



11th - 12th July 2011

Ashton Court Mansion

Bristol, UK

Poster and Oral Paper Presentations Abstract Book

Posters will be displayed throughout Ashton Court for both days of the meeting. There is no allocated viewing session so please take the time to view posters at lunch and during refreshment breaks. This abstract book provides abstracts for all posters on display.

There will also be an Oral paper presentation session on Tuesday 12th July, giving a few researchers the opportunity to present their work orally. These abstracts are also presented here.

We would like to take this opportunity again to thank everybody who submitted an abstract; your contribution to the meeting is very much appreciated and adds great value for all participants.

1. The challenges of choosing outcomes in NICE clinical guidelines: epilepsy as a case study

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Oral paper presentation

Background: Multidisciplinary guideline development groups preparing NICE clinical guidelines are expected to define the outcomes they wish to consider when reviewing evidence and making recommendations. The Cochrane Handbook suggests using seven main outcomes, although NICE has not set a formal upper limit.

Without agreed outcome sets, each guideline group has to make this decision early in the guideline process, with the risk that outcomes are chosen which may later be viewed as 'wrong' by stakeholders.

Method: This case study describes the choice of outcomes made in updating the epilepsy guideline for NICE, subsequent reactions to that choice and the attempted resolution of the scenario.

Results: The initial choices of outcomes were based on an overview of the literature, existing evidence appraisals, and the views of clinicians and patients on the guideline development group.

When the draft guideline was published for consultation, a group of stakeholders disagreed with the choice of outcomes, pointing to an apparently internationally agreed set of outcomes. This raises questions about the validity of processes used to agree sets of outcomes, and about the dissemination of outcome sets.

The guideline has been delayed at cost to the public, and delay of important guidance.

Some actions have been taken to avoid the same situation in future.

Conclusions: Agreed outcome sets need to be widely and actively disseminated to avoid unnecessary duplication in defining such sets. Guideline developers could be usefully involved in defining outcome sets

2. Developing core outcome measures for paediatric clinical trials: lessons from the development of paediatric patient reported outcomes

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Poster

Background: Selection of core outcome sets (COS) for use in clinical trials requires input from many experts to ensure that measures are accepted as credible by the scientific community and are reliably measuring correct and valid concept(s). COS in paediatric trials must also address developmental issues that increase the complexity of the challenge. We will present examples of development and selection of patient and parent/caregiver reported measures of symptoms, for use as endpoints in clinical trials. Many of these methods are applicable to COS more generally.

Methods and Results: Paediatric COS must (1) include age-appropriate outcome measures that are sensitive to developmental milestones; (2) provide comparable outcomes across tight age bands to allow pooling of data, and (3) specify how paediatric PRO and CaregiverRO data generated can be integrated and pooled.

We provide an overview of methods for addressing each of these challenges, using examples from paediatric instrument development in allergic rhinitis, asthma, constipation, irritable bowel syndrome, and restless legs syndrome.

These methods help to ensure comprehensive measurement of what is important to patients and their caregivers. In addition, to ensure the credibility that is crucial for establishing COS, paediatric PRO development is guided throughout by experts in paediatric PROs, clinical leaders for the condition under study and by GP's and/or nurses, who often have unique and helpful perspectives. We will give examples of obtaining such clinical input throughout outcome development/selection, through the use of Advisory Boards, interviews, questionnaire surveys and Delphi panels.

Conclusions: Input from a wide range of relevant experts is crucial to establishing the credibility of core outcome sets. In paediatric conditions, it is essential but challenging to get information from the patients about what is important to them and integrate it with information from caregivers and clinicians to ensure a comprehensive COS.

3. Registry of Outcome Measures (ROM); towards trial readiness

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Poster and oral paper presentation

Objective: To provide accessible self-help tools and guidelines to support identification, review and selection of OMs for studies and trials.

Background: Selecting the right OMs for clinical trials/studies is critical to success. Until done it can be a major barrier to translational research. The chance of selecting those best suited to the task at hand increases with the availability of information on existing OMs. Finding this information can be time consuming, an effort duplicated in each study. Further, the lack of an agreed set of core OMs and the resulting disparities in choice of OM has made meta-analysis or comparison of findings difficult, even within the same disease/intervention.

Method: ROM, an online database, is an attempt to address these issues, firstly by offering accessible web based information on an expanding number of existing OMs and secondly by providing on-line tools that support and facilitate the review and selection process. These tools include:

- A search engine that enables investigators to find potentially useful OMs;
- Consistently formatted OM summary information for rapid review;
- A comparison report that displays information on multiple OMs in side by side tabular format; and
- A review/selection tree that enables groups to coordinate their efforts, annotating tasks and decisions about specific OMs, while at the same time keeping the community up-to-date.

Results: ROM is appreciated by investigators and continues to grow thanks to the contributions of experts from around the world.

