J Ophthalmol. 2012 Mar;153(3):571-579.e1. Choice of Analytic Approach for Eye-Specific Outcomes: One Eye or Two

#### **Ophthalmic Section**



- 3.4.2012 meeting held at NIHR Moorfields BRC, 14 medical statisticians from various institutions across England
- Discussed statistical traps for the unwary ophthalmic researcher and merit in "raising the quality of statistics in ophthalmic publications"
- Approached the British Journal of Ophthalmology who agreed to publish a "drip-feed" series with applied ophthalmic examples

#### **Ophthalmic statistics notes**

#### **NHS** National Institute for Health Research



#### **Ophthalmic Research Section**



• Different members have led on different approaches



#### **Ophthalmic Research Section**



- Championing collaboration between statisticians and non statisticians who are working in ophthalmic research
- Promoting good statistical practise with a view to getting better research conducted and published for the benefit of patients



# Workshop



- Statisticians and trialists across academia, government and industry
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#### • Thank you!



Questions:

- What are the key areas where you have seen successful, productive interactions between statisticians and clinicians/scientists? Any less good? Any examples of value added as a result of such collaboration?
- What new challenges do you anticipate NIHR statisticians facing in the future?
- What support is available for statisticians in your organisation/institution?