Author’s response to reviews
Title: Diagnostic behaviour of general practitioners when suspecting Lyme disease: a database study from 2010-2015

Authors:
Esmée Botman (e.botman@vumc.nl)
Wim Ang (w.ang@vumc.nl)
Hanna Joosten (JHK.Joosten@vumc.nl)
Pauline Slottje (p.slottje@vumc.nl)
Hans van der Wouden (j.vanderwouden@vumc.nl)
Otto Maarsingh (o.maarsingh@vumc.nl)

Version: 3 Date: 14 Dec 2017

Author’s response to reviews:

BioMed Central

Floor 6, 236 Gray's Inn Road

London

WC1X 8HB

United Kingdom

Amsterdam, December 12th, 2017

Dear Editor, dear Donata Kurpas,

We would like to thank you and the reviewers for the additional comments and this new opportunity to improve our manuscript “Diagnostic behaviour of general practitioners when suspecting Lyme disease: a database study from 2010-2015”.

In this letter we give a point-to-point response to the points raised by the reviewers. All changes to the manuscript are indicated in the text by using track changes.

Reviewer 1 (Agnetha Hofhuis)

Agnetha Hofhuis (Reviewer 1): I agree with the authors on their answer to reviewer 2 Eugene D Shapiro.

Due to the way of health care organisation in the Netherlands, general practitioners indeed see the majority of patients with a-specific symptoms and thus the lowest pre-test probability.

The authors could consider to make this more clear for the non-Dutch readers, by incorporating some answers to reviewer 2 into their introduction or discussion.

Response:

See our answer to reviewer 2.

Reviewer 2 (Eugene D Shapiro)

I am sorry, but the authors still refuse to get it. They persist in believing that there should be different algorithms for performing diagnostic tests for Lyme disease for general practitioners and for specialists because the prevalence (pre-test probability) of Lyme disease is higher among referred patients. As a result, they did not make changes to the manuscript. They are wrong! OF COURSE the prevalence of Lyme disease is higher among referred patients! It does not follow that therefore there should be different algorithms for deciding whom to test. The reason that the prevalence of Lyme disease is higher in the referred patients is that they already have been selected as having a higher risk of Lyme disease (ie, most have been screened, at least by some implicit algorithm). If the algorithm is to select on whom to perform a diagnostic test, it would
not apply to many of the referred patients because they have already had a positive test result. The prior probability of Lyme disease in an individual patient who has not yet been tested (referred or not) is determined by the SAME risk factors. So the issue is NOT that general practitioners need a DIFFERENT algorithm, they simply need to APPLY a reasonable algorithm (which would largely be the same for a referred patient who has not yet undergone a diagnostic test)!!

Response:

We would like to thank the reviewer for his clarification. In our previous response, we used Bayes’ theorem to elaborate on the possibility of a future prediction rule for Lyme borreliosis (LB). However, we agree that there are currently no symptoms that accurately predict the prior probability of LB. And although ‘tick engorgement’ and ‘patient-estimated tick attachment duration’ [Hofhuis, PLOS One 2017] may be promising potential predictors, the current state of the evidence is that physicians – in primary and secondary care – do not have tools for estimating the risk of LB. And, consequently, when physicians are not able to perform any form of selection (contrary to other reasons for encounter, like chest pain), we agree with the reviewer that one diagnostic algorithm may be suitable for both primary and secondary care. Therefore, we made the following changes. First, we changed the sentence ‘A diagnostic algorithm tailored to primary care may decrease overuse of diagnostic tests and thereby reduce overtreatment of LB.’ into ‘The development of an easy-to-use diagnostic algorithm may decrease overuse of diagnostic tests and thereby reduce overtreatment of LB.’ (Abstract, page 2, lines 47-48). Second, we removed the sentence ‘This emphasizes the importance of a diagnostic algorithm for LB tailored to primary care.’ (Discussion section, page 8, lines 205-206). Third, we removed the sentence ‘Based on the calculated pre-test probabilities of LB in the general practice setting, the algorithm would provide the estimated risk of the patient and a diagnostic recommendation (e.g. no serological testing, serological testing, or referral to a medical specialist). An algorithm for diagnosing LB in general practice may diminish unnecessary serological testing, reduce false-positive test results and overtreatment of LB.’ (Discussion section, page 8 and 9, lines 214-218). Fourth, we changed the phrase ‘underscores the need for a diagnostic algorithm tailored to primary care.’ into ‘underscores the need for an easy-to-use diagnostic algorithm that is (also)
applicable in daily general practice.’ (Discussion section, page 8, lines 231-232). Finally, we changed the first part of Implications for clinicians and research (Discussion section) into ‘Hopefully, our study will initiate the development of an easy-to-use diagnostic algorithm for LB that is (also) applicable in daily general practice. Although the current scientific evidence for such an algorithm is limited, some promising potential predictors have been reported, like tick engorgement and patient-estimated duration of tick attachment.[10, 27]’ (Discussion section, page 8, lines 209-214).

Reviewer 3 (François Milord)
(no comments)

Reviewer 4 (Bryon Backenson)
(no comments)

Hopefully, the revised manuscript addresses the points raised by the reviewers. We look forward to the editorial decision.

Yours sincerely,
O. R. Maarsingh, MD/PhD
E. Botman, MD
J.C. van der Wouden, PhD
C. W. Ang, MD/PhD
J.K. Joosten, MSc
P. Slottje, PhD