Author's response to reviews

Title: Validity of gout diagnosis in Swedish primary and secondary care

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Author’s response to reviews: see over
To the editor of BMC Musculoskeletal Disorders

Here are the revisions made in the article “Validity of gout diagnosis in Swedish primary and secondary care” for publication in BMC Musculoskeletal Disorders. We have highlighted all changed text in the article in red.

**EDITORIAL REQUESTS:**

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- Please use initials to refer to each author's contribution.
  **Authors' contributions:** Please include an Authors' contributions section before the Acknowledgements and Reference list. For the Authors' contributions we suggest the following kind of
An "author" is generally considered to be someone who has made substantive intellectual contributions to a published study. To qualify as an author one should 1) have made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; 2) have been involved in drafting the manuscript or revising it critically for important intellectual content; and 3) have given final approval of the version to be published. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content. Acquisition of funding, collection of data, or general supervision of the research group, alone, does not justify authorship.

All contributors who do not meet the criteria for authorship should be listed in an acknowledgements section. Examples of those who might be acknowledged include a person who provided purely technical help, writing assistance, or a department chair who provided only general support.

Reviewer's report
Title: Validity of gout diagnosis in Swedish primary and secondary care
Version: 4
Date: 6 February 2015
Reviewer: Till Uhlig

We have added the following sentences to the Discussion: “The uncertainty of how representative our sample of patients with gout are to the total gout population is another limitation of this study, a question we are presently addressing as part of a large epidemiological study of gout prevalence in western Sweden.” (p 11, line 283-).
The better patients are assessed in the clinic the more likely it will be that they will be positive for any classification criteria set. Following this line, when several times an ICD-code for gout was registered, this could indicate both a higher likelihood that the patient really has gout. On the other hand the patient has been seen more often by the physician for possible gout and most likely more information is gathered and documented to reach a the necessary number of characteristics and thus the threshold for classification. The authors limit the window by only considering clinical information back to 2009. A more thorough review through the whole patient file would provide more clinical information, though that would require a lot more work. An important piece of information is that a registration of a ICD diagnosis of gout only once was alone not valid. Do the authors have reflections on how often mere coding errors could be involved (when the ICD code did not reasonably reflect the contents of the file)?

Interesting question, we identified and read all medical records with ICD 10 code for gout and found no cases of obvious coding errors.

I wonder why not exclusive categorization for ICD diagnoses was used: 1, 2, 3 or more. This would enable statistical comparisons. This and other statistics could provide information on where there were significant differences between practices and classification for gout.

We have now provided a supplementary table, Supplementary Table 1, where we statistically compare those who explicitly have one visit with a gout diagnosis to those with 2 or more. This statistical comparison shows that those with one main diagnosis had significantly lower PPVs compared to those with two more. The following sentences have been added to the Results: “Those with only one visit with a main diagnosis of gout compared to those with ≥2 visits had significantly lower PPVs (P ≤ 0.03) for all criteria evaluated (see Suppl Table 1).” (page 8, line 189-); “In similarity, but to a lesser degree than in the PC setting, the PPVs were significantly (P ≤ 0.02) lower in those with only one visit with a main diagnosis for gout compared to those with ≥2 gout diagnoses with exception of the Netherlands criteria (see Suppl table 1) (page 9, line 201-).

Minor
In the Methods section information should be given on the size of the general practitioners’ offices and on how many patients are yearly seen in the rheumatology outpatient department.

Thank you for a good comment, we have provided this information on page 6: “They both represent midsize PC clinics with 17000 (olskroken) and 8000 (Masthugget)
enlisted patients.” / and / “This clinic is a large rheumatology unit with approximately 7500 patients enlisted and 15000 outpatient appointments per year.”

In table 3 information on patient age could indirectly show to which degree a diagnosis of gout is related to time or to intensive care (several visits when first a diagnosis was made).

In the above mentioned Supplementary Table 1 we have provided the median age for the different groups with 1 or ≥2 visits with a gout diagnosis. Overall, those with ≥2 tended to be younger, but we find it difficult to further speculate about the mechanisms (more intensive follow-up, more frequent attacks etc) since we do not have detailed information regarding the possible explanatory factors.

