

# COMET IV

Wednesday 19th and Thursday 20th November 2014

Pontificia Università Lateranense

Rome, Italy



*COMET Management Group: Professor Doug Altman, Professor Jane Blazeby,  
Professor Mike Clarke, Miss Elizabeth Gargon, Professor Paula Williamson*

## COMET IV Programme

### Day 1 – Wednesday 19<sup>th</sup> November 2014

Time	
13.00-14.00	Registration and refreshments
13.30-13.50	Liz Gargon (University of Liverpool) <b>An introduction for newcomers</b>
<b>Welcome and COMET update</b>	
14.00-14.15	Roberto D'Amico (University of Modena) <b>Welcome and introduction</b>
14.15-14.30	Silvio Garattini (IRCCS-Istituto di Ricerche farmacologiche Mario Negri) <b>Surrogate and composite end-points: are they reliable?</b>
14.30-14.45	Paula Williamson (University of Liverpool) <b>COMET – looking back and going forwards</b>
<b>Core outcome sets</b>	
14.45-15.00	Christian Apfelbacher (University of Regensburg) <b>Harmonising Outcome Measures for Eczema: The roadmap of the HOME initiative</b>
15.00-15.15	Finn Gottrup (Copenhagen Wound Healing Center, Bispebjerg University Hospital) <b>Core outcome set in the wound area</b>
15.15-15.30	Alessandro Chiarotto (VU University) <b>Methods for the development of a core outcome set for non-specific low back pain</b>
<b>Poster session</b>	
15.30-16.00	Poster session
<b>Break</b>	
16.00-16.30	Break and poster viewing
<b>Cochrane links</b>	
16.30-16.45	Holger Schünemann (McMaster University) <b>Outcomes and GRADE Summary of Findings Tables: old and new</b>
16.45-17.00	Valerie Smith (Trinity College Dublin) <b>Survey of outcomes in Cochrane Reviews</b>
17.00-17.20	David Tovey (The Cochrane Collaboration) and Peter Tugwell (University of Ottawa) <b>Partnerships on core outcomes in pain: report from a conference involving OMERACT, COMET and others</b>
<b>Close of day 1</b>	
17.20-17.30	Paula Williamson (University of Liverpool)
<b>Gala dinner</b>	
19.30	

## Day 2 – Thursday 20<sup>th</sup> November 2014

<b>Time</b>	
8.30-9.00	Refreshments and poster viewing
9.00-9.05	Welcome to day 2 (Paula Williamson, University of Liverpool)
<b>Patient Engagement and Involvement in COS development</b>	
9.05- 9.15	Rosemary Humphreys (Patient Representative – HOME Initiative) <b>Core outcome sets – why are they important for us? A patient's perspective</b>
9.15-9.45	Iain Bruce (Royal Manchester Children's Hospital) <b>Meeting the challenges of public involvement in core outcome sets</b>
9.45-9.55	Heather Bagley (University of Liverpool) <b>COMET public involvement update: Involving People and the COMET PPI strategy</b>
9.55-10.00	Questions
<b>Break</b>	
10.00-10.30	Break and poster viewing
<b>Parallel workshops</b>	
10.30-12.00	<b>Workshop 1 - Methods for determining what to measure in core outcome sets</b> Paula Williamson (University of Liverpool), Angus McNair and Sara Brookes (University of Bristol)
	<b>Workshop 2 - How to measure? Selecting measurement instruments for core outcome sets</b> Caroline Terwee and Sanna Prinsen (VU University)
	<b>Workshop 3 - Involving patients in core outcome set development: identifying the challenges and potential solutions</b> Bridget Young and Heather Bagley (University of Liverpool)
<b>Lunch</b>	
12.00-13.00	Lunch and poster viewing
<b>Oral paper presentations</b>	
13.00-13.15	Liz Gargon (University of Liverpool) <b>A survey of COS developers</b>
13.15-13.30	Maria Grazia Celani (Cochrane Neurological Field) <b>Assessment of patients' and caregiver's perceived needs to start actively participated outcome measures in neurological research</b>
13.30-13.45	Lucy Hoppe (National Institute for Health & Care Excellence) <b>Qualitative systematic reviews to increase the volume and diversity of patient perspectives included in the development of core outcome sets. Tuberculosis: a case study.</b>
13.45-14.00	Chris Morris (University of Exeter Medical School) <b>Towards a shared vision for measureable and meaningful health outcomes for children and young people with neurodisability: qualitative research, Delphi survey, systematic review, and stakeholder prioritisation</b>
<b>Core outcome set development methodology</b>	
14.00-14.15	Sara Brookes (University of Bristol) <b>The impact of different stakeholder views within a Delphi process</b>
14.15-14.30	Sanna Prinsen (VU University) <b>How to select outcome measurement instruments for a 'Core Outcome Set' – a practical guideline</b>

<b>Break</b>	
14.30-15.15	Break and poster viewing
<b>Implementation</b>	
15.15-15.35	Irmgard Eichler (EMA) <b>Use of core outcome sets in European Medicines Agency's guidelines</b>
15.35-15.55	Khalid Khan (Barts and The London School of Medicine and Dentistry) <b>CROWN - Core outcomes in Women's Health</b>
15.55-16.15	Sean Tunis (Center for Medical Technology Policy) <b>Report from the first COMET Network Meeting in North America</b>
16.15-16.35	Jerry Sheehan (National Institutes of Health) <b>Common Data Elements for NIH-funded Research</b>
<b>Summary and meeting close</b>	
16.35-16.45	Mike Clarke (Queen's University Belfast)

## Invited Speakers

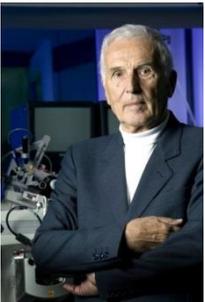


**Professor Roberto D'Amico**

University of Modena and Reggio Emilia - Italian  
Cochrane Centre

### Welcome and introduction

Roberto D'Amico is an Assistant Professor of Biostatistics at the University of Modena and Reggio Emilia, Italy. He holds a PhD in Public Health in addition to a degree in Statistics. He is the Director of a postgraduate course in Cochrane Systematic Reviews and Meta-Analysis at the University of Modena and Reggio Emilia, and organises and runs training workshops at several Italian health institutions. He has been the Director of the Italian Cochrane Centre since 2012. Roberto is an active Cochrane reviewer. He conducts systematic reviews as well as national and international randomised clinical trials on different topics. He leads a team of researchers who focus on the methodology of systematic reviews and clinical trials. He is also Editor of the Cochrane Multiple Sclerosis and Rare Diseases of the Central Nervous System Group, Testing Treatments interactive Editorial Alliance and co-convenor of the Cochrane Agenda and Priority Setting Methods Group. He coordinates a project, funded by FISM (Fondazione Italiana Sclerosi Multipla) that aims to improve the way the results of network meta-analyses are communicated to health professionals, the public and others. He is also involved in a project, funded by the Italian Ministry of Health that aims to develop a transparent, shared and evidence based process that allows the identification of low-value interventions in Neurology.



**Professor Silvio Garattini**

IRCCS-Istituto di Ricerche farmacologiche Mario Negri

### Surrogate and composite end-points: are they reliable?

Silvio Garattini qualified in Medicine in 1954, then appointed lecturer in Chemotherapy and Pharmacology. Founder and director of the IRCCS-Istituto di Ricerche Farmacologiche "Mario Negri", since 1963. The Institute has three locations, more than 750 people and has produced about 13,000 scientific publications and 250 volumes. Professor Garattini was a founder of the EORTC and has been a member of Italian National Research Council; Ministry of Health "Commissione Unica del Farmaco"; CHMP of EMA; Board of Istituto Superiore di Sanità; Chairman of the Committee for Research of the Italian Agency for Drugs (AIFA). Member of Consiglio Superiore di Sanità; Chairman of the Scientific Committee for Control of Diseases (CCM).

Awards: French Legion d'Honneur, Grande Ufficiale della Repubblica Italiana, Golden Medal of Public Health.



**Professor Paula Williamson**

University of Liverpool

### **COMET – looking back and going forwards**

Paula's research has previously been focussed on the development and application of statistical methodology in medicine. Major contributions have been made in the fields of clinical trials methodology, meta-analysis, and in the treatment of epilepsy. More recently Paula has undertaken research around the selection of outcomes for clinical research. In 2002, she was appointed Director of a new Centre for Medical Statistics, now the Department of Biostatistics, since then developing a group of over 80 staff working in health research. She has been an Associate Director of the NIHR Medicines for Children Research Network and Director of the MCRN Clinical Trials Unit since inception in 2005. In 2007, Paula became Director of the Clinical Trials Research Centre (CTRC) and has been a member of the UK Clinical Research Collaboration Registered CTU Network Steering Group since its inception.

In 2008, Paula led a successful bid to create the MRC North West Hub for Trials Methodology Research (NWHTMR), a partnership between the Universities of Liverpool, Lancaster and Bangor. The recent extension bid, 2013-2018, including the University of Manchester, was successful. Paula has recently been appointed Chair of the MRC HTMR Network. She leads the Trials Feasibility Improvement Network theme within the MRC Health e-Research Centre North, and is responsible for liaison between these two MRC networks. Paula is the lead for the European Commission- and MRC-funded COMET (Core Outcome Measures in Effectiveness Trials) Initiative, endorsed by NIHR and now referred to in NIHR HTA Guidance for Applicants. Paula has recently been appointed as an NIHR Senior Investigator, 2014-2019.



**Dr Christian Apfelbacher**

University of Regensburg, Institute of Epidemiology  
and Preventive Medicine

### **Harmonising Outcome Measures for Eczema: The roadmap of the HOME initiative**

Christian Apfelbacher gained a doctoral degree in epidemiology from the University of Heidelberg, Germany and in subsequent years a PhD in health services research from the Brighton and Sussex Medical School (BSMS) in the UK. His focal research areas are in the areas of epidemiology and prevention, evidence-based medicine and health services research. More specifically, he is interested in naturalistic observational patient cohort studies/registries, systematic reviews of both observational and intervention studies and outcomes research with a particular focus on patient-reported outcome measures. Christian Apfelbacher is a member of the executive committee of the Harmonising Outcomes Measures for Eczema (HOME) initiative and lead the quality of life working group within HOME.



**Professor Finn Gottrup**

Copenhagen Wound Healing Center, Bispebjerg  
University Hospital

### **Core Outcome Set (COS) in the Wound Area**

Professor Gottrup is a specialist in Anatomy, General Surgery and Surgical Gastroenterology. He is Professor of Surgery at the University of Southern Denmark. He has 430 publications and lectured extensively, especially in topics on clinical and experimental wound healing, wound infections, tissue perfusion and oxygenation, and organisation and education of wound healing and treatment. He has been advisor (mentor) for 4 Doctors of Medical Science (DMSci) Degrees and 8 Ph. D. Degrees. Presently he is advising for one Ph.D. Student. He has evaluated totally 17 thesis (doctoral-, Ph.D-) in different countries and 4 professor evaluations (one as chairman). Recent research is related to both basic science and clinical research topics in wound healing and education of nurses and doctors. He is member of several national and international boards, committee's, editorial boards. He is clinical science editor of Wound Repair and Regeneration and has written editorials for instance in New England Journal of Medicine. He is elected member of European Surgical Society (ESA), past president of The Danish Wound Healing Society, European Tissue Repair Society (ETRS), European Wound Management (EWMA) and has been in the board of World Union of Wound Healing Societies (WUWHS). He has received both national and international honorary awards. He has established Copenhagen Wound Healing Center in 1996 and co-established University Center of Wound Healing in Odense, Denmark in 2003. He has been head of the centres from 1996-2003 and 2003-2007, respectively. Presently he is professor and Consultant at Copenhagen Wound Healing Center, Copenhagen Denmark.



**Mr Alessandro Chiarotto**

VU University

### **Methods for the development of a core outcome set for non-specific low back pain**

Alessandro Chiarotto works as a junior researcher at the Department of Health Sciences of the VU University Amsterdam. His current research activities belong to a PhD trajectory focused: 1) on the development of a core outcome set for non-specific low back pain (NSLBP), 2) on the conduction of systematic reviews on the measurement properties of measurement instruments for NSLBP, 3) on the conduction of studies to assess the measurement properties of measurement instruments for NSLBP. Besides these projects, he is also involved on systematic reviews of health interventions and systematic reviews of observational studies. Previously, he has investigated the pain mechanisms underlying the diagnosis of thumb carpo-metacarpal osteoarthritis in elderly people. He is interested in different aspects of epidemiological research applied to musculoskeletal health, including clinimetrics, economic evaluations, association and prediction models. In Italy, he is scientific collaborator of the Italian Association of Physiotherapists (A.I.F.I.) and he has organized several post-graduate courses and congresses for physiotherapists.

After graduation, he has attended several post-graduate training courses for physiotherapists on the management of musculoskeletal disorders. He has been a teacher in courses for physiotherapists on the principles of evidence based practice and on the management of patients with whiplash associated disorders.



**Dr Holger Schünemann**

McMaster University

### **Outcomes and GRADE Summary of Findings Tables: old and new**

Succeeding eminent scientists including David Sackett, Mike Gent, Peter Tugwell and Brian Haynes, Dr. Schünemann is chair of the Department of Clinical Epidemiology and Biostatistics at McMaster University, widely considered the birthplace of evidence-based medicine. He trained in internal medicine, epidemiology, preventive medicine and public health. Having contributed to over 400 peer-reviewed publications (many focusing on guideline and systematic review methodology) he is co-developer of the guideline development tool ([www.guidelinedevelopment.org](http://www.guidelinedevelopment.org)) and the guideline checklist ([cebgrade.mcmaster.ca/guidecheck.html](http://cebgrade.mcmaster.ca/guidecheck.html)). He is co-director of the WHO collaborating center for evidence informed policy-making, co-chair of the GRADE working group, a member of the Board of Trustees of GIN, the Cochrane Collaboration Steering Group, and World Health Organization committees. He led or participated in numerous guideline panels at the WHO, the ACP, ACCP and ATS and drafted the WHO's handbook on guideline development. He enjoys his second home in Italy and long distance bike rides.



**Dr Valerie Smith**

Trinity College Dublin

### **Survey of outcomes in Cochrane Reviews**

Valerie is a part-time Assistant Prof in Midwifery at the School of Nursing and Midwifery, Trinity College Dublin and a part-time Research Fellow at the School of Nursing & Midwifery, NUI Galway. She is a registered General Nurse, Midwife and Clinical Nurse Teacher. She completed a Masters in Science (MSc) in 2006 and was awarded her PhD in July 2011. Her research interests extend to all areas of maternity care and research methods, but specifically her expertise includes methods for assessing fetal wellbeing, systematic review methodology and randomised trials. Valerie worked as a Research Fellow with the COMET team (WP2) from Nov 2012 to Mar 2014.



**Dr David Tovey**

The Cochrane Collaboration

**Partnerships on core outcomes in pain: report from a conference involving OMERACT, COMET and others**

Dr David Tovey has been the Editor in Chief of *The Cochrane Library* since January 2009. He currently leads the Cochrane Editorial Unit (CEU), based in London. The focus of the CEU is to ensure the quality and relevance of Cochrane Reviews and to support initiatives aimed at increasing their impact on decision makers. He worked previously as Editorial Director for the BMJ Evidence Centre, which is the division of the BMJ Group that produces *Clinical Evidence* and its counterpart for the public Best Treatments, BMJ Point of Care, and Best Practice. He continues to act as the series editor for the BMJ Uncertainties series. Dr Tovey worked as a General Practitioner in an urban practice in South London for 15 years until 2003 and is a Fellow of the UK Royal College of General Practitioners. During his time in practice he also undertook roles in continuing professional development for primary care professionals.



**Dr Peter Tugwell**

Centre for Global Health, University of Ottawa

**Partnerships on core outcomes in pain: report from a conference involving OMERACT, COMET and others**

Dr. Peter Tugwell is Professor of Medicine and Epidemiology & Community Medicine at the University of Ottawa and is a practicing rheumatologist at the Ottawa Hospital. In 2001, he became Director for the Centre for Global Health at the Institute of Population Health. He has built a research program and multidisciplinary team around his Canada Research Chair in Health Equity. Dr. Tugwell was Founding Director of the International Clinical Epidemiology Network Training Centre at McMaster University [1982-91] and currently serves as Secretary General to INCLEN's North American group (CanUSAClen). Dr. Tugwell is co-director of a WHO Collaborating Centre for Knowledge Translation & Health Technology Assessment in Equity. Dr. Tugwell is Coordinating Editor of the Cochrane Musculoskeletal Review Group and is Founding Co-convenor of the newly formed Cochrane Health Equity Field/Campbell Equity Methods Group and serves on the Steering Committee of the Campbell Collaboration. In 2002 he was appointed the North American Editor for the Journal of Clinical Epidemiology. He is also a Section Editor for UpToDate and a member of the Oversight committee of the Canadian Medical Association Journal. Dr. Tugwell's publication record includes over 600 journal articles, monographs, and book chapters.



**Mrs Rosemary Humphreys**

HOME Initiative

### **Core outcome sets – why are they important for us? A patient's perspective**

Rosemary is a UK consumer member of the HOME (Harmonising Outcome Measures for Eczema) initiative. Following 18 years as a Modern Language teacher she worked as a manager in Higher Education, Royal Colleges and organisations representing GPs and Community Pharmacists. Since 1975 she has volunteered in many roles with the National Eczema Society, latterly as Vice-Chair of the Trustees. Rosemary's interest in eczema and skin conditions led to membership of the Cochrane Skin Group as a consumer co-author and peer reviewer. She subsequently became involved in research more widely, as a patient representative and as an advocate of PPI (Patient and Public Involvement). She has worked with PCRN (Primary Care Research Network), with Folk.us (promoting meaningful user involvement in research) and with industry. She has been a member of a Research for Patient Benefit Funding Committee, the Royal College of GPs Patient Partnership group and local patient organisations. Rosemary is currently a member of two TSC's for eczema-related trials and one for electronic prescribing. She took part in the initial HOME Delphi studies and attended HOME II and HOME III meetings. She spoke at the 'COMET – Involving the Public' event in London in May 2014.