4. Patient partner involvement in the measurement and management of RA fatigue

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Poster

Background: At OMERACT 6 fatigue was established as an outcome that is important to patients and at OMERACT 8 delegates voted overwhelmingly to measure the symptom in studies wherever possible. As a result, our group has developed and validated a patient reported outcome for fatigue (the Bristol RA Fatigue Scales) and conducted a randomized controlled trial (RCT) of a cognitive-behavioural intervention to reduce fatigue impact. We present our perspectives on how patient partner involvement has shaped the research.

A patient partner perspective: Patient partners are not representing all patients but see things from a point of view that someone without RA cannot:

- *Enhancing researchers' understanding of the symptom:* When a researcher joined the BRAF team, two patient partners discussed the symptom and its impact, providing insights that could not be gained from the literature.
- *Making patient reported outcomes user-friendly:* Two patient partners fed back on the question order in relation to flow, presentation and broaching more personal questions.

A researcher perspective: Three patient partners, who all participated in the RCT cognitive-behavioural intervention, are involved in evaluating its effectiveness:

- *Data analysis:* A patient partner independently analysed a subset of data from a focus group study nested within the RCT, enhancing the rigour and credibility of the findings.
- *Study materials:* In our recent application for a further multi-centre RCT of the cognitive-behavioural intervention, two patient partners advised on patient information sheets, the content and wording of patient handouts and practical considerations for patients attending the intervention.

Conclusions: Researchers need to ensure their work is communicated appropriately to enable patient partners to make a useful contribution. Ultimately efforts to build a collaborative relationship will improve the research. Patient partners bring their experiential knowledge of RA to the team, making the research more acceptable, accessible, relevant to patients and rigorous.

5. Health Outcomes Research at the Clinical Trials Research Unit (CTRU), University of Leeds

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Poster

Background: Health outcome data are an integral aspect of patient care, policy decision making and healthcare delivery. The CTRU has an active portfolio of outcomes research including development of statistical methodology and disease-specific outcome measures that underpin clinical trials research.

Methods and Results: Systematic reviews have been conducted to identify and appraise outcome measures, based on international guidelines, to identify research gaps and make informed decisions about appropriate outcomes:

- PRO measures for chronic wounds (UK NIHR)
- Content comparison of PRO measures for children with musculoskeletal impairments based on international classification of functioning, disability and health
- Physical and social factors in the home related to diet and eating behaviours (American NIH)
- Outcome measures used to evaluate childhood obesity treatment interventions (UK HTA)

The following conceptual framework development, informed by literature and interviews with patient and/or experts, has been completed:

- Pressure ulcer-specific health-related quality of life (HRQL) outcomes and contributory factors
- HRQL in Rheumatoid arthritis and foot ulceration: care pathways and experiences of care provision
- Pain in pressure ulcers
- Factors within home environments hypothesised to relate to childhood obesity

Methods for development and evaluation of outcome measures, completed or in progress:

- Myeloma disease-specific QoL module adopted by EORTC
- Development of new design for phase III international field study validation of QoL measures
- Pressure ulcer-specific PRO measure of HRQL (PU-QOL)
- Researcher conducted and self-report Home Food Availability Inventories (HFAI and FAI checklist)
- Home environmental measure related to childhood obesity (HomeSTEAD)

Clinical interpretation

- Guidelines for the clinical interpretation of EORTC QLQ C30

Psychometric evaluation is performed using traditional and Rasch methods.

Conclusions: The presentation will demonstrate the ongoing application within the CTRU of mixed methods approaches to the development, evaluation and interpretation of PROs across a number of disease areas.

6. Defining the outcome set for thrombosis research in palliative care

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Poster

The TRAD Alliance was developed in response to a growing need expressed from palliative care clinicians and patients that there is insufficient applicable data to inform the management of VTE in patients with incurable disease. Following a scoping exercise amongst palliative care physicians at the last EAPC and a focus group of patients affected by VTE, the TRAD Alliance was born. Whilst there is a large body of clinical trial evidence on the epidemiology, diagnosis, prevention and treatment of VTE in all clinical subgroups of patients, those with advanced disease (ECOG >2, prognosis < 3 months) are rarely included in such studies. The outcome measures used in VTE studies are less applicable to patients in the palliative stages of their disease. The majority of studies use endpoints such as asymptomatic VTE, major bleeding complications and survival upon which to base clinical recommendations. Within the palliative care setting these outcome measures have less meaning, whilst symptomatic disease burden and quality of life are considered more appropriate. There is evidence to suggest the pathophysiology, complication rates and pharmacokinetics change with progressive disease and that calls into question how much one can extrapolate the data from other trials. In addition, the sequelae of complications of VTE in advanced disease are likely to be catastrophic since such patients have higher bleeding risks and greater likelihood falls e.g. elderly patients, compliance with medicines (e.g. dementia, elderly) of bleeding into critical areas (e.g. stroke patients and patients with brain metastases). This poster will report on a process, including an expert group meeting, of defining the research agenda required to specify the core outcomes in this population at high risk, but with low levels of appropriate evidence at least partial due to lack of appropriate outcomes being studied.

