

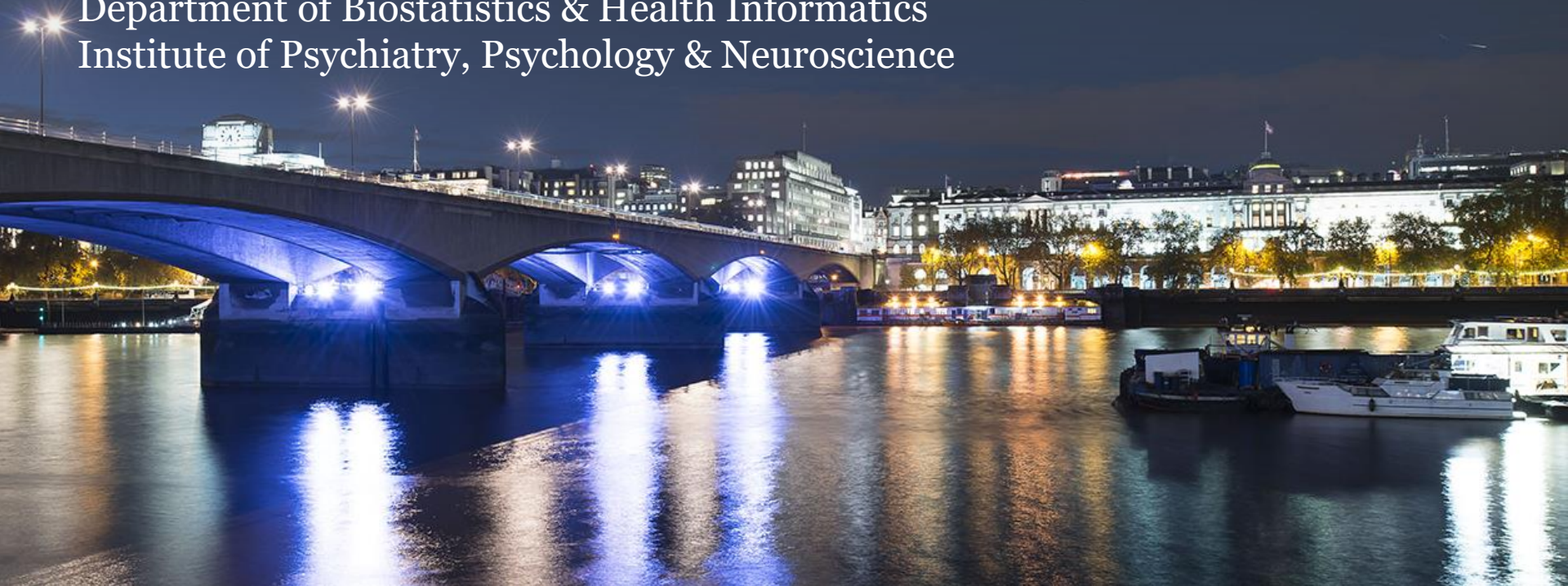
Personal experience of successfully securing methodology funding as PI

Richard Emsley

Professor of Medical Statistics and Trials Methodology

Department of Biostatistics & Health Informatics

Institute of Psychiatry, Psychology & Neuroscience



 KING'S HEALTH PARTNERS


National Institute for
Health Research


Biomedical Research Centre for Mental Health

KING'S
College
LONDON

Personal experience of successfully securing methodology funding as PI

- Personal (a bit about me)
- Experience (examples of grants)
- Successfully (and unsuccessfully...)
- Methodology funding (what is it)
- PI (why is this important)



Personal: background and education

- From Stockport, Greater Manchester



Personal: background and education

- 2000 – 2003 BSc (Hons) Maths with Statistics
University of Manchester

Undergraduate module on
Medical Statistics taught by
Prof Chris Roberts &
Prof Roseanne McNamee



- 2003 – 2007 PhD in Biostatistics (MRC Studentship)
University of Manchester

Supervised by
Prof Graham Dunn &
Prof Andrew Pickles



Personal: research and academic posts

The University of Manchester

- 2006 – 2009 Research Associate (post doc on MRC Grant)
- 2009 – 2012 MRC Career Development Award in Biostatistics
- 2011, 2013 Visiting Researcher, Harvard School of Public Health
- 2012 – 2015 Lecturer in Biostatistics
- 2015 – 2016 Senior Lecturer in Biostatistics
- 2016 – 2018 Professor of Medical Statistics, CTU Deputy Director

