Towards a core outcome set for hip fracture trials:

A protocol for the development of a consensus statement.

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Warwick
Medical School
CLINICAL TRIALS UNIT

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ABSTRACT

Background Fragility fracture of the proximal femur (hip fracture) is a very considerable cause of morbidity and mortality worldwide. The lack of a consensus for the core outcomes that should be reported in clinical research in this field has hampered study design and evidence synthesis.

Objective To reach a UK consensus for a core outcome set to be used in clinical trials involving patients with a hip fracture, including patients with cognitive impairment.

Data sources A synthesis of the evidence from research undertaken in advance of the consensus meeting: patient/carer dyad interviews, focus groups, and systematic reviews of patient-reported and performance outcome measures. The data synthesis will inform a nominal group questionnaire listing candidate domains and outcome measures.

Participants Relevant stakeholder groups in the UK will be identified and approached to be represented on the consensus panel. These stakeholders include funders, systematic reviewers, clinical researchers and health professionals. Patient and public representation on the panel will be sought from several partner organisations.

Consensus methods The participants will complete the nominal group questionnaire, rating the candidate domains and outcome measures in order of importance in advance of a consensus meeting. Pre-meeting source data and questionnaires will be summarised at the subsequent consensus meeting followed by facilitated discussion of candidate domains and potential outcome measures. A core outcome set will then be determined using a closed voting system.

INTRODUCTION

Fragility fracture of the proximal femur (hip fracture) is one of the greatest challenges facing the healthcare community. In 1990, a global incidence of 1.31 million was reported and was associated with 740,000 deaths.[1] Hip fractures constitute a heavy socioeconomic burden worldwide. The cost of this clinical problem is estimated at 1.75 million disability adjusted life years lost; 1.4% of the total healthcare burden in established market economies.[1]

In evaluating the effectiveness of care for patients who have sustained a hip fracture, it is important to assess the full array of outcomes considered important and relevant by patients, clinicians and other key stakeholders in the healthcare system.[2] However, consensus regarding the key outcomes, or core outcome sets (COS), that should be assessed following hip fracture does not currently exist. This has hampered the conduct of both clinical trials and systematic reviews.[3] The UK National Hip Fracture Audit/ Database (NHFD)[4] was created following a series of stakeholder meetings involving healthcare professionals and patients. The NHFD has been hugely successful in defining a standard for the collection of process and mortality data. However, the audit was not designed for use in clinical research and in particular lacks patient-centred measures.

We describe a protocol for the development of a UK-based consensus on the key outcomes to measure in clinical trials of patients following a fracture of the hip; both those with and without cognitive impairment. This consensus will recommend a core outcome set (COS), which will include both clinical and patient-reported outcomes.

The objective of the study is to define a 'core outcome set 'for use in clinical trials involving patients with fracture of the hip where:

- Hip fracture is defined as any fracture of the proximal femur in a patient over the age of 60 years; including intracapsular, extracapsular and subtrochanteric fracture.[4]
- The outcome set will be designed for use in all clinical trials of pre-, peri- and post-operative interventions for patients with hip fracture.

METHODOLOGY

Summary

An agreed methodology for the best approach to achieve consensus on a core outcome set for use in clinical trials does not exist. However, evidence suggests that a more formal, explicit approach is preferable,[5] for example, (modified) Nominal Group Techniques (NGT), Delphi methods, or a Consensus Development Conference.

We have integrated key aspects of the modified NGT (RAND version)[5-8] with an approach towards achieving consensus in core outcome sets described by the Outcome Measures in Rheumatology and Clinical Trials (OMERACT) initiative.[9] This approach aims at deriving consensus from a group of experts through highly structured, facilitator-led discussion.[5-7] A flow diagram for the process is at Appendix A.

Aims

We aim to achieve consensus on the following questions:

- What core outcome domains must be included in clinical trials of patients with hip fracture?
- What outcome measures are most relevant and acceptable for the proposed domains?

