Proposal to develop EULAR Recommendations for the Prevention and Treatment of Osteoporosis associated with Inflammatory Musculoskeletal Conditions

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Objective

To develop recommendations for the prevention and treatment of osteoporosis associated with inflammatory musculoskeletal conditions that can be implemented in routine clinical practice by rheumatologists or internists across Europe.

Project group

Convenor
Professor Anthony D Woolf (UK)

Experts (tbc)
Dr Willem Lems (The Netherlands)
Prof Glenn Haugeberg (Norway)
Dr Luigi Sinigaglia, Milan / Dr Gerolamo Bianchi, Genoa (Italy)
Professor Christian Roux (France)
Professor Tore Kvien (Norway)
Professor Piet Guessens (Belgium)
Professor David Reid (UK- Scotland)
Professor Hans Bijlsma (The Netherlands)
Professor Gulya Poor (Hungary)
Professor Josef Rovensky (Slovakia)

Outside Europe:
Professor Philip Sambrook (Australia)
Dr Nancy Lane (USA)
Professor Ken Saag (USA)

Patient representative:
tbc

Clinical epidemiologist
Dr Terence O’Neill

Person supervising Literature Review
Dr Ken Stein, PENTAG*, Peninsula Medical School, Exeter, UK

* The Peninsula Technology Assessment Group (PENTAG) carries out independent Health Technology Assessments for the UK HTA Programme and other local and national decision-makers and has considerable experience in carrying out systematic reviews and meta-analyses, particularly of health care interventions, including Cochrane reviews.
Justification

Osteoporosis and increased risk of fracture is associated with several inflammatory musculoskeletal conditions (Sinigaglia et al 2006). Risk is reported as being increased in rheumatoid arthritis, and there are studies also showing an increased risk in ankylosing spondylitis, SLE, polymyalgia rheumatica and vasculitides. Corticosteroids are a major risk factor but other determinants of osteoporosis and fracture are related to the disease itself (inflammation), reduced physical activity, low BMI, increased risk of falls and other factors. Outcome following fracture is likely to be often worse because of compounded causes of disability. However the level of risk and the determinants of that risk of osteoporosis and fracture are not clearly established.

There is a body of evidence and evidence-based guidelines for various interventions for the prevention and treatment of osteoporosis and reduction in fracture risk in postmenopausal women and for corticosteroid-associated osteoporosis but much less evidence specifically acquired in those with osteoporosis associated with inflammatory musculoskeletal conditions, many of whom will not have received significant doses of corticosteroids and many who will be premenopausal or male. There are no agreed strategies for the prevention and management of osteoporosis in these situations.

Despite the existence of recommendations for the prevention and treatment of corticosteroid-associated osteoporosis, audits have shown that these are seldom implemented in routine clinical practice.

There is therefore a need for recommendations for the prevention and management based on a review of existing literature and expert opinion that can be readily implemented in everyday clinical practice across Europe.

The specific questions to be addressed

- What is the risk of osteoporosis and fracture associated with inflammatory musculoskeletal conditions
  - RA
  - Ankylosing spondylitis
  - SLE
  - Other connective tissue diseases and vasculitides
  - Polymyalgia rheumatica
- What are the determinants of any increased risk of osteoporosis and fracture
  - Disease-related
  - Related to consequences of disease eg reduced physical activity, low BMI
  - Related to treatment of disease eg corticosteroid
- Who is most at risk
- Evidence for interventions in target populations
  - Interventions
    - Lifestyle
    - Disease management
    - Pharmacological interventions
      - Bisphosphonates
      - Strontium ranelate
      - PTH
      - HRT
      - Other
    - Non-pharmacological
- Fall prevention
- other
  - Direct evidence in target populations (literature review)
  - Indirect evidence in other populations (review of guidelines)
- Who will benefit most from treatment (expert opinion supported by evidence)
- Developing algorithms / decision trees based on who is most at risk for whom an intervention will be most cost-effective (expert opinion supported by evidence)

Evidence base

The quantity and quality of evidence that addresses these questions is variable, with most related to rheumatoid arthritis and corticosteroid therapy. Recommendations will be made where it is considered that there is sufficient evidence of appropriate quality or where there is a consensus of expert opinion.

Literature search strategy

Literature searches will be undertaken focusing on key questions that have been agreed by the expert group. Original studies, systematic reviews (Cochrane), meta-analyses and guidelines will be identified. The likely questions are

- What is the risk of osteoporosis and fracture associated with inflammatory musculoskeletal conditions
- What are the determinants of any increased risk
- Who is most at risk
- Evidence for interventions in target populations
  - Direct evidence in target populations
  - Indirect evidence in other populations
- Who will benefit most from treatment

There may be insufficient data to develop recommendations for all of the different inflammatory musculoskeletal different conditions.

Quality scoring of the evidence

All scientific studies will be objectively scored. Systematic reviews must meet the Cochrane criteria. Guidelines must meet AGREE criteria.

The level of evidence to support any statement will be categorised (Ia to 4)

The literature review will be undertaken under the supervision of PENTAG and the Convenor.

Developing recommendations

Recommendations for the prevention and treatment of osteoporosis associated with inflammatory musculoskeletal conditions will be developed from the evidence where possible. However there are likely to be areas where evidence is deficient or contradictory and expert opinion will be considered. The strength of evidence supporting the recommendations will be made transparent by using a standard grading system (A to D).

Presentation and dissemination of recommendations

Algorithms in the form of decision trees will be developed. These will be similar to the format of other guidelines that exist for osteoporosis, such as in postmenopausal women or
with the use of glucocorticoids. These will be based on who is most at risk for whom an intervention will be most cost-effective. The use of a familiar style of format will improve the chances of the clinical use of the recommendations. The algorithms will also be piloted to ensure they are practical for use in a routine clinical setting. Clinician and patient information sheets will also be developed.

**Dissemination of recommendations**
The recommendations will be submitted for presentation at the Annual Congress of Rheumatology and for publication in the Annals of Rheumatic Diseases. They will also be submitted for presentation at osteoporosis related meetings (e.g., ECTS, WCO).

**Implementation of the recommendations**
An audit protocol will be developed that can be used to audit the uptake of the recommendations.

**Practical aspects**
An expert group of up to 18 people will be developed.
A fellow will be appointed to undertake the literature search.
3 meetings will be held at the EULAR House, Zurich.
The project duration will be a year.

**Financial aspects**
- Meeting costs: ? SF
- Grant for fellow: ? SF
- Statistical analysis: ? SF