Abstracts from Invited Speakers

I-1 OARSI AND NICE: ARE THEY BETTER THAN PREVIOUS GUIDELINES?

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Purpose: In recent years guidelines for the treatment of osteoarthritis (OA) have been criticised for lack of methodological rigour, stakeholder involvement and applicability. The Osteoarthritis Research Society International (OARSI) has recently published global evidence-based, expert-consensus treatment guidelines for OA hip and knee [1,2]. The National Institute for Health and Clinical Excellence (NICE) has also recently published a National Clinical Guideline for the Care and Management of OA in the National Health Service (NHS) in Great Britain [3]. The aim of this study was to attempt to assess whether the OARSI and NICE recommendations were any better than previous guidelines.
Methods: The quality of the guidelines was assessed using the AGREE (Appraisal of Guidelines for Research and Evaluation) instrument and standardised percent scores for scope, stakeholder involvement, rigour, clarity, applicability and editorial independence, as well as overall quality were calculated. Assessments were undertaken by an international panel of 7 independent experts from a variety of health professional disciplines. Scores were also compared with AGREE appraisals of the OARSI guidelines undertaken by 4 scientists from the American Academy of Orthopaedic Surgeons (AAOS) and with the appraisals of the 23 previously published guidelines [2].
Results: Both OARSI and NICE guidelines had higher scores for each domain of quality than previously published guidelines. The OARSI recommendations scored higher than the NICE guidelines for methodological rigour (70% v 59%), editorial independence (75% v 48%) and overall quality (58% v 50%), but had lower scores for stakeholder involvement (42% v 49%), clarity (59% v 64%) and especially applicability (22% v 43%).
Conclusions: Appraisals of the OARSI and NICE guidelines suggest that they are better in overall quality and in most quality domains than previous guidelines. Nevertheless the quality of both could be significantly improved by wider stakeholder involvement and greater attention to applicability. This is clearly a greater challenge for globally applicable international guidelines than it is for a national guideline. The OARSI guidelines can be adapted for national and regional application through translation and liason with patients and professional groups representing stakeholders in primary and secondary care worldwide [1].

References

[1] 1. Zhang W et al *Osteoarthritis and Cartilage* 2008; 16: 137–62.
[2] 2. Zhang W et al *Osteoarthritis and Cartilage* 2007: 15: 981–1000.
[3] 3. National Collaborating Centre for Chronic Conditions. adults. Osteoarthritis: National clinical guidelines for care and management in http://www.nice.org.uk/nicemedia/pdf/CG059FullGuideline.pdf

I-2 NEW EVIDENCE 2006–2008: WHAT IMPACT ON CURRENT RECOMMENDATIONS?

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Purpose: The Osteoarthritis Research Society International (OARSI) developed global, evidence-based consensus treatment guidelines for osteoarthritis (OA) of the hip and knee based on a systematic review (SR) of the literature up to January 2006 [1,2]. Since then a large number of new studies have been published. This study was designed to update the evidence and to examine whether the more recent evidence would influence the profile of recommendations for core therapies for OA.
Methods: A systematic literature search was undertaken for new guidelines, SRs, randomised controlled trials (RCTs) and economic evaluations (EEs) published between 31 January 2006 and 31 January 2008. The quality of guidelines was appraised by an independent group of experts and the core set of treatment modalities was determined by the level of evidence and the frequency of recommendations. The quality of the RCTs included in the SRs and of others retrieved from the literature search were appraised, and where possible effect size (ES), number needed to treat (NNT), relative risks (RR) or odds ratio (OR) and cost per quality adjusted life years (QALY) gained were estimated. Statistical pooling was undertaken as appropriate. Sensitivity analysis and cumulative meta-analysis were conducted to examine the impact of studies published after 2006 and the stability of the effect.
Results: The literature search yielded 1347 citations in the last 2 years. Of these 2 guidelines, 57 SRs, 200 RCTs and 16 EEs met inclusion criteria. Core therapies, defined as treatments supported by Ia level evidence and a recommendation by all guidelines which addressed that therapy, remained unchanged. These included exercise, education, self-management, acetaminophen and COX-2 selective or non-selective NSAIDs with PPI. Whilst the evidence for weight reduction was upgraded from Ib to Ia, the frequency of recommendations for joint lavage was reduced from 100% to 75%. ES changed with inclusion of additional trials. For example the ES for pain relief was reduced from 0.21 (95% CI 0.02, 0.41) to 0.18 (0.04, 0.33) for acetaminophen, but was increased from 0.13 (−0.12, 0.38) to 0.20 (0.06, 0.33) for weight reduction. Cumulative meta-analysis indicated stability of efficacy for some therapies (eg, NSAIDs) but not for others (eg, glucosamine and chondroitin sulphate). New treatment modalities such as celecoxib plus PPI and Tai Chi exercise had been assessed in RCTs. Cost per QALY had been estimated for behavioural graded activity, class based exercise, unicompartment knee arthropathy, and hip versus knee replacements.
Conclusions: Recent research evidence has resulted in changes in the calculated risk-benefit ratio for some treatments for osteoarthritis. The rapid increase of new evidence presents challenges to guideline developers. A regularly updated, evidence-based osteoarthritis research database of well characterised trials of all modalities of treatment for OA would be very useful.