Institute of Psychiatry, Psychology & Neuroscience, King's College London

- Jan 2018 - Professor of Medical Statistics and Trials Methodology

Experience: methodology grant applications

- 2006 MRC/ESRC Fellowship
- 2006 MRC Methodology Research Programme
- 2009 **MRC Career Development Award in Biostatistics**
- 2009 MRC Methodology Research Programme
- 2012 MRC Early Career Centenary Award
- 2012 **MRC Methodology Research Programme**
- 2013 MRC Hubs for Trials Methodology Research (HTMR)
- 2013 MRC Methodology Research Programme
- 2014 NIHR Research Methods Fellowship
- 2015 NIHR Research Methods Fellowship
- 2014 MRC Methodology Research Programme
- 2015 **HTMR Network award**
- 2016 MRC Methodology Research Programme
- 2016 NIHR Research Methods Fellowship
- 2016 MRC Methodology Research Programme
- 2016 HTMR Network award
- 2016 MRC Methodology Research Programme
- 2016 **NIHR Research Professorship**
- 2017 HTMR Network award
- 2018 ...

Key:

Black = PI

Black = 'Successful'

Red = 'Unsuccessful'

What is “methodology research”?

- Methodology research is the study of how best to design, conduct, analyse and evaluate medical and health research
- Aim is to develop the best methods in areas that underpin biomedical science, experimental medicine, clinical trials, population health sciences, health services research and health policy
- Methodology development supported by MRC MRP must:
 - Underpin an evidenced research need within the remit of MRC or NIHR;
 - Be generalisable beyond a single case-study
 - Demonstrate early engagement with a broad range of end-users for developed methodology

Some thoughts on the 'unsuccessful' 2006 Fellowship application

- Built on work in PhD thesis:
 - Write up papers arising from PhD
 - Relevance to both social and medical sciences
- Problems with application:
 - Wrong scheme
 - Very hurriedly written (1 week)
 - Content not sufficiently thought through
 - Not considered resources properly
 - Lack of peer review
- All reflected in the referee's comments
 - No interview stage for response
- Didn't know the J-ES software for submission.



The 'successful' MRC Fellowship application

- Much better overall proposal;
 - Learnt from previous experience
 - But built on work in previous application, PhD and post-Doc.
- Spent two months preparing the application;
 - This probably still wasn't long enough!
- Identified the ideal scheme for the project and my development
- Identified ideal collaborators and overseas partners
- Thorough justification of costs (maximum words allowed)
- Peer reviewed and took advantage of internal training opportunities when preparing

Motivation for the research topic



What are your 'magic beans'?

- Clinical problem:

“This is an important clinical question,
but we don't know how to answer it”

- Methodological problem:

“The assumption this method makes
is unlikely to hold in real settings”

- Data driven problem:

“The availability of new forms of high-dimensional
data require new methods to answer
the new important clinical questions”

Example of a motivating clinical problem

- Does the therapeutic alliance influence the outcome in therapy?