Participants

Due to the relative uncertainty with regards to the proposed research questions, we have defined a heterogeneous group with whom to explore a consensus.[5, 8] Although little guidance exists regarding the appropriate number or composition of consensus groups, the target sample will be weighted to reflect the relative contributions of different health and social care groups to the treatment and rehabilitation of patients with fragility hip fracture.[8] A total of 24 participants have been invited to participate in the consensus process:

- End-users
  - » *Patient and public representatives*
- Health Care Professionals
  - » *Nurses*
  - » *Orthogeriatrician*
  - » *Trauma surgeons*
  - » *Anaesthetists*
  - » *Therapists*
  - » *General Practitioners*
- Clinical Research
  - » *Chief investigators*
  - » *Research managers and trial co-ordinators*
  - » *Research associates*
  - » *Statisticians*
  - » *Health Economists*
  - » *Mixed Methods Researchers*
  - » *Experts in Clinical Outcomes*
- NHS
  - » *Department of Health*
  - » *National Hip Fracture Database*
  - » *NHS Management*

- Other stakeholder organisations
  - » *Cochrane Bone Joint and Musculoskeletal Trauma Group*
  - » *National Institute for Health and Clinical Excellence*
  - » *Funding Bodies*

National Institute of Health Research INVOLVE guidelines[10] were followed in order to include appropriate patient and public representatives. The consensus meeting, a description of the work involved and the training and support available were advertised through the local Patient Advisory Liaison Service[11] and on the website People in Research.[12] Additionally, a formal application for interested persons was made to the University of Warwick University/User Teaching and Research Action Partnership (UNTRAP).[13]

A list of the proposed members of the consensus panel is at Appendix B..

Methods

We describe three key stages:[5-9]

Stage 1 Preparation of information for participants.

Stage 2 Postal completion of nominal group questionnaire with rating of candidate domains and outcome measures.

Stage 3 Nominal Group Consensus meeting — discussion of scores, candidate domains and outcomes, and arrival at a final consensus.

Stage 1: Preparation of information for participants

Synthesis of research evidence in support of domain and outcome measure selection

An evidence synthesis of research undertaken in advance of the consensus meeting — patient/carer dyad interviews, focus groups, and systematic reviews of patient-reported and performance outcome measures — will be produced and presented in summary format.[5, 9] In addition, the synthesis will include the current NHFD dataset.

Generation of candidate domains and potential outcome measures for the nominal group questionnaire

A questionnaire listing candidate domains and outcome measures will be developed.[5-8] The questionnaire will have two key sections:

a) What to measure: potential outcome domains and definitions

The results of an interview study of patient/carer dyads and focus groups with health professionals conducted in hospital and community settings will inform the generation of a list of key domains regarded as important to outcome assessment following hip fracture. Overlap and discrepancies between data sources will be highlighted. This list will be supplemented by additional outcome domains identified from the NHFD dataset, and the systematic review of PROMs evaluated following completion by people sustaining a fragility hip fracture.

The proposed core domains will be underpinned by reference to the International Classification of Functioning, Disability and Health Framework (ICF).[14] The ICF is a classification of health and health-related domains classified from body, individual, and societal perspectives. The conceptual framework will assist in the definition of domains that may be of relevance to our population.[15]

b) How to measure: potential methods of assessment

A short-list of candidate ('best evidence') outcome measures will be produced which map against the list of potential outcome domains,[16] and reflect both PROM-based and clinical-based approaches to assessment.

The short-list of PROMs will be informed by two systematic reviews of PROM quality, relevance and appropriateness in firstly, older people in general and secondly older people with hip fracture. Additional systematic reviews of alternative outcome measures used with older people, such as physical activity questionnaires, will also be reviewed.[17]

Clinical-based outcome measures will be listed from the NHFD dataset, as described above.

Response options

Each participant will be invited to rate the relative importance of each domain, as well as the relevance and feasibility of each outcome measure for clinical trials of patients with a hip fracture.

What to measure?

Domain importance ratings will be made on the GRADE[18] scale, a 9-point Likert scale (1 to 3 = not important; 4 to 6 = important; ; 7 to 9 = critical). Importance will be defined as 'how important is it that this domain of measurement is included in a future core outcome set for clinical trials of hip fracture?'