**Professor Iain Bruce**

Royal Manchester Children's Hospital

### **Meeting the challenges of public involvement in core outcome sets**

Professor Bruce is a Consultant Paediatric Otolaryngologist working at the Royal Manchester Children's Hospital, UK. He is an Honorary Clinical Professor of Paediatric Otolaryngology, Manchester Academic Health Science Centre, University of Manchester. His research interests compliment his clinical subspecialist interests, including Hearing Loss in Childhood, Implantable Hearing Devices in Children and Airway Disease in Children. Currently, he is the chief investigator for the NIHR RfPB SLUMBERS study regarding sleep disordered breathing in children with cleft palate and was a co-investigator for the NIHR HTA MOMENT study regarding the management of glue ear in children with cleft palate.



**Mrs Heather Bagley**

University of Liverpool

### **COMET public involvement update and future plans (Involving People and the COMET PPI strategy)**

Heather Bagley is Patient and Public Involvement Facilitator at COMET. Heather originally trained as a nurse and then moved into research, training materials development and NHS service improvement. Heather has worked on a range of projects including: epilepsy, mental health, long term care of older people, cancer services, emergency services, hospital admissions and medical education. Heather became actively involved as a parent representative in the Medicines for Children Research Network 5 years ago and now sits on three of their committees providing a parent perspective on research. Heather is also a consumer on the North West People in Research Forum Executive Committee and is involved as a patient representative in a number of other projects. Previously she was involved in the EPIC (Evidence Base for Patient and Public Involvement) project and the Public Involvement Impact Assessment Framework project as a patient representative. Heather attended the launch event of COMET as a consumer. Following Heather's passion for patient and public involvement in research (PPI) she began pursuing a career professionally in PPI in November 2012. Heather works part time for both COMET and for the Liverpool Clinical Trials Research Centre.



**Dr Sara Brookes**

University of Bristol

### **The impact of different stakeholder views within a Delphi process**

Dr Sara Brookes is a senior lecturer in health services research at the University of Bristol. Her research is in the conduct and methodological development of pragmatic randomised controlled trials (RCTs) in health care contexts. As joint lead for the outcomes theme within the ConDuCT-II Hub (Collaboration and Innovation for Difficult or Complex Randomised Controlled Trials In Invasive procedures), an MRC Hub for Trials Methodology Research hosted by the School of Social and Community Medicine at Bristol, the main theme of her current methodological research is the development, assessment and communication of clinical and patient reported outcome measures. She has contributed to the methodology and development of a number of core outcome sets for surgical interventions. Dr Brookes is also joint-lead for the MRC Hubs for Trials Methodology Research Working Group for 'Outcomes'.



**Dr C.A.C. (Sanna) Prinsen**

VU University Medical Center

### **How to select outcome measurement instruments for a 'Core Outcome Set' – a practical guideline**

C.A.C. (Sanna) Prinsen graduated from the University of Amsterdam and acquired her Master's degree in Clinical Epidemiology (2009). She wrote her Master's thesis at the Department of Dermatology, at the Academic Medical Center, University of Amsterdam (AMC-UvA) where she investigated the interpretation of quality-of-life scores as measured with a multi dimensional, dermatology-specific, health-related quality of life instrument. This publication received the '*Herman Musaph Literature Prize 2010*' awarded by the Dutch Society of Psychodermatology, and founded the basis of her PhD thesis entitled: '*Health-related quality of life in dermatology: measurement, interpretation and application*' (2013). Sanna currently works as a Post Doctoral researcher at the Department of Epidemiology and Biostatistics at the EMGO+ Institute, VU University Medical Center, Amsterdam, The Netherlands. She is involved in the Core Outcome Measures in Effectiveness Trials (COMET) initiative ([www.comet-initiative.org](http://www.comet-initiative.org)), which aims to bring together researchers interested in the development and application of agreed standardized sets of outcomes (i.e., core outcome sets). To this aim, Sanna is working on a guideline on instrument selection for outcomes included in a core outcome set. In addition, Sanna is a member of the Harmonizing Outcome Measures for Eczema (HOME, [www.homeforeczema.org](http://www.homeforeczema.org)) 'Quality of Life' and 'Symptoms' research groups, and of the European Academy of Dermatology and Venereology (EADV) Taskforce on Quality of Life. She supervises PhD and Master students with their theses. Sanna has special interests in clinimetrics and core outcome set development.



**Dr Irmgard Eichler**

European Medicines Agency

### **Use of core outcome sets in European Medicines Agency's guidelines**

Irmgard Eichler is Professor of Paediatrics and is currently Scientific Administrator in Paediatric Medicines Section at the European Medicines Agency (EMA). She qualified in medicine at the Vienna University Medical School and subsequently completed clinical training in Austria, South Africa and the US. Irmgard undertook research training in Paediatric medicine in Austria before completing a Postdoctoral Fellowship in the Division of Allergy & Pulmonary Diseases, at the Children's Hospital at Stanford, Stanford University Medical Center in California. Before joining the paediatric team at the EMA, Irmgard worked at the University Children's Hospital in Vienna. She held positions as the Director of the CF-Center, Head of Pulmonary Function Lab and as the Head of the Paediatric Allergology/Pulmonology Working Group. Irmgard has been involved in a number of other professional activities including Senior Clinical Specialist, Pediatric Pulmonology at the Prince Court Medical Center, Kuala Lumpur, member for Austria of the WHO Working Group on Health Promotion for Children and Adolescents in Hospital,

expert for cystic fibrosis with the European Medicines Agency and investigator for several national and international clinical trials.



**Professor Khalid Khan**

Barts and The London School of Medicine and Dentistry

### **CROWN - Core outcomes in Women's Health**

Khalid Khan graduated from Medical School in 1989. Currently, he is Professor of Women's Health and Clinical Epidemiology at Barts and the London School of Medicine. His academic expertise is in patient-oriented health research and medical education. He has published over 200 peer reviewed journal articles making contribution in systematic reviews (meta-analyses), trials of treatments and tests, health technology assessments, and evaluation of educational methods. His book on Evidence-based Medicine has won the BMA medical book competition. He is Editor-in-chief of British Journal of Obstetrics and Gynaecology.



**Dr Sean Tunis**

Center for Medical Technology Policy

### **Report from the first COMET Network Meeting in North America**

Sean Tunis, MD, MSc. is the Founder, President and Chief Executive Officer of the Center for Medical Technology Policy in Baltimore, Maryland. CMTP is an independent, non-profit organization that provides a neutral platform for multi-stakeholder collaborations that are focused on improving the quality, relevance, and efficiency of clinical research. His work currently focuses on expanding infrastructure for the conduct of pragmatic clinical trials within the health care delivery systems, developing condition-specific evidentiary standards for reimbursement, and promoting greater engagement of patients and consumers in clinical research. Dr. Tunis serves on the Board of Health Technology Assessment International, the Health Sciences Policy Council for ISPOR and a number of other advisory boards for public and private sector organizations focused on issues of comparative effectiveness, innovation, health technology assessment, evidence-based medicine, clinical research, and reimbursement. Through September of 2005, Dr. Tunis was the Director of the Office of Clinical Standards and Quality and Chief Medical Officer at the Centers for Medicare and Medicaid Services (CMS). In this role, he had lead responsibility for clinical policy and quality for the Medicare and Medicaid programs, which provide health coverage to over 100 million US

citizens. Dr. Tunis supervised the development of national coverage policies, quality standards for Medicare and Medicaid providers; quality measurement and public reporting initiatives, and the Quality Improvement Organization program. As Chief Medical Officer, Dr. Tunis served as the senior advisor to the CMS Administrator on clinical and scientific policy. He also co-chaired the CMS Council on Technology and Innovation. Dr. Tunis joined CMS in 2000 as the Director of the Coverage and Analysis Group. Before joining CMS, Dr. Tunis was a senior research scientist with the Technology Assessment Group, where his focus was on the design and implementation of prospective comparative effectiveness trials and clinical registries. Dr. Tunis also served as the Director of the Health Program at the Congressional Office of Technology Assessment and as a health policy advisor to the U.S. Senate Committee on Labor and Human Resources, where he participated in policy development regarding pharmaceutical and device regulation. He received a B.S. degree in Biology and History of Science from the Cornell University School of Agriculture, and a medical degree and masters in Health Services Research from the Stanford University School of Medicine. Dr. Tunis did his residency training at UCLA and the University of Maryland in Emergency Medicine and Internal Medicine. He is board certified in Internal Medicine and holds adjunct faculty appointments at Johns Hopkins (Baltimore), Stanford (Palo Alto), Tufts (Boston) and the University of California San Francisco Schools of Medicine.



**Mr Jerry Sheehan**

National Institutes of Health- National Library of Medicine

Jerry Sheehan is Assistant Director for Policy Development at the National Library of Medicine. He is a key figure in the formulation and implementation of NIH policies related to scientific data sharing, clinical trial registration and results information, genomic data sharing, public access to NIH-funded publications, and the Big Data To Knowledge (BD2K) initiative. Mr. Sheehan manages the trans-NIH Biomedical Informatics Coordinating Committee and chairs its Common Data Elements (CDE) Working Group, which aims to improve coordination and communication of CDE initiatives across NIH and beyond. Mr. Sheehan is chairman of CENDI (the interagency group of U.S. federal science, technology, and medical information managers), chairman of the OECD Working Party on Innovation and Technology Policy, and vice president of the International Council for Scientific & Technical Information. He previously co-chaired the Interagency Working Group on Digital Data. Prior to joining NLM, Mr. Sheehan held positions of increasing responsibility in the Congressional Office of Technology Assessment, the Computer Science and Telecommunications Board of the National Research Council and the Science & Technology Policy Division of the Organization for Economic Cooperation and Development (OECD). He holds B.S. and M.S. degrees in Electrical Engineering and Technology & Policy, respectively, from the Massachusetts Institute of Technology.

## Contributed Oral Paper Presentations

**E Gargon, B Young, P Williamson**

### **A survey of core outcome set developers**

**Background:** A systematic review of core outcome sets (COS) identified 250 reports relating to 198 studies. The review showed that a range of methods have been used, in a variety of ways, to develop core outcome sets. Furthermore, we found that of the 178 studies that described the methods they used to determine the core outcome set, 164 (92%) did not provide an explanation regarding their choice of methodology. To our knowledge, there is no guidance about how to conduct or report COS studies and it is currently uncertain which of these methods are the most suitable, feasible and efficient. It is important to investigate COS developers' choice of approach as this is a new area of research, and in order to formulate guidance in this area we need to try and understand the current situation, including the influences of methodological choices being made.

**Methods:** We have used a mixed methods approach, using qualitative methods (semi-structured interviews) and an online web-based survey. This presentation will focus on the web based survey, the content of which has been informed by the first 9 interviews conducted.

**Results:** Preliminary results will be reported.

**Conclusion:** This study will contribute to a larger research project that is aiming to develop methodological guidance for COS development. In order to develop this guidance we need to try to understand what factors have informed the ways in which researchers have developed COS. These survey results will contribute to a more comprehensive account of COS development, ultimately facilitating the formulation of guidance in this area.

**MG Celani, M Bianchi, A Bignamini, S Maccone, K Mahan, R Papetti, C Piersanti, A Sgoifo, TA Cantisani**

### **Assessment of patients' and caregiver's perceived needs to start actively participated outcome measures in neurological research**

**Background:** The Cochrane Neurological Field endeavors to create a research environment that reflects the needs of patients and caregivers, alongside health professionals, decision-makers, and including pharma. Collecting "the end-user of treatments" perspectives, ideas and values to reach agreement between these different partners will facilitate awareness of all stakeholder needs.

**Methods:** The study was conducted in Umbria (Italy) on three adult populations affected by disabling neurological diseases: Epilepsy, Stroke and Dementia. It was structured through the use of Focus Groups. Two psychologists conducted recruitment, used pre-determined semi-structured questions to interview attendees, and moderated group discussions. These were digitally recorded and transcribed into text-files, blindly analyzed and elaborated into key semantic meanings expressing perceived needs and emotions. Codes were analyzed using «Concordance» software.

**Results:** Preliminary results of focus groups in Epilepsy are presented: 49 patients and carers participated, organized into 4 groups of patients, with the exception of those with severe grade Epilepsy, and 4 groups of Caregivers with the exception of mild grade Epilepsy. Most frequently expressed needs were "assistance", expressed 3 times more frequently by carers than patients, "Experience sharing" and "need for knowledge" expressed 2 times more

frequently by patients. The need for assistance was directly proportional with disease severity, while the need for knowledge inversely proportional with disease severity. Emotions most frequently expressed were anger and fear, proportional with disease severity, but also hope, resignation and acceptance. These two were 2 and 5 times each more frequently expressed by patients. Anger and hope were equally distributed among patients and carers.

**Conclusions:** These preliminary data support the idea of a gap in research between different interest groups. Patient and carers' priorities are based on intense personal insight, representing a starting point to work for shared outcome measures in clinical trials and shared agenda in research.

## **L Hoppe**

### **Qualitative systematic reviews to increase the volume and diversity of patient perspectives included in the development of core outcome sets. Tuberculosis: a case study**

**Background:** Patient involvement in decision-making is a core value of contemporary healthcare, and patient consultation is an emerging component of COS methodology. This project explores: – use of qualitative systematic reviews (QSRs) of patient perspectives on outcome prioritisation in COS development; and – contribution(s) of QSR to the development of a COS for tuberculosis. Why QSR? It is proposed that QSR will provide additional outcomes for refinement in focus groups and/or surveys. QSRs allow all relevant literature, without prejudice, to inform the selection of COS, increasing the volume and diversity of the perspectives incorporated. Why tuberculosis? The World Health Organisation estimates that there are 8,600,000 cases of tuberculosis worldwide. The fight has been hampered by numerous factors, including the burden of regimens and the emergence of drug resistance. Research is on-going, and a COS for tuberculosis will ensure that trials produce useful, consistent data, free from outcome selection bias.

**Methods:** MEDLINE, EMBASE, CINAHL, PsycINFO and ASSIA were searched for studies of patient perspectives on tuberculosis outcomes and their importance. Inclusion: – direct contact or observation; – English; – publication after 2000. Reference and citation tracking were performed on included papers. Studies will be appraised using the CASP checklist and synthesised by thematic analysis.

**Results and conclusions:** Outcomes that impair physical and social functioning are emphasised, with their importance often linked to fear or stigma. Few studies were designed with outcome prioritisation in mind, reflecting the novelty of the research question. Much evidence is 'indirect' and often 'concealed' in the results. The paucity of direct information represents justification for future qualitative research in this area. Data extraction in QSR is complex, with substantial irrelevant data due. Searching for relevant studies is demanding due to poor refinement of qualitative indexing and a lack of conceptualisation and representation of the phenomenon (patient outcome prioritisation).

**C Morris, A Janssens, V Shilling, A Allard, A Fellowes, R Tomlinson, J Williams, J Thompson Coon, M Rogers, B Beresford, C Green, C Jenkinson, A Tennant, S Logan**

### **Towards a shared vision for measureable and meaningful health outcomes for children and young people with neurodisability: qualitative research, Delphi survey, systematic review, and stakeholder prioritisation**

**Objective:** To seek a shared vision between families and clinicians regarding key aspects of health as outcomes, beyond mortality and morbidity, for children and young people with neurodisability. To appraise the appropriateness and measurement properties of multidimensional patient reported outcome measures (PROMs) to assess the outcome domains.

**Methods:** Relevant outcomes were identified from (i) qualitative research with children and young people with neurodisability and parent carers, (ii) Delphi survey with health professionals, and (iii) systematic review of PROMs. The International Classification of Functioning Disability and Health provided a common language to code aspects of health. A stakeholder group participated in a prioritisation Q-sort task. Participants 54 children and young people with neurodisability and 53 parent carers participated in either focus groups or interviews; 262 multidisciplinary health professionals took part in one or more rounds of a Delphi survey. 15 stakeholders participated in a consensus meeting: 3 young people, 5 parent carers, and 7 multidisciplinary health professionals.

**Results:** The qualitative study and Delphi survey suggested a range of aspects of health that are important to service users and targeted by health professionals. There was partial but not complete overlap. Key outcome areas prioritised were: communication, emotional wellbeing, pain, sleep, mobility, self-care, independence, mental health, social activities; behaviour, toileting, and safety were also important to many parents. No single multidimensional PROM was identified that captured all the key aspects of health. Evidence was lacking of one or more measurement properties for all candidate PROMs in children and young people with neurodisability, and especially for preference-based measures.

**Conclusions:** This research proposes a core suite of outcome domains for children and young people with neurodisability that can be used to assess health services routinely and in trials. Further work is required to produce a single PROM to measure these outcomes efficiently across neurodisability.

# Workshops

## **Workshop 1: Methods for determining what to measure in core outcome sets**

Selection of outcomes is crucial to trials designed to compare the effects of different interventions. For findings to influence policy and practice, chosen outcomes need to be relevant to patients, public, healthcare professionals and others making decisions about health care. Trials in a specific condition often report different outcomes, or address the same outcome in different ways. So much could be gained if an agreed core outcome set (COS) of a minimum number of appropriate and important outcomes was measured and reported in all clinical trials in a specific condition. There are, however, no agreed best methods for selection of outcomes for COSs. This workshop will comprise a mixture of presentations, exercises and participant discussion to consider the various methods that have been used to date for COS development. A presentation will introduce methodological issues and considerations involved in developing COS. This will be illustrated with examples of COS developed for different healthcare settings (e.g. primary, secondary care, acute and chronic illnesses). Participants will be given examples of existing work to design COS for clinical trials, and work in groups to discuss potential issues. Participants will also consider different methods and their role in COS development. The importance of including key stakeholders in establishing COS will be emphasised to ensure consideration of appropriate outcomes.

**Professor Paula Williamson**, University of Liverpool

Paula Williamson is Professor of Medical Statistics and Director of the Clinical Trials Research Centre (CTRC) at the University of Liverpool. She is an Associate Director of the NIHR Medicines for Children Research Network, and Director of the MCRN Clinical Trials Unit. In 2008 she led a successful bid to create the MRC North West Hub for Trials Methodology Research (NWHTMR), focussing on three themes (early phase trial design and analysis, later phase trial design and analysis, patients' perspectives), and developing methods for application across key clinical areas including paediatrics, drug safety, cancer and epilepsy. Paula chairs the management group for the MRC-funded COMET (Core Outcome Measures in Effectiveness Trials) Initiative.