Richard Bentall

Journal of Personality and Social Psychology
1986, Vol. 51, No. 6, 1173–1182

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0022-3514/86/\$00.75

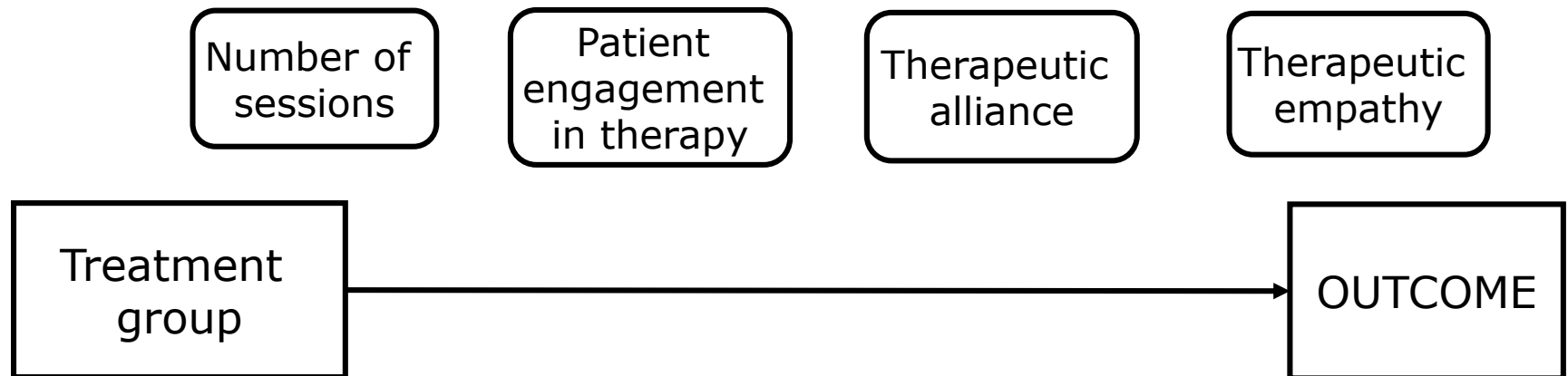
The Moderator–Mediator Variable Distinction in Social Psychological Research: Conceptual, Strategic, and Statistical Considerations

Reuben M. Baron and David A. Kenny
University of Connecticut

In this article, we attempt to distinguish between the properties of moderator and mediator variables at a number of levels. First, we seek to make theorists and researchers aware of the importance of not using the terms *moderator* and *mediator* interchangeably by carefully elaborating, both conceptually and strategically, the many ways in which moderators and mediators differ. We then go beyond this largely pedagogical function and delineate the conceptual and strategic implications of making use of such distinctions with regard to a wide range of phenomena, including control and stress, attitudes, and personality traits. We also provide a specific compendium of analytic procedures appropriate for making the most effective use of the moderator and mediator distinction, both separately and in terms of a broader causal system that includes both moderators and mediators.

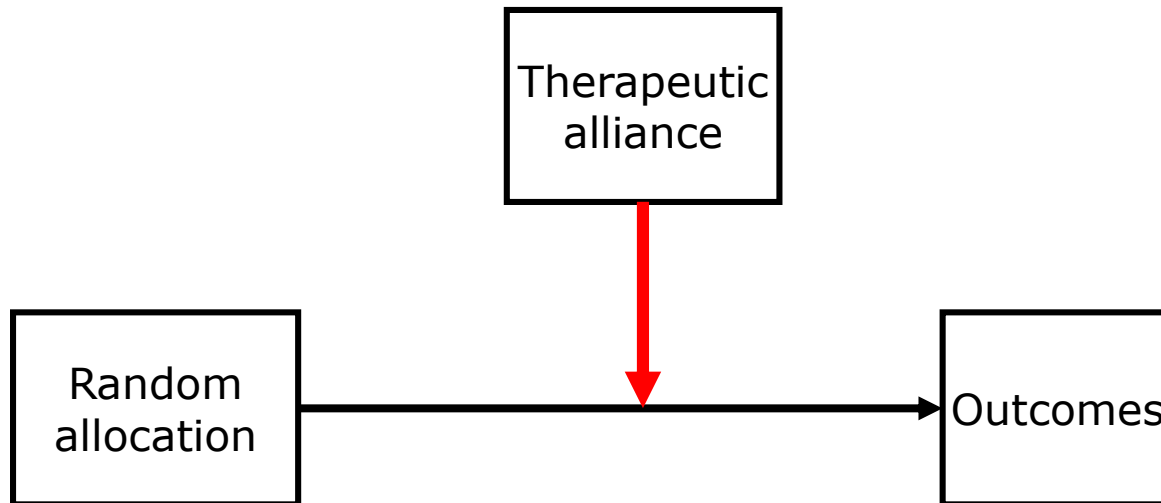
Example of a motivating clinical problem

- Process variables: characteristics of therapy
- It is plausible that these may only be measured in the therapy arm of a randomised trial. For example, if the control arm has some form of treatment as usual which doesn't contain an active 'therapy' on which they can be measured.



Example of a motivating clinical problem

- Why do we say these aren't mediators?
 - Generally interested in some other causal question, such as how do they account for heterogeneity?
 - Are they post-randomisation effect modifiers?