It should be stated whether comorbidities in table 2 were assess by ICD diagnoses in the files or by reading them.

In the Methods section we define that “Comorbidity was considered to be present if it was mentioned in the clinical record or medication for the comorbidity was prescribed.” We have now added this information to Table 2.

New ACR/EULAR classification criteria are around the corner. They have been presented at the recent ACR congress in Boston/USA in November 2015 and are likely to be published within weeks or months. They do not specifically address chronic gout. Further some useful information on the strengths and weakness of existing classification criteria sets are given in the recent publication by Taylor et altera in Annals of the Rheumatic Diseases, online accessible October 2014.

Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests: I declare that I have no competing interests.

Reviewer's report
Title: Validity of gout diagnosis in Swedish primary and secondary care
Version: 4
Date: 10 February 2015
Reviewer: Frank Wollheim

Reviewer's report:
This is an valuable and interesting study of validity of criteria for gout in primary care and in a hospital based rheumatologic unit. It confirms the unfortunate nonor underuse of joint fluid examination among physicians and confirms apparent high validity of the Mexican and Dutch criteria which do not contain joint fluid examination. The study is based on routine hospital and primary care unit records. This reviewer would like the authors to clarify some points below.
Comments

1. It is stated that the primary care units were “randomly” selected. Please describe how this was done.

We selected two primary care units located in large apartment complex areas we deemed fairly representative of the city as a whole although knowing that we could never achieve any true representativeness. We have now omitted the word “randomly” and the text runs like this. “The two PC clinics were chosen from the 30 PC centers in Gothenburg. They both represent midsize PC clinics in average income areas with approximately 17000 (Olskroken) and 8000 (Masthugget) enlisted patients, respectively.” (page 6, line 120-)

2. It seems likely that some patients were referred from primary care to the only specialist unit. Please supply information on whether this applied to any of the 132 hospital cases

The majority of the 132 hospital cases were referred from primary care to the only specialist unit – 4 of these cases were also identified in the two primary care units under investigation. This has now been added to p6 line 134: “Only four patients included, were present in the patient selections from both PC and the rheumatology department.”

3. Page 4 line 49 “It mainly affects the lower extremities” Although this may be correct it I would rather stress that it may involve any joint and therefore be misdiagnosed and mixed with e.g. RA. Furthermore if the authors want to raise awareness they should present better characteristics of acute gout, e.g. the acute onset and the nocturnal onset etc.

Thank you for the comment! We have changed this to “It may affect any joint although most commonly in the lower extremities with nocturnal onset, where the inflammation generally subsides within two weeks.” (page 4, line 49-50).

4. P4, Line 53ff. The crystals should be intracellular

Thank you for this remark – the word “intracellular (IC)” has been added on page 4 Line 54-55 and page 5 Line 101 and in Abbreviations.

5. P5, Line 90: please specify the term “specialized”. It obviously includes primary care physicians, which in many countries would not be called “specialists”

Thank you for this comment. We have changed this to “In 2001, an outpatient register for specialized care (non-primary care) was added to the NPR” (page 5 Line 90-91).

6. P8, Lines 153 ff. Please define the term “attended”. –does it refer to the number of individuals who visited the units or the total catching population?

Thank you for this remark. The term “attended” refers to number of individuals enlisted at the primary care unit. We have changed this to: “who were enlisted to” this center during the study period, (page 8 Line 159 and 161).
7. The identification of 173 and 89 patients at the two primary care centers should not be extrapolated to indicate a prevalence of around 1% since one does not know the point prevalence, and thus one does not now what proportion of all gout individuals in the area actually were diagnosed. The same of course applies to the 132 cases identified at Sahlgrenska Hospital. Therefore one needs to discuss how representative the identified cases are for all patients with gout. The reviewer realizes that the answer to this question requires an epidemiologic study which is out of the scope of this report, but nevertheless the issue must be discussed and have implication on the conclusions regarding criteria validity. The authors touch upon the problem in the last paragraph of the discussion, P11, line 265

This is very true and in fact we have addressed this question in a large epidemiological study of gout prevalence in western Sweden which we are conducting now. To further emphasize this we have added the following sentence to the discussion: “The uncertainty of how representative our sample of patients with gout are to the total gout population is another limitation of this study, a question we are presently addressing as part of a large epidemiological study of gout prevalence in western Sweden.”, (page 11, Line 283-).