**Dr Angus McNair**, University of Bristol

Angus is a National Institute of Health Research Academic Clinical Lecturer in General Surgery at the University of Bristol, UK. His academic expertise focuses on randomised trial methodology, and specifically the study of outcome measurement and reporting. He has led the development of the colorectal cancer core outcome set. In addition, he has a strong interest in the communication of trial results to improve patient decision-making and inform consent for surgery. Angus is also a surgical registrar specialising in colorectal cancer.

**Dr Sara Brookes**, University of Bristol

Dr Sara Brookes is a senior lecturer in health services research at the University of Bristol. Her research is in the conduct and methodological development of pragmatic randomised controlled trials (RCTs) in health care contexts. As joint lead for the outcomes theme within the ConDuCT-II Hub (Collaboration and Innovation for Difficult or Complex Randomised Controlled Trials In Invasive procedures), an MRC Hub for Trials Methodology Research hosted by the School of Social and Community Medicine at Bristol, the main theme of her current methodological research is the development, assessment and communication of clinical and patient reported outcome measures. She has contributed to the methodology and development of a number of core outcome sets for surgical interventions. Dr Brookes is also joint-lead for the MRC Hubs for Trials Methodology Research Working Group for 'Outcomes'.

## **Workshop 2: How to measure? Selecting measurement instruments for core outcome sets**

Once a COS is agreed, it is then important to determine how the outcomes included in the set should be defined and measured. We recently performed a Delphi study to reach consensus on the methods for selecting outcome measurement instruments for inclusion in a COS. Consensus was reached on three important steps, that will be discussed in the workshop: 1) Conceptual considerations in the selection of outcome measurement instruments, for example agreement on the construct to be measured and the target population before starting to search for instruments; 2) Finding all relevant outcome measurement instruments, for example by performing a systematic review of outcome measurement instruments or by updating a literature search; and 3) Evaluation of the measurement properties and feasibility of identified outcome measurement instruments. This workshop offers guidance for finding available outcome measurement instruments, for comparing the measurement properties and feasibility aspects of existing instruments, and for selecting the best instrument for a given outcome. The workshop will be a combination of presentation and practice.

**Dr Caroline Terwee**, VU University Medical Center

Caroline Terwee is an epidemiologist with expertise in the development and evaluation of outcome measures. She is coordinator of the Knowledge Center on Measurement Instruments of the VU University Medical Center, Department of Epidemiology and Biostatistics, in Amsterdam, which aims to optimize the quality of measurement and quality of measurement instruments used in medical and health science research, through consultation, education, and research. Her main expertise is the development and evaluation of Patient-Reported Outcome Measures (PROMs). Caroline has a special interest in the methodology and performance of systematic reviews of measurement instruments. She is founder of the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) initiative ([www.cosmin.nl](http://www.cosmin.nl)), an international group who developed consensus-based standards for performing and evaluating studies on the measurement properties of outcome measures. She is also coordinator of the Dutch-Flemish PROMIS group, who aims to translate, validate and implement the Patient Reported Outcomes Measurement Information System (PROMIS) in the Netherlands and Flanders ([www.dutchflemishpromis.nl](http://www.dutchflemishpromis.nl)).

## **Workshop 3: Involving patients in core outcome set development: identifying the challenges and potential solutions**

For a core outcome sets (COS) to have credibility, the chosen outcomes need to be relevant and meaningful to all stakeholders, including patients and carers. Participants in this interactive session will work together to identify the challenges that researchers may encounter when planning to involve patients and carers in COS development (such as how to access patients/carers, how to maintain their involvement over time and how to elicit their views on COS etc.) Participants will also exchange ideas about potential solutions to address these challenges in different contexts and with different stakeholder groups. After brief introductory presentations to set the scene, participants will join breakout groups to discuss the challenges and solutions. A plenary session at the end will provide the opportunity for groups to share their ideas and experiences. The workshop will be suitable for people who have no prior experience of working with patients/carers to develop COS, as well as those who have some experience. The aim of the workshop is not to teach people how to involve patients/carers in COS development, but rather to raise awareness of the challenges and to discuss some potential ways to tackle these challenges.

**Professor Bridget Young**, University of Liverpool

Bridget Young is Professor of Psychology at University of Liverpool and co-lead for the Patient Perspectives Theme of the Northwest Hub for Trials Methodology Research. Her research focuses on psychosocial processes in healthcare and clinical research, with the ultimate aim of improving patient care. Much of her work has used qualitative

methods to investigate patient-practitioner communication in complex chronic illness, recruitment to clinical trials, and most recently, the development of core outcome sets.

**Ms Heather Bagley**, University of Liverpool

Heather Bagley is Patient and Public Involvement Facilitator at COMET. Heather originally trained as a nurse and then moved into research, training materials development and NHS service improvement. Heather has worked on a range of projects including: epilepsy, mental health, long term care of older people, cancer services, emergency services, hospital admissions and medical education. Heather became actively involved as a parent representative in the Medicines for Children Research Network 5 years ago and now sits on three of their committees providing a parent perspective on research. Heather is also a consumer on the North West People in Research Forum Executive Committee and is involved as a patient representative in a number of other projects including two projects exploring the impact of patient involvement in research. Heather attended the launch event of COMET as a consumer. Following Heather's passion for patient and public involvement in research (PPI) she began pursuing a career professionally in PPI in November 2012. Heather works part time for both COMET and for the Liverpool Clinical Trials Research Centre.

## Poster Presentations

### 1. Validation and application of a core set of patient-relevant outcome domains to assess the effectiveness of multimodal pain therapy (VAPAIN) - a study protocol

Ulrike Kaiser, Stefanie Deckert, Christian Kopkow, Rainer Sabatowski, Jochen Schmitt

**Introduction:** Multimodal pain therapy (MPT) has been established internationally considering a bio-psycho-social perspective in diagnostic and therapy. There is convincing evidence of effectiveness of programs according to MPT. Still, the comparability of those studies is strongly limited due to the diversity of study design and outcome measurement methodology.

**Aim:** A core outcome set (COS) deemed necessary for medical and therapeutic decision making by an international Delphi and Consensus Process according to methodological standards (OMERACT, COSMIN).

**Methods:** VAPAIN is a comprehensive, multi-methodic approach consisting of several steps. Step 1: Aim-identification of most important outcome domains in MPT. A systematic review on existing and most common domains in effectiveness trials and intervention studies will prepare a subsequent Delphi process. The panel consisting of 25 interdisciplinary professionals and patient representatives will rate domains according to their importance in effectiveness studies and daily record keeping during two online exercises. A consensus on COS domains will be targeted during a presence meeting at the end of step 1. Step 2: Aim- identification of valid and reliable instruments. At the end of step 2 there will be a recommendation of candidate instruments to measure preliminary COS from step 1. For this concern systematic reviews on relevant instruments will be conducted and finally recommended in a Consensus-meeting by the Delphi-panel. In case of problematic information levels the Delphi panel will define further research questions according to specific candidate instruments. Step 3: Aim-validation of COS on patients with chronic pain attending MPT A prospective multicenter study in 4 comprehensive, multimodal pain centers on approx. 300 patients with chronic pain will be conducted to evaluate and validate preliminary COS. At the end of the described process there will be a finalization and defining of further concerns of research by the Delphi-panel.

### 2. Multimodal pain therapy for chronic pain: A systematic review of reported patient-relevant outcome domains

Stefanie Deckert, Ulrike Kaiser, Christian Kopkow, Freya Trautmann, Rainer Sabatowski, Jochen Schmitt

**Introduction:** A variety of outcomes have been reported in the literature to determine the effectiveness of multimodal pain therapy (MPT) for chronic pain. The pronounced diversity amongst those reported outcomes interferes comparisons between measured endpoints and studies.

**Aim:** The aims of this systematic review were to summarize the choice of outcome domains used in randomized controlled trials (RCTs) and longitudinal non-randomized studies assessing the effects of MPT for chronic pain, and to subsequently form a consensus-based development of a core set of patient-relevant outcome domains (COS) in this field.

**Methods:** Medline, Embase, and AMED (until 30th August 2013) as well as systematic reviews were searched for studies reporting on chronic pain that applied MPT and investigated patient-relevant endpoints based on Randomized Controlled Trials (RCTs) and longitudinal non-randomized studies. From eligible articles, we

extracted study characteristics and all reported patient-relevant outcomes. For conceptual classification of all outcomes, the Patient-Reported Outcomes Measurement Information System (PROMIS) was used.

**Results:** From 3.626 potentially relevant titles, 71 studies were included (20 RCTs and 51 longitudinal non-randomized studies). The median and maximal numbers of patient-relevant outcomes were 8 and 34, respectively. Although most studies (39/71) assessed a combination of all three core health areas, i.e. physical, mental and social health, there was great variation in the specific domains chosen to address these core health areas. No outcome domain was measured consistently in all studies. We identified 21 different outcome domains, mostly operationalized through the domains pain intensity (n=50/71), depressive symptoms (n=42/71) and functional/physical disability (n=40/71).

**Conclusion:** The current lack of standardization of outcome domains in MPT studies hinders us to readily compare interventions from different trials and is a barrier towards evidence-based decision making. Based on these results the development of a COS for MPT has been initiated.

### 3. Core outcome set to assess effectiveness in multimodal pain therapy – preliminary results of an interdisciplinary Delphi exercise

Christian Kopkow, Stefanie Deckert, Jochen Schmitt, Rainer Sabatowski, Ulrike Kaiser

**Background:** Initiatives such as OMERACT and COMET develop standards to identify and establish core outcome sets (COS) consisting of reliable and valid instruments to assess effectiveness in health care settings. Following their recommendations, VAPAIN targets an accepted and valid COS for multimodal therapy in chronic pain (MPT).

**Methods:** 25 stakeholders (patient representatives, methodological experts, physicians, psychotherapists and physiotherapists) were nominated by their associations and asked to participate. Two rounds of online exercises were conducted prepared by a systematic review on common outcome domains. The exercises were provided by MOMENT-software (COMET). Response rates ranged from 100% (round 1) to 88% (round 2). In both rounds participants were asked to rate the provided domains according to their importance to effectiveness studies (ES) and daily record keeping (DRK). In round two they received a feedback on their first rating and the rating of the complete panel of round 1. Additionally they were asked to decide of the minimum/maximum number of required domains for ES and DRK. In both rounds the identical domains were provided additionally of those supplemental domains participants had recommended in round 1.

**Results:** Participants recommended 4 domains minimum and 9 domains maximum for ES, 3 vs 6 for DRK. Most important domains in round 2 for ES were pain intensity/severity (18/22; Md 9), health related quality of life (17/22; Md 8), and pain related disability (11/22; Md 8). For DRK they rated most important pain intensity (15/22; Md 9), psychological distress (9/22; Md 7,5) and both analgesic medication intake and pain related disability (7/22; Md 7).

**Conclusions:** Recommendations differed partly between ES and DRK. This has to be considered in future study designs of clinical trials or intervention studies in routine care. The next step will be to identify valid and reliable instruments to cover the recommended domains.

#### 4. Core Outcome Measures for Perioperative and Anaesthetic Care (COMPAC)

O.Boney, R.Moonesinghe, M.Grocott

**Background:** There is increasing recognition that generic outcomes of surgery, such as mortality and complications, length of hospital stay and time off work, are fundamental to informed consent and shared patient-doctor decision making. Generic outcomes cannot be meaningfully assessed, however, unless measured and reported consistently between trials. In current anaesthetic and perioperative research, outcome reporting often varies between RCTs, so that comparing trials, and combining them into systematic reviews, is difficult or impossible. This systematic review of the recent surgical, anaesthetic and perioperative medicine literature aims to identify what generic outcomes are commonly reported, and how they are defined.

**Methods:** We will conduct database searches of EMBASE, Medline and the Cochrane Library to identify all RCTs and systematic reviews published from 1st January 2013 to 31st March 2014 in surgery, anaesthesia and perioperative medicine. RCTs involving patients undergoing major surgery and reporting any generic outcome will be included. Generic outcomes reported in each trial will be listed, and categorised by domain, to generate a comprehensive database of reported generic outcomes, grouped by domain, showing the frequency of reporting of each outcomes.

**Results and conclusion:** We define a generic outcome as 'any outcome of universal relevance to any type of surgery or anaesthesia'.

#### 5. Patient reported outcomes (PROs) in randomized controlled trials (RCTs) on age-related macular degeneration (AMD)

Aniela K. Krezel M.D. , Ruth E. Hogg Ph.D., Augusto Azuara-Blanco Ph.D., FRCS(Ed), FRCOphth

**Aim:** The purpose of this systematic review is to identify the frequency and type of patient-reported outcomes (PROs) used in recent randomized controlled trials (RCTs) for age-related macular degeneration (AMD).

**Methods:** The authors conducted a systematic search between January 2010 and November 2013 in MEDLINE, EMBASE, Scopus, Cochrane Library and the clinical trials' registries ([www.controlled-trials.com](http://www.controlled-trials.com) and [www.ClinicalTrials.gov](http://www.ClinicalTrials.gov)) according to defined criteria. Two independent reviewers evaluated studies for inclusion and data collection content. Only RCTs for AMD and articles published in English were included. Reference lists of included papers were scanned to identify other relevant RCTs. Information collected on extracted outcomes was analysed using descriptive statistics.

**Results:** Literature and registry search yielded 3816 abstracts of journal articles and 493 records from trial registries. A total of 177 RCTs were deemed to have met inclusion criteria. Of the 860 outcomes reported, 38 outcomes were identified as PROs (4.4%). Of the 177 RCTs examined, PROs were used in 25 trials (14.1%). The National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25) was the most frequently used PRO instrument (42.1% of PROs).

**Conclusion:** This review highlights that a small proportion of AMD RCTs included PROs as outcome measures and that there was a wide variety in the instruments used.

## 6. BISON (Bloodstream Infections and Sepsis Outcomes measurement Network) initiative: an ESGBIS proposal

Luigia Scudeller, Jesús Rodríguez Baño, Winfried V. Kern on behalf of the European Society of Clinical Microbiology and Infectious Diseases working group on bloodstream infections and sepsis (ESGBIS)

**Background:** Outcome of a bloodstream infection/sepsis (BSI/S) is defined in different ways in different research projects. In this, BSI/S share the characteristics of other fields of medicine; specific issues are related to diversity of causative agents, the clinical focus of infection, severity of comorbid conditions, presence of indwelling devices, multiplicity of affected patient populations, and others. A preliminary list of putative core outcome set (COS) might be: • mortality • time-to-clinical stability • time-to-microbial clearance • development/resolution of metastatic foci • adverse events of treatment • salvage of infected device • relapse • compliance. Therefore, the European Society of Clinical Microbiology and Infectious Diseases working group on bloodstream infections and sepsis (ESGBIS) is currently designing a project for the development of a COS in BSI/S. Objectives 1. generate a comprehensive long-list of all outcome variables reported in recent randomised controlled studies on BSI/S 2. refine the outcome long-list into a COS agreed by key stakeholders 3. define the best measurement methods of proposed COS 4. identify unresolved issues for further research 5. publish the proposed COS in the relevant scientific journals 6. build a COS database with standard fields easily shared across studies 7. monitor uptake of the selected core outcomes in future relevant publications

**Methods:** Overall timetable: 2 year from first meeting. The ESGBIS group is composed by approximately 30 people with different backgrounds (infectious disease, microbiology, intensive care medicine, epidemiology and statistics). We will adopt a combination of methods: two preparatory meetings, restricted and extended Delphi rounds (via email exchanges), semi-structured interviews with patients, systematic review of the literature, final consensus conference.

**Results and conclusion:** Expected outputs publication of the systematic review and of the COS in medical journals and development of a standard set of database fields, to be included in eCRF of future studies.

## 7. Which method is best for the induction of labour: a systematic review and analysis of the outcomes reported in trials

Nancy Medley, BA, MA, Zarko Alfirovic, MD, PhD, Deborah M Caldwell, BA, MA, PhD, Therese Dowswell, BSc, PhD, Edna Keeney, MSc, Leanne Jones, BSc, and Nicola J Welton, BSc, MSc, PhD.

**Background:** Labour inductions have increased over the past two decades, with rates in many countries now exceeding 20% of all births. We conducted a systematic review, network meta-analysis and cost-effectiveness analysis to determine which labour induction method performed best on pre-specified safety and efficacy outcomes. The original protocol can be found here: [http://www.crd.york.ac.uk/PROSPERO/display\\_record.asp?ID=CRD42013005116](http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42013005116). This abstract describes the methods of the systematic review and the outcomes reported in randomised trials of labour induction.

**Methods:** We searched the Cochrane Pregnancy and Childbirth Group database of trials. Randomised clinical trials of all induction methods for women near term (37 weeks) were eligible.(4) Full papers were reviewed for assessment and data extracted independently by two researchers (NM and TD). Data were extracted for seven outcomes: vaginal delivery not achieved within 24 hours; uterine hyperstimulation with fetal heart rate (FHR) changes; caesarean section; serious neonatal morbidity or perinatal death; serious maternal morbidity or death; maternal satisfaction; and cost outcomes. After data extraction began three frequently-reported outcomes were identified and additional data were extracted. Effect modifiers were also recorded.

**Results:** 1,190 studies relating to 1,508 primary reports were identified as eligible through searching. 613 studies (902 reports) were included in the systematic review. 577 studies (607 reports) were excluded with clear reasons. Of the 613 included trials only 77 reported maternal death or serious maternal morbidity (defined as uterine rupture or ICU admission). These 77 trials (19,112 women) reported a total of 5 maternal deaths, one ICU admission and 15 instances of uterine rupture. Results will be provided for all of the outcomes specified above.

**Conclusions:** Most labour induction trials neglect to report the outcomes of X, Y and Z. An analysis of the outcomes reported in trials is a first step toward improved evidence synthesis and clearer decision-making for women undergoing labour induction.

## 8. Evaluation of Interventions for informed Consent for randomised controlled Trials (ELICIT): developing a core outcome set.