7. Disaster Data - Urgent Need for a Common Core Data Set

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Poster

Background: At the second session of the Global Platform for Disaster Risk Reduction in 2009, the United Nations International Strategy for Disaster Reduction (UNISDR) Science and Technical Committee recognised the need for review and consolidation of the various disaster information sources and databases, to improve the consistency, comparability, quality and value of the data available to the international disaster community.

Methods: As part of the mid-term review for the Hyogo Framework for Action, we examined the applicability of systematic review methods to the synthesis of evidence from disaster databases. Two health-related questions were posed as "case studies", to focus our analysis.

Findings: Key findings were categorised as process or content related.

Process - The systematic review approach was successfully applied to the analysis of databases. . As in reviews of research studies, systematic reviews of databases helped to summarise existing evidence, to identify gaps in knowledge and to articulate these gaps.

Content - The databases interrogated were not able to meet our needs as healthcare professionals seeking to answer questions on the health impacts of disasters. The databases were limited by the quality of data they contained and its relevance to healthcare decisions. This included a lack of comparability and standardisation across different data sources.

Conclusions: Much of the publicly available data relating to the health impacts of disasters is inadequate for practitioners and policymakers trying to make decisions about health care in these settings. This is largely due to the quality and relevance of primary data being collected, and inconsistencies in these data. There is an urgent need for these data issues to be addressed. Consensus is needed on a common core set of disaster data to be collected across agencies and events, the methods and case definitions to be used, and means for sharing these data.

8. Reporting Bias in Systematic Reviews of Psychological Interventions

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Poster

Background: Studies of psychological and behavioral change interventions frequently include multiple measures of the same construct (e.g. depression) or related constructs (e.g. the Hospital Anxiety and Depression Scale), and they often include measures that are derived from these (e.g. recovery). These conditions create opportunities for outcome reporting bias. That is, when trialists select outcomes to report on the basis of their results, reported outcomes may be biased (Hutton, 2000) through non-reporting, selection of subgroup analyses, or choice of cut-offs such as recovery (Williamson et al., 2005; Naggara et al., 2001). More than a third of Cochrane Reviews include a trial at risk of outcome reporting bias, and many primary results become non-significant after adjustment for bias. However, the extent of reporting bias in secondary outcomes and continuous outcomes requires further examination (Kirkham et al., 2010).

Objectives: This pilot study will examine Cochrane Reviews of anxiety and depression for evidence of outcome reporting bias.

Methods: All outcome data for symptoms of anxiety and depression, including clinical recovery, will be extracted from the 108 reviews in the Cochrane Depression, Anxiety, and Neuroses group (as of March 14th, 2011). Effect size data for every study included in a symptom or recovery meta-analysis from these reviews will be extracted. In the absence of selective outcome reporting:

- 1) Within each review, there should be no relationship between study effects and the number of outcomes reported.
- 2) Effects on symptoms in studies reporting recovery should be no larger than effects on symptoms in studies that do not report these dichotomized results.
- 3) Those studies reporting long-term follow-up should not differ from studies reporting results only at post-treatment.

Finally, this study will classify each review according to their susceptibility to outcome reporting bias based on how the authors chose to extract data from the original trial reports.

9. BEST Platelet Study Group: Devising Reporting Guidelines For Clinical Platelet Transfusion Studies

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Poster

Background: A systematic review of randomized controlled and observational studies in platelet transfusion demonstrated that descriptions of trial design, platelet products, transfusions, and outcomes were not adequately described. We aimed to develop a reporting checklist to aid authors and editors in creating and critiquing platelet trials.

Method: An initial checklist of 23 items necessary to be included in a platelet transfusion trial manuscript was developed. A panel of experts from the BEST Collaborative was queried on the importance of including these items in the platelet trial guideline using the Delphi technique. Delphi is a validated, systematic, interactive forecasting method, used to achieve consensus among experts. Panelists graded each item using a 7 point Likert scale from "definitely should not" to "very important to" include. Three rounds were undertaken. Items receiving an average rank of ≥ 5.5 were accepted; 2.6-5.4 were edited by the authors and sent out in the subsequent round; < 2.5 were eliminated.

Results: Initially 33 panelists participated, but this decreased to 25 by the third round. After round I, 18 (78%) of the items were accepted and 5 were indeterminate. Indeterminate items were reworked and added to based on panelist comments, thus 15 items were sent out for round II. Following round II, 3 of 15 items (10%) were indeterminate and reworded for round III. After round III, 33 items were established for the final checklist with ranks of ≥ 5.5 . One indeterminate item was reviewed by the authors and accepted for a total of 34 items.

