

New vaccine strategies to finish polio eradication



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For the **Global Polio Eradication Initiative** see <http://www.polioeradication.org/Dataandmonitoring.aspx>

The Global Polio Eradication Initiative (GPEI) currently faces two specific challenges. First, all the cases in the past 9 months caused by ongoing wild-virus transmission were in Afghanistan and Pakistan—Africa has had a remarkable 9 months without detection of the disease. Second, circulating vaccine-derived polioviruses are continuing to cause poliomyelitis in a few countries, a rare outcome associated with continued use of the live-attenuated oral poliovirus vaccine (OPV). In *The Lancet Infectious Diseases*, the results of two clinical trials of OPV that address these challenges are reported by Fatima Mir and colleagues¹ and Concepción Estívariz and colleagues.²

The persistent, widespread transmission of wild polioviruses in Pakistan (and to a lesser extent Afghanistan) is arguably the biggest hurdle for global polio eradication. Armed conflict, a ban on vaccination in parts of the country, and targeted killing of polio vaccinators severely limit the ability of the eradication programme to deliver all the doses of OPV that are needed to ensure that a child is protected against poliomyelitis.³ Vaccination campaigns must be opportunistically planned, taking advantage of windows of opportunity to reach children during periods of improved security (eg, ceasefires) or mass migrations. These vaccination campaigns have traditionally occurred with at least a 4-week interval between doses. This interval is used because replication of a specific serotype of vaccine poliovirus associated with seroconversion after giving trivalent OPV could interfere with the response to the other two serotypes in a subsequent dose if given too soon. However, during the past decade monovalent OPV (mOPV) and bivalent OPV (bOPV) have been introduced in campaigns to target the remaining circulating wild poliovirus serotypes (currently only wild serotype 1 still circulates; serotype 2 was last detected in 1999 and serotype 3 in 2012). The mOPV and bOPV vaccines have better immunogenicity and efficacy than the trivalent formulation as a result of absent (mOPV) or reduced (bOPV) interference between each serotype of vaccine poliovirus.⁴⁻⁶ The mOPV and bOPV vaccines are also less likely to be affected by interference from successive doses of vaccine. Indeed, in the case of mOPV no such interference would be expected—because vaccine response is all-or-nothing, a failure of the first dose would not alter the likelihood of response to a subsequent dose. This reasoning has driven a short-interval additional

dose strategy in parts of Pakistan and Afghanistan, where two vaccine doses are given in succession within a period of 2 weeks or less, which the GPEI believes is effective in rapidly immunising children during periods of access. The clinical trials in Pakistan¹ and Bangladesh² show that two or three doses of mOPV given with a 1-week or 2-week interval^{1,2} or bOPV given with a 2-week interval² are as effective (ie, non-inferior) at inducing serum-neutralising antibodies as the same vaccines given with the standard 4-week interval. These findings support the use of short-interval campaigns with other strategies to maximise the immunogenicity of each vaccination contact with children in Pakistan. These strategies include giving inactivated poliovirus vaccine (IPV) simultaneously with OPV. This particular strategy began in some districts in Pakistan in 2014 after it was shown that IPV substantially boosts intestinal and systemic immunity.^{7,8}

The clinical trials in Pakistan¹ and Bangladesh² gave OPV as part of the routine immunisation series for infants beginning at age 6 weeks. The trials therefore also provide evidence to support the regulatory approval and licensing of bOPV on this schedule, which is important for the GPEI strategy to tackle the challenge of circulating vaccine-derived polioviruses. To prevent emergence and spread of such polioviruses, the use of OPV will eventually have to cease. The current GPEI strategic plan envisages a globally synchronised withdrawal of serotype 2 OPV in April, 2016, at a time of heightened surveillance and investment in polio, followed by withdrawal of serotypes 1 and 3 OPV when the corresponding wild-type viruses are confirmed as eradicated.⁹ The withdrawal is a major undertaking, needing sufficient quantities of licensed bOPV, coordinated changes to vaccination schedules, careful destruction of unused stock of trivalent vaccine, and the introduction of at least one dose of IPV to the routine schedule as recommended by WHO as insurance against any potential emergence or reintroduction of serotype 2 vaccine-derived or wild-type polioviruses.¹⁰ The results of the clinical trial reported by Estívariz and colleagues² suggest there might also be some benefit from the global withdrawal of serotype 2 OPV for the eradication of remaining wild polioviruses, because they showed bOPV to be more immunogenic on the routine schedule than trivalent OPV for serotypes 1 and 3.² A third challenge and a key objective for the GPEI is to reap this

benefit and leave a legacy by supporting improvements in routine immunisation coverage in underserved, low-income areas.

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I declare no competing interests.

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Sequelae after Ebola virus disease: even when it's over it's not over



Although still far from over, the Ebola virus disease outbreak in west Africa seems to be waning. With almost 25 000 cases reported up to now and an estimated case fatality rate of 50–70%, about 10 000 to 15 000 survivors of this disease exist in the region. What health problems do these survivors face? Some answers are provided by a study in *The Lancet Infectious Diseases* by Danielle Clark and colleagues,¹ who assessed 49 adult survivors of Ebola virus disease matched with 157 controls 29 months after an Ebola virus outbreak in Uganda in 2007.² Survivors were at significantly increased risk of ocular deficits (retro-orbital pain and blurred vision), hearing loss, neurological abnormalities, sleep disturbance, arthralgias, memory loss, and various other constitutional symptoms and chronic health problems.

Although the study by Clark and colleagues is of a different virus species (Bundibugyo Ebola virus) and population than the ones implicated in the continuing crisis in west Africa, there is much reason to believe that their findings nevertheless apply to survivors of the Zaire Ebola virus presently circulating in Guinea, Liberia, and Sierra Leone. Similar findings have been shown from early anecdotal reports from those west African countries and published reports and smaller studies^{3–7} on Ebola virus disease survivors in the Democratic Republic of the Congo (Zaire Ebola virus) and northern Uganda (Sudan

Ebola virus).^{3–7} Neither can these post-Ebola virus disease sequelae be cast off as minor aches and pains. In one report, survivors were unable to perform their previous work up to 1 year after infection, with obvious economic consequences.⁷

In view of these findings, services for Ebola virus disease survivors should be established, a task that is easier said than done considering that many of the governmental and non-governmental agencies involved are still grappling with the heavy burden of acute outbreak control activities while trying to re-establish the broader health-care system. A further challenge is that Ebola virus disease survivors might need subspecialised services not readily available in the afflicted countries, such as ophthalmic care (including slit lamp examination to diagnose possible uveitis, which seems to be common) and mental health services.

Despite the findings of Clark and colleagues, many questions remain and much research needs to be done to better understand the frequency and severity of post-Ebola virus disease sequelae and ensure optimum clinical management. The study was observational and cross-sectional, with data collected at one time point years after acute disease. Although cursory physical exams were done, investigators were not able to assess more episodic problems (eg, bouts of acute uveitis) as they happened.

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