Katie Gillies, Cynthia Fraser, Vikki Entwistle, Shaun Treweek, Paula Williamson, Marion Campbell

**Background:** The process of obtaining informed consent for participation in randomised controlled trials (RCTs) was established as a mechanism to protect participants against undue harm from research and allow people to recognise any potential risks, or benefits, associated with the research. A number of interventions have been put forward to improve the informed consent process. Outcomes reported in trials of interventions to improve the informed consent process for decisions about trial participation tend to focus on 'understanding' of trial information. However, the operationalization of understanding as a concept, the tools used to measure it, and the timing of the measurements are heterogeneous. The measurement tools are often study-specific non-validated tools with only a handful of validated tools being implemented. Moreover, there is a lack of clarity regarding which outcomes matter (to whom) and why. This inconsistency between studies results in difficulties when making comparisons across studies. As such, no optimal method for measuring the impact of these interventions aimed at improving informed consent for RCTs has been identified. The ELICIT project aims to develop a core outcome set for the evaluation of interventions intended to improve informed consent for RCTs.

**Methods:** The project will adopt and adapt methodology previously developed and used in projects developing core outcome sets for assessment of clinical treatments. Specifically, the work will consist of three stages: 1. A systematic methodology review of existing outcome measures of trial informed consent interventions; 2. Interviews with key stakeholders to explore additional outcomes relevant for trial participation decisions; and 3. A Delphi study to refine the core outcome set for evaluation of trial informed consent interventions.

**Conclusion:** This presentation will discuss the key issues relevant for this work and present data generated to date from the systematic literature review, which is reviewing both quantitative and qualitative evidence.

## 9. Consensus on Outcome Measures for Glaucoma Effectiveness Trials: A Modified Delphi Approach

Rehab Ismail, Augusto Azuara-Blanco, Craig Ramsay

**Aim:** Comparing the relative effectiveness of interventions across glaucoma trials can be problematic due to differences in definitions of outcome measures. We sought to identify a key set of clinical and quality of life outcomes and how best to measure them from the perspective of glaucoma experts.

**Methods:** A two-round electronic Delphi survey was conducted. A 10-point Likert scale was used to quantify importance and consensus of outcomes. Round one involved 25 items identified from a systematic review. Round two was developed based on information gathered in round one. Items were classified as demonstrating 'agreement' as follows: median scores in the 1–4 range were considered as “not important”, those in the 5–6 range were considered as “uncertain” and those in the 7–10 range were considered as “highly important”. Experts were identified through two glaucoma societies membership-the UK and Eire Glaucoma Society (UKEGS) and European Glaucoma Society (EGS) (UKEGS, n= 122& EGS, n= 198). Delphi items were analysed using descriptive statistics.

**Results:** A total of 65 participants completed round one; of whom 56 completed round two (86%). Agreement on the importance of outcomes was reached on 48/51 items (94%). Clinical outcomes that were classified as highly important were: intraocular pressure (IOP), visual field (VF), safety and anatomical outcomes. Regarding methods of measurement of IOP, “mean follow up IOP” achieved the highest importance and for evaluating VFs- “global index mean deviation/defect (MD)” and “rate of VF progression” were equally important. With reference to instruments, IOP measured by the Ocular response Analyser had an equivocal importance.

**Conclusion:** Consensus was reached among glaucoma experts on how best to measure IOP, VF, and anatomical outcomes in glaucoma trials. The results of this study will improve the standardization of outcome measures and hence improve data synthesis and reduce outcome-reporting bias in glaucoma trials.

## 10. Selective or stepwise removal of deep caries lesions in deciduous molars: A multi-center randomised controlled trial

Falk Schwendicke, Sebastian Paris, Hardy Schweigel

**Background:** For treating deep caries lesions, selective or stepwise excavations seem advantageous compared with complete caries removal, but current evidence is sparse and focusses mainly on clinical success. Given that no core outcomes are defined for trials investigating caries removal and restorative dental treatments, we aim to compare different excavations of primary teeth using clinical, patient-centered and economic outcomes.

**Methods:** We plan a prospective multi-center, two-arm parallel group, randomised controlled trial comparing selective and stepwise excavation in sensible, asymptomatic deciduous molars with deep caries lesions. Trial outcomes were decided after systematic assessment of the literature and discussions with clinicians, patients and health economists.

**Results:** We will recruit 300 children aged 3-9 with minimum one deeply carious molar. After inclusion, sequence generation will be performed. During initial treatment, leathery, moist and reasonably soft dentin will be left in proximity to the pulp followed by adhesive restoration. Afterwards, patients', dentists' and parents' assessment of the treatment will be recorded using visual-analogue- and Likert-scales, respectively. Treatment and opportunity costs will be calculated. Re-examination will be performed after six months. Then, teeth will be allocated to one of the two interventions. Selectively excavated teeth will not be treated further, whilst for stepwise caries removal, a second excavation will be performed until only hard dentin remains. Clinical re-evaluation will be performed after 12, 24 and 36 months. Restorations will be re-assessed using modified Ryge-criteria. Objectively or subjectively required re-treatments will determine success or survival. Re-treatments will be evaluated both subjectively and regarding the generated costs.

**Conclusions:** Available core outcomes for caries trials are not applicable for comparing different excavations. The planned trial will comprehensively assess different treatments for deep lesions, and could identify discrepancies between conventionally used and alternative outcome parameters.

## 11. Evaluating outcomes used in cardiothoracic surgery intervention based research – a systematic review of reviews to develop a core outcome set

Benstoem C, Moza A, Stoppe C, Goetzenich A, Autschbach R

**Background:** Comparing relative effectiveness of interventions across studies is problematic due to the inconsistency in choice and definition of outcome measures. In cardiothoracic surgery, research has focused habitually on the identification of risk factors and on the reduction of adverse outcomes with less consideration of factors that contribute to well-being and positive health outcomes.

**Methods:** We conducted a systematic review of reviews to determine the type and number of outcomes reported in current cardiothoracic surgery intervention based research. Special focus was laid on outcomes that emphasise salutogenesis. We searched Issue 7 (July 14) of the Cochrane Database of Systematic Reviews. Systematic reviews of randomised trials on non-minimal-invasive off- or on-pump cardiothoracic surgery (elective and emergency, excluding transplants) investigating pre-, intra- or postsurgical interventions related to the outcome of the procedure were eligible for inclusion. We excluded protocols and withdrawn systematic reviews. Unique lists of salutogenically and non-salutogenically-focused outcomes were established.

**Results:** In 15 included systematic reviews (363 RCT's, n = 57.482) patient-centred, salutogenically-focused outcomes are barely reported. One third did not assess salutogenically-focused outcomes at all, two third did intend but were not able to perform meta-analyses due to absence of data, heterogeneity in outcome measurement and reporting. This compares unfavourably to 36 non-salutogenically-focused outcome categories representing 112 individual non-salutogenically-focused outcomes. Measures of mortality, cerebrovascular complications and hospitalisation are reported most frequently. Applied definitions are inconsistent for all categories. Composite endpoints vary significantly, are not validated with regard to population and combined components. Pooled analysis was not possible, as required data was not reported per patient for all components.

**Conclusion:** There is an absence of salutogenically-focused outcome parameters in cardiothoracic surgery intervention based research. Choice and definition of non-salutogenically-focused single and composite outcomes are inconsistent. We recommend the development of a core outcome set of salutogenically-focused and non-salutogenically-focused outcomes.

## 12. Reported Outcomes in Phase II Studies of Newly-Diagnosed Pulmonary Tuberculosis

L. J. Bonnett & G. Davies

**Background:** Tuberculosis (TB) remains a major killer amongst infectious diseases. Current treatment involves a four-drug regimen for at least six months. New drugs and regimens are required to shorten treatment duration, reduce toxicity and combat drug resistance however the optimal methodology to define the critical path for these regimens is not well-defined. We undertook a literature review to summarise outcomes reported in phase II trials of patients with newly-diagnosed pulmonary TB to determine the necessity for a core outcome set in TB.

**Methods:** Relevant studies were identified by searching MEDLINE, EMBASE, LILACs and reference lists of included studies. All reported outcomes were considered.

**Results:** 49 included phase II studies presented data on 24 historic drug combinations. The most commonly reported outcome (35 studies) was early bactericidal activity (EBA) although there was disagreement regarding a definition. The majority of studies defined EBA as the fall (sometimes mean rate of change) in log<sub>10</sub> colony forming units (CFU) per ml sputum over various time points. Related outcomes such as CFU count were

sometimes reported in preference (12 studies). Other popular outcomes included number of positive (20 studies) or negative cultures (4 studies) at selected time points while in others time to culture negativity was favoured (3 studies). In all cases there was disagreement as to which time points should be chosen with options ranging from two days to eight weeks. Results for novel drug combinations are currently being analysed and will be presented.

**Conclusion:** There is large variation in the outcomes reported across phase II studies in TB. To utilise results of multiple studies, and thus identify the best treatment regimens for TB, a core outcome set needs to be developed. This would enable trial results to be more easily compared and combined, potentially leading to improved treatment strategies for patients with TB.

### 13. Do outcome measures used in neurological clinical research realistically represent the needs and the expectations of patients and their caregivers?

Celani MG, Bassi MC, Bignamini A, Candelaresi P, Carlini M, Cecconi M, Congedo M, Cusi C, Cuzzubbo S, Guerra D, Macone S, Melis, M, Motto C, Nardi K, Oppo V, Papetti R, Piersanti C, Piras V, Serafini A, Sgoifo AL, Susani E, Tremolizzo L, Cantisani TA . Cochrane Neurological Field

**Background:** There is an increasing recognition that Neurological diseases, both chronic and disabling, are effected by multiple domains. It is crucial to select outcome measures and their rating scales to assess the meaningful results of a clinical study. The aim of the study is to address the mismatch between what clinical researchers do and what patients need.

**Methods:** Stroke, dementia and epilepsy, considered in this study, are the greater and most common debilitating neurological diseases. . For each of these diseases all clinical trials published in any language over the last 5 years were reviewed with the aim of identifying and analysing the outcome measures used in the evaluation of any kind of intervention. Patients affected by disability at different levels and their carers were enrolled in the study and agreed to attend facilitated focus groups. Once all the data were collected a qualitative analysis was performed to understand patients' expectations.

**Results:** The measurement of health outcomes is a new and intriguing field. While working on this study we critically reconsidered the construction of the study protocol and approached new perspectives by virtue of the reevaluation of our own work and experience. In the interim of the study we ran into four different orders of problems: the needs of patients and cares are different from the needs of researchers, the quality of the trials do not always match good methodological criteria. Clinical trials require rating scales and/or tools that actually measure the health constructs that they claim to measure, correct reporting and analysis of the measures is also often missing.

**Conclusion:** For a beneficial application of health outcomes, measures used in clinical trials need to fit the study purpose, but at the same time the aim and goal of research needs to be tailored to patients' needs.

### 14. Focus group in Multiple Sclerosis as a tool to increase active patient involvement. A preliminary experience.

Annalisa Sgoifo, A. Bignamini, M. Celani, M. Esposito, L. La Mantia, R. Marazzi, V. Prone, A. Protti, V. Sangalli, E. Agostoni

Unmet needs may influence emotional status, life style and care. Focus group (FG) was organized after an educational MS Open-Day at Niguarda Hospital, to involve pwMS to actively take care of themselves and to disclose patient-centered outcome measures. FG was explained individually and a collectively to attendance. PwMS filled out a registration form to declare their consent to participate. FG was conducted by two psychotherapists. Conversation was recorded, computerized and examined anonymously, using qualitative and quantitative text analysis. 25 registration form were distributed, 12 subscriptions were collected and six pwMS participated (5w;1m). Mean age was 50 (26-81); EDSS mean was 2.6 (1-6.5). 5 patients were affected by relapsing remitting and one by secondary progressive MS. Disease duration ranged from 2 up to 34 years. FG lasted 72 minutes. Delivered questions: A->What did you wish for yourself? B->What do you consider most important to improve MS care? All patients described an emotional reaction (hate, fear, anger). Replies reveal: A->Strong wish to continue with personal life, avoiding disability. B->Importance of: clear information, empathic care, multidisciplinary approach to disease. Preliminary text analysis showed that patients had a fighting reaction, supporting an active coping. They expressed the need to appear normal in the social setting, preserving a referent point (mainly the neurologist) to show and express themselves as fragile and affected people. Data are preliminary for a larger project and limited by small size and selection bias. FG may facilitate the relationship with clinicians and guide research. In our experience, FG appears an intriguing technique to investigate patients needs, involving them in care and research. In conclusion, MS can be accepted and perceived as a part of life. Decentralizing MS, patients clearly revealed better ability to cope with disease, focusing on the present, without delaying their needs.

## 15. Developing meaningful public involvement in a cancer clinical trials unit

Baillie J, Fitzgibbon J, Simon N and Nelson A

**Background:** Public involvement in clinical trials has developed rapidly and is now expected by funders, research ethics committees, researchers and members of the public. Despite benefitting the research, researchers and public members involved, public involvement can be challenging and tokenistic. For several years, a cancer clinical trials unit (CTU) in Wales, in association with a government funded public involvement organisation, has made serious efforts to meaningfully and appropriately include members of the public across all its clinical trials.

**Method:** With input from the aforementioned public involvement organisation, research infrastructure and cancer research institute, the CTU established an involvement group, overseen by a senior staff member. An experienced health research volunteer was appointed as Research Partner Coordinator to oversee and advocate for the public members (Research Partners), also acting as a contact for trial managers.

**Results:** In total, 30 Research Partners have been recruited, with two individuals working on each clinical trial. The Research Partner Coordinator has developed terms of reference and standard operating procedures for recruitment, training and remuneration. Research Partners are offered comprehensive training through the public involvement organisation, and in-house training as required. Research Partners contribute to prioritising trials adopted by the CTU, study and protocol development, participant information sheets, publications, and Trial Management Group and Trial Steering Group meetings. Feedback is sought from Research Partners through questionnaires and optional debrief after each meeting, and periodic discussion sessions with the senior staff member and Research Partner Coordinator. An evaluation of CTU staff and Research Partner experience has been undertaken and will be reported separately.

**Conclusion:** The CTU has sought to increase and improve inclusion of Research Partners across all its studies. Future planned CTU developments, which Research Partners will be involved with, include developing appropriate trial outcomes and ensuring patients' understanding of clinical trials.

## 16. Core outcomes set for studies on primary prevention of preterm birth

Janneke van 't Hooft, George R. Saade, Zarko Alfirevic, Ben Willem J. Mol, Khalid S. Khan. A CROWN and GONet collaborative project

**Objective:** There is a lack in consistency in the choice and definitions of outcomes in research on preterm birth, thus hampering clinically useful conclusions through evidence synthesis. In an international collaboration, Our objective was to develop a consensus around a minimum set of critical outcomes for studies, reviews and guidelines on primary prevention of preterm birth.

**Methods:** We registered our protocol on the Core Outcome Measures in Effectiveness Trials (COMET) database. Between May and November 2014 we approached 162 participants representing different stakeholder groups: patients (n=15), neonatologists (n=31), obstetricians (n=42), midwives, (n=21), and researchers (n=53) from 25 low and high resource countries. They were identified through purposive sampling in relevant networks: patient organisations, Global Obstetrics Network (GONet), midwife networks, the Cochrane collaboration and journal editors from the Core Outcomes in Women's health (CROWN) initiative. Potential relevant outcomes for inclusion in the core outcome set were drawn from systematic reviews, interviews and questionnaires. After establishment of this initial list, we used an online 3-round Delphic survey and a consensus meeting to define the core outcome set.

**Results:** Out of an initial list of 249 items, 29 outcomes have been identified for consensus in the Delphi survey. The results of the survey will be discussed at a consensus meeting in November. We aim to get consensus on a set of 10 to 12 outcomes. The results from initial consensus will be presented at COMET November 2014. Six current trials focussing on the use of pessary for prevention of preterm birth have already expressed their intention to implement this core outcome set.

**Conclusion:** We have developed a core outcome set to facilitate uniform presentation of outcome measures for preterm birth. Dissemination will be facilitated through the CROWN initiative journal editors.

## 17. Development of a core outcome set for colorectal cancer surgical trials

Angus McNair, Robert Whistance, Rhiannon Macefield, Kerry Avery, Jane Blazeby on behalf of the CONSENSUS-CRC working group

**Aim:** To develop an evidence based core outcome set for use in colorectal cancer surgical trials

**Methods:** Systematic literature reviews identified all clinical and patient reported outcomes of colorectal cancer surgery in prospective studies published between 2001-10. Outcomes measured only once were excluded, and similar outcomes were grouped into domains. Delphi consensus methodology was used to gain agreement between patients, surgeons and nurses as to which outcome domains were "core". Stakeholders completed

questionnaires which asked them to rate the importance of domains on a scale of 1 (not essential) to 9 (absolutely essential). Responses were analysed by retaining outcomes rated between 7-9 by over 50% of respondents and 1-3 by less than 15%. Participants were provided feedback, and the process repeated with a second questionnaire. A face-to-face meeting was then conducted to gain consensus on the final core set.

**Results:** Systematic reviews and interviews identified 1686 separate outcomes that were grouped into 116 domains. A total of 99 patients (mean age 65, 57% male) and 97 healthcare professionals (70% male, 49% >10 years' experience) participated in the Delphi process. 51 domains were retained after the first round, 24 after the second and 7 following the consensus meeting. The final core outcome set is 1) the need for, and potential problems with, stomas; 2) cancer recurrence; 3) long term survival; 4) quality of life including: physical function, sexual function, faecal urgency and faecal incontinence; 5) anastomotic leak; 6) post-operative infections; and 7) conversion to open operation (where appropriate).

**Conclusions:** A "core outcome set" for trials in colorectal cancer surgery is now available, the use of which may aid meta-analysis and reduce reporting bias.

## **18. The COMMENT Working Group on Acute Diarrhea. Development of a core outcome set for clinical trials in acute diarrhea**

Jacek Karas, Shai Ashkenazi, Alfredo Guarino, Andrea Lo Vecchio, Raanan Shamir, Yvan Vandenplas, Hania Szajewska on behalf of the Consensus Group on Outcome Measures Made in Paediatric Enteral Nutrition Clinical Trials (COMMENT)

**Background:** Outcome sets are the baseline for what should be measured in clinical research and thus should serve as a guide for what should be collected and reported. The Consensus Group on Outcome Measures Made in Paediatric Enteral Nutrition Clinical Trials (COMMENT), established in 2012, agreed that consensus on a core set of outcomes with agreed upon definitions that should be measured and reported in nutritional trials was needed. To achieve this goal, six working groups (WGs) were set up, including the WG on Acute Diarrhea, whose main goal was to develop a core outcome set for clinical trials in acute diarrhea.