Conclusion: The use of the Delphi method with an expert panel was successful in finding consensus for items to include in a platelet study report. The final checklist will be useful for authors and editors to improve the reporting and evaluation of platelet transfusion trials.

10. The use of an e-delphi method to identify core maternity outcome measures

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Poster and oral paper presentation

Background: Variation in maternity care outcome measures, both in the variety of outcomes reported and disparity in the definition of terms, makes comparison between studies and meta-analysis highly problematic. The aim of this Delphi study then was to identify a minimum data set of outcome measures that could be proposed to evaluate models of maternity care and provide the basis for comparison between models.

Methodology: A three round, electronic Delphi study design was used as a means to reach a degree of consensus between key maternity care stakeholders internationally. The use of electronic, on-line resources allowed the participation of a wide variety of key stakeholders and greatly facilitated international collaboration. 320 participants from 28 countries expressed willingness to take part with representation from maternity service users, midwives, obstetricians, general practitioners, policy makers, and maternity care researchers. 218 participants completed round 1, 173 completed round 2 and 152 completed round 3 (47% of the original expression of interest).

Results: Delphi response patterns, participating countries, respondents' primary interest in Maternity care are reported. From 299 items identified at systematic review and 73 further items suggested at round 1, a core set of 48 outcomes that scored above the mean or which were scored 4 or 5 (out of 5) by 70% or more of the respondents during iterations of the Delphi process are presented.

Conclusion: The predominance of European and midwife respondents may mask the priorities of other groups for example women and obstetricians. Nonetheless, consideration should be given to routinely reporting the outcomes reported in the evaluation of models of maternity care. The data set could be useful to identify primary outcome measures for multicentre trials. Adoption of the data set would allow more fruitful comparisons of models of maternity care nationally and internationally.

11. The development of a core outcome set for studies of children with Cleft Palate and Otitis Media with Effusion

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Poster

Background: Cleft lip and palate (CLP) is a congenital malformation with an incidence of around 1 in 700 individuals. Cleft palate results in impaired Eustachian tube function and approximately 90% of these children have non-trivial Otitis Media with Effusion (Glue ear). Recently a systematic review of the management of OME for children with CLP has revealed that previous studies reported multiple outcome measures: mostly selected by clinicians with limited consistency between studies. As OME can impair hearing at stages important in the development of language, behavioural and social relationships, it is clear that outcomes relevant to these issues should be used in future studies. As a result, the aim of this study is to develop a set of core outcome measures that are relevant to parents and children with Cleft Palate and OME.

Method: This study will have several interrelated work streams.

- (i) An updated systematic literature review to identify outcomes that have previously been used in OME and cleft research
- (ii) A Delphi exercise to gather clinician's opinions on the relevant outcomes that may be used in a potential study.
- (iii) Qualitative interviews to explore patient and parent opinions on outcomes that are important to them.
- (iv) Finally, the outcomes will be evaluated by the project team, a Study Advisory Group and a panel formed from the UK Cleft Centres to identify the most appropriate core outcomes for future studies of the care for children with Cleft Palate who have OME.

12. National Audit to Measure Outcomes in Lung Cancer

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Poster

Introduction: The National Lung Cancer Audit is run jointly by the Royal College of Physicians and The Information Centre for health and social care. Its development was driven by the realization that lung cancer outcomes vary widely across the UK and are poor compared to other western countries. The aim of the audit is to record outcomes in lung cancer on a large scale and through case-mix adjustment, start to explain the wide variations noted. Originally piloted in 2005 in a few trusts in England, the audit now covers the whole of England, Wales, Scotland, Northern Ireland and Jersey.

Results: For patients first seen in 2009, 37,304 cases were submitted from England (30,096), Wales (1,973), Scotland (4,379), Northern Ireland (819) and Jersey (37), representing >97% of the expected number of cases. Completeness of data on individual cases has also improved such that stage and performance status are recorded in over 80%.

Results suggest that the quality of care is improving, with increases in histological confirmation rate (68% to 76%), proportion having anti-cancer treatment (45% to 59%) and proportion having surgery (9% to 14%). However, these mean results hide significant variation across the cancer networks and individual hospital trusts, which persists even after adjustment for case-mix (age, sex, stage, performance status, socio-economic status).

Conclusions: These results highlight the considerable achievement of the National Lung Cancer Audit in collecting data and are a testament to the hard work of lung cancer teams across the country in achieving such high quality data on such a large scale. The results suggest that care for lung cancer patients is slowly improving, although some of the apparent improvement is likely to reflect the rise in data quality. However, wide variations in outcomes persist between organisations, which need to be the focus of on-going service improvement work.