References

[1] 1. Zhang W et al *Osteoarthritis and Cartilage* 2008; 16: 137–62.
[2] 2. Zhang W et al *Osteoarthritis and Cartilage* 2007: 15: 981–1000.

I-3 IS BEST AVAILABLE EVIDENCE THE BEST?

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Purpose: Evaluation of some of the pitfalls associated with comparisons of the numerous interventions used in osteoarthritis management.
Methods: Literature review of systematic reviews and overviews with sensitivity analysis of patient selection bias, interpretation of effect estimates, level of evidence and strength of recommendation in osteoarthritis.
Results: Guidelines are often seen as the end results of a stringent synthesis of the available literature. However, the picture of an unblemished and rigorous scientific method for synthesizing scientific evidence has been taking several blows lately. The method quality scoring of randomized controlled trials (RCT) has proved less reliable than we hoped for, and the interpretation of meta-analyses with mixed results seems unreliable even among experienced reviewers. Methods for grading levels of evidence are drifting from quantification of a number of well-designed RCTs or a single meta-analysis number to achieve the highest evidence level, to qualitative evaluation of the likelihood for future change in evidence. And recommendations are subject to a qualitative balancing act of benefit and harms. Guidelines can be seen as an anchor point on a continuous line from (a) perfect consensus of experts on one side

to, (b) the result of hard quantitative data on the other side. If we use the perfect consensus model, then we are back to where evidence-based medicine (EBM) started twenty years ago. EBM proponents then demanded that clinical experts should step down as review authors because of their notoriously unsystematic evaluations of the literature. In this perspective, a high level of consensus may rather be a measure of the opinions among stakeholders, than synonymous with best evidence. On the other hand, we still struggle with the handling of quantitative data to make trustworthy comparisons across interventions.

A systematic review of non-steroidal anti-inflammatory drugs (NSAID) in knee osteoarthritis which we performed, can serve as an example of the difficulties associated with quantitative data. We found that some trials only recruited known responders to NSAID who had 49.4% higher effect size compared to patients in trials which did not. The inflated effect size in the subgroup of biased trials, led to an overall inflated effect size by 24.3%. This fact hampers valid comparisons between NSAID and other interventions. Because of the strict exclusion of co-interventions in most NSAID-trials, there is also a lack of data for the effect of NSAID in combination with potentially effective exercise therapy. There are examples of trials with other interventions which do the opposite, and recruit known non-responders in addition to allowing effective co-interventions. Comparisons across interventions may then be flawed.

Conclusions: There is still a way to go before we can be satisfied with our methods for synthesizing best evidence. When a consensus-oriented approach is selected, it seems important to balance guidelines developer groups with involved stakeholders. If best evidence is sought from hard quantitative data, more attention should probably be paid to differences in patient selection criteria, intervention characteristics and allowed co-interventions.

I-4 RESOURCES FOR FUTURE GUIDELINES & RESEARCH: AN OARSI 'TOOLBOX' AND AN 'EVIDENCE-BASED OA RESEARCH DATABASE' (EBOARD)

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Purpose: More than 50 pharmacological, non-pharmacological and surgical therapies are available for treating osteoarthritis (OA) [1] and there are now 25 published guidelines for the management of OA. The Osteoarthritis Research Society International (OARSI) has recently published 25 recommendations for the management of hip and knee OA [2]. However guidance for patients and clinicians on the order in which such treatments, or combination of treatments, should be offered is much less secure. While ***algorithms*** are frequently promulgated as simple aids to guide physicians and patients through the welter of options, evidence to support the use of one treatment prior to another is rarely available, The clinical application of algorithms is also restricted by the need to tailor treatment to the individual patient depending on the severity of symptoms, the stage of disease, the presence of comorbidities, the risk of side effects and the use of other drugs, etc.

An alternative approach which OARSI is developing is a ***toolbox*** containing all effective treatment options. This is more flexible to apply and in many instances better supported by research evidence. It also has the advantage that decisions to use one and/or another recommended treatment is made by the users themselves, rather than by the guideline developers.