**Methods:** In order to achieve the main goal, four steps were planned. The first identified how outcomes related to acute diarrhea were reported. The second focused on the methodology for determining which outcomes to measure in clinical trials. The third employed a 2-phase questionnaire study using the Delphi technique, first identifying a long list of potential outcomes (Phase 1) and then defining a short list of clinically important outcomes (Phase 2).

**Results:** Three core outcome sets were created. The therapeutic core outcome measures for outpatients include: diarrhea duration; degree of dehydration; need for hospitalization; proportion of patients recovered by 48 hours; adverse effects associated with therapy. The therapeutic core outcome set for inpatients include: diarrhea duration; degree of dehydration; duration of hospitalization; proportion of patients recovered by 48 hours; adverse effects associated with therapy. The prophylactic core outcome set include: prevention of diarrhea; prevention of dehydration; prevention of hospitalization; adverse effects associated with therapy.

**Conclusions:** These outcome sets for outpatients and inpatients for therapy and prevention can be recommended for use in future nutritional trials for gastroenteritis. Their aim and envisioned goal is to decrease study heterogeneity and ease the comparability of studies.

## 19. TACT: what impact does Research Partner involvement have on the working practices of a cancer clinical Trial unit and Academic research CenTre

Hopewell-Kelly N, Baillie J, Fitzgibbon J, Simons N and Nelson A.

**Background:** Since 2005 lay representatives ('Research Partners' – RP) have been involved in the work of a clinical trials unit and academic research centre as members of trial management groups, reviewing documents and chairing and presenting at sub-committees. Where recruitment of RPs was once opportunistic, RPs are now more formally recruited in conjunction with a national public involvement organisation. The impact of RPs at the centre has not been examined in-depth, nor research partners' or staff members' experiences been explored. The TACT study was conducted to investigate the input and impact of RPs to ensure the best possible working partnership between the centre and the public is achieved.

**Method:** Semi-structured interviews were conducted with RPs (n= 10) and staff members (n=8). The data were analysed using a Framework approach.

**Results:** Research partners and members of staff see the RP role as an advocacy role for patients. Although some RPs feel welcomed into the centre and are happy with their level of involvement, others identify more negative points including an apparent a bias in the centre's tendency to use more experienced RPs, the RP role being a funding requirement that is tokenistically implemented and the need for greater monitoring and support within the RP role. Staff members stated that they were unclear about the degree to which RPs should be involved in their work; the processes involved in working alongside RPs were also unclear and although there was a general recognition that greater commitment was required of them in the RP initiative, time pressures and stresses were cited as barriers in achieving this aim.

**Conclusion:** The evaluation demonstrated that the RP role is generally valued and enjoyed by RPs but this is only theoretically reciprocated by members of staff who face challenges and barriers in fully committing to the RP initiative.

## 20. Systematic review of Goal Attainment Scaling as an Outcome Measure in Drug Trials

C.M.W. Gaasterland, MSc; M.C. Jansen-van der Weide, PhD; J.H. van der Lee, MD, PhD.

**Introduction:** Goal Attainment Scaling (GAS) is a technique aimed to measure change induced by treatment. GAS enables patients to set goals and to determine the relative success in achieving these goals on a 5-point scale that is precisely defined beforehand. Since the goals are individually determined, goals may differ in actual content. Its individual and patient oriented approach is one of the appealing aspects of GAS when used as an outcome measure for trials, particularly in orphan diseases. GAS may be more responsive than standardised questionnaires, making it useful in smaller and more heterogeneous samples. In this systematic review, we aim to investigate whether the measurement properties of GAS have been evaluated in drug trials.

**Methods:** We have conducted a sensitive search in Medline, PsycINFO and Embase . Included are papers that either describe a study in which a drug intervention is tested using GAS as an outcome measure, or in which the measurement characteristics of GAS are evaluated, in terms of validity, reliability, responsiveness, and/or feasibility. Selection, data extraction and critical appraisal is performed by 2 independent reviewers.

**Results:** The search yielded a total of 3271 abstracts after removal of duplicates. The final results of this review will become available at the end of 2014.

**Conclusion:** GAS may be a useful personalised approach to outcome measurement in rare conditions. We expect that further validation of the method will be needed.

## 21. Development of a method to involve patients in the determination and appraisal of outcomes in clinical trials

C.M.W. Gaasterland, MSc; M.C. Jansen-van der Weide, PhD; J.H. van der Lee, MD, PhD.

**Introduction:** Involving patients in the early stages of trial design may be relevant from an ethical point of view, since the patients are those who are most likely to benefit from the research. Also, the quality of the research may benefit from the involvement of patients, who may suggest research questions and outcome measures that are relevant to them, as well as procedures that may lead to better recruitment and retainment. In drug trials, for instance, it may be relevant to ask patients what they expect of a new medication and what they hope the effects are. The instruments used to measure these effects are of pivotal importance for the result of the trial and the subsequent decision-making. In rare diseases the choice of outcomes, and the relative value of several outcomes in a possible composite outcome is even more important. However, until now there is no standard method to involve patients in the choice and appraisal of outcomes. Therefore, we want to develop a methodology to involve patients in the decisions about relative weights of outcomes in the trial design stage.

**Methods:** First, we have performed a literature review on patient involvement in research design, and consulted professional patient representatives. Based on these meetings and the literature, we have developed a draft method to involve patients in the determination and weighing of outcome measures. We will elicit feedback from professional stakeholders, e.g. clinical researchers, pharmaceutical companies, regulators, and from a group of patient representatives, which will be used to improve our methods. Subsequently, we will test the methods by applying them in the developmental stage of an actual trial. All contacts with external parties are arranged through the ASTERIX consortium ([www.asterix-fp7.eu](http://www.asterix-fp7.eu)).

**Results:** Results will become available in 2015.

## 22. Making core outcomes more clinically meaningful: 2-for-the-price-of-1 with a distributional approach

Janet Peacock, Odile Sauzet

**Background:** In RCTs with a continuous outcome, it is easier to interpret a difference in proportions at high risk than the difference in means. For example when comparing lung function in two groups, a difference in proportion <10th centile may be more clinically meaningful than the difference in means. However choosing a dichotomised continuous outcome at the outset requires a larger sample than using the raw data and may also distort the true difference since data are discarded on dichotomisation.

**Method:** We have derived a dual-outcome solution where the difference in means and difference in proportion at high risk are equivalent inference-wise (Peacock). The distributional approach treats the proportion below a cut-point as a function of the mean and standard deviation of the distribution, assuming the data are Normal or can be transformed to Normal. The method is robust in situations commonly encountered (Sauzet). We illustrate here with lung function (LF) outcome data.

**Results:** This trial compared LF (FEF<sub>75</sub>) in adolescent children. They had been randomised to one of two types of ventilation at birth. The primary LF outcome differed significantly between the groups (difference in z-scores

0.23; 95% CI: 0.02, 0.45,  $p=0.04$ ). The difference in percentage <10th centile-for-normal was calculated using the distributional approach as: 10.3%; 95% CI: 0.7, 20.0%,  $p=0.04$ .

**Conclusion:** Using the distributional approach an outcome can be presented as both a difference in means and difference in proportions at high risk without penalty due to loss of power or multiple testing since the test of the means is equivalent to the test of the proportion at high risk.

**References:** Peacock 'Dichotomising continuous data while retaining statistical power'. *Statistics in Medicine* 2012. Sauzet 'Estimating dichotomised outcomes in two groups with unequal variances: a distributional approach'. *Statistics in Medicine* 2014.

### 23. Heterogeneity in outcomes meta-analyzed among systematic reviews in renoprotective field: a systematic review

Bénédicte Sautenet, Laetitia Contentin, Adrien Bigot, Bruno Giraudeau

**Background:** The COMET (Core Outcome Measures in Effectiveness Trials) initiative aims at developing sets of outcomes to favor the measure of relevant outcomes, decrease heterogeneity in outcomes among trials, and limit the selective reporting of outcomes. In nephrology, to our knowledge, no guidelines exist regarding outcome measures which should be assessed. Objectives To identify outcomes used in the renoprotective field and to assess the proportion of trials and patients pooled for each studied outcome in previously published systematic reviews (SR) of renoprotective treatments.

**Methods:** We searched SR with meta-analyses of renoprotective treatments in the Cochrane Central Register of Controlled Trials, and Medline through Pubmed. All the outcomes meta-analyzed were listed. For each outcome and for each SR, we assessed both the proportion of trials and patients which could have been meta-analyzed.

**Results:** 66 SR were included. The median number of trial by review was ([Q1, Q3]) 8 [5, 13] and the median number of outcomes meta-analyzed by review was 8 [4, 12]. 622 outcomes were meta analyzed, 222 (35.7%) were renoprotection outcomes (with 36 distinct outcomes), 32 (5.1%) were mortality all cause, 28 (4.5%) were cardiovascular outcomes (with 14 distinct outcomes), 6 (1.0%) were quality of life (with 1 distinct outcome), 38 (6.1%) were remission outcomes, 172 (27.6%) were adverse events and 124 (20.0%) were others types of biological or clinical outcomes. Work is still in progress to assess the proportion of trials and patients which could have been meta-analyzed for the different identified outcomes.

**Conclusion:** This study would be the first step to develop a set of outcomes in the renoprotective field.

### 24. Useability and consistency of harm information in drug product descriptions: a matched comparison of data between the US and Europe

Victoria R Cornelius, Kun Liu, Janet Peacock, Odile Sauzet

**Background:** Regulators require pharmaceutical companies to produce product information documents (Europe:SmPC, US:USPI). These documents contain comprehensive and valuable publicly available information which have the potential to inform harm-benefit decisions which are important to patients, prescribers,

researchers and policy makers. We reviewed the usefulness of the data presented and compared the harm profile of matched brand drug data in Europe and the US. Objectives: To assess the usability and consistency of harms reported in matched SmPC and USPI drug documentation.

**Methods:** Brand drugs included were antidepressants or antiepileptic drugs evaluated in randomised trials of neuropathic pain since 1965 which have been marketed in both the United States and Europe. Data extracted included; number of adverse events (AEs), how AEs were selected for reporting and the dictionary used for coding.

**Results:** Ten drugs with matched documents were reviewed. More USPIs than SmPCs specified the criteria for reporting AEs (9 v 3) but these rules often differed within a document and no two criteria were the same across all documents. More USPIs than SmPCs specified the dictionary used (6 v3) but only one document pair specified the dictionary in both and these were not the same. The number of AE contained in a documents ranged from 56 to 413. On average 95 more AEs were reported in the USPI compared to the SmPC.

**Conclusions:** Pharmaceutical companies are inconsistent in how they report harm outcomes of their drugs between Europe and USA. The development of core outcomes for adverse events and clear reporting criteria would significantly improve the usability of this valuable and publicly available information. Core outcome sets for harms may be more useful by drug than disease.

## 25. TINNET COST Action BM1306: an international standard for outcome measurements in clinical trials of tinnitus

Deborah Hall, Alain Londero, Winifred Schlee,

**Background:** Over 70 million people in Europe experience tinnitus, for 7 million it creates a debilitating condition. In spite of its enormous socioeconomic relevance, research funding is somewhat limited. The European Union has approved funding for a COST Action TINNET (2014-2018) to create a pan-European tinnitus research network. One of the Working Groups will address outcome measurement; building upon the 2006 consensus meeting organised by the Tinnitus Research Initiative (Langguth et al., 2007). This Working Group seeks to embrace inclusivity and brings together clinicians, experts on clinical research methodology, statisticians, and representatives of the health industry. The primary objective is to establish an international standard for outcome measurements in clinical trials of tinnitus.

**Methods:** The first step towards the objective is to seek a consensus about appropriate and relevant outcome domains, using Delphi survey methodology. Details of the study design and collaborative approach will be confirmed at the first Working Group management team on November 14th. On November 13th, we are also holding a COST Action workshop in Amsterdam, "Agreed Standards for Measurement : An International Perspective" with invited talks on the COSMIN and the HOME initiatives, and the World Health Organisation International Classification of Functioning, Disability and Health (ICF) core sets for assessment of hearing loss.

**Conclusion:** Once our methodology is confirmed we will register our work on the COMET database. Furthermore, by working with the COST Action Clinical and Database Working Groups we can achieve standards for outcome measurement both in clinical trials and in clinical routine and support data collection of treatment results in a centralised database.

Reference Langguth, B. Goodey, R. Azevedo, A. et al. (2007) Consensus for tinnitus patient assessment and treatment outcome measurement: Tinnitus Research Initiative meeting, Regensburg, July 2006. Progress in Brain Research, 166: 525-536.

## 26. Achieving consensus over the assessment of clinical signs in eczema trials

Kim S Thomas, Jochen Schmitt, Phyllis I Spuls, Eric Simpson, Masutaka Furue, Stefanie Deckert Magdalene Dohil, Christian Apfelbacher, Joanne Chalmers, Hywel C Williams on behalf of the Harmonizing Outcome Measures for Eczema (HOME) initiative.

**Background:** Eczema (atopic dermatitis, atopic eczema) is a chronic, itchy, skin disease that commonly starts in childhood. Over 500 randomised controlled trials of eczema treatment have been conducted, but a core outcome set is lacking, leading to inefficiency and waste. The Harmonizing Outcome Measures for Eczema (HOME) initiative aims to agree a core set of outcomes for future research, and has previously agreed key outcome domains: clinical signs, patient-reported symptoms, quality of life and long-term control.

**Methods:** Two systematic reviews were conducted as per the HOME methodology: i) review of outcome measures used to capture clinical signs, and ii) review of validation studies of the identified scales. Results of these reviews and other data were presented at a face-to-face consensus meeting. The principle focus of the HOME III meeting, (April 2013, San Diego, USA), was to achieve consensus over the measurement of eczema clinical signs. The meeting included 56 participants (clinicians, patients, researchers and industry representatives) from 10 countries including Asia, Europe, South America, and the US. Consensus methodologies included: presentation of evidence, small and large group discussion, and anonymous key-pad voting with pre-defined consensus criteria.

**Results:** Of the 16 identified scales that assess eczema clinical signs, the Eczema Area and Severity Index (EASI) and the Scoring Atopic Dermatitis index (SCORAD) were identified as valid and reliable. The EASI has adequate validity, responsiveness, internal consistency, and intra-observer reliability. The SCORAD has adequate validity, responsiveness, inter-observer reliability, but unclear intra-observer reliability. HOME III delegates agreed that EASI was the preferred instrument to measure the core outcome of eczema signs in future AE-trials (90% of delegates in favour of EASI).

**Conclusion:** Those involved in designing, reporting and using evidence from clinical trials on eczema are asked to comply with this consensus to enable better evidence-based decision making and improved patient care.

## 27. Development of a Core Domain Set for Non-Specific Low Back Pain: Results from an International Delphi Study

Alessandro Chiarotto, Caroline B. Terwee, Maarten Boers, Raymond W. Ostelo; on behalf of the International Steering Committee for the Core Outcome Set for Low Back Pain

**Background:** Heterogeneous reporting of outcomes in clinical trials on non-specific low back pain (LBP) can be the consequence of selective reporting bias, hinder comparison of findings and statistical pooling. The existence of a core outcome set (COS) to be reported in all clinical trials on a particular health condition can address these issues. In 1998 Deyo et al. proposed a standardized set of outcomes for LBP clinical research, but the time has come to update those recommendations. This study purported to develop a COS for non-specific LBP following methodological guidance from the OMERACT initiative.

**Method:** An international Steering Committee (SC) selected participants for a Delphi study aimed at reaching consensus on core domains. Members of the SC and Delphi participants were researchers, clinicians and patients. The OMERACT Filter 2.0 framework was used to generate a list of potential core domains. This list was presented to Delphi participants to judge the importance of each domain for inclusion in this COS. A-priori

thresholds for consensus were established before each round. Participants' substantial arguments regarding importance, overlap, aggregation or addition of potential core domains were considered.

**Results:** 280 experts were selected and invited to the Delphi; response rates of the three rounds were 52%, 50% and 45%, respectively. Among 41 potential core domains, six were excluded in round 1 and 22 in round 2. The remaining 13 were presented for rating in round 3 where consensus for inclusion in the COS was reached for 'Physical Functioning', 'Pain Intensity' and 'Health-Related Quality of Life'. Ratings across stakeholder groups were consistent for these domains.

**Conclusion:** A core domain set for clinical trials on non-specific LBP was developed and represents the update of the set proposed by Deyo et al. in 1998. Future research should determine the measurement instruments that best cover the included domains.

## 28. Variation in the reporting of outcomes in studies on pregnant women with epilepsy: A systematic review

B.H.Al Wattar, J. Troko, Alexander.M.Pirie, Manny Bagary, Lyn Greenhill, Khalid.S.Khan, Dougall McCorry, Shakila Thangaratinam

**Background:** Pregnant women with epilepsy (WWE) and their offspring are at increased risk of adverse health outcomes. Clinical studies on pregnant WWE vary in the reported outcomes, contributing to significant clinical heterogeneity in meta-analysis. Mapping of the reporting of the outcomes is the first step in the development of core outcomes for reporting in clinical trials. We systematically reviewed the various outcome measures reported in clinical studies on pregnant WWE.

**Methods:** We searched major electronic databases MEDLINE, Embase, CINAHL, AMED and Cochrane Library. Bibliographies of relevant articles were manually searched. We combined the Mesh terms for pregnancy, anti-epileptic drugs and epilepsy using AND or OR. There were no language restrictions. Quality of included studies was assessed using the Newcastle-Ottawa Scale and the CONSORT checklist.

**Results:** We have reviewed 318 full articles, out of which 172 studies met our inclusion criteria. We did not identify any randomised controlled trials. There were 145 prospective cohort studies (84%), 19 retrospective cohorts (11%) and 8 case control studies (4%). The studies were conducted in many countries, with the most studies from the USA (22%), and the UK(17%). Fourteen maternal outcomes were reported with special emphasis on seizure control in pregnancy (54/172, 31%) and the risk of pre-eclampsia(20/172, 11%). Fourteen fetal and neonatal outcomes were reported with large focus on the rate of congenital abnormalities (89/172, 51%) and the subsequent neurodevelopment of the offspring(39/172, 22.6%). We have also captured 9 obstetric related outcomes. Pregnancy outcome, mode of delivery and rate of preterm labour were the most frequently reported.

