

centre of interest for public health purposes.⁶ Finally, the decline in the global prevalence of subtype C, which dominates in South Africa, raises hope about the potential to eliminate new transmissions through the implementation of the UNAIDS 90-90-90 global target.

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Pneumococcal vaccines in Nepal

Worldwide, pneumococcal conjugate vaccines (PCV10, PCV13) are included in many national immunisation schedules to prevent severe pneumococcal disease, particularly meningitis and pneumonia. PCV schedules vary from country to country.¹ A 2012 WHO Position Paper on PCV endorses either a 2+1 (two primary, one booster) or 3+0 (three primary, no booster) vaccination schedule depending on disease epidemiology, coverage, and timeliness of immunisation.² Many countries have adopted a 2+1 schedule, with the first two doses administered early in infancy, approximately 8 weeks apart, and the third dose given late in the first year or early in the second year of life. The rationale for this approach is that two PCV doses are likely to offer similar protection for infants to three doses in the first year of life,³ with the booster dose offering longer lasting immunity and therefore protection, and better indirect protection. The effectiveness of this schedule has been shown in many settings.⁴

Studies of PCV7 have shown that two doses have similar immunogenicity to three doses for most serotypes, exceptions being serotypes 6B and 23F.⁵ Many African countries continue to use a 3+0 schedule which has been shown to be effective in the two African efficacy trials of a nine-valent PCV, which was a precursor of PCV13.^{6,7} In the trials, the vaccine was immunogenic for serotype 1, the dominant cause of pneumococcal disease in less developed countries, but surprisingly showed little efficacy against serotype 1 disease. Data from South Africa, which has implemented a 2+1 schedule, suggests that this

schedule might provide better long-lasting protection and better herd protection especially for serotype 1, which is more prevalent in older children.⁸

As part of the Global Polio Eradication Initiative, WHO now recommends that countries using oral polio vaccine should add a single dose of inactivated polio vaccine (IPV) at or after 14 weeks of age. For many countries, this has necessitated the administration of three injectable vaccines (PCV, IPV, and diphtheria, tetanus, whole-cell pertussis, hepatitis B virus, Haemophilus influenzae type B) at a single clinic visit at 14 weeks. The Nepali Ministry of Health was concerned about the acceptability of this policy. To address this concern, Rama Kandasamy and colleagues⁹ did an open-label randomised clinical trial of two different 2+1 PCV10 schedules to compare the immunogenicity of the second dose of PCV10 given at 10 weeks of age (6+10) with that given at 14 weeks of age (6+14).

The authors found that for six of the ten serotypes in the vaccine, immunogenicity was inferior in the 6+10 group by one or both of the standard measures. The most substantive differences were seen for serotypes 6B and 23F, and these were largely corrected by the time the booster was due at 9 months. Following the booster there were no significant differences between the groups. The clinical relevance of these findings is not known. The risk of pneumococcal disease is age dependent. Giving the second dose at 10 weeks would provide protection earlier, but the level of protection might be less for up to six serotypes



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for part of the time up to 9 months of age. After the booster, the levels are similar, so herd immunity is likely to be similar. Therefore, the authors conclude that the 6 week, 14 week, and 9 month schedule is superior, but that the 6 week, 10 week, and 9 month schedule might be used where programmatic issues dictate, as the herd effects would be similar. The 6 week, 10 week, and 9 month schedule might leave infants more susceptible to some serotypes, but this would soon be covered by herd immunity. If countries were to introduce this schedule with poor coverage and therefore limited herd immunity, this could lead to vaccine failures in children yet to receive a booster dose.

The study rationale was based on the perception that caregivers would not accept the administration of multiple injections at a single visit.¹⁰ A systematic review found high caregiver acceptance of multiple injections in a single visit, even when concerns were expressed about the number of vaccine injections children received.¹¹ Countries need to balance concerns such as this against the superior immunogenicity seen when the two primary doses of PCV are separated by 2 months rather than 1 month.

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Socioeconomic disparities and infection: it's complicated

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The associations between low socioeconomic status and poor health have long been appreciated and are supported by a vast body of evidence.¹ Although this overall relationship remains robust, in *The Lancet Infectious Diseases*, Alessandro Pini and colleagues² show that the association between markers of low socioeconomic status and incidence of infectious diseases in Sweden, a high-income country, is not at all straightforward. Pini and colleagues² used 10 years of Swedish national notification data to study the association between 29 infectious diseases and socioeconomic characteristics. They used a matched case-control design and analysed the data of more than 1 million people aged 18–65 years.

Pini and colleagues² grouped their findings into three patterns. The first pattern supports the overall premise of the social determinants of disease—people with markers of lower socioeconomic status had higher disease incidence. This association was seen for invasive bacterial infections, hepatitis B, hepatitis C, tuberculosis, and antimicrobial-resistant infections. These infections are the ones that could be affected by public health campaigns to address social determinants of disease. The second pattern was the opposite—ie, markers of lower socioeconomic status were associated with lower disease incidence. Diseases in this group included food-borne and water-borne diseases and dengue. The authors postulate that this pattern could be partly