How to measure?
Participants will be asked to indicate if they are familiar with the outcome measure (yes/no). If yes, they will be asked to consider if it is feasible to collect the measure within the context of clinical trials (yes/no), and to consider if the synthesised measurement properties (i.e. reliability, validity, responsiveness) were adequate (yes/no). The relevance and feasibility of the measures to each domain (content) will then be rated on separate 9-point GRADE[18] scales (1 to 3 = not relevant / not feasible; 4 to 6 = relevant/ feasible; 7 to 9 = most relevant / highly feasible).

The research team will be responsible for developing and agreeing the content of the evidence synthesis and questionnaire. The questionnaire content will be piloted with stakeholders representative of the proposed survey group (n=5; to include a patient, clinician, nurse, methodologist/ researcher).

Stage 2: Postal completion of nominal group questionnaire with ranking of candidate domains and outcome measures
Each member of the consensus group will receive the evidence synthesis and questionnaire three weeks in advance of the Nominal Group Consensus meeting. A structured agenda will be included so that participants are aware of the purpose of the meeting, the requirements for completion of the enclosed questionnaire and the subsequent Nominal Group Consensus meeting.

Participants will be asked to return all completed questionnaires in advance of the meeting to allow results to be collated. Where appropriate, participants will be encouraged to provide additional comments or contributions to the candidate lists of domains and outcome measures for further discussion at the meeting. The distribution of ratings for each domain and outcome measure will be summarised; including the group median and interquartile range for each outcome on a line below the Likert scale, together with a reminder of their own personal score for each outcome. The results will be given to each participant at the beginning of the Nominal Group Consensus meeting.

Stage 3: Nominal Group / Consensus meeting – discussion of ratings, candidate domains and outcomes, and arrival at a final consensus
A one-day Nominal Group Consensus meeting will be held. The meeting will seek to converge on a common view on the core outcome set to be included in all clinical trials involving patients with hip fracture. The meeting will be structured into three discrete sections:[8,9]

First, the evidence synthesis will be re-presented to, and considered by, representatives of the stakeholder groups. In addition, the pre-meeting median ratings of potential domains and outcome measures will be presented. Additional domains or outcomes highlighted by participants will also be included. Copies of all candidate measures will be made available at the meeting. Participants will be advised to consult the detailed summary of evidence provided in advance of the meeting at this stage.[8]

Second, a semi-structured group discussion will be facilitated by a trained, independent chair with experience of such meetings. Participants from each of the stakeholder groups (patients and public, healthcare professionals, clinical researchers and other stakeholder organisations) will be assigned into two break-out groups. Both groups will address the same key research questions. Each group will include a moderator to smooth the group process and to allow everyone's opinion to be heard and to help the reporter to summarise the group session. Participants will be given the opportunity to explore core domains, re-write and add potential domains and associated definitions, to explore reasons for any differences in ratings, and to consider candidate outcome measures.[5-9]

After the group sessions, the moderator and reporter of each break-out group will quickly prepare their report to feedback at the summary session at the end of the conference in advance of the final voting.

Finally, a plenary session will be convened and the results from both group sessions fed back to all participants. The chair of the session will endeavour to engage all participants in a discussion that focuses on the key research questions and key points identified by the groups.

The group will then be invited to consider firstly the domains and secondly the outcome measures again. They will be asked to vote as to whether each domain (yes/no) and each outcome measure (yes/no) should be included in the proposed core outcome set, using a secure interactive voting process.

Although all votes will be made in private and independently, the level of agreement will be immediately communicated via the voting procedure.[9] If 70% of the participants indicate that the domain/measure should be included then this domain/outcome measure will form part of the proposed core outcome set.

The group will be sent a draft report to confirm whether views have been appropriately captured before the final report is produced.

