

child mortality) and MDG 5. At that time, the US Agency for International Development (USAID), the UK Department for International Development, the Australian Agency for International Development, and the Bill & Melinda Gates Foundation launched the International Alliance for Reproductive, Maternal, and Newborn Health to coordinate the efforts of donors and partner countries to reduce the unmet need for family planning and maximise outcomes in maternal and neonatal health. In 2011, the high-level Commission on Information and Accountability for Women's and Children's Health⁹ was established, to inform relevant global reporting, oversight, and accountability standards, and the Global Plan Towards the Elimination of New HIV Infections Among Children by 2015 and Keeping their Mothers Alive,¹⁰ supported by PEPFAR and UNAIDS, was released with the aim to reduce by half maternal deaths among HIV-positive women. This year the Commission on Life-Saving Commodities for Women and Children¹¹ was formed, to recommend solutions to eliminate access barriers to key maternal and child health and family planning commodities. The US Government has, with the Governments of Uganda and Zambia and key partners, initiated Saving Mothers Giving Life, focused on the dangers that occur during the 24 hours of labour and delivery. A global consortium of non-governmental organisations and countries joined USAID to launch Saving Lives at Birth, a grand challenge for new and transformative solutions to help newborn babies and mothers during their most vulnerable hours. In June, 2012, the US Government and UNICEF, along with the Governments of Ethiopia and India, will be hosting a Child Survival Call to Action, followed shortly by the UK Government and the Bill & Melinda Gates Foundation's forum on family planning in July. And in July, the world will gather at the XIX International AIDS Conference to discuss, among other issues, investments in prevention of mother-to-child transmission of HIV and saving mothers' lives.

For **Saving Mothers Giving Life** see http://www.savingmothersgivinglife.org/about_smgl.html

For **Saving Lives at Birth** see <http://www.savinglivesatbirth.net>

For the **Child Survival Call to Action** see <http://5thday.usaid.gov/pages/ResponseSub/Event.aspx>

For the **Family Planning Forum** see <http://www.dfid.gov.uk/News/Latest-news/2012/Family-planning-UK-to-host-summit-with-Gates-Foundation/>

The life—or death—of a mother in labour and delivery can be viewed as a decisive indicator in the health of a nation. The Oslo conference will help shape the integration of health and diplomacy and lift up the vital link between maternal mortality, the strengthening of health systems, and the fate of nations.

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Oral cholera vaccine and integrated cholera control in Haiti

On April 14, 2012, some 18 months after the first cases of cholera were documented in Haiti, a group of Haitians were offered the first of two doses of oral cholera vaccine as part of the Haiti cholera vaccination project. The epidemic is not only the first in this region in nearly

two decades, it is also the worst epidemic of the post-antibiotic, post-vaccine era.¹ This vaccine rollout, linked to efforts to increase access to safe drinking water, seeks to vaccinate 100 000 people with a low-cost vaccine recently prequalified by WHO. It is, we hope, a modest

For the **Haiti cholera vaccination project** see <http://www.pih.org/cholera-vaccine-campaign>

first step towards comprehensive and integrated prevention and control of cholera in Haiti and the region.

On April 23, 2012, the Haitian Ministry of Health reported 536 943 cases of cholera and 7112 deaths, with 144 cases seen on that day.² The epidemic has continued to expand despite case-finding campaigns and treatment linked to prevention, education efforts about proper hygiene and sanitation, and calls for investment in sanitation and water infrastructure. The start of the rainy season in mid March has been associated with an increased number of cases. Moreover, the *Vibrio cholerae* strain is evolving,³ which renders even those previously infected at risk of reinfection.

This epidemic has exploded with such ferocity in large part because of the long-standing fragility of the Haitian health system.⁴ Most providers, local and international, have already spent the lion's share of their available "relief" funds.⁵ But water and sanitation have not attracted the attention they merit, even in cities. The impact of cholera on the household assets of the rural and urban poor is poorly measured but likely to be far-reaching; medical catastrophe and high costs of care are a common cause for tipping households into destitution in Haiti and many poor countries.⁶ It is for this reason that we argued, soon after the first cases of cholera in Haiti, that only fully integrated prevention and care would do.⁷

Safe and effective oral cholera vaccine is part of this agenda. The ongoing vaccination effort is led by the Haitian Ministry of Health; our organisations, Partners In Health and GHESKIO, are working as technical and implementing partners. Despite the scepticism of some international public health agencies,⁸ Partners In Health purchased all available doses (200 000) of Shanchol vaccine. The programme will assess the feasibility of providing the two-dose oral vaccine (in cold chain) in Haiti.⁹ The vaccine protects about 67% of those who receive both doses over 2–3 years,¹⁰ which affords time to promote true water security.

