serotypes 6B (0·16 μg/mL), and 2·2 times higher than that for serotype 19F (1·17 μg/mL).[7,11]

In summary, Temple and colleagues' study showing non-inferiority of PCV10 versus PCV13 in terms of immunogenicity against invasive pneumococcal disease provides important endorsement of existing WHO advice on the use of PCVs for infant immunisation.[12] Furthermore, these data indicate that an individual country's decision on which vaccine to use in a 2+1 schedule to directly protect against vaccine-serotype invasive pneumococcal disease might well be influenced primarily by the cost of vaccine procurement. The effects of the differences between the vaccines in terms of absolute antibody concentrations are unclear, but might have implications for the effect of vaccines on non-invasive disease, carriage, and indirect protection for at least some serotypes. However, these questions require further study.

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Control of scabies and secondary impetigo: optimising treatment effectiveness in endemic settings


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For **WHO list of neglected tropical diseases** see http://www.who.int/neglected_diseases/diseases/en/

Scabies is more than a common parasitic skin disease[1] and health authorities in low-income and middle-income countries now recognise it as a public health issue. In 2017, WHO added scabies to the list of neglected tropical diseases for the following reasons: it is very common (point prevalence of up to 200 million),[2] has a substantial global burden in disability-adjusted life-years,[3,4] has notable psychosocial and economic effects caused by stigma and work disruption, and the major sleep disturbances and damage to the skin barrier caused by scratching. *Sarcoptes scabiei* also inhibits complement pathways, leading to streptococcal and staphyloccocal super-infection of the skin.[5]

Controlling secondary bacterial pyodermas caused by scabies is crucial. Patients in tropical areas with *Staphylococcus aureus* bacteraemia and scabies have a higher mortality than those without scabies;[6] but other life threatening infections such as cellulitis or necrotising soft tissue infection might occur, and impetigo might lead to haematuria or post-streptococcal glomerulonephritis and acute rheumatic fever or rheumatic heart disease.[7,8]

In *The Lancet Infectious Diseases*, Lucia Romani and colleagues[9] report on the efficacy of the

coadministration of oral ivermectin and azithromycin for control of scabies and impetigo in the Choiseul Province of the Solomon Islands. Using the opportunity of a trachoma mass drug administration campaign in the general population, the investigators added ivermectin (or permethrin 5% cream) in a subgroup of the population using a single-arm intervention study design. Primary outcome data, published elsewhere,[10] showed that combining ivermectin and azithromycin is safe and achievable. As a secondary outcome, the authors measured the prevalence of scabies and impetigo using a before-and-after design with two different sets of ten randomly selected villages (only four of the ten villages were actually visited twice, with change in prevalence assessed via a paired sensitivity analysis). A parallel relative reduction in prevalence was found for scabies (88%, 95% CI 76·5–99·3) and impetigo (74%, 63·4–84·7). And a comparison of outpatient attendance at government clinics across the province in the 3 months before and after mass drug administration showed that the number of people presenting with skin sores, boils, and abscesses decreased by 50·9% (95% CI 48·6–53·1).[9]

Compared with interventions in individuals, a lot of data is now available in endemic or epidemic settings from mass drug administration for treatment of scabies, whether adults or children, or other diseases—eg, onchocerciasis.[11,12] Which drug should be used for scabies and whether it should be combined with antibiotics are important decisions. David Taplin[13] first used a mass drug administration approach in 1986 for control of scabies in Panama, and showed that application of 5% permethrin cream substantially decreased the prevalence of scabies for up to 3·8 years after treatment (33% at baseline to 12% at 3·8 years). A parallel sustained decrease in bacterial skin infections, without any oral or topical antibiotic, was also noted (32% at baseline to 2% at 3·8 years).[13] However, wide use of this community treatment appeared impractical because of the logistics involved in mass topical therapy. Subsequently, the SHIFT scabies cluster randomised controlled trial in Fiji showed a significant response after oral ivermectin (1–2 doses) versus 5% permethrin cream and the normal standard of care. As in Panama, the response included a parallel and sustained 12 months (24-month data are yet unpublished) decrease in the prevalence of scabies and impetigo (relative reduction of 94%, 95% CI 83–100 and 67%, 95% CI 52–83).[14] Finally, in a randomised controlled trial involving six communities in the Solomon Islands, coadministration of azithromycin with ivermectin led to similar decreases in the prevalence of scabies and impetigo compared with ivermectin alone;[15] however, a transient increase in the proportion of macrolide-resistant *S aureus* strains was reported after azithromycin mass drug administration.

