Why pneumococcal surveillance must continue

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Pneumonia, two-thirds of which is caused by *Streptococcus pneumoniae*, is the single most common vaccine-preventable cause of death in children younger than 5 years, leading to approximately 700 000 deaths per year in those younger than 5 years.[1] To continue to monitor the effectiveness of pneumococcal vaccines to prevent invasive pneumococcal disease (IPD) is important.

In this issue of *The Lancet Global Health*, Anne von Gottberg and colleagues[2] present the analysis of surveillance data generated between 2005 and 2019 from more than 50 000 cases of IPD in adults and children in South Africa. The data stem from a national, laboratory-based active surveillance system that also includes serotyping and antibiotic susceptibility testing with good quality assurance standards. Such substantial national surveillance is not routinely carried out in most low-income countries, primarily because of resource constraints.

With documented decline of 76·0% in overall IPD rates and 95·5% (7-valent pneumococcal conjugate vaccine [PCV7]) and 93·8% (13-valent PCV [PCV13]) decline in vaccine-specific serotypes in children younger than 2 years in South Africa, the results are definitely good news for the control of pneumococcal disease. The dataset clearly supports evidence from both high-income and low-income settings that PCV protects against an important infectious disease (IPD), which causes high morbidity and mortality, especially in both very young and very old age groups, as well as in those who are immunocompromised and have comorbidities.[3] The results also support previously published findings from research settings in The Gambia, Kenya, Malawi, and Zambia,[4–7] and enable comparisons of trends of direct and indirect effects of PCV between settings in Africa.

In South Africa, PCV7 and PCV13 were introduced into the routine infant vaccination schedule in 2009 and 2011 respectively, following a two plus one dosing schedule with average cover rates of more than 85%. As illustrated in figure 3 of the Article, the analysis showed a vaccine-serotype-specific significant decrease in the numbers of IPD in all age groups. The authors show that the highly invasive serotype 1 had almost completely disappeared, but there were some concerns regarding vaccine efficacy against serotype 3. Notably, there was also an increasing and significant effect on the decline of IPD in non-vaccinated older age groups and in infants too young to have received the primary vaccination schedule.

The evolution of IPD due to serotypes not covered by the PCV in use is a global concern and has been observed in many countries that have implemented routine PCV programmes, and South Africa is no exception.[8] In particular, unvaccinated older people benefited from a decline in IPD caused by serotypes contained in PVC, but are increasingly noted to develop IPD with non-vaccine type (NVT) pneumococci, especially with serotype 8. This finding corroborates data from other countries, be it with different regional and age-associated serotype patterns and affecting in particular individuals older than 64 years.

Although it is, of course, important to monitor the evolution of NVTs going forward with a view to possibly develop vaccines for future adult vaccination incorporating these serotypes, current concerns regarding the evolution of NVT should not distract from the indirect effect of PCV on preventing cases of pneumonia and meningitis overall, as well as in the older age group and in infants still too young to receive their vaccines.

Further indirect effects might not be anticipated in view of the 15-year surveillance data, provided the serotypes covered by the PCV vaccines and schedules are the same. However, the switch to the WHO prequalified and licensed preparation of a PCV10 produced by the Serum Institute in India will occur later this year in South Africa. In a substantial clinical trial in The Gambia, this vaccine had shown non-inferior immunogenicity to that of polysaccharide protein D-conjugate vaccine and had shown efficacy and effectiveness against pneumococcal disease, and this vaccine represents a cost-effective alternative to existing PCVs.[9] After the switch, there will be a need to closely monitor IPD for any reappearance of disease from serotypes 4 and 18C, serotypes not covered by the Serum Institute in India PCV10. Further efforts to identify levels of vaccine coverage in rural areas are also needed to predict direct and indirect effects.

IPD is an infectious disease with high mortality in South Africa. With 64% of all cases of IPD occurring in

people living with HIV, this group is over-proportionally represented with a high susceptibility and mortality risk. Additional sensitivity analyses could further identify factors that are associated with poor outcomes and influence improvements in diagnosis and care for people living with HIV. Other confounders over a long period would include nonspecific, preventive measures such as water, sanitation, housing, and other respiratory diseases (eg, SARS-CoV-2, respiratory syncytial virus, and tuberculosis).

In conclusion, given the robust evidence of the direct and indirect effects of PCV on IPD in all ages with a sustained reduction in IPD and also drug-susceptible pneumococci, there can be no doubt that PCV vaccines need to be available in an equitable and cost-effective manner to children and possibly also adults.[10] In view of evolving NVTs, the battle has not yet been won against the pneumococcus because development continues to play the catch-up game, and surveillance efforts as reported here should continue.

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