Title:

EunetHTA guideline on data requirements for the assessment of health technologies used for the treatment of osteoarthritis of the hip and knee

EUnetHTA disease-specific guidelines aim to give recommendations about type of data to be produced during the development of technologies (initial evidence generation) to support relative effectiveness and cost-effectiveness assessment in a given condition.

Introduction:

Osteoarthritis (OA) refers to a clinical syndrome of joint pain accompanied by varying degrees of functional limitation and reduced quality of life due to chronic degenerative arthropathy. It is by far the most common form of arthritis and one of the leading causes of pain and disability worldwide. Any synovial joint can develop osteoarthritis but knees, hips and small hand joints are the peripheral sites the most commonly affected. Although pain, reduced function and participation restriction are important consequences of osteoarthritis for a patient, structural changes commonly occur without accompanying symptoms. Such frequent discordance between osteoarthritis structural changes, symptoms and disability means that each of these need separate consideration in the development of osteoarthritis treatments.

Osteoarthritis is a metabolic dynamic process that involves all joint tissues (cartilage, bone, synovium/capsule, ligaments and muscle). Key pathological changes include localised loss of articular (hyaline) cartilage and remodelling of adjacent bone with new bone formation (osteophyte) at the joint margins.

Osteoarthritis is a common complex disorder with multiple risk factors. These risk factors could be broadly divided in:

- genetic factors (heritability estimates for hand, knee and hip osteoarthritis are high at 40–60%, though the responsible genes are largely unknown)
- constitutional factors (for example, ageing, female sex, obesity, high bone density)
- Other factors, largely biomechanical risk factors (for example, joint injury, occupational/sport usage, reduced muscle strength, joint laxity, and joint mal-alignment).

Importantly, many risk factors are reversible (for example, obesity, muscle weakness) or avoidable (for example, occupational or recreational joint trauma) which has important implications for primary and secondary prevention. According to risk factors and their influence on disease progression in different locations, treatment success at one joint site can not necessarily be extrapolated to all joint sites. Therefore, specific trials should be designed and conducted for different OA joint sites.

Current treatments of hip and knee OA can be broadly divided in non-pharmacological and pharmacological. Among the former we could find non-invasive treatments such as: exercise and manual therapy, weight loss, electrotherapy, aids and devices,

nutraceuticals, and invasive treatments such as arthroscopic debridement for knee osteoarthritis. Among the latter, main treatments are: topical treatments, oral analgesics, NSAIDs, highly selective COX-2 inhibitors and intra-articular injections. Pharmacological treatments aim to improve symptoms such as pain or disability or to slow or prevent structural damage and thus progression of the pathology.

Objective and scope (problem statement): The scope of this EUnetHTA guideline is to raise relevant issues related to the clinical evaluation and provide non-binding recommendations on evidence requirements for the clinical and cost-effectiveness assessment of health technologies (including drugs, medical devices and procedures) intended to be used for the treatment of OA of the hip and knee before considering joint replacement.

Discussion on items of interest

Current treatments (pharmacological and non-pharmacological) have been evaluated according to a variety of health outcomes measures and endpoints. Some trials define a dichotomous endpoint of clinically significant pain relief as improvement having been achieved above a specific threshold on a pain score. However, there is no standard threshold and each such trial should be individually considered. Moreover, some endpoints and time points of maximum effect for treatments have been recently established but not agreed among different parties and stakeholders. Functional disability is considered as an important co-primary variable and validated disease-specific and joint-specific instruments should be used to measure it. Finally, in order to establish cost-effectiveness comparisons quality of life measurements both specific and generic together with appropriate utility measures are proposed to be considered as endpoints in OA trials.

Specific points to be addressed (including options for solutions when applicable)

The guideline on osteoarthritis will address the following topics and issues:

- Diagnosis of the disease (clinical, imaging, metabolic and/or genetic diagnosis)
- Patients' characteristics and selection of relevant patient populations.
- Primary and secondary endpoints of interest according to joint sites, risk factors and characteristics of patients.
- Methods/measurements and scales to be used for primary and secondary endpoints.
- Treatment comparators
- Time points to assess maximum effect for treatments.
- Types of studies to be designed and possible comparators.
- Adverse events to be monitored and follow-up periods.

Timetable for release of draft and final disease specific guideline

Final agreed concept paper will be available in September 2013, after public consultation. The first guideline draft will be elaborated in December 2013. Second draft will be elaborated by February 2014 and opened to further discussion. Final draft will be considered for public consultation in March-April 2014.

Specific interested parties potentially affected by this particular topic to be identified for appropriate consultation

1. HT assessors in national HTA agencies
2. **Healthcare professionals**.
    a. Family Physicians and their Associations,
    b. Orthopaedic Surgeons and their Associations
    c. Rheumatologists and their Associations.
    d. Associations of physiotherapist and of specialists in non traditional medicine.
3. **Patients** with osteoarthritis and relatives.
4. **Service providers**. Specifically National, Regional Health Services
5. **Industry and manufacturers**: Specifically Medical Devices Associations – EUCOMED and Pharma Industry Associations EFPIA, AESGP (European Self-Medication Industry Association) Biotechnological Companies Associations EuropaBIO as well as individual companies.

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