Comparative effectiveness of Tumor Necrosis Factor alpha inhibitors (TNFi) in ankylosing spondylitis: a Bayesian network meta-analysis

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Review question(s)
The purpose of this study is to compare the efficacy and safety of five tumor necrosis factor alpha inhibitors (TNFi) in treatment of ankylosing spondylitis.

Searches
We conducted a systematic search of PubMed, EMBASE and Cochrane Database for published randomized control trials of TNFi in ankylosing spondylitis up to May 20th, 2014 in all languages, and supplemented it with manual searches of reference lists from previous systematic review articles.

Types of study to be included
Inclusion criteria:
- Adult Patient fulfills the modified New York criteria for diagnosis of ankylosing spondylitis;
- intervention: TNFi; comparator: placebo or a different TNFi;
- Randomized controlled trials.

Exclusion criteria:
- Case series, case report;
- Abstract, unpublished data;
- studies on Axial SpA, if a subgroup analysis of AS was not reported.

Condition or domain being studied
ankylosing spondylitis

Participants/ population
Adults diagnosed with ankylosing spondylitis, defined by modified New York criteria.

Intervention(s), exposure(s)
TNFi, including adalimumab, certolizumab, etanercept, golimumab, infliximab. Concomitant use of non-steroidal anti-inflammatory drugs, corticosteroid, non-biologic immunosuppressants, such as methotrexate, sulfasalazine, hydroxychloroquine, is allowed.

Comparator(s)/ control
placebo or a different TNFi.

Outcome(s)
Primary outcomes
BASDAI and BASFI
at week 12 and week 24

Secondary outcomes
ASAS20;
CRP;
BASMI;

Number of adverse events, including adverse events, serious adverse events, serious infections, and tuberculosis.

Data extraction, (selection and coding)
Literature review and data extraction were done by two independent reviewers. Any disagreement was resolved by discussion. Extracted data included study design, participant characteristics, and relevant outcomes.

Risk of bias (quality) assessment
We used the Cochrane Collaboration’s tool for assessment of risk of bias. This tool addresses six domains, including sequence generation, allocation concealment, blinding, incomplete outcome data, selective reporting and other sources of bias. Each study was scored on these domains, as high, low or unclear risk of bias. Studies that have high risk of bias will be excluded in sensitivity analysis.

Strategy for data synthesis
Bayesian network meta-analysis will be carried out to synthesize the results from the studies. This will be implemented using Markov Chain Monte Carlo (MCMC), via the R package gemtc (http://cran.r-project.org/web/packages/gemtc/index.html). We assume consistency (i.e., indirect effects can be derived from differences in the corresponding direct effects) during modeling. The relative effect sizes are reported as posterior mean differences along with 95% credible intervals. Drug rankings are derived from the MCMC results by evaluating the rank of each drug at each MCMC iteration based on size of the effect of the drug compared to placebo, and evaluating the relative frequency of each ranking over the MCMC iterations. We modify the standard ranking method by having two drugs have the same rank if the drug with the larger effect size is within 10% of the effect size of the second drug.

Analysis of subgroups or subsets
We will examine the treatment effects by baseline duration of AS, baseline BASDAI and CRP, and year of study to investigate if temporal trends in severity varied over time and affected relative effect sizes.

Dissemination plans
Conference and Journal publication.

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**Anticipated completion date**
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Intramural Research Program, National Institute of Arthritis and Musculoskeletal and Skin Diseases, NIH

**Conflicts of interest**
None known

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English

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United States of America

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Subject indexing assigned by CRD

**Subject index terms**
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**Stage of review**
Ongoing

**Date of registration in PROSPERO**
15 October 2014

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15 October 2014

**Stage of review at time of this submission**

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