13. An objective measure of time to recovery – a core outcome following cardiac surgery?

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Poster

Background: Clinical trials in cardiac surgery are often unmasked. In such trials there is a need for objective measures of post-operative recovery as the commonly used post-operative hospital stay is susceptible to bias. We describe a measure of recovery developed and used in a randomised trial of a median sternotomy (OPCAB) versus anterolateral left thoracotomy (ThoraCAB) incision in patients having off-pump coronary artery bypass surgery. It was hypothesised that recovery would be faster with ThoraCAB.

Methods: Recovery time was defined as the time from surgery until the patient was considered fit for discharge. Patients were classified fit (a) when the x-ray was clear (no evidence of pleural effusion requiring drainage, lung collapse/consolidation, pneumothorax); (b) there was no suspected systemic, lower respiratory tract or wound infection; (c) routine blood results and temperature were normal and (d) when physically mobile (walking 70m, bowels open and oxygen saturation >95%). Patients were recruited from two centres and these recovery criteria were monitored daily until discharge.

Results: 184 patients were recruited (91 randomised to ThoraCAB, 93 to OPCAB). In the OPCAB group 77% were classified fit at or before discharge versus 68% in the ThoraCAB group. For the remainder, the recovery time was censored because discharge occurred before all the criteria were met. Insufficient mobility also accounted for the majority of censored observations. The median recovery time was 6 days, IQR [4,7] in the ThoraCAB group versus 5 days, IQR [4,7] in the OPCAB group ($p=0.53$). In contrast, the median time to discharge was 5 days in the ThoraCAB group versus 6 days in the OPCAB group.

Conclusion:

A faster recovery with ThoraCAB was not found and a significant proportion of patients were discharged before all the recovery criteria were met. The measure (with slightly modified criteria) is being used in other cardiac surgery trials.

14. Systematic review of measurement properties to enable development of a core outcome set for evaluating effectiveness of physiotherapy post lumbar discectomy

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Poster

Background: Variability in outcome measures across trials contributed to uncertainty in conclusions from our systematic review evaluating effectiveness of physiotherapy post lumbar discectomy, and limited the potential for meta-analyses [1]. A combination of patient-reported and performance-based measures is required to define a core outcome set. Selection of measures must be informed by key measurement properties [2], and coverage of the components of the International Classification of Functioning, Disability, and Health (ICF) [3]. The objective of this study was to conduct a systematic review of measurement properties of outcome measures that have been used to evaluate effectiveness of physiotherapy post lumbar discectomy, with the focus of subsequently informing the process of defining a core outcome set.

Method: A systematic review was conducted following guidance [4] and PRISMA [5]. Measures were identified from our recent systematic review [1] that included 16 trials (1336 participants). Studies published in English prior to 30th April 2011, investigating at least one key measurement property (content validity, construct validity, criterion validity, internal consistency, reliability, absolute measurement error, and responsiveness) of an identified measure were included. The characteristic of interpretability was also included to address potential clinical usefulness. Two reviewers independently searched information sources, assessed studies for inclusion, evaluated methodological quality of studies [6], and tabulated included measures against the main components of the ICF [3]. Standardised criteria were used to assess the measurement properties of each measure [7].

Results: Preliminary findings will be reported.

Conclusion: Findings from this systematic review of properties of measures will be used to inform consensus discussions regarding definition of a core outcome set for future trials investigating effectiveness of physiotherapy management post lumbar discectomy. This will reduce the use of inappropriate outcome measures, reduce the risk of bias from selective outcome reporting, and facilitate comparison and synthesis of findings from future trials.

References:

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15. A Systematic Review of Studies That Aim to Determine Which Outcomes to Measure in Clinical Trials in Children

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Poster

Background: The process of selecting the most suitable outcomes to include in clinical trials can be complex. Our aim was to systematically review studies that address the process of selecting outcomes or outcome domains to measure in clinical trials in children.

Methods and Findings: We searched Cochrane databases (no date restrictions) in December 2006; and MEDLINE (1950 to 2006), CINAHL (1982 to 2006), and SCOPUS (1966 to 2006) in January 2007 for studies of the selection of outcomes for use in clinical trials in children. We also asked a group of experts in paediatric clinical research to refer us to any other relevant studies. From these articles we extracted data on the clinical condition of interest, description of the method used to select outcomes, the people involved in the selection process, the outcomes selected, and limitations of the method as defined by the authors. The literature search identified 8,889 potentially relevant abstracts. Of these, 70 were retrieved, and 25 were included in the review. Two groups utilised the Delphi technique, one used the nominal group technique, and one used both methods to reach a consensus about which outcomes should be measured in clinical trials. Other groups used semistructured discussion, and one group used a questionnaire-based survey. The collaborations involved clinical experts, research experts, and industry representatives. Three groups involved parents of children affected by the particular condition.

