Author's response to reviews

**Title:** Conceptualization of Common LR: A useful Tool for Clinical Diagnostic Reasoning

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**Author's response to reviews:** see over
Dear editor

According to reviewers' comments, new version of article has been changed a lot. Thanks for your cooperation and offering more time to do revisions. We hope that all the changes that were required are made. Kindly let us know if more changes are necessary.

**Reviewer: Doctor Chris Del mar**

Dear Doctor Chris Del mar

We thank you for your review and pointing out our mistakes. New version of article has been changed a lot. We hope that all the changes that were required are made.

**Comment 1:** decide who it is for (EBM teachers of GPs?)

_Reply:_ The audiences of article are researchers in the field of clinical teaching and teaching of EBM

**Comment 2:** perhaps put in some 'worked examples', starting with the presentation ("a XX year old patient came in with a fever...")

_Reply:_ it’s done. New version of article starts with 2 cases and continues through thinking about them.

**Comment 3:** get some LRs and show how the probability of prior probabilities changes with the application of the LR – (and perhaps also explain what they are for un-initiated!)

_Reply:_ it's done. It discussed by case 1, LRs for diagnosis of UTI in table 1, and calculating post test probability according to formula.

**Comment 4:** Better explain the notion of classification helping with the diagnostic process (Perhaps with concrete rather than theoretic examples).

_Reply:_ We think it's done in new version in examples of approaching fever and tiredness.

**Comment 5:** explain how to obtain the LRs from the literature.

_Reply:_ it's explained in "Conclusion, Implications and Future Directions".

**Comment 6:** show how they might be applied in the clinical examples that would be a useful contribution.

_Reply:_ it's done in format of 2 cases.
Reviewer: Doctor Jean Karl Soler

Dear Doctor Jean Karl Soler

We thank you for your extensive review and pointing out our mistakes. New version of article has been changed a lot. We hope that all the changes that were required are made.

Comment 1: Page 4. Paragraph 1. If this is the introduction it should be labelled as such. The part on deficiencies in diagnosis by doctors is reductionist, and does not reflect the broad literature on the topic, including the controversy about whether Bayesian approaches and intuitive/pattern matching approaches to diagnosis are superior in all situations. In fact, from my perspective it seems that either may be better in different situations, with different doctors.

Reply: it's done. The part on "experts based diagnosis and its drawbacks" has been re-written and also explained your point in the first paragraph of this part.

Comment 2: Page 4, last paragraph. “A Bayesian approach and objective refining of the probabilities...” Different categories of diseases – this term/concept should be defined and explained, and referenced to previous literature. There is a short explanation of the purpose of the article, which should be carried over to the abstract. There is no mention of prior probabilities, only likelihood ratios, and this is an important issue to be discussed. LRs cannot be used to predict a posterior probability without the prior probability.

Reply: Concepts of category and category assignment is defined through explanation of scheme inductive diagnostic reasoning. Purpose of the article is explained at the end of introduction more clearly than the past. Calculating post test probability from pre test probability and Likelihood ratios is explained in resolution of case 1 in part " Evidence Based Clinical Diagnosis and its limitations".

Comment 3: Page 5. This article is missing an appropriate methodology section. It should not be published without it.

Reply: The article has been submitted as a debate article. Further paragraphs for better explanation and conceptualization have been written in this version especially in the parts of "Conceptualization of category oriented or common LR" and" Conclusion, Implications and Future Directions".

Comment 4: Page 5. Paragraph 1. This is an example of poor use of the article in English: “Studies on the diagnostic decision-making...” “The physicians' lack...”

Reply: they're reworded.
Comment 5: Page 5. Para 1. This is a sweeping statement based on one reference only, and should be removed, reworded, or else supported by more literature. The authors have not studied doctors’ decision making, and cannot conclude that it is deficient in general, on the basis of one reference.

Reply: it's reworded and re-written precisely.

Comment 6: Page 5. Paragraph 2. “In the field of clinical diagnosis, a central notion of EBM is the application of LRs in diagnostic decisions. LRs can be used to assign a probability ranking to a particular disease through refining its probability, i.e. disease assignment.”

Reply: it's reworded.

Comment 7: Page 6. Paragraph 1. The condition of malaise has been studied by Kenter et al, in the European Journal of General Practice. You may consider including data from this study.

Reply: Data from one of studies by kenter et al about differential diagnosis of tiredness that was available for us (reference 29), has been used in this version for better conceptualization and calculation of common LR of fever for an exemplar infectious category.

Comment 8: Page 6. Paragraph 1. English correction: “When the physician encounters non-specific problems which lead to a wide set of differential diagnoses related to...”

Reply: it's reworded.

Comment 9: Page 6. Section on expert-based decision making and its drawbacks, the argument on the potential failure of clinician expertise and in favour of analytical approaches to diagnosis is far more complex than stated in this section. I have reviewed the literature on clinician decision making, and in summary, there are various theories of the diagnostic process and clinical reasoning, but there seems to be agreement that various types of reasoning and pattern recognition are at play, from the more analytical to the more intuitive. More experienced clinicians are able to use different types of mental diagnostic processes depending on the context of the problem. Common problems may be solved by pattern matching or intuition, requiring less information and less time, whilst more complex or infrequent problems may be solved by returning to basic skills of analytical processing of information gathered much more systematically. Thus experienced clinicians tend to indeed perform better than less experienced clinicians, and possess superior knowledge of many kinds, formal and informal. The process may fail due to a number of biases, and in some cases which are complex; the step-by-step analytical deductive process may produce better results. However, the Bayesian approach is not the best one in all circumstances. The authors need to re-write this section entirely to reflect current realities. The paragraph is too simplistic, and denigrates clinician experience.

