Reviewer's report

Title: Health-Economic evaluation of vaccination strategies for the prevention of herpes zoster and postherpetic neuralgia in Germany

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Reviewer: Albert Jan van Hoek

Reviewer's report:

Review Health-economic evaluation of vaccination strategies for the prevention of herpes zoster and postherpetic neuralgia in Germany.

The authors present a well documented analysis including an extensive sensitivity analyses. However due to the abundant (uncertainty) analyses the authors might have shifted the focus from the main issues towards less important factors.

Major issues:

For my feeling there are three main outcomes for this analysis: the absolute values of the cost per case/PHN/QALY (by age), the optimal age of vaccination, and subsequently how robust these absolute estimates are as well as the conclusion regarding the optimal age.

The absolute cost-effectiveness of a vaccine depends on the probability to experience disease (disease incidence) and the capacity of the vaccine to prevent this burden (vaccine efficacy). Within the methods, results and discussion of these two important factors deserve more attention.

Although the incidence analysis was published before it would be good to remind the reader in the method section of the exact source, disease definition (HZ + PHN) and years included in the incidence data.

Can the authors add a small paragraph highlighting the incidence of HZ and PHN by age (on top of just a reference to the table) in the result section? And make this explicit as possible in context of the model; this can be by presenting the numbers per cohort of 1 million, or for Germany as a country (why was a cohort of 1 million chosen?). Ideally the authors should do this in such a way that it enables a comparison with the model, as the authors mention a difference between the two.

The authors should include a discussion on the similarity between the definition of HZ, and especially PHN in their incidence data, and the definition used in the clinical trial. As both underpins the applied vaccine efficacy in the CEA.

A major short coming is the investigation of the uncertainty around the vaccine efficacy. The authors should include a more focussed analysis of the uncertainty around VE-related parameters in relation to the optimal timing of vaccination and
the overall cost-effectiveness. For example the 10 years of fixed protection should be justified and investigated, this in combination with the waning rate (perhaps by age), and a declining protection against PHN by age. There is actually quite a lot of uncertainty around all these parameters and this matters in context of the optimal age of vaccination. When the protection is shorter vaccination of older people becomes perhaps relatively more cost-effective and there is an increased need for boosters. Related to the booster doses; I would expect to see a table of the cost-effectiveness of these booster doses related to the moment when you give the first dose. E.a. cost-effectiveness when you vaccinate at 50 and at 70, 60 and 80 etc.

Much more emphasis can be given in the discussion on the uncertainties regarding the incidence, the vaccine efficacy and the optimal age of infection. As the robustness of the analysis does depend solely on the robustness of the used parameters and it does not depend on the outcome of the PSA or on the comparison with other cost-effectiveness studies. Therefore the authors should focus the discussion on the parameterisation. This will require re-writing most of the discussion, as the comparison with the other CEA is not of so much value (as the authors say). Also can the authors include more discussion on the wide differences between the best- and the worst scenario – the ICER per QALY is between 235 (very low) to 157,845 (very high).

Minor:

The shown clouds on the cost-effectiveness planes are not very informative without the reference of a cost-effectiveness threshold. Can the author present cost-acceptability curves instead (for perhaps some applicable scenarios).

The problem with recurrence is new and unclear to me. Can the authors expand on this issue if it is very important or leave it out if it is too hypothetical. Please make sure no scenario is included where actually acquiring disease has a shorter protection as vaccination, as this seems logical inconsistent.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.