Conclusions: Very few studies address the appropriate choice of outcomes for clinical research with children, and in most paediatric specialties no research has been undertaken. Among the studies we did assess, very few involved parents or children in selecting outcomes that should be measured, and none directly involved children.

16. Using the Delphi technique to determine which outcomes to measure in clinical trials: a systematic review of existing studies and recommendations for the future

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Poster

Background: There is little guidance relating to the use of the Delphi technique for developing core outcome sets. Issues which may affect the credibility of the results of studies which use the Delphi technique for this purpose include inappropriate group composition, poor questioning technique, attrition bias, analysis which can miss or overstate the importance of certain outcomes, and incomplete reporting of results.

Our aim was to systematically review studies that use the Delphi technique to determine which outcomes to measure in clinical trials or systematic reviews of clinical trials, to identify variations in the methods applied within these studies.

Methods and findings: We searched Medline (no date restrictions) in January 2010, for relevant studies. From these, we extracted data on methodological aspects including the participants involved, the types of questions they were asked, whether the study was completely anonymised, whether non-responders in earlier rounds were included or excluded from subsequent rounds and the definition of consensus used by the authors.

The literature search identified 656 potentially relevant abstracts. Of these, 15 were included in the review. There was variation between the studies in terms of the composition of the groups, and the manner in which the Delphi process was conducted. The reporting quality of studies was variable. Patients were rarely involved in the process of determining which outcomes to measure in clinical trials.

Conclusions: Researchers who use the Delphi technique to design core outcome sets should be aware of issues which may affect the credibility of their study, and explain methodological decisions, in relation to the study aims, in the main publication.

17. Outcomes in Clinical Trials of Inhaled Corticosteroids for Children with Asthma Are Narrowly Focussed on Short Term Disease Activity

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Poster

Background: Little work has been done to determine which outcomes should be measured in randomised controlled trials (RCTs) in children with asthma. We aimed to identify whether any domains were underrepresented in RCTs of regular therapies for children with asthma over a 20 year period, and to examine what consistency there was between RCTs in the outcomes used to assess the domains.

Methodology/Principal Findings: By searching the Cochrane Central Register of Controlled Trials in January 2008, we identified all parallel-group RCTs, published between January 1988 and December 2007, which assessed inhaled corticosteroids (ICS) as regular therapy for children with asthma. We evaluated how frequently RCTs measured the following pre-defined domains: disease activity; disease damage; functional status; quality of life; health resource utilisation; and adverse effects of therapy. Our initial search identified 1668 abstracts, of which 412 were retrieved in full. 159 RCTs, were included in the review. Disease activity was measured in 157 RCTs, adverse effects of ICS in 135, functional status in 25, quality of life in 21, and health resource utilisation in 17. No RCT measured long term disease damage, although two used FEV1 as a measure of 'lung growth'. RCTs were inconsistent in the outcomes used to measure the domains.

Conclusions: Short term disease activity is the most frequently measured outcome domain in RCTs in children with asthma. Effects of regular therapies on functional status, quality of life, and long term consequences of asthma are infrequently assessed. A core set of outcomes, developed using consensus techniques, would standardise the measurement of appropriate outcomes in these RCTs. Involving patients would identify outcomes which are most relevant from their perspective.

18. The selection, measurement, and reporting of outcomes in clinical trials in children – guidance for trialists

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Oral paper presentation

Background: It is crucial in clinical trials that appropriate outcomes are selected, that they are measured using scientifically rigorous methods, and that they are reported completely. Research suggests that in clinical trials in children, there are problems with the selection, measurement, and reporting of outcomes.

The Star Child Health group is a global initiative to improve the quality of clinical trials in children http://www.ifsrc.org/index.php?option=com_content&view=article&id=30&Itemid=2. This initiative comprises several working groups, which aim to produce 'Standards', or guidance documents for trialists. We describe the progress of one of these groups, which aims to provide guidance around the selection, measurement, and reporting of outcomes, in clinical trials examining the effectiveness of interventions for children.

Methods: The international working group comprises 18 members, including clinicians, trialists, methodologists, and biostatisticians. Through a series of teleconferences, meetings, and an online Delphi process, the group has formulated a series of statements that form the basis of a guidance document for trialists.

Results: The main points in the current version of the guidance relate to the following issues:

1. Selection of important outcomes
2. Core outcome sets
3. Measurement of outcomes in a rigorous manner
4. Description of the methods used to measure outcomes
5. Complete reporting of results
6. Documentation of changes to outcomes as the trial progresses

Discussion: The work of this group should help improve the quality of the selection, measurement, and reporting of clinical trials examining effectiveness of interventions in children. This includes guidance relating to core outcome sets. This version of the guidance is being sent for wider consultation to clinical trial networks and people involved in clinical trials in children, before it is disseminated in its final form.