**Conclusion:** Developing a set of core outcomes that are specific to epilepsy in pregnancy to be minimally reported in future research in this field is important in order to ensure the synthesis of good quality evidence.

## 29. Towards core outcome sets (COS) development: A follow-up survey of outcomes in Cochrane Reviews

Francesca Wuytack, Dr Valerie Smith, Prof Mike Clarke

**Background:** The COMET Initiative aims to link the development of COS for trials with the specification of outcomes for Cochrane Reviews. As part of this work, a survey of outcomes in Cochrane Reviews, published for

the first time in 2007 and 2011, was performed. The results showed that 37% (1996/5363) of outcomes specified in the methods section of 702 reviews were not reported. For 14% (732) of cases, reasons for this non-report were not found in the text of the review. To determine possible changes in outcome reporting over time, a repeat survey, using newly published 2013 Cochrane Reviews, was conducted.

**Aim:** To survey the outcomes used in newly published 2013 Cochrane Reviews as a follow-up survey of outcomes used in 2007 and 2011 reviews. Methods A descriptive survey of outcomes in Cochrane Reviews published for the first time in 2013. Outcomes specified in the methods sections and reported in the results section of the reviews were examined. The use of Summary of Findings (SoF) tables, the number of outcomes included in these and the quality of the evidence was explored.

**Results:** Four hundred and forty reviews were included, specifying a total of 3142 outcomes. Of these outcomes, 32% (1008) were not reported. For 7% (233), no reason was identified in the text of the review for this non-report. Of the 375 reviews with studies included, 57% used a SoF table, an increased use from 31% in the 2011 reviews. Of these, the number of outcomes most commonly included was 5.

**Conclusion:** Outcomes reported in Cochrane Reviews have increased over time, from 61% in 2007 and 65% in 2011, to 68% in 2013. Importantly, reasons provided in the text of the reviews for non-reporting of specified outcomes have increased two-fold. The use of SoFs in Cochrane Reviews is gaining momentum.

### 30. Epilepsy in pregnancy core outcomes (E-CORE): A Delphi survey

B.H.Al Wattar, Alexander.M.Pirie, Manny Bagary, Lyn Greenhill, Khalid.S.Khan, Dougall McCorry, Shakila Thangaratinam

**Background:** Clinical studies on pregnant women with epilepsy(WWE) vary in the reported outcomes, contributing to significant clinical heterogeneity in meta-analysis. Developing a set of core outcomes that are specific to epilepsy in pregnancy to be minimally reported in future research in this field is important in order to ensure the synthesis of good quality evidence that includes the points of interest of both clinicians and patients. We have systematically reviewed the various outcome measures reported in clinical studies on pregnant WWE in order to develop a specific set of core outcomes to epilepsy in pregnancy. Using the Delphi technique we aim to refine the outcome list into a core outcome set agreed by key stakeholders.

**Methods:** A three round Delphi survey of stakeholders will be carried out to reach consensus. Stakeholders involved are clinical experts (Obstetricians, neurologists, neonatologists, epilepsy specialist midwives and nurses), international experts through the Global Obstetric Network (GONet) and patients representatives through the Katherine Twining Network and Public involvement Group. The project aims to finish by end of August 2014.

**Results:** Round one results: we had 42 obstetricians and specialist midwives, 26 neurologist and epilepsy specialist nurses, 15 neonatologists and 5 patient representatives. The majority of participants (>70%) agreed on the inclusion of the following outcomes: Seizure control in pregnancy, maternal mortality in pregnancy, Status epilepticus in pregnancy, Epilepsy Sudden Death in pregnancy, Anti-epileptic agents maternal toxicity and Neonatal neurodevelopment after in utero AED exposure. There was no apparent consensus on which outcomes to be excluded. Complete analysis will be carried out at the end of the third round.

**Conclusion:** Developing a set of core outcomes that are specific to epilepsy in pregnancy to be minimally reported in future research in this field is important in order to ensure the synthesis of good quality evidence.

### 31. Outcomes reporting in randomised clinical trials with diet and lifestyle interventions in pregnancy: a systematic review

Rogozinska E., Yang F., Marlin N., Molyneaux E., Khan K.S., Thangaratinam S. for the i-WIP Collaborative Group

**Background:** High maternal weight at the beginning of gestation or its excessive increase in pregnancy is associated with serious consequences to the mother and the baby. Interventions based on diet and physical activity minimise gestational weight gain with varied effect on a number of clinical outcomes. Although randomised clinical trials are considered the 'gold standard', not much attention has been placed on outcomes selection and quality of their reporting. We systematically evaluated range and frequency of reported outcomes as well as quality of their reporting. Additionally, we explored correlation between the quality of outcome reporting, study design and journals' characteristics.

**Method:** We searched the major (Cochrane Library, MEDLINE, EMBASE) and specialized (CINAHL, PsychInfo) databases from inception to October 2013 with no language restrictions. The quality of outcome reporting was assessed using a 6-point scale following current recommendations. The quality assessment was performed using Cochrane's risk of bias tool and Jadad scoring system. Spearman rank correlation coefficients and regression analysis were used to evaluate the association between quality of outcomes reporting and study quality and various journal characteristics such as impact factor, type and focus.

**Results:** 61 publications meet the inclusion criteria. 10% of them were published in high impact factor journals and around half come from journals specializing in obstetrics and gynaecology. Results of this ongoing project will be available for the COMET conference.

**Conclusion:** Our systematic review will highlight the variation in the quality of outcome reporting in trials on diet and lifestyle in pregnancy. Our work will inform development of a minimum set of core outcome that should be reported in future trials in this area.

### 32. Effects of diet and lifestyle interventions in pregnancy: Development of composite maternal and fetal outcomes for Individual Patient Data (IPD) meta-analysis

Rogozinska E., D'Amico M., Khan K.S., Thangaratinam S. on behalf of the iWIP Collaborative Network

**Background:** Interventions based on diet and lifestyle have the potential to influence adverse maternal and fetal outcomes in addition to gestational weight gain. An Individual Patient Data meta-analysis allows exploring the differential effects of interventions in subgroups not available on aggregated-data level. The individual trials varied in the choice of outcomes used to assess interventions effectiveness and it is not clear which of them is the most informative for mothers care in pregnancy. Composite outcome is a way to overcome problem of low incident rates in clinical trials which is also a hurdle in IPD meta-analysis projects. Our aim was to identify outcomes that are considered to be very important in the reporting of clinical trials by a Delphi survey, and developed composite maternal and fetal outcomes for the iWIP IPD meta-analysis project.

**Methods:** A two-generational Delphi using previously identified list of outcomes was conducted between June and August 2013. The survey was completed by members of the iWIP Collaborative Network gathering experts in the area of weight management in pregnancy. Development of the composite outcomes was guided by criteria of biological plausibility, independence from each other, similar frequency of occurrence and level of importance.

**Results:** The final maternal composite outcome included: pre-eclampsia, pregnancy induced hypertension, gestational diabetes mellitus, elective and emergency caesarean section, preterm delivery and admission to High Dependency Unit. The neonatal composite consists of intrauterine death, small for gestational age, large for gestational age, admission to neonatal intensive care unit, birth trauma and shoulder dystocia.

**Conclusion:** Prospective IPDs and clinical trials should consider inclusion of the identified components in composite outcomes

### 33. UK validation of the Tinnitus Functional Index (TFI) in a large research population

K. Fackrell, D. A. Hall, J. G. Barry and D. J. Hoare

**Background:** Questionnaires are essential for measurement of tinnitus severity and treatment-related change. Yet no standard measure is used across clinical and research settings. Current tinnitus questionnaires are limited to measure either severity or change, but not both. The Tinnitus Functional Index (TFI) was developed as both a diagnostic measure of the functional impact of tinnitus and to be a sensitive measure of treatment-related change. This first study evaluates validity of the TFI as a diagnostic measure of tinnitus severity in a UK research population.

**Methods:** 283 participants completed a series of questionnaires; the TFI, Tinnitus Handicap Inventory (THI), Tinnitus Handicap Questionnaire (THQ), tinnitus loudness VAS, tinnitus annoyance percentage scale, Beck's Depression Inventory (BDI), Beck's Anxiety Inventory (BAI), and the World Health Organisation Quality of Life Bref (WHOQOL). 100 participants completed the TFI at a second visit. Analyses included (1) Exploratory Factor Analysis (EFA) to identify all possible inter-item relationships; (2) Confirmatory factor analysis (CFA) using the current eight subscales proposed for the TFI development and the newly identified EFA structure; (3) Convergent and discriminant validity; and (4) Test-retest reliability and agreement.

**Results:** EFA indicated that two questions loaded onto alternative factors than previously proposed. For CFA, although the TFI structure showed acceptable model fit (RMSEA = 0.65), it was not optimal with some questions showing poor loading. Convergent and discriminant validity of the TFI revealed high correlations with the THI ( $r = 0.82$ ) and THQ ( $r = 0.82$ ), and moderate correlations with a tinnitus loudness VAS ( $r = 0.46$ ), tinnitus annoyance scale ( $r = 0.58$ ), the BDI ( $r = 0.57$ ), BAI ( $r = 0.38$ ) and WHOQOL ( $r = -0.48$ ). Test-retest reliability was extremely high (ICC = 0.86). Test agreement was 93%.

**Conclusion:** Overall, the TFI does appear to reliably measure tinnitus and multiple symptoms domains. However, at this point we cannot confirm the proposed TFI structure.

### 34. Complexity, Context and Considerations for Treatment in CFS/ME: Children's versus Health Professional's Conceptual Model

Roxanne Potgieter, Aarti Patel, Lucy Beasant, Kirstie Haywood, Debbie Johnson, Alison Heawood and Esther Crawley

**Background:** Paediatric CFS/ME is relatively common and disabling. However, little is known about which outcomes are important to children and the clinicians who treat them.

**Methods:** We conducted semi structured interviews with young people with CFS/ME. Paediatric CFS/ME clinicians participated in focus groups or semi-structured interviews. Data was analysed thematically, descriptive accounts produced, and theoretical explanations developed.

**Results:** Thirty young people with CFS/ME were interviewed (15 males, 15 females; mean age 13.2 years (SD 2.3), and 15 clinicians from a range of clinical disciplines and experience in paediatric CFS/ME (2 months to 25 years) of which 10 (67%) were female. Both young people and clinicians identified similar outcomes: symptoms, activity, social participation and emotional wellbeing influenced by management and contextual factors. Disrupted school attendance was the impact described most often by young people. Clinicians said that changing sleep was fundamental for improvement. Clinicians described problems with using school attendance as an outcome measure as it is often reduced during treatment and did not necessarily reflect a child's disability or whether they were coping. Young people described a unidirectional relationship of anxiety, low mood and stress as a consequence of their symptoms and the reduction in usual activities, socialising and ability to keep up with school. Clinicians revealed the circularity of low mood with children becoming more vigilant to symptoms and lower thresholds for activity and participation driving further low mood.

**Discussion:** Analysis supported the development of separate conceptual models of CFS/ME described by young people and clinicians. Both the young person and health professional's perspective is important for understanding the impact of this complex disabling illness. .

### 35. Primary outcomes and power calculations in clinical RCTs in urogynecology – need for improvement?

M. Koch, P. Riss, W. Umek, E. Hanzal

**Background:** Except for studies where composite outcomes are chosen a randomized controlled trial must have a primary outcome parameter. The primary outcome must be unambiguous, reliably assessable and clinically relevant. The estimated difference between the primary outcome in the study and control group(s) is used for the power calculation to determine the number of subjects needed for the trial.

**Method:** We reviewed all RCTs published in 3 urogynecology journals (International Urogynecology Journal - IUJ, Neurourology and Urodynamics - NAU, Female Pelvic Medicine and Reconstructive Surgery - FPMRS) and 3 general gynecology journals (Obstetrics and Gynecology - GREEN, American Journal of Obstetrics and Gynecology – AJOG, and BJOG – an International Journal of Obstetrics and Gynecology) in the field of Urogynecology in the year 2013. The journals were hand searched for clinical randomized controlled trials, and the following variables were noted: type of primary outcome, number of secondary outcomes, power calculation.

**Results:** After excluding secondary analyses a total of 34 randomized controlled trials were identified in the 6 journals in 2013 (IUJ 19, GREEN 6, NAU 5, FPMRS 3, BJOG 1) . In 3/34 articles several outcome variable were called “primary outcome”. In 26/34 studies secondary outcomes were also used, the average number of secondary outcomes was 3.5 per study (range 1-11). The most common primary outcomes chosen by the investigators were results of questionnaires (n=8), and POPQ (pelvic organ prolapse quantification system) statements and bladder diaries (5 each). Correct power calculations were done in 25/34 studies, and in 3 studies power calculation were reported in the methods section without giving the variable on which the power calculation was performed.

**Conclusion:** We conclude that there is room for improvement for authors and journals in regard to identification of primary outcomes and to correct power calculation in RCTs.

### 36. Development of a core outcome set based on Case Report Form (CRF) to assess laboratory biomarkers and clinical parameters in Onco-Hematology area

Mariangela Vanalli, RN, MSN<sup>1</sup>, Francesca Rio, RN<sup>1</sup> <sup>1</sup>Mariangela Vanalli, RN, MSN, is a nurse researcher at Division of Immunohematology and Transfusion Medicine, Hospital Papa Giovanni XXIII, Bergamo and University of Milan Bicocca, Milan, Italy; <sup>1</sup>Francesca Rio, RN, is a nurse researcher at Division of Immunohematology and Transfusion Medicine, Hospital Papa Giovanni XXIII, Bergamo, Italy.

**Background:** The number of cases, the crude and age-standardized incidence, mortality rates and the prevalence proportions estimated by the Italian Association of Cancer Registries presently providing the epidemiological indicators for the major cancers used in ICD-O-3.1. Aim of this study is to examine the relationships among the incidence of genera-cancer-associated risk factors and routine laboratory in cancer patients through CRF.

**Methods:** The CRF database has been developed by a dedicated working group using Delphi process. It contain anonymous records on patient characteristics and one set of biomarker laboratory data identified in several variables.

**Results:** Between 2012 and 2014, 1373 cancer patients were enrolled at three Italian Oncological Institutions after informed consent. Among these patients, 36% were men and 64% were women (mean age 71±45 years) and breast was the most frequent type cancer (43%) followed by lung (29%), colon-rectum (18%) and stomach (9%). 72% (n=85) of the lung, 67% (n=24) of the stomach, 33% (n=25) of the colon-rectum, 4% (n=7) of the breast cancer patients had comorbidities weighted with 3 point and above (Age Unadjusted Charlson-Comorbidity-Index=4; HR=6.38; 99% CI [3.07,13.24]). Multivariate analysis determined that comorbidity was highly associated with cancer type, stage and ECOG PS (p=0.01). Evaluation between cardiovascular disease, risk of bleeding, deep-vein thrombosis and colon-rectum cancer stage (p=0.01), breast (p=0.03), lung (p=0.01) compared into comorbidities. The other tested variables Hgb level, neutrophil and platelet counthad the strongest relationship with breast and lung cancer stage (p=0.02), stomach (p=0.002) and colon-rectum (p=0.1).

**Conclusion:** The current study confirmed that cancer staging, comorbidity and poor performance status were a significant predictive factor. The appropriateness of results could be useful to better describe the role of CRF and biomarkers recorded in patient charts as well as the other variables could allow nurses to identify patients at risk for shorter survival time following hospitalization.

### 37. Completeness of outcome description in studies for low back pain rehabilitation interventions: a survey of trials included in Cochrane reviews

Greta Castellini, Silvia Gianola, Pamela Frigerio, Michela Agostini, Rosa Bolotta, Davide Corbetta, Monica Gasparini, Paolo Gozzer, Erica Guariento, Linda Li, Valentina Pecoraro, Valeria Sirtori, Andrea Turolla, Valsecchi MariaGrazia, Lorenzo Moja

**Background:** Selection of appropriate outcome measures is crucial in clinical trials in order to minimize bias and allow for precise comparisons of effects between interventions.

**Objective:** We aimed to assess the frequency and completeness of outcome measures in randomized controlled trials (RCTs) included in Cochrane systematic reviews (SRs), focusing on evaluations of the efficacy and safety of rehabilitation interventions for mechanical LBP.

**Methods:** We performed a cross-sectional study of all RCTs included in all Cochrane SRs (full-text) published on The Cochrane Database of Systematic Reviews in February 2013. Two authors independently evaluated the type and frequency of each outcome measure reported in the full-text of RCTs, the methods used to measure outcomes, and the proportion of outcomes fully replicable based on the reported information.

**Results:** Our literature search identified 11 Cochrane SRs, including 185 RCTs. Across all RCTs, thirty-six different outcomes were investigated. The outcomes most commonly reported were pain (165/185; 89,2%, 95% Confidence Interval (CI) 84.7% – 93.7 %), disability (118/185; 63,8%, 95% CI 56.9% – 70.7 %), range of motion (72/185; 38.9%95% CI 31.9% – 45.9%), and quality of life (45/185; 24,3%, 95% CI 18.1% – 30.5%) measured respectively by 70, 43, 41, 19 different measurement instruments. The procedure of blinding assessment was reported in 49.7% of the RCTs for pain (n= 82 RCTs) and 45% of RCTs for disability (n=53 RCTs). Pain, disability, range of motion, and quality of life outcomes were reported as fully replicable in 10.3% (n= 17 RCTs), 10.1% (n= 12 RCTs), 5.5% (n= 4 RCTs), and 6.6% (n= 3 RCTs) of the RCTs, respectively.

**Conclusions:** A large number of outcome measures and a myriad of measurement instruments were used across all RCTs. The reporting was largely incomplete, suggesting better opportunities for the standardization of approaches and reporting.

### 38. Development of core outcome set for pediatric health conditions: A systematic review

Mufiza Kapadia, Winnie Chan, Thivia Jegathesan, Martin Offringa

**Background:** Standardized selection of outcomes has been advocated to allow comparison and syntheses of clinical trials' results in systematic reviews and to avoid outcome selection bias. As health outcomes in children are different from adults, the methodology behind selecting and measuring outcomes should be acceptable, responsive and valid to pediatric research. Our aim was to determine what methods are used for “developing” and “validating” core outcome sets (COS) in pediatric studies, and to determine what domains (common as well as specific) are identified within the studies.

