[1] School of Health, Wellington Faculty of Health, Victoria University of Wellington, Wellington, New Zealand

[2] Usher Institute, University of Edinburgh, Edinburgh, UK

Correspondence to: C R Simpson
colin.simpson@vuw.ac.nz

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Long term effectiveness of live herpes zoster vaccine

New data will help to inform improvements to vaccination programmes for shingles

James F Mbinta, [1] Colin R Simpson[1, 2]

With a growing ageing population, the prevention of herpes zoster (known as shingles) and its associated complications is an important public health issue. Herpes zoster is a painful dermatomal vesicular disease that results from the reactivation of latent varicella-zoster virus in nerve ganglia.[1] Advancing age and immunosuppression are prominent risk factors.[2] In some patients, reactivation occurs on the ophthalmic branch of the fifth cranial nerve, causing herpes zoster ophthalmicus with an increased risk to the eye.[3-5] A substantial minority of patients can also develop postherpetic neuralgia (8-21% according to published estimates[6]), a prolonged neuropathic pain in areas of the skin supplied by sensory neurons arising from a spinal nerve ganglion. In their linked BMJ study, Klein and colleagues (doi:10.1136/bmj-2023-076321) used data from a large US healthcare provider (Kaiser Permanente Northern California) to determine the long term effectiveness of live zoster vaccine among just over half a million adults aged 50 years and older.[7] Key outcomes were herpes zoster infection, admission to hospital with herpes zoster, postherpetic neuralgia, and herpes zoster ophthalmicus.

This work is timely because herpes zoster vaccination programmes, such as those introduced in the UK in 2017 and New Zealand (Aotearoa) in 2018, are expanding to include people who are younger, older, and at risk from immunocompromised status (live zoster vaccine, for instance, is not currently recommended for people with immunocompromising conditions).[8] Further evidence is also needed to reassure policy makers on the effectiveness of live zoster vaccine in preventing herpes zoster in these populations for a sustained period of time.[9-13]

Klein and colleagues' new research is an excellent example of a real world observational study, using high quality health data, relevant epidemiological designs, and methods to control for biases. Real world studies are increasingly considered a valuable (and cost effective) contribution to the evidence base and are complementary to randomised controlled trials.[14] The authors made extensive efforts to improve data quality to enhance the precision of outcomes by including diagnoses, prescriptions, laboratory tests, and by conducting a review of medical charts for incident case identification.

As vaccine uptake in the study population exceeded 60% in adults aged 60 years or older, and 5.7% of the vaccinated cohort were immunocompromised at the time of vaccination, the study had sufficient power for an analysis of subgroups based on age, sex, ethnicity, and immunocompromised status. The authors also included a novel method for examining waning vaccine effectiveness by using a calendar timeline rather than from time since vaccination when fitting their Cox proportional hazards regression models. This method avoided bias caused by changes in herpes zoster incidence unrelated to vaccine effectiveness waning .

In Klein and colleagues' study, the effectiveness of live zoster vaccine against herpes zoster in the first year after vaccination (67%) was similar to the efficacy reported in prelicensure clinical trials (60%).[15] However, the 83% effectiveness they found against postherpetic neuralgia was considerably higher than the 67% reported in clinical trials.[16] Although a previous meta-analysis of trials was not able to determine a precise estimate of efficacy against herpes zoster ophthalmicus,[16] Klein and colleagues reported a precise estimate of 71% (95% confidence intervals 63% to 76%).[7]

Their reported 90% vaccine effectiveness against admission to hospital for herpes zoster is also notable because this strong evidence shows that live zoster vaccine can prevent severe infection related outcomes, particularly in older people at higher risk. This information is crucial for vaccination programmes that are limited to individuals aged 70-79 years. This research also adds to evidence that live zoster vaccine is effective against herpes zoster among immunocompromised adults.[9 17]

A further advantage of observational study designs is that vaccine effectiveness can be followed up in a cost effective way over long periods of time. Klein and colleagues' observed waning of vaccine effectiveness over a 10 year period for all outcomes. The capability to determine precise estimates of waning effectiveness over time, provides new and valuable information on the need for and timing of follow-up or booster doses. If, for instance, 50% is the limit of acceptable vaccine effectiveness for prevention of herpes zoster,[18] vaccine effectiveness (>50%) was sustained for five years only among adults younger than 70 years.

Evidence suggests that high vaccine effectiveness can be reached with a subsequent dose of herpes zoster vaccine, so booster or second doses for people in the older groups could be considered.[9] Further research is also needed to evaluate the trajectory of vaccine effectiveness against herpes zoster and severe outcomes over time in people with chronic diseases such as those of the kidney, heart, and autoimmune system.

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