19. Feasibility of recruitment and training of carers of people with dementia as a route to Cochrane-NHS engagement

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Poster

Background: Relatives of people with dementia often want to participate in research, but their time is limited because of their caregiving role.

Objectives: The first, innovative part of the proposal is to recruit carers and former carers of people with dementia to a well-defined task: reading trial reports, extracting basic information, and entering it into the Dementia Group's online register of studies - ALOIS.

The volunteers are also invited to work through a series of modules about EBM using examples, all directly related to dementia.

Methods: A range of publicity and outreach methods were used to recruit volunteers. Also an EBM skills workshop for carers was held in Oxford which was very well attended. We will conduct a before-and-after study where the participants' skill at the coding task will be rated, and a questionnaire will be used to assess changes in involvement with dementia-related NHS activities, primary dementia research, and attitudes.

Results: At the project half-way point, we had recruited 35 volunteers (20 carers or former carers). We have now reached 40, and this has translated into 65 new study records being coded by new volunteers and published on ALOIS, and a further 70 studies currently assigned to volunteers for coding.

A slightly unexpected but welcome development is that schools are now interested in participating, and we are currently looking at how adapt the model for this purpose. We are also hopeful that the model might be further adapted as a Cochrane-wide "citizen science" initiative in conjunction with the development of the Cochrane Register of Studies.

Conclusion: Involving and training volunteer 'expert carers' in maintaining a trial register is feasible. We will explore whether the model can be adapted to bring wider benefits for public engagement with the NHS and participation in primary research.

20. Systematic reviews of measurement properties – a standardized methodology

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Poster

Background: The selection of appropriate outcomes and measurement instruments is crucial to the design of clinical trials. Systematic reviews on the measurement properties of all available instruments to measure an outcome of interest, are the best tool for evidence-based instrument selection. The methodology and quality of such reviews, however, varies widely. There is an urgent need for a standardized methodology for performing such reviews.

Methods: We made an overview of all published systematic reviews on the measurement properties of health status measurement instruments (published up to March 2011). Based on general guidelines of the Cochrane Collaboration for systematic reviews of clinical trials and diagnostic studies, a standardized methodology for systematic reviews of measurement properties was developed. This includes methodological search filters, and a consensus based checklist to assess the methodological quality of the included studies. A 10-step procedure was developed and applied in a systematic review of neck disability questionnaires.

Results: A methodological search filter for finding studies on measurement properties was developed for PubMed with a sensitivity of 97.4%. The filter was translated for Embase. In an international Delphi study the COSMIN checklist was developed to assess the methodological quality of studies on measurement properties. A scoring system was also developed. For data synthesis, we present levels of evidence, taking the number of studies, their quality, and their results into account. In a systematic review of neck disability questionnaires 8 questionnaires were identified. The Neck Disability Index seems most appropriate to be used in clinical trials. However, lack of evidence on the measurement of other possibly appropriate questionnaires was found, which hampers instrument selection.

Conclusion: More high-quality systematic reviews of measurement properties are needed, to select the best outcome measures for clinical trials and to identify the need for studies on the measurement properties of promising measurement instruments.

21. Core Outcome Domains for Controlled Trials and Clinical Recordkeeping in Eczema: International Multi-perspective Delphi Consensus Process

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Poster

Background: There is wide variation in the use of outcome measures for eczema. The aim of this project was to develop a consensus based set of core outcome domains for eczema that can be used for controlled clinical trials, and for clinical recordkeeping.

Methods: We performed a three-stage web-based international Delphi exercise to develop consensus-based sets of core outcome domains for eczema for “controlled trials” and “clinical recordkeeping”. A total of 57 individuals from four stakeholder groups (consumers, clinical experts, regulatory agency representatives, and journal editors) representing 13 countries were asked to rate the importance of 19 outcome domains for eczema and to choose which domains should be included in two core sets of outcomes. Participants received standardized feedback, including the group median, inter-quartile range, and previous responses, and the assessment was repeated in two subsequent rounds. We defined consensus a priori as at least 60% of the members of at least three stakeholder groups, including consumers, recommending domain inclusion in the core set.

Results: Forty-six individuals (81%) participated. Consensus was achieved for inclusion of symptoms, physician-assessed clinical signs, and a measurement for long-term control of flares in the core set of outcome domains for eczema trials. For medical recordkeeping, consensus was reached to regularly monitor eczema symptoms in clinical practice.

Conclusions: We recommend including eczema symptoms, physician-assessed clinical signs, and a measurement for long-term control of flares as core outcomes in future eczema trials, in order to enhance clinical interpretability and to enable meta-analyses across different studies. Future work is needed to select which existing or new scales should be used to measure the domains identified as relevant for the core set.

