Reviewer’s report

Title: The HUMTICK study: Protocol for a prospective cohort study on Post-Treatment Lyme Disease Syndrome and the disease and cost burden of Lyme borreliosis in Belgium.

Version: 0 Date: 22 Feb 2017

Reviewer: Charline Maertens de Noordhout

Reviewer's report:

Geebelen et al. proposed a paper entitled: « The HUMTICK study: Protocol for a prospective cohort study on Post-Treatment Lyme Disease Syndrome and the disease and cost burden of Lyme borreliosis in Belgium ». This is the protocol of a very ambitious study aiming to evaluate the incidence and possible risk factors to develop PTLDS and to estimate the disease and cost burden of borreliosis in Belgium. This will be a very interesting study that will bring new knowledge on borreliosis disease. I think that after some improvement of the method section, which I find not detailed enough, the paper would be acceptable for publication. I also would like to review the questionnaire (not SF-36, CFQ, EQ5D, GALI) that will be used to collect the risk factors, comorbidity, tike-bite exposure, prescribed treatment…., because it is not available in the supplementary appendix.

L8 (p2): "Lyme borreliosis…".
I would "add and having been treated?"

L6 (p3): "a red expanding rash…".
I would explain what the risk factors for having an expanding red rash are. I suppose it would depend for instance on the location of the bite or on the time the tick remained hanging.

L9 (p3): "If left untreated…".
How do you define the treatment? I mean is the tick removal a treatment?
I would also better explain that some people may be bitten, have a red rash, remove the tick and never developed disseminated Lyme borreliosis.

Do you have any ideas of the risk factors linked with disseminated Lyme borreliosis (very young children, immunocompromised people, season,…)?
L13 (p3): "Cognitive difficulties".
This concept seems very broad, maybe it would be useful to give an example.

L18 (p3): "Incidence estimation…".
Is "incidence" the correct term?
Where this incidence come from? Belgium? Europe? I would be more specific.

L10 (p4): "."
To be deleted

L16 (p4): "been assessed".
Has the burden of borreliosis already been assessed by other countries?

L20 (p5): I would add "Having already suffered of borreliosis" as an exclusion criteria.

L3 (p6): Will be? (June 2016) Has the study already started?

L6 (p7): Would it be possible to have to access to the formula/code you used for the sample size
calculation? I don't find exactly the same results as you. Thank you!

L17-18 (p7): Would it be a printed questionnaire?
Will the "follow-up" questionnaires be sent by email? Or it will be a face to face interview?
This is not well explained.
L6 (p9): To my knowledge, there are no Belgian tariff for EQ-5D-5L (only for 3L and only based on Flemish population).

L15 (p9): Could you describe which socio-demographic variables you plan to collect?

L21 (p9): + severity + occurrence + duration…

"The latter is calculated based on incidences".

I would correct the sentence. The latter is calculated based on incidences if incidence-approach is used (which is commonly the case in burden of infectious diseases estimates). If you are using prevalence approach, then morbidity is calculated on prevalence data.

L1 (p10): How do you plan to translate 5L into 3L (as no tariff for 5L are available)?

How do you plan to merge questionnaire and VAS answers?

How do you plan to translate utilities from EQ-5D-5L to DW?

+ justify your choices, thank you!

L6 (p10): How do you plan to calculate the YLLs?

Do you expect some mortality rate linked with borreliosis disease?

If so, which life expectancy table do you plan to use?

Do you plan to perform a time-discounting? Or age weighting? + justify your choices, thank you!

I found the burden paragraph not detailed enough.

L10 (p10): I don't understand the link between the minimization of recall bias and the cost diary. Could you better explain?
I would be clearer in the "Costs" paragraph. I don't understand how you will merge the answers of the participants regarding the 'direct medical costs' with the data you will collect from official sources, what is the interest to have two data sources for direct costs?

Do you plan to attribute more weight to "official" sources than to participant's answers?

L23 (p10): On which confounding variables you're expecting to adjust your model?

GR: Please could you also add your questionnaire in supplementary appendix?

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