Reply: it's done. The part on "experts based diagnosis and its drawbacks" has been re-written.
Comment10: Page 8. Section on use of common LRs to refine the probability of disease, this section is full of English grammatical errors. I also have a major issue with the exemplar category of infectious diseases, and the likelihood ratio thus calculated. Many important and common infectious diseases have been excluded from the category (such as URTI and gastroenteritis, for example), and as such the category is incomplete. This missing information would have a major influence on the common LRs for all infectious diseases. Furthermore, the combination of these LRs assumes that these diseases contribute equally, but we know that this is not the case. Meningitis is far less common than influenza, and the LR for influenza is far more important than that of meningitis for a common LR for infectious disease. By ignoring the prior probabilities of these conditions, the theory presented by this paper is seriously weakened and rendered clinically inapplicable.

Reply: it's done. This part has been re-written too. As new paragraphs in this version, in this article, only for showing more objectively the conceptualization of common LR, this value is calculated by considering diagnostic values from current best evidence and by using a simple formula that we constructed for this purpose (a hypothetical category of febrile diseases that their diagnostic accuracy was available in the series of the JAMA systematic reviews (Rational clinical examination) are considered and listed in table 3, but for future we need to calculate real values by using routine episode of care data from patient databases including reason for encounter, clinical and paraclinical data and final diagnosis. Also for calculation of common LR of fever for the exemplar infectious category more precisely than the past, Prevalence of diseases is derived from an article entitled "Tiredness in Dutch family practice." studied by Kenter et al, and has been used in this version (reference 29).

Comment11: Page 8. Second paragraph. The statement that “this approach still lacks objectivity” and that GPs should use common LRs to refine category assignment more objectively, is a sweeping statement not supported by evidence. Firstly, the data used for this example are not all based on primary care data, and the LRs can be wrong for primary care. Secondly, there is no evidence that this approach to diagnosis, using category assignment, is more accurate than actual clinical practice for common infectious disease. The authors are not experts in diagnosis in GP and should not jump to conclusions on the quality of the diagnostic process in GP without objective evidence. Proposing a “better” system without evaluation is not scientifically acceptable. The method should be described without such value judgments.

Reply: it's reworded and re-written precisely.

Comment12: Page 9. Paragraph 1. “However, there are major pitfalls in using these key clues and all physicians may not reach to the stage of using these clues. In addition there are variable diagnostic biases in using experience and heuristics.” This is again judgemental – there is no evidence that Bayesian methods provide superior results to clinician diagnoses in all situations. In fact, this is known not to be true.

Reply: it's reworded and re-written precisely.
Comment 13: Page 9. Paragraph 1. “...the hallmark of the disease is only about 1.9 [28]”. Is this a percentage or a LR? In that case the statement should be made more clearly.

Reply: 1.9 is LR (+) of rebound sign for diagnosis of acute appendicitis. It's reworded and re-written for more clarity.

Comment 14: Conclusions. Please only include conclusions that are supported by the results of your study.

Reply: This part has been re-written, too.

Comment 15: Table 1. Please define LR+, LR-, and category (in this table, maybe term it as category of infectious disease?)

Reply: it's done.

Reviewer: Doctor Kees van Bove

Major compulsory revision: working as a GP you "know" the prior probability of diseases/problems for many complaints and symptoms presented by the patient. The prior probability depends on the prevalence, sex, age etc. For example the if a patient has the complaint tiredness/ general weakness the top 20 end diagnosis will be different in the age and sex classes. Mostly the "diagnosis" stays tiredness but the older the population the higher the chance for having a depression. In my opinion you only consider broader categories of diseases when patients present unusual complaints, complaints with a very low frequency in family practice. And when you consider a serious disease as for example meningitis the common LR will not help the GP. But when you know the prior chance it is very important to know the posterior probability of a diagnosis in the presence of a complaint or symptom. When I use your table 1 you can see that the symptom fever does not contribute to the diagnosis otitis media (the what H. Lamberts called the posterior Odds = LR+/LR- = 0,7) and from other research the the symptom pain in the ear has a posterior Odds of 15.8 (LR+ = 7.8 and LR- = 0.5) and contributes a lot to the diagnosis. So my conclusion is that common LR are not very helpfull. But this is really something to discuss!! I am waiting for your answer.

Dear Doctor Kees van Boven

We thank you for your review and pointing out our mistakes. We agree with you about missing the consideration to value of pretest probability in estimation of post test probability. In new version of article submitted herewith, we have explained it. Estimation probability of disease has been discussed by 2 scenarios. According to scenarios, otitis media as you said that the symptom fever does not contribute to the diagnosis of it has been removed from table. Since odds are technical and LRs are more common and user friendly for clinicians, we only consider to mention LRs. Also for more objectivity and reliance on evidence, we have used data from the transition project for pretest probabilities of differential diagnosis of tiredness in table. We hope that all the changes that were required are made.