**Methods:** We searched Medline, EMBASE and PsychInfo for relevant articles in English language from their inception to June 2014. Titles and abstracts were screened for inclusion by two reviewers. The reference list of the included article was screened for further studies.

**Results:** The literature search identified 7,100 non-duplicate abstracts. 72 eligible full text articles were retrieved and 29 studies were included in this systematic review. Eleven studies focused on pediatric rheumatic diseases. The common domains identified were disease activity, disease damage and health related quality of life. Growth and development as a domain was recommended for chronic conditions. Other less common domains included health resource utilisation, adverse effects, functional status, neurodevelopment and mortality. Only 38% of the studies employed a formal consensus technique such as a Delphi survey, Nominal group technique or a questionnaire survey to develop a COS. Involvement of parents or patient representative in the consensus process was minimal (10%). 6/29 studies undertook validation of the proposed COS.

**Conclusion:** Published experience showcasing the methodology of development and validation of COS in pediatric clinical research is limited. Methods used for outcome selection vary widely. Most reports are in pediatric rheumatic conditions. Development of standardised methodology for outcome selection and validation is recommended.

**39. A comprehensive survey of hearing questionnaires: How many are there, what do they measure, and how have they been validated?**

Michael.A Akeroyd, Kay Wright-Whyte, Jack Holman, William M Whitmer

The self-report questionnaire is a popular tool for measuring outcomes in trials of interventions for hearing impairment. Many have been designed over the last fifty years, and there is no single standard questionnaire that is widely accepted and used. We felt it would be a valuable resource to have a comprehensive collection of all adult hearing-loss questionnaires (excluding those wholly devoted to tinnitus, children, or cochlear implants) and to survey their degree of validation. We collated copies of every published hearing difficulty questionnaire that we could find. The search was primarily done by iterative reference searching. Questionnaire topics were obtained by mapping the text of each questionnaire onto a set of categories; reports of validation methods were taken from the primary paper(s) on each questionnaire. In total we found 139 hearing-specific questionnaires (though many others were found that were primarily about something else). Though not formally systematic, we believe that we have included every questionnaire that is important, most of those of some notice, and a fair fraction of those obscure. We classified 111 as “primary” and the remaining 28 as “contractions”, being shortened versions of a primary without any new questions. In total, there were 3618 items across all the primary questionnaires. The median number of items per questionnaire was 20; the maximum was 158. Across all items, about one third were concerned with the person’s own hearing, another third with the repercussions of it, and about a quarter with hearing aids. There was a wide range in validation methods, from only using items chosen statistically from wider pools and with formal validation against independent measures of clinical outcomes, to just reporting a correlation with an audiogram measure of hearing loss. The “state of play” of the field of hearing questionnaires will be discussed.

**40. Measuring patient outcome using data capture by mobile app.**

Carol Fawkes, Dr Robert Froud, Dr Dawn Carnes

The use of Patient Reported Outcome Measures (PROMs) to measure effectiveness of care, and supporting patient management is being advocated increasingly in clinical and research settings. Current patient data capture involves completion of paper questionnaires which is costly and environmentally challenging. New innovations are required to balance the challenges of introducing data capture directly from patients while considering budgets, access to Information Technology, and the capability to use technological devices. The development of content for a mobile and web app for capturing PROM data has been informed by two qualitative studies, and a systematic review. The qualitative studies involved interviews and focus groups with patients and clinicians (osteopaths) concerning their views on using PROMs in clinical practice, and a selection of specific PROMs. The systematic review compared the measurement properties of three PROMs (the Roland Morris Disability Questionnaire, the Oswestry Disability Index, and the Bournemouth Questionnaire). Patients (N=18) have been enthusiastic about using PROMs in practice welcoming the opportunity to provide feedback, and undaunted by use of technology. It was shown to be important to include PROMs with numerical scales, and text descriptions of symptoms. Clinicians (N=30) also recognised the value of PROMs and the importance of outcome data being collected independently of their clinics. However, there were some concerns. Patients wanted clarity concerning the use of data, and to whom it would be accessible. In addition patients were concerned about the potential disruption to the consultation process. Clinicians were concerned about fitting the collection of PROM data into the consultation process, and how this could affect the relationship with patients. The findings of these three studies have informed the development of a mobile and web app. Both apps are currently being piloted in private and training clinics for osteopaths.

#### 41. PARTNERS2: A protocol for the development of a core outcome set for use in mental health trials involving people with schizophrenia or bipolar in a community setting

Thomas Keeley\*, Humera Khan, Jonathan Mathers, Ruth Sayers, Paula Williamson, Elizabeth England, Vanessa Pinfold, Andrea Roalfe, Linda Davies, Linda Gask, Michael Clark, Peter Jones, Peter Huxley, Peter Lewis, Richard Byng, Simon Love, Siobhan Reilly, Max Birchwood, Melanie Calvert\*. \*denote corresponding authors

**Background:** Randomised controlled trials can provide robust evidence to inform clinical care of mental health service users. A core outcome set (COS) for use in research into schizophrenia and bipolar has the potential to reduce reporting bias and increase the ability of reviewers to synthesise results of randomised controlled trials. There is no core outcome set currently available for use in this research area.

**Aim:** The aim of this study is to develop a COS for use in research into schizophrenia and bipolar disorder in a community setting.

**Methods:** A group of participants representing the key stakeholder groups, including service users, carers, health and social care professionals and commissioners, will be recruited from the United Kingdom. Focus groups and one-to-one interviews, led by academic and service user researchers, will seek to identify clinical, social, psychological and physical outcomes that are important to key stakeholders. An iterative, constant comparative and thematic analysis will identify key outcomes and will be supplemented by outcomes identified through a review of literature. An online, three round, Delphi study with key stakeholders will reduce the range of potential outcomes to a smaller core set. On completion of the Delphi Study a face-to-face consensus meeting will be held to ratify the final outcomes. A systematic or rapid literature review will assess the properties of existing measures used in research with bipolar and schizophrenia populations. Measures identified will be matched with the outcomes from the Delphi study for consideration and confirmation at a later stakeholder meeting.

**Discussion:** A COS represents the minimum measurement requirement for trials within a research area. It is anticipated that this work will increase the use of stakeholder relevant outcomes and improve our ability interpret and compare the results of studies involving people with schizophrenia and bipolar living in a community setting.

*This abstract is dedicated to the memory of Helen Lester, Professor of Mental Health at the University of Birmingham UK who led the PARTNERS-2 programme grant development and is sadly missed by colleagues. Funded by an NIHR Programme Grant (RP-PG-0611-20004)*

#### 42. The concept of physical limitations in knee osteoarthritis – the view of patients and health professionals

Louise Klokke PT MSc, Richard H Osborne PhD, Eva Ejlersen Waehrens OT PhD, Ole Norgaard MSc, Elisabeth Bandak PT MSc, Henning Bliddal MD, DMSc, and Marius Henriksen PT PhD

**Background:** Recommendations of core outcomes in clinical trials on knee osteoarthritis (OA) include ‘physical function’ but no definition is provided. The objective of this study was to comprehensively identify components of the ‘physical limitation’ concept in knee OA, and to rate the clinical importance of these by using the perspective of both patients and health professionals.

**Method:** Concept Mapping, a structured group process, was used to identify and organize components of the ‘physical limitation’ concept. Statements were generated through workshops with patients and through e-mail and an international web-based survey with health professionals. Ideas were elicited through a nominal group

technique and organized using multidimensional scaling, hierarchical cluster analysis, participant validation, rating of clinical importance, and thematic analyses, to generate a conceptual model of physical limitations in knee OA.

**Results:** Fifteen Danish patients and 200 international professionals contributed, producing 1739 statements. Omitting redundancies, 361 individual statements were thematically grouped by participants. Five clusters emerged: 'Limitations/physical deficits'; 'Everyday hurdles'; 'You're not the person you used to be'; 'Need to adjust way of living' and 'External limitations', each with sub-clusters. Twelve sub-clusters were rated significantly more important by patients, and one was rated higher by professionals.

**Conclusion:** Patients and professionals agreed largely on the physical limitation concept in knee OA. Some limitations of high importance to patients were underestimated by the professionals, highlighting the importance of patient involvement. These data offer new knowledge to guide selection of clinically relevant outcomes and development of outcome measures in knee OA.

#### **43. The Development of a Measure of Participation in Adults with Hearing Loss: A Qualitative Study of Professional and Patient Views**

Eithne Heffernan, Neil Coulson, Helen Henshaw, Melanie Ferguson

**Background:** The International Classification for Functioning, Disability and Health (ICF) proposes that the primary healthcare outcomes are body functions/structure, activity and participation. Recently, ICF core sets for hearing loss (HL) have been developed. This is of the utmost importance, as HL is not simply a physical condition; it also substantially affects communication, which in turn affects participation. However, it has been argued that the measurement of participation has been impaired by inadequate conceptualisation. A second impediment is the highly personal nature of participation, which is difficult to capture in a standardised tool. The aim of this research is to address these issues whilst developing a new measure of participation in adults with HL. The first stage of this research is the consultation of HL experts in order to better understand participation and to provide a foundation for its measurement.

**Method:** Semi-structured interviews were conducted with nine hearing healthcare professionals and 25 adults with HL. Maximum variation sampling was used to recruit adults with HL who varied in terms of age, gender, hearing loss duration and hearing aid use, as well as various hearing healthcare professionals, including audiologists, hearing therapists and international opinion leaders. The data were analysed using an established thematic analysis technique. A sample of interview transcripts were independently analysed by a second researcher.

**Results & Conclusion:** Preliminary results show that adults with HL experience participation restrictions in work, education, social life, community life and personal relationships. One of the reasons why they become socially withdrawn is due to diminished confidence, suggesting that a measure of participation centred on self-belief could be of value. The results also show the complexities of participation in adults with HL, as they may be unaware of their own isolation and they may find their attempts to participate blocked by those with normal hearing.

#### **44. Interventions for caries in primary teeth; mapping reported outcomes in clinical trials over the last 30 years**

Nicola Innes, Felicity Borrie, Neeraj Gugnagni, Alex Keightley, Thomas Lamont, Zoe Marshman, Ruth Santamaria, Falk Schwendicke

**Background:** Dental caries (decay) is the most prevalent disease in school age children and carries a burden of pain and infection. Clinical trials investigating interventions (fillings and other caries management techniques) to alleviate these have no agreed core outcome set. This makes research design difficult and complicating evidence synthesis. The first step in addressing these issues is to map the current status. Research question: what outcomes have been measured in clinical trials investigating management of carious primary teeth over the past 30 years?

**Objectives:** • Identify and categorise outcomes/ outcome measures of all published randomised and controlled clinical trials investigating primary tooth restoration, including pulp therapy; • Assess quality of reporting; and • Look for trends/gaps/ patient reported/ patient oriented outcomes.

**Methods:** Inclusion: • Population: Individuals 6 months- 14 years (Human studies) • Interventions: Management techniques for carious primary teeth/ pulp therapy (tooth, patient, clinician, practice levels). • Comparisons/Control: No intervention/different interventions/Self • Outcome: all outcomes • Study design: randomised and controlled clinical trials Search strategy: Cochrane Oral Health Group's Trial register/ Cochrane Central Register of Controlled Trials (CENTRAL): ((((((Dental Restoration, Permanent[Mesh] OR Dental Restoration, Temporary[Mesh]) OR Dental Cements[Mesh]) OR Pulp Capping and Pulpectomy Agents[Mesh]) OR Resins, Synthetic[Mesh]) OR Dental Pulp Capping[Mesh]) OR Pulpectomy[Mesh]) OR Pulpotomy[Mesh] AND (Clinical Trial[ptyp] AND (1983/11/01[PDAT] : 2013/11/01[PDAT])) AND humans[MeSHTerms] AND (infant[MeSHTerms] OR child[MeSHTerms] OR adolescent[MeSHTerms])) Data extraction: titles/abstracts reviewed independently and in duplicate; obtain manuscripts for those meeting inclusion criteria, or where this is unclear; piloted proforma for data extraction, independently and in duplicate (3rd person to resolve disagreement). Data analysis: Outcomes/ outcome measures listing; Independent categorisation by 3 researchers; consensus; Reporting quality according to Cochrane methodology; Outcome/ outcome measure categories mapping against intervention type, year of publication, country of publication and author group; Discussion to interpret the findings, agree trends and look for gaps.

#### 45. Outcome measures in Cochrane reviews and protocols for the prevention and treatment of periodontal disease

Thomas Lamont, Jan Clarkson, Craig Ramsay

**Background:** Periodontal disease (gum disease) is the most common oral disease to affect adults. The importance of core outcome sets for effectiveness trials is well established. However, there is currently great debate in the field as to the most appropriate clinical outcomes to investigate. The recently published Scottish Dental Clinical Effectiveness Programme Guidelines "Prevention and Treatment of Periodontal Diseases in Primary Care" highlighted the need for a set of core outcome measures for periodontal outcomes. This study was conducted to assess the variability of outcome measures reported in periodontal Cochrane reviews and protocols prior to the development of a set of core outcomes involving patients and key stakeholders.

**Method:** Published Cochrane reviews and protocols (search up to August 2014) investigating the prevention and treatment of periodontal disease were assessed. The type of intervention, outcome measures (clinical, patient and economic) and duration of follow up was recorded. From included trials all indices reported were also noted.

**Results:** This study included 8 Cochrane reviews, involving 141 trials with 23,108 patients and 3 protocols. Descriptions of outcomes were varied but, following deduplication 27 unique outcomes were identified, as either primary or secondary, in the Cochrane reviews/protocols. In the published reviews 15 of these 27 outcomes had data available and in the included trials an additional 6 reported outcomes were found. Gingivitis and plaque (surrogate outcomes) were the most commonly reported outcomes and were each measured by 17 different indices in 110 and 117 trials respectively.

**Conclusion:** This study demonstrates the variety of outcome measures available for periodontal studies and highlights the number of indices used to record them. There is ongoing debate as to which outcomes should be investigated; reinforcing the need of a core set of outcomes for periodontal studies whilst also highlighting the need for agreed measurement instruments.

#### **46. The CONSENSUS Study: Preliminary results of a mixed methods study to develop a core outcome set for late phase clinical trials in Oropharyngeal Cancer**

Aoife M I Waters, Catrin Tudur Smith, Bridget Young, Terry M Jones

**Introduction:** Contemporary treatments for Oropharyngeal cancer (OPSCC) are associated with a number of debilitating side-effects. Whilst these have a significant impact on the patient's quality of life, they are often not measured in clinical trials. Additionally there is no standardisation of outcome selection and reporting, even amongst trials of comparable interventions. This reduces the volume of data available for meta-analyses leading to difficulties in both interpreting treatment effect and in making evidence based healthcare decisions. The development of a Core Outcome Set (COS) is proposed to address these problems.

**Methods:** 1. Systematic review to establish which outcomes are measured in OPSCC trials 2. Qualitative interviews with patients and carers to identify which outcomes they prioritise 3. Delphi study to refine long list of outcomes from review and interviews +/- consensus meeting of key stakeholders to ratify which outcomes should be included in the final COS

**Results:** Systematic Review Electronic searches of Pubmed, EMBASE and CENTRAL identified 42 eligible studies. There are significant disparities in the number and type of outcomes measured between trials with a significant focus on outcomes related to survival and disease control. Interviews We recruited 34 patients and carers across 3 centres; two in the UK (NHS Trusts in Liverpool and Sunderland) and one in the US (MD Anderson Cancer Center, Houston, TX). Patients and carers agree that survival outcomes are a priority and must be measured in clinical trials, however functional and health-related quality of life outcomes are also important and should be measured to help patients and clinicians differentiate between treatments. The short and long-term functional and psychological impact of such radical treatments must be considered when making treatment decisions. We will present the findings of the systematic review and interviews and discuss the Delphi Consensus Study development process and results.

#### **47. Encephalitis in children-Which outcomes are Important?**

Jennifer Lemon, Jessie Cooper, Harsha Hanumanthiah, Sylviane Defres , Ruth Backman, Paula Williamson, Tom Solomon \*, Rachel Kneen\* (joint last authors)

**Background:** Encephalitis, inflammation of the brain tissue, is a rare but serious neurological disorder with different causes. Survivors frequently experience sequelae including seizures, limb weakness, communication difficulties, behavioural and neuropsychological problems. There is no published review of previously measured outcomes and no studies have investigated which outcomes are most important to affected children and their families. This pilot study aims to explore these knowledge gaps.

**Methods:** Systematic review: Cochrane CENTRAL, MEDLINE, Embase and trials registries were searched to identify clinical trials, involving acute treatment interventions for encephalitis. Participants were any age, with any acute encephalitis aetiology. Outcome measures data are currently being extracted and classified using the 'International Classification of Functioning, Disability and Health, Children and Youth version'. Qualitative interviews: Semi-structured interviews were undertaken with carers of children previously diagnosed with encephalitis. Interviews focused on impact, future concerns, expectations and important outcomes for the child and family. Thematic analysis is underway.

**Results:** Systematic review: 36 of 6475 studies screened are included to date (636 duplicates, 5772 excluded, 31 awaiting final classification). Outcomes measured varied considerably between studies. The Liverpool Outcome Score (<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2908971/>) was the only validated encephalitis-specific composite outcome measure. 21/36 (58%) assessed outcome after discharge. Most studies included measures of function/independence, however only 2/36 (5%) assessed Quality of life and none formally assessed school performance, participation or neuropsychological sequelae. Qualitative interviews: 12 interviews were undertaken with 15 carers. Children were median of 2 years 3 months post encephalitis and were heterogeneous regarding age, encephalitis aetiology and sequelae. Eight transcripts have been coded to date. Recurring important outcomes included survival, independence, participation, cognition and communication, school performance and quality of life. Carer views evolved over time.

**Conclusion:** Preliminary data suggests a mismatch between outcomes previously measured and carer views, supporting the need for a paediatric encephalitis 'Core Outcome Set'.