ADDITIONAL INFORMATION

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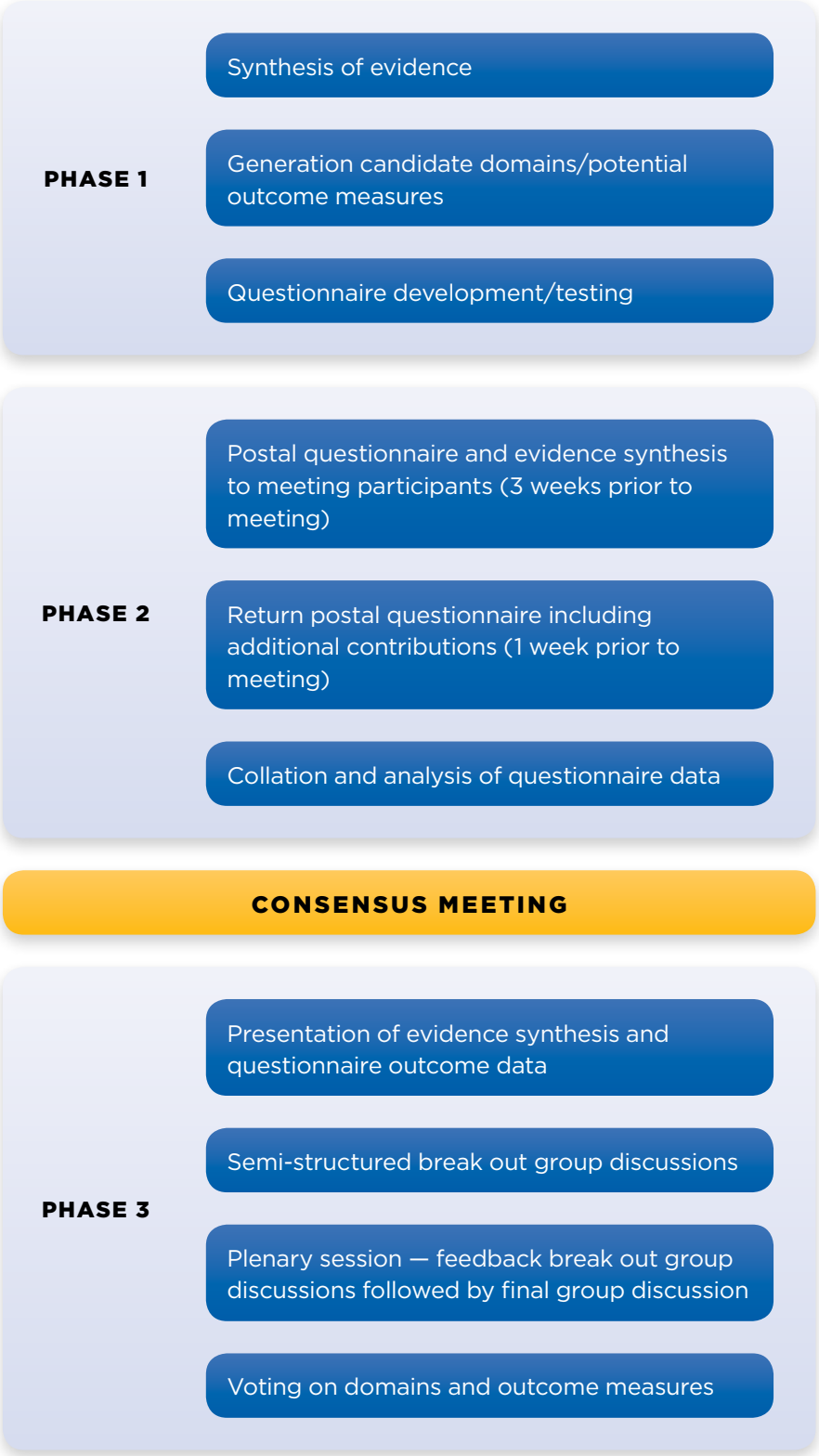
Conflict of interests None declared.

Contribution XLG, KLH, JA and MLC contributed to the design of the study, XG and KLH wrote the manuscript, JA and MLC provided critical revisions.

