Author’s response to reviews

Title: Trends in diagnostic prevalence and treatment patterns of male and female ankylosing spondylitis patients in the United States, 2006-2016

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Author’s response to reviews:

Thank you for the feedback. The following comments have been addressed in the revised version of the manuscript.

Reviewer 1:

1) The results on treatment patterns of male and female patients with ankylosing spondylitis are interesting. The results on the prevalence of AS are however less interesting because the authors mention in the discussion chapter that this is not the prevalence among the adult population but the prevalence among the employed and thus insured population only. Since unemployment may be larger among patients with AS than in healthy persons, their results must not be compared with results among the adult population.

   a. I clarified in the discussion that this study did not exclude unemployed patients, but may not be generalizable to patients who are uninsured or receive a different insurance not covered in this database.

2) That the prevalence results do not concern the adult population but employed persons only, should also be mentioned in the abstract and in the introduction, results and conclusion chapters. The small prevalence found in this study is nevertheless surprising.
A description of the database has been added to the abstract introduction results and conclusion sections.

3) In line 14 of page 5, “adult patients” should be replaced by “employed and insured persons”.
   a. This has been updated.

4) In reference 2 and reference 14, Landewe has to be replaced by Landewé.
   a. This has been updated.

5) In reference 3, fo has to be replaced by of.
   a. This has been updated.

6) In many references, the usual order of year;volume number:pages has to be regarded.
   a. This has been updated

7) In reference 9, assessment has to be replaced by Assessment.
   a. This has been updated.

8) In reference 11, Van Der Heijde has to be replaced by van der Heijde.
   a. This has been updated.

9) In reference 13, Heijde has to be replaced by van der Heijde.
   a. This has been updated.

10) In reference 17, Rheumatology 2014;4(12) has to be replaced by BMJ Open 2014;4(12):e006634.
a. This has been updated.

Reviewer 2: This study assessed the annual AS diagnostic prevalence in a US adult population using the IBM MarketScan® for the period from 2006 to 2016 based on the ICD diagnostic codes for AS. The authors found quite a low prevalence estimate for AS (0.09% in 2016), which is considerably lower than the previously reported diagnostic prevalence of AS using another US population registered in another database.

The authors did not attempt to test the validity of their approach and provided no data for the sensitivity and specificity of these ICD codes for a true diagnosis of AS. Therefore, the validity and reliability of the reported prevalence estimates are highly uncertain.

• These codes have been used in numerous AS studies to report diagnosis.

It is very probable that some of the patients who were using TNF-inhibitors actually might have had nr-axSpA, rather than AS, but were recorded with a diagnostic code for AS to meet the insurance coverage criteria, since nr-axSpA is not an approved indication for anti-TNF treatment in the US. This may have partially contributed to the increase in the rate of the use of TNF inhibitors, as well as in the prevalence of AS, diagnosis codes over the study period.

• This has been added to the discussion section.