

Reviewer's report

Title: The incidence of varicella and herpes zoster in Massachusetts as measured by the Behavioral Risk Factor Surveillance System (BRFSS) during a period of increasing varicella vaccine coverage, 1998-2003

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Reviewer: Sara L Thomas

Reviewer's report:

General

The question of whether widespread vaccination against varicella will increase incidence of herpes zoster (by reducing circulating wild-type varicella-zoster virus) is a topic of major public health importance in countries that have ageing populations and that have introduced (or are considering) childhood varicella vaccination programmes. Until recently, research on this topic was hampered by lack of data on trends in zoster incidence from communities with high vaccine coverage over a sufficient period of time. Such data are finally beginning to be available from selected sites in the USA.

The current study by Yih et al attempts to answer this question using data from successive Behavioural Risk Factor telephone surveys in the Massachusetts area, and finds a marked increased trend in zoster incidence coinciding with increasing vaccine uptake and declining varicella incidence. There are limitations to these data (for example, the reliance on self-report of zoster, their method of estimating annual zoster incidence from age at interview and age at zoster, and low survey response rates). However, as the authors point out, these limitations are unlikely to fully explain the trends seen. Therefore, the study findings are of considerable interest.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. The trends in the crude and age-specific incidence rates of zoster need to be interpreted with caution. The risk of zoster increases sharply with age, and the age groups chosen in this study encompass a wide age range (because zoster numbers were small). Therefore, differences in crude or age-group-specific zoster incidence over time may partially be due to a differing age composition for the overall sample or within age-groups (particularly amongst those aged 65+) at different time periods. The key issue is that the age-standardised zoster rates also increased markedly over time. These data are only mentioned briefly in the Results (and not at all in the Tables). The authors need to provide 95% CI for the annual age-standardised zoster incidence estimates, and to clarify that the highly significant increasing trend applied to the standardized (as well as the crude) rates.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. Overall incidence of varicella was higher in 2003 than in 2002. The authors mention in the Discussion that this increase was not statistically significant (this statement would be better placed in the Results). They do not comment on the corresponding decrease in overall (crude and age-adjusted) zoster incidence between 2002 and 2003. Was this decrease also not statistically significant?

2. The authors state in the Results that the large apparent increase in 2002 response rates was mainly due to 'changes in disposition codes and formulas'. I do not know what this means; a short explanation is needed.

3. Some individuals were excluded from each analysis because either their age and/or their varicella or zoster status were missing. These numbers need to be reported (perhaps in the Tables?)

4. The authors state that previous studies of zoster have reported unadjusted incidence rates ranging from 1.3-4.6/1000 population. In fact, the study by Chidiac et al (Ref 13) reported zoster incidence of 4.8/1000 population, and the study by McGregor (Ref 10) does not explicitly state incidence but is usually quoted as finding zoster incidence of 4.8/1000 population (81 zoster cases over a seven year period in a population of 2400 patients).

5. The authors summarise data from three previous studies of trends in zoster incidence, all of which report increasing incidence over time. In one of these studies, the reported increase in overall zoster consultation rates between 1979-97 in UK general practice data (Brisson et al, Ref 37) is rather misleading. It is more useful to consider the detailed analyses of the same data reported by Fleming et al (Eur J Epidemiol 2004; 19 (12): 1113-8). This analysis examined age-specific and age-standardised annual zoster incidence between 1970 and 2001. In contrast to the crude incidence rates reported by Brisson et al, Fleming et al found consistent mean annual incidence within all age groups over the period of the study except amongst those aged greater than 65 years (where there was a gradual increase in incidence over time, although this could simply reflect an increasing mean age of patients over time in this age group). Sex-specific age-standardised trends over a shorter period (1994-2001) did not demonstrate an increasing trend in incidence for either males or females.

Discretionary Revisions (which the author can choose to ignore)

1. I found the Tables a little difficult to read, and the layout hampered comparison of incidence between study years. Perhaps comparisons could be facilitated by reducing the number of rows for each study year, reporting each age-specific number of cases and respondents in a single cell (for example, 4/144), and then reporting incidence and 95% CI in a single cell directly below?

2. As the risk of zoster increases markedly with age, the authors might want to check whether the trends in age-standardised zoster incidence remain after controlling more finely for age (for example, standardising by five-year groups).

3. I doubt that background levels of underlying immunosuppressive conditions would have increased very much between 1999 and 2003. However, the number of individuals randomly selected for the survey who had underlying immunosuppression may have varied over time, and this could have affected the results. Perhaps this could be stated a little more clearly in the Discussion?

4. The authors make numerous comparisons between their incidence findings and those of previous studies, stressing that their estimates are mostly higher. As they rightly point out later in the Discussion, this is probably because their method of estimating annual zoster incidence is likely to have resulted in an overestimate of incidence (it would perhaps be useful to make this point directly after the incidence comparisons). I agree with their argument that such overestimates could be expected to occur uniformly over time. This argument could be investigated a little further if the months of birth of the participants and the months of the surveys were known. The interval of interest is (month of the survey minus month of participant's birthday), and the likelihood of overestimating incidence is greater when this interval is longer. So, if the distribution of this interval was similar for all survey years, this would provide some reassurance that overestimation of incidence was unlikely to have contributed to the trends seen.

5. I agree that self-report of zoster by older individuals has been shown to be accurate compared with physician diagnosis (Schmader et al, Ref 41). However, self-report may be less reliable amongst younger individuals, because herpes simplex infection is sometimes misdiagnosed as zoster in these individuals. Could such misdiagnosis partially explain some of the apparent increasing zoster trend amongst the younger age groups?