REFERENCES

1. Johnell O, Kanis J. An estimate of the worldwide prevalence, mortality and disability associated with hip fracture. Osteoporosis International. 2004; **15**(11): 897-902.
2. Mease PJ, Arnold LM, Crofford LJ, Williams DA, Russell IJ, Humphrey L, et al. Identifying the clinical domains of fibromyalgia: contributions from clinician and patient Delphi exercises. Arthritis Rheum. 2008; **59**(7): 952-60.
3. Williamson PR, Altman DG, Blazeby JM, Clarke M, Devane D, Gargon E, et al. Developing core outcome sets for clinical trials: issues to consider. Trials. 2012; **13**: 132.
4. National Hip Fracture Database. [cited 26/11/2012]; Available from: http://ww.nhfd.co.uk
5. Murphy MK, Black NA, Lamping DL, McKee CM, Sanderson CF, Askham J, et al. Consensus development methods, and their use in clinical guideline development. Health Technol Assess. 1998; **2**(3): i-iv, 1-88.
6. Vella K, Goldfrad C, Rowan K, Bion J, Black N. Use of consensus development to establish national research priorities in critical care. BMJ. 2000; **320**(7240): 976-80.
7. Sarre G, Cooke J. Developing indicators for measuring Research Capacity Development in primary care organizations: a consensus approach using a nominal group technique. Health Soc Care Community. 2009; **17**(3): 244-53.
8. Fitzpatrick R, Chambers J, Burns T, Doll H, Fazel S, Jenkinson C, et al. A systematic review of outcome measures used in forensic mental health research with consensus panel opinion. Health Technol Assess. 2010; **14**(18): 1-94.
9. Tugwell P, Boers M, Brooks P, Simon L, Strand V, Idzerda L. OMERACT: an international initiative to improve outcome measurement in rheumatology. Trials. 2007; **8**: 38.
10. National Institute of Health Research. INVOLVE Guidelines. [cited 30/11/2012]; Available from: http://www.invo.org.uk/resource-centre/resource-for-researchers
11. National Health Service. Patient Advice and Liasion Service. [cited 30/11/2012]; Available from: http://www.pals.nhs.uk
12. People in Research. [cited 26/11/2012]; Available from: http://www.peopleinresearch.org
13. University of Warwick University/User Teaching and Research Action Partnership. [cited 26/11/2012]; Available from: http://www2.warwick.ac.uk/fac/cross_fac/healthatwarwick/untrap
14. Organisation WH. International Classification of Functioning, Disability and Health (ICF). Geneva; 2001.
15. Hoang-Kim A, Beaton D, Bhandari M, Kulkarni AV, Schemitsch E. The Need to Standardize Functional Outcome in Randomized Trials of Hip Fracture: a Review Using the ICF Framework. Journal of orthopaedic trauma. 2012.
16. Mease P, Arnold LM, Choy EH, Clauw DJ, Crofford LJ, Glass JM, et al. Fibromyalgia syndrome module at OMERACT 9: domain construct. J Rheumatol. 2009; **36**(10): 2318-29.
17. Forsen L, Loland NW, Vuillemin A, Chinapaw MJ, van Poppel MN, Mokkink LB, et al. Self-administered physical activity questionnaires for the elderly: a systematic review of measurement properties. Sports Med. 2011; **40**(7): 601-23.
18. The Grading of Recommendations Assessment, Development and Evaluation Working Group. GRADE Guidelines. [cited 30/11/2012]; Available from: http://www.gradeworkinggroup.org/index.htm

Appendix A Study Flow Diagram



Appendix B Nominal Group Consensus Panel Members

NAME
Mr Phil Glanfield (Chair)
Mrs Pauline Fenwick-Wilson
Mrs Karen Keates
Mr Alwin McGibbon
Mrs Filo Eales
Dr Neil Pendleton
Mr Martin Parker
Dr Stuart White
Prof Sallie Lamb
Prof Martin Underwood
Prof Frances Griffiths
Prof Ray Fitzpatrick
Dr Nick Parsons
Prof Stavros Petrou
Dr Juul Achten
Dr Becky Kearney
Dr Kirstie Haywood
Prof Keith Willett
Mr Sam Keong
Prof Chris Moran
Dr Colin Currie
Mr Xavier Griffin
MrTim Chesser
Prof Ian Pallister
Dr Sarah Smith