8. In view of the high prevalence of hypertension and cardiovascular disease, one would like to know what drugs they were treated with

Indeed an interesting point, although we have not recorded the specific drugs. We are however presently addressing this issue in a large register-based study in our region.

9. P10, lines 250 ff: “the administration of allopurinol may support the diagnosis of gout.” Does one mean the false diagnosis?

In the context, where it is mentioned in the article the interpretation is that allopurinol may indicate a possible true case of gout with efficient treatment over many years, therefore normal s-urate and no medical records of acute attacks of gout or what the gout diagnosis is based upon.

10. In table 3 one notes that patients with 3 gout diagnoses showed slightly lower validity with the Dutch criteria. Chance?

Considering the data we see no obvious explanation for this, but would as the reviewer suggest consider reflecting chance.

Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests: None
Reviewer's report
Title: Validity of gout diagnosis in Swedish primary and secondary care
Version: 4
Date: 19 February 2015
Reviewer: Changfu Kuo

Reviewer's report:

Major compulsory revisions:

1. The authors did not mention the timing of information collected for determination of gout status. If the authors used the entire medical records to judge whether patients fulfilled classification criteria then the PPV would be overestimated. Indeed, the patients were identified through having an ICD-10 code of gout from 2009 to 2013 and the medical records were reviewed over these years but when possible also back in time.

2. Gout is characterised by repetitive acute attacks. In the primary care group, only 1/3 of patients have two diagnoses and 10% have 3 diagnoses. This is a bit strange, please comment on this point. This could have several explanations which were beyond the scope of the present study, including that patients largely are treated well with normalized s-urate and few attacks, patients may seek health care at emergency units (these records were not reviewed) night time due to nocturnal onset and to the fact that their PC units only are open at daytime or that patients to a large degree have gained knowledge on how to treat acute attacks themselves. These are all questions, which we aim to address in a planned questionnaire survey.

3. I assume the two PC centres are in the catchment area of the specialised centres. Some patients would have been referred by these two PC centres. In Rheumatology group, did you include the history of patients recorded in the PC centres? Indeed, the two PC centres are in the catchment area of the specialized unit. Four of the 132 hospital cases were referred from the two primary care centers in the study. This is now specified on p6 l 134 (also see answer to point 2, reviewer 2). However, in the Rheumatology group only medical records from the specialized center was studied so the history of patients recorded in the PC centres was not reviewed in this context. Please also read comment to reviewer 2 (item 2).

4. I thought the Rheumatology department should have a better PPV but it's not. I suspect the authors did not include medical history recorded in PCs. Indeed, in this study we have only reviewed the medical records “written / recorded” by the physician at each unit.

5. Please report confidence intervals for PPV.
The confidence intervals for all PPVs are now included in Table 3 and in Supplement Table 1.
6. In Table 4, missing values should be included in denominators. We have now changed Table 4 by including missing values in the denominators in the row with increased s-urate. Percentages are given with both all examined and those with available test results used in the denominator.

Minor
1. Page 10, line 213 Netherlandcriteria --> Netherland criteria
Thank you - this has been corrected.

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests: I have no competing interest.

The following sentence has been added to Methods:
"When comparing categorical data Chi-2 test, or when appropriate Fisher´s exact test, were used." (page 7, line 158 -).

The following writing errors have been corrected (highlighted with red here and in Table 3):
Table 3, Primary Care, ≥1 ICD-10 gout, Rome: 34, changed to 18
Table 3, Primary Care, ≥1 ICD-10 gout, Netherlands: 115, changed to 110

Regards
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