From the point of view of health policy decision making, mass drug administration with oral ivermectin in highly endemic or epidemic settings is clearly effective, producing a relevant long-term effect on both scabies and impetigo. Adding an antibiotic to an active mass drug administration-based scabies strategy does not appear to provide additional benefit, although combining drug administration with mass drug administration for trachoma (or yaws) is a potential option. Many of these studies have involved island populations and similar work needs to be assessed in continental programmes and in refugee camps or institutions—eg, nursing homes, and in high-income countries. Efforts should be made to facilitate access to oral ivermectin, including listing in the WHO essential list of medicines or through donor programmes, such as for onchocerciasis. Alternative regimens such as a single dose of moxidectin, which is already approved for onchocerciasis, might be an even better alternative because of its pharmacokinetic properties;[16] but this option needs to be studied.

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Tuberculosis active case-finding: more than just finding cases

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In *The Lancet Infectious Diseases*, Matthew Saunders and colleagues[1] describe a long-term active case-finding intervention for tuberculosis among households in shanty towns in Callao, Peru. They used home visits over a 10-year period to screen household contacts of an index patient for tuberculosis disease. Although the absolute number of cases found through the active case-finding intervention was modest compared with the number diagnosed by passive case-finding at health facilities, women were preferentially diagnosed through the home visits (36 [68%] of 53 cases diagnosed through active case-finding were female *vs* 85 [47%] of 179 diagnosed through passive-case-finding; p=0·009). Saunders and colleagues propose that the visits might have overcome a health-care access gap that leads to disproportionate underdetection of tuberculosis among women in this setting. Sparse prevalence survey data from Latin America make it difficult to know whether the case detection gap is truly larger for women in this region, distinct from other parts of the world.[2] Regardless, the study by Saunders and colleagues shows that patients found through active case-finding can differ from those who are routinely diagnosed in health facilities. Thus, active case-finding can promote equity through preferential detection of tuberculosis in populations who face barriers to accessing health services.[3] These vulnerable individuals are probably over-represented among the so-called missing 4 million tuberculosis patients—that is, the gap between the 6 million people diagnosed and 10 million estimated patients with tuberculosis annually.[4]

The study by Saunders and colleagues also emphasises a benefit of active case-finding that is ignored when people focus solely on increasing the numbers of cases detected—namely, the benefit of early diagnosis. The greater proportion of sputum smear-negative cases found through active case-finding in the study (33 [62%] of 53 *vs* 62 [35%] of 179 found by passive case-finding; p=0·0003) highlights that contact investigations diagnose people earlier, when they are less infectious, thus reducing transmission. However, more sensitive diagnostic technologies—eg, chest radiography[5] and molecular testing for *Mycobacterium tuberculosis* and rifampicin resistance mutations[6]—will be vital if programmes are to maximise the benefits of active case-finding.

The study by Saunders and colleagues also highlights the opportunity lost by not giving preventive treatment to adult contacts of tuberculosis patients—a group for whom such treatment is considered optional, according to latest WHO guidance.[7] Adult contacts had a substantially increased risk of developing tuberculosis that persisted for 3–4 years. Only a third of contacts who ultimately got sick were diagnosed within a year of the index patient; more cases were diagnosed over the