Duration of pertussis vaccine effectiveness in New Zealand

Funded by a Partnership between Health Research Council of New Zealand and Ministry of Health

Investigators:

Dr Helen Petousis-Harris (Principal Investigator)

Dr Sarah Radke (Principal Epidemiologist and Co-Investigator)

Associate Professor Nikki Turner (Co-Investigator)

Ms Donna Watson (Project Manager)

Summary

The Effectiveness of Pertussis Immunisation in Children (EPIC) study data provides good evidence that the current National Immunisation Schedule protects against severe pertussis in infants and children. The pertussis vaccine provides moderate protection against severe disease after two doses and good protection after three doses. No evidence of waning protection was shown following dose three up to age four years or following 3P+1 doses up to age seven years. Further investigations are required to investigate protection against mild disease and duration of protection in older children and adolescents, and to evaluate the effects of delays between doses one and three.

The study was led by Dr Helen Petousis-Harris, Director of Immunisation Research at the Immunisation Advisory Centre, with funding and assistance provided by the Health Research Council of New Zealand and Ministry of Health.

Discussion

The EPIC case-control study was conducted in 2015 to evaluate the effectiveness and duration of protection provided by the National Immunisation Schedule against pertussis. The data were sourced from the National Immunisation Register (NIR), the National Minimum Dataset (NMDS), EpiSurv, school-based vaccination systems (SBVS), the National Health Index (NHI), Primary Health Organisation enrolment collection, and practice management systems (PMS).

There were two ages of interest – children aged six weeks to four years and children aged four to eight years enrolled on the NIR. Cases for children aged six weeks to four years included pertussis-related hospitalisations or pertussis notifications between 2006 and 2013. Cases for children aged four to eight years were limited to non-hospitalised pertussis notifications between 2006 and

2013. For every case, 20 controls were randomly sampled from children enrolled on the NIR and matched by age and DHB of residence. Demographic characteristics between cases and controls were compared using appropriate statistical tests. Vaccine effectiveness was calculated using multivariable conditional logistic regression and the formula (1-Odds Ratio) x 100%. Sex, ethnicity and socioeconomic deprivation were examined as potential confounders. Various sensitivity analyses were performed to test the robustness of the study design.

For children aged six weeks to four years, significantly more reported cases were unvaccinated than matched controls (29% vs 12%, respectively; $p<0.001$). Vaccine effectiveness increased from 41% after the first dose of the primary series, to 78% and 89% following the second and third doses, respectively, and maintained until the children's fourth birthday. Adjusting for confounders resulted in the vaccine effectiveness for the first dose dropping from 41% to 25% for the youngest infants (six weeks – two months), which was predominantly driven by differences in ethnicity between the vaccinated and the unvaccinated groups. No confounding was seen for the other ages and doses.

In children aged four to eight years, the difference in the proportions cases and controls who were immunised widened – 31% of non-hospitalised notified pertussis cases were unimmunised compared with 4% of the cohorts. Vaccine effectiveness following the primary series plus the first booster at age four years was 92% and was maintained until the children's eighth birthday. No evidence of confounding was seen.

Overall, the vaccine effectiveness following the primary series was approximately 84% (95% CI 82-86) and following the first booster dose increased slightly to 91% (95% CI 89-92). A series of sensitivity analyses did not change our primary finding that protection against pertussis disease was sustained through to children's fourth birthday following the primary series of vaccinations recommended by the National Immunisation Schedule.

In the first sensitivity analysis, the EpiSurv notification data were matched with the NMDS to examine differences between vaccine effectiveness and duration of protection for hospitalised and non-hospitalised notifications: a third of hospitalisations were not notified. The second sensitivity analysis limited cases to laboratory confirmed pertussis – approximately, half of the cases were laboratory confirmed. In the third sensitivity analysis, improved timeliness in recent birth cohorts was taken into account. The fourth sensitivity analysis reduced the wash-out period between vaccination and disease detection from 14 to seven days and again to zero days. To examine

reporting behaviour of individual practices, controls were selected from the NIR and matched by general practice enrolment in addition to age and DHB of residence in the fifth sensitivity analysis. The final sensitivity analysis examined healthcare seeking behaviour by selecting controls from the matched case's general practice and randomly sampling from among children who had a non-cough visit within two weeks of the case disease date.

A strength of the EPIC study was utilising existing New Zealand health data. NHI numbers facilitated linking information across data sources at the individual level. Results could be reported separately for hospitalisations and notifications, and the validity of control sampling was verified. The electronic data linking methodology is timelier and less costly than traditional research methods that require prospective data collection. The ability to conduct a range of sensitivity analyses confirmed the robustness of the results.

A limitation of this and all observational studies is that there may be unmeasured residual confounding. The study was also limited to evaluating vaccine effectiveness in children less than age eight years because immunisation data for older children aggregated and available from a central source, such as the NIR is not yet available. Obtaining data for older children involves either waiting until 2017, when the children enrolled on the NIR age up, or extracting data from individual PMS, requiring additional funding and resources. Another limitation is that the results are not generalisable for all pertussis disease – because notifications are collected through passive surveillance, our analysis likely captures only cases at the severe end of the disease spectrum.