There have been objections to integrating vaccine into the response. Initial resistance to deploying vaccine as a complementary tool in the fight against cholera occurred for various reasons: fear that using only the limited number of available doses would be inequitable and might trigger social unrest during an election year; fear that logistics capacity (especially for cold chain storage) would be insufficient to implement the programme effectively;⁸ concerns that use of the vaccine would reduce

other prevention practices of good hygiene and use of potable water;⁸ concern that the project would interfere with a planned national campaign to reinforce other basic childhood vaccinations, including polio;¹¹ and uncertainty about the use of vaccine in epidemic settings compared with endemic settings, in which oral cholera vaccines have been better studied.^{10,12} A new Haitian President and the nomination, in October, 2011, of a Minister of Health who viewed the situation with urgency and called for integrating vaccination into the ongoing response to cholera, brought a change in political will.

The debate has occurred largely among those not at risk of waterborne disease. During the early stages of this pilot in both rural and urban Haiti, we found that communities were interested in the vaccine and uptake of the first dose has been high. Within 2 weeks of commencement, 52 000 first doses of the vaccine have been administered. The capacity of the health system in the region is being reinforced by the cholera vaccination programme through the promotion of the national childhood immunisation campaign; community health workers have been trained to better prevent and, failing that, refer cases; cold chain capacity has been expanded; and a new vaccine has been delivered through the public sector vaccination programme. There have, of course, been challenges. Days before the launch of the cholera vaccine programme, a national bioethics committee wrote to the Minister of Health objecting to the use of cholera vaccine, which delayed the start date beyond the onset of the rainy season. Some villages are now flooded making it difficult to access health posts. The delay also caused a scheduling overlap with a national polio campaign, which led to reduced cold chain storage space and additional planning to ensure an appropriate interval between cholera vaccine and oral polio vaccine for children. These challenges, however, have been far from insurmountable.

Lasting improvements in access to clean water, hygiene, and sanitation are a backbone of public health, and the effect of such improvements in Haiti will be seen not just on cholera case loads but also on diarrhoeal disease and malnutrition—major killers of children in Haiti. Such improvements require sustained investment, and building public infrastructure, such as municipal water and sewage-treatment plants, takes time. In the interim, oral cholera vaccine—imperfect as it is—offers an opportunity to help save lives and protect the most vulnerable.



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For GHESKIO see <http://www.gheskio.org>

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Carotid intima-media thickness and cardiovascular events

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The association between carotid intima-media thickness (cIMT) and cardiovascular disease is well established. A single measurement of cIMT and plaque assessment improves predictions of risk of cardiovascular disease,^{1,2} and ACC/AHA guidelines³ support the use of cIMT and plaque measurement for cardiovascular risk stratification with a Class IIA recommendation (ie, evidence suggests that it is a reasonable test). However, the relation between cIMT progression over time and cardiovascular events has not been established. Although two meta-regression analyses of clinical trial data^{4,5} reported conflicting results about cIMT progression and cardiovascular events (one reported that less cIMT progression was associated with a lower likelihood of non-fatal myocardial infarction for each 0.01 mm per year decreased rate of change of cIMT [odds ratio 0.82, 95% CI 0.69–0.96; p=0.018], while the other reported that no relation exists between cIMT regression and coronary heart disease events [$\tau=0.91$, p=0.37]), no such data exist for the general population.

In *The Lancet*, Matthias Lorenz and colleagues⁶ report results of an individual patient data meta-analysis, which show that cIMT progression is not associated with incident myocardial infarction, stroke, or vascular death in the general population (hazard ratio 0.98, 95% CI 0.95–1.01, adjusted for age, sex, mean common carotid artery intima-media thickness, and vascular risk factors). Individual patient data meta-analyses

have advantages compared with conventional meta-regression analysis of published work, including greater power and lower risk of ecological bias.⁷ However, several other potential sources of bias,⁸ partly discussed by the authors, merit consideration.

First, selection bias and quality of primary studies. Six of 22 eligible study populations did not contribute data. An additional 21 423 of 58 407 eligible patients (36%) were excluded (several studies had >50% of their eligible patients excluded) because of a cardiovascular event before or between ultrasounds and loss to follow-up; excluded participants were older and had more risk factors than those included. In one study, only 784 of 1804 (43%) patients were eligible because of lack of complete outcome adjudication. Exclusion of these patients might have biased the results towards the null hypothesis, which raises questions about generalisability of the findings. Furthermore, although epidemiological studies are appropriate for questions of prognosis, the investigators should have assessed study quality and its effect on the results.⁹

Second, heterogeneity. Absence of statistical heterogeneity in the model for cIMT progression does not necessarily indicate absence of clinical heterogeneity, which is a qualitative judgment. Although heterogeneity in the study populations can help generalisability, differences in variables such as ultrasound protocols