PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	The Rate of Adherence to Urate-Lowering Therapy among Gout Patients: A Systematic Review and Meta-analysis
AUTHORS	Yin, Rulan; Li, Lin; Zhang, Guo; Cui, Yafei; Zhang, Lijuan; Zhang, Qiuxiang; Fu, Ting; Cao, Haixia; Li, Liren; Gu, Zhifeng

VERSION 1 – REVIEW

REVIEWER	Gérard Reach APHP and Paris 13 University, France
REVIEW RETURNED	01-Jun-2017

GENERAL COMMENTS	This is a very interesting paper comparing the rate of adherence in gout according to the method used to estimate quantitatively adherence. I have only a few concerns. In the introduction,page 6, 21, in non-medication therapy, the authors forget to mention the adherence to diet recommendations. page 6. 21: were excluded articles "that used the term "adherence" but actualy measured persitence or retention rate or treatment gaps". This should be justified. The discussion is rather short. A major point shown by this study is that adherence rate from prescription claims is 42 %, and is 71, 66 and 63 % with the other methods. Is this really non significant? This should be discussed. The authors quote Briesacher et al. who compared adherence rates in 7 chronic diseases and who found unexpectedly that non-adherence was the worst in gout, while usually, one expects that it should be worse in "silent diseases". This could also be discussed.

REVIEWER	Dr A Abhishek Academic Rheumatology University of Nottingham UK No Competing Interest
REVIEW RETURNED	23-Jun-2017

GENERAL COMMENTS	This is a well written manuscript. The authors have not searched Embase and Cochrane databases. The reasons for this should be discussed. They note significant difference in adherence in claims database, especially from the USA, and also from UK. The reasons for this need discussing. Could it be that interview studies or postal surveys are prompting patients to self-report higher adherence. Adherence also depends on

	[1] the healthcare system in which the study is done - private (with billing for drugs used) vs. government funded; primary care vs. secondary care.
	[2] severity of gout and age of patients (older typically will have higher adherence).
	This ought to be discussed.
	I would like to draw the authors' attention to a study where we reported an adherence rate of 85% (Rheumatology (Oxford). 2017 Apr 1;56(4):529-533. doi: 10.1093/rheumatology/kew395.). This and the related study by Rees et al. should be discussed as there are excellent adherence rates after nurse led treatment of gout.
	A discussion on how to improve adherence will enhance the quality of the work.

VERSION 1 – AUTHOR RESPONSE

For Reviewer 1
Comment 1. In the introduction,page 6, 21, in non-medication therapy, the authors forget to mention the adherence to diet recommendations.

Response: Thanks for your suggestions very much! On pages 6 and 21, we have added the part of the adherence to diet recommendations in non-medication therapy.

Comment 2. page 6. 21: were excluded articles "that used the term "adherence" but actualy measured persitence or retention rate or treatment gaps". This should be justified.

Response: Thanks very much for your great suggestions! "Articles on persistence, discontinuation, switching, treatment gap, or retention rate" was one of the exclusion criteria. When browsing articles, we found that some articles used the term "adherence" but actualy measured persitence or retention rate or treatment gaps, so these articles were also excluded.

Comment 3.The discussion is rather short. A major point shown by this study is that adherence rate from prescription claims is 42 %, and is 71, 66 and 63 % with the other methods. Is this really non significant? This should be discussed.

Response: Thanks very much for your great suggestions! We have added a discussion about the adherence rate from prescription claims and the other methods.

Comment 4. The authors quote Briesacher et al. who compared adherence rates in 7 chronic diseases and who found unexpectedly that non-adherence was the worst in gout, while usually, one expects that it should be worse in "silent diseases". This could also be discussed.

Response: Thanks very much for your helpful suggestions! Gout is similar to silent disease, which refers to a disease that produces no clinically obvious symptoms or signs, such as, hypertension, many forms of cancer, and hearing loss, which may be either not noticed or denied by the individual. Many diseases begin silently, becoming obvious only when they are advanced. Gout is so named because the pain is coming faster and going too fast. The pain of gout is self-limiting, often automatically disappear in a few days or weeks.

After the pain disappears, the patient ofthen thinks the gout is cured and stops taking drugs. So it is possible that non-adherence in gout is as bad as in silent disease, even worse. We have added a lot of discussion based on the comments you, the other reviewer, editor and the associate editor have given, so we will not discuss this part of the article. Nevertheless, I would like to thank you for your great suggestions.

For Reviewer 2
Comment 1. The authors have not searched Embase and Cochrane databases. The reasons for this should be discussed. They note significant difference in adherence in claims database, especially from the USA, and also from UK. The reasons for this need discussing. Could it be that interview studies or postal surveys are prompting patients to self-report higher adherence.

Response: Thank you for the helpful suggestions! We have discussed the reasons for not searching Embase and Cochrane databases, as well as the reasons for significant difference in adherence in claims database, especially from the USA, and also from UK the revised proof.

Comment 2. Adherence also depends on
[1] the healthcare system in which the study is done - private (with billing for drugs used) vs. government funded; primary care vs. secondary care.

[2] severity of gout and age of patients (older typically will have higher adherence).
This ought to be discussed.

Response: We feel very honored to your affirmation and thanks for your suggestions very much. In the revised manuscript, we have added the discussion of this part.

Comment 3. I would like to draw the authors' attention to a study where we reported an adherence rate of 85% (Rheumatology (Oxford). 2017 Apr 1;56(4):529-533. doi: 10.1093/rheumatology/kew395.). This and the related study by Rees et al. should be discussed as there are excellent adherence rates after nurse led treatment of gout.

Response: Thanks very much for your helpful suggestions! In the revised proof, we have discussed the two studies that you mentioned above.

Comment 4.A discussion on how to improve adherence will enhance the quality of the work.

Response: Thank you for the helpful suggestions! We have added a discussion on how to improve adherence will enhance the quality of the work in the revised manuscript.

VERSION 2 – REVIEW

REVIEWER	Gérard Reach
	Assistance Publique Hôpitaux de Paris and Partis 13 University
REVIEW RETURNED	01-Aug-2017

| GENERAL COMMENTS | I think that authors answered the reviewers' comments |

VERSION 2 – AUTHOR RESPONSE

For Reviewer
Please state any competing interests: None declared.

Response: Thanks very much for your helpful suggestions! According to your suggestion, we checked the article and found that "The authors declared that they have no competing interests" was stated after "Acknowledgments" in the manuscript. Nevertheless, thank you so much.