The relevance and utility of treatment guidelines is also time limited by the rapid accumulation of new research evidence. Risk-benefit ratios for some therapies currently recommended by OARSI have already changed and some of the differences in the recommendations for the treatment of OA contained in the NICE guidelines published in February 2008 [3] are attributable to such new research evidence. So which guidelines should one follow and how should one assess and weight the quality of evidence? While one can criticise the OARSI guidelines for pooling results from all RCTs regardless of quality, one must also be aware of potential bias when different quality criteria are used for determining recommendations for different modalities of therapy. It is, however, impossible to apply the same quality criteria to all modalities of therapy unless all individual trials are collected and characterised.

We therefore propose to develop an **E**vidence based **OA R**esearch **D**atabase **(eBOARD).** This will be a comprehensive and coherent database of well characterised trials of all modalities of treatment for OA. In addition to containing details of patient demographics, disease characteristics and treatments it will include quality assessments using a single, standard instrument and measures of outcomes such as ES, NNT, RR/OR and cost/QALY. The database will be updated annually with the key messages and summary statistics for each therapy. We believe that this database will be useful for (1) developing and updating treatment guidelines; (2) answering specific clinical questions concerning the efficacy or side effects of any modality of therapy; undertaking evidence based research, such as meta-analysis, sensitivity analysis, and cumulative meta-analysis. It will also provide an unconstrained hypothesis-free database of OA therapy that can be used to generate and test new hypotheses.

References

[1] 1. Zhang W et al *Osteoarthritis and Cartilage* 2008; 16: 137−62.
[2] 2. Zhang W et al *Osteoarthritis and Cartilage* 2007: 15: 981–1000.
[3] 3. National Collaborating Centre for Chronic Conditions. Osteoarthritis: National clinical guidelines for care and management in adults. http://www.nice.org.uk/nicemedia/pdf/CG059FullGuideline.pdf-.

I-5 MOVING FROM GUIDELINES TO STANDARDS OF CARE

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Purpose: Treatment guidelines are designed to assist clinical decision-making by defining a set of optimal patient care strategies. The best treatment guidelines are evidence-based, but there are often limitations in the availability of data from clinical trials to inform their development. Guidelines are therefore frequently a combination of expert opinion and the best available evidence.

What are the next steps after the development of treatment guidelines? Ideally, guidelines also identify gaps in knowledge and areas where more evidence would be helpful. Guidelines need to be disseminated to the target audience of providers. Effective dissemination often requires a multi-pronged approach.

The ultimate goal of treatment guidelines is to improve the quality of care for a given condition through improved patient outcomes, enhanced physician efficiency and/or greater health system productivity. Quality indicators or performance standards are designed to define a minimally acceptable level of care. Quality indicators may address a combination of overuse, underuse or misuse of diagnostic and/or treatment modalities. Quality indicators should be relevant, have scientific validity and be feasible for implementation into clinical practice.

Methods: Quality indicators are used to assess the quality of care delivered by providers, hospitals, health systems and/or other health care organizations. Benchmarking can be used to summarize the performance of a specific group of entities on a set of quality indicators to identify the highest and lowest performing entities. Quality indicators can also be used to identify/define/recognize the highest quality providers or health systems. Risk adjustment may be needed to control for differences in case-mix among providers or health systems.

Quality improvement is based on measurement. A performance measure is a set of technical specifications that define how to calculate a "rate" for a particular quality indicator. This rate is equivalent to the numerator, or number of eligible patients who meet the quality indicator divided by the denominator, or number of patients who meet inclusion criteria minus the number of patients excluded due to medical, patient, or health system reasons.

Results: The development of quality indicators is similar to the process of developing treatment guidelines. A priority area is identified; a panel of experts is convened; the available evidence is summarized through a literature review; a draft set of measures is defined; the expert panel evaluates the draft set of measures; specifications are developed to define the numerator of eligible patients who meet the quality indicator, the denominator of patients who meet inclusion criteria, and potential reasons for excluding patients from the denominator. The performance measure undergoes field-testing to assess feasibility.

Conclusions: Existing examples of quality indicators for knee and hip osteoarthritis will be presented.

I-6 RISK STRATIFICATION FOR OA PROGRESSION

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Purpose: The medial compartment of the knee is the most common site of involvement in knee OA, and has been the subject of the most previous studies in this context. Although many joint structures are affected in OA, OA manifests prominently in the articular cartilage. Traditionally the progression of knee OA has been assessed by measuring changes in the width of the space between the medial femoral condyle and medial tibial plateau on plain x-rays. More recently interest has grown in the