#### **48. Towards the development of a core set of outcomes in pediatric appendicitis: A protocol of a systematic review of randomised trials**

NJ Hall, MZ Kapadia (Presenting author), S Eaton, W Chan, A Pierro, M Offringa

**Background:** Acute appendicitis is the commonest surgical emergency in children. However, there is no consensus on the outcomes that should be measured in all the randomised control trials (RCTs) in children with appendicitis. A core outcome set (COS) represents the minimum that should be measured in a clinical trial for a particular health condition. We strive to develop such a COS and first aimed to identify outcomes in existing RCTs.

**Methods/Design:** A search of MEDLINE, EMBASE and Cochrane Register databases were performed from their inception till April 2014. Included studies were RCTs published in English and investigated the effect of one or more interventions in children aged = 18 years with appendicitis. The titles and abstracts were screened by two reviewers and discrepancies were resolved by discussion. In the next step of this systematic review, the full text of the included studies will be reviewed and data will be extracted by two reviewers. Primary (if defined) and all other outcomes will be noted. To visualise the variety of outcomes used, adjacency matrix will be developed listing the outcome domains reported in each trial in rows and the trials listed in columns. The outcome reported

by >30% of the trials will then be assigned to the domains 'disease', 'pathophysiological manifestations', 'life impact' and 'resource use', using the OMERACT filter 2.0. Other domains not fitting in the OMERACT filter will be identified.

**Discussion:** We expect to complete the full text review by September 2014. The consensus on the COS will then be achieved by undertaking a two-stage Delhi survey with clinicians, patients (12-18 years) and patient representatives of children <12 years. The COS developed can be used in future trials of the management of appendicitis in children, improving the consistency of research in this clinical area and minimising the outcome reporting bias.

#### **49. How could clinical researchers', patients' and investigators' preferences influence study hypotheses and reported outcome results of clinical randomized controlled trials? A critical appraisal from a reader's perspective**

Paola Rosati\*, Roberto D'Amico, Valerio Balassone, Gabriella Ricciotti, Rita Inglese, Ferruccio Giustini, Giuseppina Testa, Ersilia Fiscarelli, Cecilia Carlino, Marco Zazza, Roberto Fiorito, Franz Porzsolt.

**Background:** An emerging problem that has rarely been investigated concerns the human preferences that undermine clinical randomised controlled trials (RCTs). Ample evidence shows that human preferences exert a major influence at various stages in RCTs. When patients or doctors have a strong preference for one of the two options participation rates will decrease. Conversely, only doctors and patients who find the two options acceptable -- namely equipoise -- will accept randomization.

**Aim and methods:** To analyse researchers', patients' and investigators' preferences in designing and conducting RCTs we did a preliminary scoping study analysing a sample of 40 published RCTs from two influential medical and surgical journals (Pediatrics and Annals of Surgery). All co-authors from each specialty gathered and assessed 20 RCTs going backwards from the November 2013 issue. The RCTs chosen had to compare an active intervention with another active intervention or placebo or no treatment. From each RCT all co-authors mapped and coded different variables using published data and categorised the main outcome; statistical method stated (one side or two sided); reported difficulties in conducting RCTs (including recruitment, drop-outs); which kind of statement the results reported and reader's assumption on the researchers' possible preferences (strong, weak or none) related to funding reasons. To evaluate how researchers', patients' and investigators' preferences influenced the calculation and interpretation of the conclusive statements and consistency of the reported results, each categorised variable in published RCT was then compared with the same data from the registered clinical trials (from [www.clinicaltrial.gov](http://www.clinicaltrial.gov)) to find more detailed unpublished results, and a possible change in primary outcome undermining internal validity and transparency.

**Results and conclusion:** In our poster we will synthesise the results of the coded categorised variables and show the comparative results from the published RCTs and variables recorded from the corresponding registered clinical trials.

#### **50. Heterogeneity of wound bed outcome measures in RCTs of VLU a systematic review**

Georgina Gethin; Fiona Killeen; Declan Devane

**Background:** Venous leg ulcers (VLU) affect up to 2% of the population. The outcomes of RCTs in VLU are important to guide treatment choices and for allocation of resources. The use of inappropriate or poorly defined

or validated outcomes can lead to misleading information that overestimate or underestimate the potential benefits of an intervention.

**Aims:** to identify the endpoints and wound bed outcomes that were assessed in RCTs of interventions in VLU; how these outcomes were assessed and what reference was made to the validity and reliability of such methods.

**Methods:** a systematic review of all full text, published, RCTs from 1998-2013 and in English language.

**Results:** 102 studies met our criteria. 78 different endpoints were recorded. The majority (n=34) of endpoints related to healing and were evaluated at 12 different time points. 62% of studies did not define healing. Of those who did, seven different definitions were provided the most frequent being 'full or complete epithelization'. Size was recorded in 99% of studies but 18% did not describe the method used; photographs were used by 40% and of these 70% did not provide details of the protocol; tissue type was assessed in 38% of trials and of these 26% did not describe the method used; exudate was assessed in 27%, oedema in 14%, odour 8% and pain 34% with 31-54% not reporting the methods used in assessment. Only five studies made specific reference to validity or reliability of methods used to assess wounds.

**Conclusions:** Identification of future research needs VLU call for standards for measuring outcomes with acceptable inter rater reliability and validated measures of patient-reported outcomes. The lack of agreed definitions of healing and core outcome measures must be addressed if we are to provide robust evaluations of wound management.

## 51. A Study within a Study: Exploring the Methodology of the Delphi Technique

Bronagh Blackwood, Suzanne Ringrow, Danny McAuley, Mike Clarke

**Background:** The Delphi technique using sequential rounds of questionnaires is a widely used consensus-gathering technique [1]. Feedback and statistical group response takes place between the rounds, when results from the previous round are analysed and communicated back to the participants. We plan to use the Delphi technique in our study to develop a core outcome set (COS) for trials of interventions which aim to modify the duration of mechanical ventilation in critically ill patients. Our panel will comprise various stakeholders including critical care trial groups, bedside clinicians, industry, funders and patient representative groups. The diversity of the panel provides an opportunity for us to explore (a) if the COS is influenced by the method of feedback provided in the Delphi; and (b) if participants rank the importance of outcomes differently depending on their knowledge of the other groups' ranking.

**Methods:** We will use a nested randomised controlled trial within a three round Delphi study. In Round 1, participants will be asked to rank the importance of a list of outcomes identified from our review of ventilation trials [2] and to add additional outcomes if necessary. Prior to Round 2, participants will be randomised into one of three groups. Group 1 will receive collated responses without identifying the stakeholder group; Group 2 will only receive responses from the stakeholder group to which they belong; and Group 3 will receive the breakdown of responses from each stakeholder group. After Round 3, we will explore any variance in COS between groups and we will bring all three COS to a consensus meeting for discussion and final agreement.

**Conclusion:** This study will provide valuable information that will (a) inform Delphi methodology by showing the impact of different feedback mechanisms; and (b) provide a much needed COS for critical care trials involving mechanically ventilated patients.

1. Dalkey N, Helmer O. An experimental application of the Delphi method to the use of experts. *Management Science* 1963; 9: pp458-467.
2. Blackwood B, Clarke M, McAuley DF, et al. How Outcomes are defined in Clinical Trials of Mechanically Ventilated Adults and Children. *American Journal of Respiratory and Critical Care Medicine*. 2014; 189(8): pp886-893

## **52. Consensus on the Need for a Hierarchical List of Patient-Reported Pain Outcomes for Meta-Analyses of Knee Osteoarthritis Trials**

Robin Christensen, Lara J. Maxwell, Peter Juni, David Tovey, Paula R. Williamson, Maarten Boers, Niti Goel, Rachelle Buchbinder, Lyn March, Caroline B. Terwee, Jasvinder A. Singh, And Peter Tugwell

The selection of appropriate outcomes is crucial when designing, and subsequently interpreting clinical trials, in order to directly compare the effects of different interventions in ways that minimize bias. The same is likely to apply for systematic reviews and meta-analyses. Although protocol registration for systematic reviews is still not mandatory, reviewers should be strongly encouraged to register the protocol, in order to identify - a priori - the proposed methodological approach, including all outcomes of interest. This will help to minimize the likelihood of biased post hoc decisions in review methods, such as selective outcome reporting. A group of international experts convened to address issues regarding the need to develop hierarchical lists of outcome measurement instruments for a particular outcome for meta-analyses. Meta-analysis of knee osteoarthritis (OA) trials, and the assessment of pain as an outcome, was used as an exemplar to assess how 'Outcome Measures in Rheumatology' (OMERACT) and other international initiatives might contribute in this area. The meeting began with formal presentations of background topics, empirical evidence from the literature, and a brief introduction to two existing hierarchical lists of pain outcome measures recommended for meta-analyses of knee OA trials. After discussions most participants agreed that there is a need to develop a methodology for generation of hierarchical lists of outcome instruments for use to guide meta-analyses. Tools that could be used to steer development of such a prioritized list are the COSMIN checklist and the OMERACT filter 2.0. For future research we suggest that among outcome measures frequently reported in trials for the same domain, those with the best measurement properties (e.g., validity and reliability) would achieve high, if not the highest rankings for use on a hierarchical list.

## COMET Management Group

**Doug Altman**



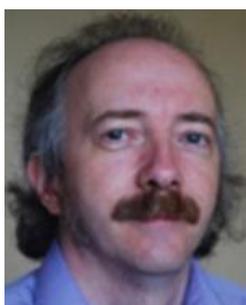
Doug Altman has been director of the Centre for Statistics in Medicine in Oxford since its inception in 1995. He has published over 400 peer reviewed articles, many aimed at clarifying statistical ideas for medical researchers. He is author of Practical Statistics for Medical Research. His varied research interests include the use and abuse of statistics in medical research, studies of prognosis, regression modelling, systematic reviews and meta-analysis, randomised trials, and studies of medical measurement. Doug is senior statistical editor at the BMJ and co-editor-in-chief of Trials. He is actively involved in developing guidelines for reporting research, including CONSORT, STROBE, and PRISMA, and in 2006 founded the EQUATOR Network which seeks to improve the quality of scientific publications by promoting transparent and accurate reporting of health research.

**Jane Blazeby**



Jane Blazeby is Professor of Surgery at the University of Bristol and an Honorary Consultant Surgeon at University Hospitals Bristol NHS Foundation Trust. She is Director of the MRC ConDuCT Hub (Collaboration and Innovation for Difficult and Complex Randomised Controlled Trials) for trials methodology research. ConDucT focuses on several themes including developing methods for integrating clinical and patient reported outcomes to influence clinical decision-making.

**Mike Clarke**



Professor Mike Clarke is Chair of Research Methodology at Queen's University in Belfast and Director of the all-Ireland Hub for Trials Methodology Research, since March 2011. He was Director of the UK Cochrane Centre from

2002 until then and has spent more than twenty years working on systematic reviews and large randomised trials in a range of areas. He has a strong interest in increasing capacity for the conduct of randomised trials and systematic reviews, and in improving accessibility to their findings, in particular in low and middle income countries. This includes his work on Evidence Aid, to make it easier for people and organisations planning for and responding to natural disasters to make well informed decisions about health care and other areas.

### **Paula Williamson**



Paula Williamson is Professor of Medical Statistics and Director of the Clinical Trials Research Centre (CTRC) at the University of Liverpool. She is an Associate Director of the NIHR Medicines for Children Research Network, and Director of the MCRN Clinical Trials Unit. In 2008 she led a successful bid to create the MRC North West Hub for Trials Methodology Research (NWHTMR), focussing on three themes (early phase trial design and analysis, later phase trial design and analysis, patients' perspectives), and developing methods for application across key clinical areas including paediatrics, drug safety, cancer and epilepsy. The MRC have recently funded NWHTMR for a further five years.

### **Elizabeth Gargon**



Elizabeth Gargon obtained a First class Bachelor of Science Degree in Psychology and Health Science from the University of Liverpool in 2007. She joined the University of Liverpool as a research assistant for a research programme funded by the National Institute of Health Research (NIHR), and worked in collaboration with Alder Hey Children's NHS Foundation Trust. She is now a member of the COMET (Core Outcome Measures in Effectiveness Trials) Initiative Management Group and the Project Coordinator, and is undertaking a part-time PhD in the Institute of Translational Medicine (Biostatistics) at the University of Liverpool.

## COMET FP7 International Advisory Group

### **Professor Jacques Demotes-Mainard (ECRIN)**

Jacques Demotes-Mainard, MD-PhD-MBA, is Professor of Cell Biology, has a background in clinical neurology and a research curriculum as a basic neuroscientist, then as chair of a clinical research centre. Since 2004, he co-ordinates the European Clinical Research Infrastructure Network (ECRIN, [www.ecrin.org](http://www.ecrin.org)), funded by the FP6, then FP7 as the ESFRI-roadmap European infrastructure for clinical trials. Since 2005 advisor, then deputy director of the Biology and Health research department at the French Ministry of Higher Education and Research. Chair of the working group on risk based approach in the OECD initiative to facilitate international collaboration in clinical trials.

### **Dr Irmgard Eichler (EMA)**

Irmgard Eichler is Professor of Paediatrics and is currently Scientific Administrator in Paediatric Medicines Section at the European Medicines Agency (EMA). She qualified in medicine at the Vienna University Medical School and subsequently completed clinical training in Austria, South Africa and the US. Irmgard undertook research training in Paediatric medicine in Austria before completing a Postdoctoral Fellowship in the Division of Allergy & Pulmonary Diseases, at the Children's Hospital at Stanford, Stanford University Medical Center in California. Before joining the paediatric team at the EMA, Irmgard worked at the University Children's Hospital in Vienna. She held positions as the Director of the CF-Center, Head of Pulmonary Function Lab and as the Head of the Paediatric Allergology/Pulmonology Working Group. Irmgard has been involved in a number of other professional activities including Senior Clinical Specialist, Pediatric Pulmonology at the Prince Court Medical Center, Kuala Lumpur, member for Austria of the WHO Working Group on Health Promotion for Children and Adolescents in Hospital, expert for cystic fibrosis with the European Medicines Agency and investigator for several national and international clinical trials.

### **Professor David Flum (PCORI, Surgical Outcomes Club)**

Dr. David Flum is a gastrointestinal surgeon and outcomes researcher at the University of Washington. He holds the rank of Professor in the Schools of Medicine, Public Health, and Pharmacy, and serves as the Director of the Surgical Outcomes Research Center (SORCE) and Associate Chair for Research in the Department of Surgery. He earned a Masters Degree in Public Health in the field of health services research while in the Robert Wood Johnson Clinical Scholars Program at the University of Washington. Dr. Flum has developed a national reputation as a surgical epidemiologist and outcomes researcher, becoming a leader in bridging clinical care and public health issues. His work is aimed at improving healthcare by studying the impact of surgery by identifying processes of care that work and encouraging their use. Dr. Flum is Medical Director of CERTAIN (<http://www.becertain.org>), a patient-centered research network focused on conducting comparative studies of healthcare treatments and technology. He also was the founder and Medical Director (2005-2011) and currently serves as Research and Development Lead of the Surgical Care and Outcomes Assessment Program (SCOAP), a quality of care improvement program providing hospital-specific data feedback and best practices regarding processes of care and outcomes to over 55 Washington State hospitals. In 2011, Dr. Flum was appointed to the Methodology Committee of the federal Patient-Centered Outcomes Research Institute (PCORI). He is also the Chair of the American College of Surgeons' Surgical Research Committee.

### **Dr Piero Olliaro (WHO)**

Piero has been working for WHO/TDR in Geneva for the last 20 years covering positions in R&D, capacity building and applied field research. Currently he leads a unit on biomedical intervention and implementation research on tropical diseases (NTDs, malaria and tuberculosis). Before TDR he has worked in academia, public health and the private pharmaceutical sector. His background spans over bench and field research and his work bridges research and policy, academia and public health. Developing methodologies is one of his main current themes. MD, PhD, HRD (Habilitation à Diriger les Recherches, Grenoble), infectious diseases specialist, member of the French Académie

Nationale de Médecine, Visiting Professor U. Oxford, Honorary Research Fellow with the LSTM; 240 papers indexed in Pubmed.

#### **Dr Sean Tunis**

Sean Tunis, MD, MSc. is the President and Chief Executive Officer of the Center for Medical Technology Policy in Baltimore, Maryland. CMTP's main objective is to improve the quality, relevance and efficiency of clinical research by providing a neutral forum for collaboration among experts, stakeholders and decision makers. Dr. Tunis was a member of the Institute of Medicine Committee on Initial National Priorities for Comparative Effectiveness Research. He advises a wide range of domestic and international public and private health care organizations on issues of comparative effectiveness, evidence based medicine, clinical research, reimbursement and health technology policy. Through September of 2005, Dr. Tunis was the Chief Medical Officer at the Centers for Medicare and Medicaid Services (CMS), where he had lead responsibility for clinical policy for the Medicare and Medicaid programs. Previously he served as the Director of the Health Program at the Congressional Office of Technology Assessment and as a health policy advisor to the U.S. Senate, where he worked on pharmaceutical and device policy issues. Dr. Tunis trained at the University of California in Los Angeles and the University of Maryland in Internal Medicine and Emergency Medicine, and holds adjunct faculty positions at the Center for Health Policy at Stanford University, the Department of Internal Medicine at the Johns Hopkins School of Medicine, and the Department of Surgery at the University of California at San Francisco.

#### **Ms Liz Whamond**

Liz is past President of the Canadian Breast Cancer Network (CBCN). Her advocacy activities have been at the local, province, national and international level. She has lobbied for research funds as well as working to make sure survivors are on national research committees. She co-founded a community support group called Breast Cancer Survivor's Fredericton shortly after she was diagnosed with breast cancer in 1993. Liz has sat on Peer Review Panels with the National Cancer Institute of Canada. In April 2001, she graduated from "Project Lead". Liz co-founded the Canadian Cancer Action Network in 2001 and has been a consumer reviewer for the US Department of Defense. She has been a Board Member of the Canadian Partnership Against Cancer; is now Past Chair of the Canadian Cancer Advocacy Network; and Co-Chair of the Executive Committee of the Cochrane Consumer Network. Liz has had invited articles published in the Journal of Cancer Prevention and Control, the Cochrane Collaboration Consumers' Network Newsletter and various other venues. Liz is in her second term as a member of the Steering Group of the Cochrane Collaboration.

## COMET FP7 Collaborators

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