Author's response to reviews

**Title:** Factors affecting the accuracy of the urine dipstick test for the detection of bacteriuria or urinary tract infections. A meta-analysis.

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PDF covering letter
Dear Editor,

We are pleased to submit the revised version of our manuscript. We are addressing the comments made by the three reviewers, one by one. Reviewer two suggested to drop some tables and figures. We have done so and mentioned that some data are available on request.

We hope that the changes made to the manuscript make it suitable for publication.

With kind regards,

Walter Devillé

**Addressing comments of Reviewer one, Masahiro Hiraoka**

We thank the reviewer for his/her useful comments and we are confident that we responded suitably to most of it.

**General Comments**

The reviewer considers that either nitrites or esterase tests alone are not accurate enough to confirm diagnosis and believes therefore that disjunctive pairs of both tests should be used, but only as a screening test. Positive tests should be confirmed by urine culture.

This view is similar to the view of the authors in the Conclusion section were we state that a negative test may exclude the presence of infection. Furthermore, we state that although sensitivities of disjunctive pairs may be higher than positive tests of one separate test alone, still disjunctive positive results should be confirmed by culture, except in case of high pre-test probabilities.

**Major Compulsory Revisions**

Most of the comments of the reviewer are related to the problem of at what level of a post-test probability an infection should be ruled-in. We consider a post-test probability of a positive test result of 80% high enough to start treatment, while a post-test probability of 90% should be high enough to rule-out infection. Of course a physician takes in the evaluation more into consideration than the test result of a dipstick only.

- Comments 1-3: we agree to clarify “a negative test result” by “a negative test result of one of both tests” (p18, line 19). We still assume that a post-test probability of 89% of a positive test result gives enough confidence to rule in infection when both tests are positive in the general population. We changed “confirms” into “rules in” throughout the manuscript.

- Comment 4: To address the comment of the reviewer and the different post-test probabilities in the different population subgroups we adapted and nuanced the statement as follows: “while a positive nitrite test rules in infection in elderly and increases the probability of an infection considerably in surgery and urology patients”. (p18, lines 24-26)

- Comment 5: We deleted the sentence and replaced it by “Post-test probabilities of positive leucocyte-esterase remain low in all population subgroups”. (p18, lines 26-27)

- Comment 6: In common patients in general practice the post-test probability of a positive nitrite result is 84%. We consider this high enough to start treatment in this specific situation: the already considerably higher pre-test probability in general practice still increases from 55% to 84%. On the other hand, if both test results are available and one of them is negative (disjunctive pair) confirmation should be sought. We added this comment to the text. (p19, lines 3-5)

- Comment 7: Although perhaps unexpected, still Table one shows that in case of using a very low cut-off point in culture the meta-analysis results in a mean diagnostic odds ratio of 32. This DOR is statistically not different from the diagnostic odds ratio’s at higher cut-off points. The sensitivity of nitrites in this case is significantly higher than for the other cut-off points as can be seen in the same table.
**Addressing comments of Reviewer 2, Y. Waisman**

We thank colleague Dr. Waisman for his positive comments and suggestions for improving the manuscript. As some of the General comments are repeated in the Discretionary or Compulsory sections we will address them jointly.

- **Comment general 4, discretionary 4:** We are aware about the length of the manuscript and the amount of tables and figures. The length results from the fact that 2 tests are evaluated in one meta-analysis. In the covering letter to the editor we made the suggestion that some of the tables could be made available on request of the readers of the manuscript. We included all tables for the reviewers to facilitate a sound evaluation of the systematic review and meta-analysis. We would suggest the editors – if necessary for the BMC journal at issue – to keep tables one to four, figures 4 and 5 and appendix one and three. Figures one and two can be dropped and appendices two and four can be made available on request. We adapted the manuscript accordingly.

- **Comment general 5, major compulsory 5:** This reviewer assessed that the Conclusions are adequately supported by the data. We added a sentence to the conclusion to discuss the meaning and the validity of the results “Although this meta-analysis…” (p19, lines 25-26 through p20, lines 1-4).

- **Comment general 6, major compulsory 6:** The abstract is rewritten to address the comments about style and specificity. A short version of the clinical recommendations of the main manuscript is used for the conclusions part of the abstract.

- **Comment general 7, discretionary 4a, major compulsory 7:** The manuscript is submitted to and corrected by a native English translator. Title is rewritten into: “The urine dipstick test useful to rule-out infections. A meta-analysis of the accuracy.” The terms disjunctive and conjunctive pairs were copied from the published meta-analysis in 1991. We changed the terms now in “Nitrites and Leucocyte-esterase: one or both positive” and “Nitrites and Leucocyte-esterase positive”, respectively, also according the definitions of the former meta-analysis.

**Addressing comments of Reviewer 3, P.J. Nogueira**

We thank P. J. Nogueira for his comments and suggestions. We will address them point by point.

**Discretionary revisions**

We do not understand why the reviewer doubts if this research is a meta-analysis? The authors are confident that the study is performed according all existing standards for a diagnostic meta-analysis. (see Devillé et al. BMC Research Methodology, 2002, 2, e9)

Original studies about the accuracy of the urine dipstick report a wide range of results. Former meta-analyses were limited to a specific population group as children (Gorelick, Pediatrics 1999) or were not able to study heterogeneity (Hulrbut, Am J Clin Path 1991). Our meta-analysis identifies the major sources of heterogeneity and confirms the limitations of the dipstick in different clinical settings and in different patient populations.

**Minor Compulsory Revisions**

As the other reviewers did not mention anything about the inclusion and exclusion criteria, we think that they are clear enough. We added a few words to clarify a few criteria (page 6, lines 14 and 16).

Concerning the literature search we clarified the contacts with experts and dropped a part of the first sentence in the second paragraph under literature search (p. 6, lines 5-6).

**Major Compulsory Revisions**

Background, results and conclusions are rewritten in the abstract in a more understandable way for clinicians.