



Letter to the Editor

Herpes zoster and dementia risk



Dear editor,

We read with interest the recent study by Blandi and colleagues, which makes an important contribution to understanding the potential long-term neurocognitive risks associated with severe Herpes Zoster (HZ), particularly through its robust use of large-scale population data [1]. Their results were compatible with previous studies [2,3].

One key result is the elevated sub-distribution hazard ratio (SHR) of 2.43 (95 % CI: 2.15–2.75) for dementia incidence within the first year post-HZ hospitalization compared to the general population [1]. This figure represents the highest SHR reported across all follow-up intervals in Blandi and colleagues' study. Given the magnitude of this short-term association, it may be valuable to explore the potential influence of early dementia diagnosis on the overall effect size.

We would like to respectfully suggest the potential value of conducting a sensitivity analysis incorporating a one-year wash-out period. This would exclude dementia diagnosis occurring within one year of the index HZ event. Such an approach could help:

1. Minimize the effects of reverse causality, where early-stage undiagnosed dementia may predispose individuals to more severe HZ episodes and subsequent hospitalizations. In this scenario, dementia is already developing before the onset of HZ, increasing the likelihood of a severe HZ episode. Thus, the observed association may not be causal — HZ did not cause dementia.
2. Reduce detection bias, which can occur when hospitalization increases the likelihood of diagnosing dementia. This may create a false impression that HZ elevates dementia risk, when in fact, dementia was already present but remained undiagnosed until the hospital visit.
3. Assess the independence and stability of long-term dementia risk beyond the acute post-exposure period. This helps determine whether the association persists over time and is not merely a short-term artifact of the initial medical event.

For example, if a large portion of all observed dementia cases occurred within the first year post-HZ, after removing these cases, the overall strength of the observed association might reduce, possibly to the point of losing statistical significance. It suggests that the initial strong association might have been influenced by factors like detection bias or reverse causality, rather than a true long-term risk.

To our mind, a sensitivity analysis excluding dementia diagnosis within the first year (i.e., a wash-out period) could help separate short-term detection bias from long-term associations. Even if such an analysis has been considered internally but not presented, its inclusion—even with non-significant results—would add transparency and further strengthen the interpretability of the findings. We recognize that results from such analyses may vary in statistical significance; however,

including them in supplementary material could help readers better understand the strength and independence of the observed effect.

Thank you for considering our suggestions. We look forward to your response.

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Ethical considerations

This article is a letter and informed consent is waived.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Shih-Wei Lai: Conceptualization, Writing – original draft, Writing – review & editing. **Kuan-Fu Liao:** Conceptualization.

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