Efficacy and mechanisms evaluation research programme

- EME: four key questions about treatments
 1. Does it work?
 - Efficacy analysis
 2. How does it work?
 - Mediation analysis
 3. Who does it work for?
 - Stratified/personalised medicine
 4. What factors make it work better?
 - Process evaluation

Efficacy and mechanisms evaluation research programme

- MRC Methodology grant 2006 - 2009
 - Designs and methods of explanatory (causal) analysis for randomised trials of complex interventions in mental health
- MRC Methodology grant 2009 - 2012
 - Designs and analysis for the evaluation and validation of social and psychological markers in randomised trials of complex interventions in mental health
- MRC Career Development Award 2009 - 2012
 - Estimation of causal effects of complex interventions in longitudinal studies with intermediate variables
- MRC Methodology grant 2013 - 2015
 - Developing methods for understanding mechanism in complex interventions

Efficacy and mechanisms evaluation research programme

- Dunn G, Emsley RA, Liu H, Landau S, Green J, White I and Pickles A (2015) Evaluation and validation of social and psychological
Statistical Methods in Medical Research 2010; **19**: 237–270

Mediation and moderation of treatment effects in randomised controlled trials of complex interventions

Richard Emsley, Graham Dunn Health Methodology Research Group, School of
Community Based Medicine, University of Manchester, UK and **Ian R White** MRC Biostatistics
Unit, Cambridge, UK



Use motivating clinical examples

- Unsuccessful MRC Methodology grant in 2012
- Trial designs fully integrating biomarker information for the evaluation of treatment-effect mechanisms in personalised (stratified) medicine
- **“Ethics and research governance** All the analyses proposed in this project will use only simulated data, informed by reference to real data through our Project Partners, and so there are no ethical concerns.”
ARTICLE Clinical Trials 2013, 10: 709–719
- **“Data preservation for sharing.** There is no proposed data collection in this project. Please see the Data Management Plan for further detail.”
Integrating biomarker information within trials to evaluate treatment mechanisms and efficacy for personalised medicine
- Graham Dunn^a, Richard Emsley^a, Hanhua Liu^a and Sabine Lindt^b Reviewers questioned the strengths of our links with clinical researchers
- Several reviewers also questioned whether we would be able to analyse any data from real trials

Patient and Public Involvement

- Public Engagement in Science – from 2006 and 2009 MRC grants
- “The general public is exposed through the media to countless

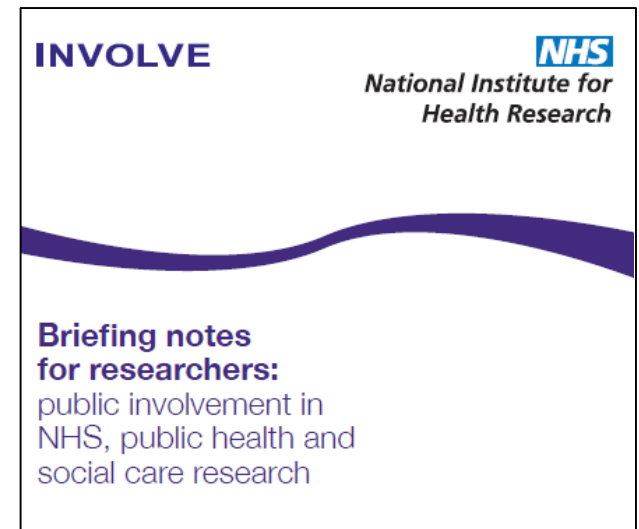
Basically says the public should care about our findings.

No PPI involvement at all!

might be manipulated so that the therapies can be refined and improved. Equally, if a particular form of therapy does not appear to be very effective, we can use the same sources of information to develop an improved version that might be.”

Patient and Public Involvement

- NIHR Involve: <http://www.invo.org.uk/>
- Funded involvement of PPI members
- Advisory panels of patients and clinicians
- Take opportunities to present at PPI/service user groups
- Sessions by Roy and Laura this afternoon...



The research funding challenge



Some concluding thoughts

- How important is it to be PI?
 - Build a good team of co-applicants and collaborators
- Look for all available schemes from a range of funders to find the right one
- If it is a good idea...keep persisting...
 - But don't be afraid to switch topics
- Demonstrate that there is an evidenced research need
 - Be generalisable beyond a single case-study
- Demonstrate early engagement with a broad range of end-users for developed methodology
 - Beyond papers, conferences...

Thank you for your attention



Email: richard.emsley@kcl.ac.uk