22. The relationship between prioritising gaps in knowledge about the effects of treatment and identifying core outcome sets

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Poster

Background: This study addresses the challenges of service users, clinicians and researchers working together to achieve two different goals:

- 1) identifying the most important gaps in knowledge about the effects of treatments (treatment uncertainties),
- 2) identifying a core set of outcomes to be used by trialists and systematic reviewers.

Service users and clinicians have similar roles for both challenges: deciding which 'treatment uncertainties' and 'core outcomes' are important to them. Researchers have had a greater role in identifying core outcome sets than they have had in identifying important treatment uncertainties.

This study uses the example of preterm birth to explore how the roles of these groups differ for achieving the two different goals, and how methods of working together differ. Preterm birth is the most important single determinant of adverse infant outcome in terms of: survival; quality of life; psychosocial and emotional impact on the family; and costs for health services. The combination of highly technical research and highly emotive issues presents particular challenges to partnership working.

Methods: A James Lind Alliance Priority Setting Partnership will be established to identify treatment uncertainties shared by service users and clinicians. Simultaneous discussions between service users, clinicians and researchers will consider how best to draw on the priority setting work to inform the development of a core set of outcomes. Diaries, observations and interviews will investigate the roles of the different players as each stream of work progresses.

Results: This poster will present an evolving study design for identifying both 'treatment uncertainties' and core outcome sets. It will consider the new challenges are they appear, and suggest possible solutions.

Conclusion: Efforts to identify treatment uncertainties and core outcome sets share principles of being research based and collaborative, but they draw on research in different ways and shape collaborations differently.

Keywords: Priority Setting Partnership, preterm birth, research priority, uncertainties

23. Building a database of validated pediatric outcomes

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Poster

Background: Pediatric populations have increasingly been included in clinical research, which relies on availability and use of appropriate outcome measurement tools. Objective: To develop an inventory of valid and reliable pediatric outcome measurement tools.

Methods: The top 6 general medicine journals and top 4 pediatric journals were searched for pediatric randomized controlled trials (RCTs) published since 2000. Two independent reviewers conducted screening and data extraction.

Results: Searches identified 2229 unique references. Screening of 2.5% of references determined that the vast majority (96.5%) would be included, thus full text for all references was obtained. Inclusion screening and data extraction will occur simultaneously and are currently underway. Preliminary extraction of 61 RCTs has been completed; full results will be presented in July. Most (70%) were identified from pediatric journals, with ages ranging from 33 weeks gestation to 21 years. The most common condition studied was psychological disorders (12). A single intervention was tested in 57% trials and more than one intervention was tested in 36% of trials. Half (48%) reported one primary outcome, while 31% did not identify a primary outcome, and a further 13% identified more than one. We identified 79 different scale or questionnaire-type measurement tools, from 31 studies, that measured outcomes in 21 different conditions. For 41% of these 79 tools, authors provided information on psychometric properties and included relevant citations in 28% for these properties. The most commonly reported properties were reliability (59%) and validity (41%).

Conclusions: A wide variety of pediatric outcome measurement tools are in use by researchers. Psychometric properties of measurement tools are inconsistently reported in pediatric RCTs, thus it is unclear to readers if the tools are of high quality. Developing a comprehensive database of validated pediatric outcome measures may facilitate use of high quality pediatric research.

24. The need for a core outcome set in colorectal cancer: a systematic review of current outcomes

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Poster

INTRODUCTION: Evidence suggests that there is inconsistent outcome selection, measurement and reporting in clinical trials of colorectal cancer (CRC), which hinders meta-analyses and leads to outcome reporting bias. The aim of this study is to determine the extent of heterogeneity in clinical outcomes reported in prospective studies of colorectal cancer surgery.

METHODS: A systematic literature review identified prospective studies in adults over a two year period. Included were studies reporting outcomes from patients treated with surgery for colorectal adenocarcinoma, including neoadjuvant and adjuvant chemotherapy and radiotherapy. Excluded were articles of:

- 1) non-English language;
- 2) non-biomedical interventions;
- 3) non-curative, non-surgical treatments;
- 4) screening for CRC; and
- 5) treatment of colorectal metastases.

Data extracted will include:

- 1) study design;
- 2) whether outcomes are primary or secondary;
- 3) the degree of bias in the study; and
- 4) journal impact factor.

Planned analyses include the number and frequency of outcome reporting, whether endpoints were defined and whether a validated system for grading outcomes was used. A long-list of outcomes will be produced, and these will be categorised into themes. This will form the basis of a comprehensive list of outcomes to be refined into a shorter list. Delphi methodology will refine the lists and it is intended to identify a core clinical outcome set (n=7).

RESULTS: Literature reviews have identified 3735 abstracts which have been screened and 275 potentially eligible articles identified. Full papers are being retrieved and data extracted. By the July meeting results of the long list of outcomes, the frequency of outcome reporting and the methods used to define and grade will be summarised for presentation.