Report on an Expert Colloquium

Past, Present and Future Partnerships In Disease Elimination and Eradication

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Former U.S. President Jimmy Carter welcomes GlaxoSmithKline CEO Andrew Witty to The Carter Center
BACKGROUND: A COLLOQUIUM OF EXPERTS

Past, Present and Future Partnerships in Disease Elimination and Eradication was an expert colloquium held at The Carter Center in Atlanta, Georgia on 4 December 2008. The event brought together health experts from around the world to measure progress in disease elimination and eradication and to discuss strategy for future efforts. The conversation focused on the role that partnerships–across sectors and continents–can play in addressing some of the world's most intractable health problems.

The event also marked the 10th anniversary of The Carter Center’s successful collaboration with GlaxoSmithKline to eliminate lymphatic filariasis (LF), a debilitating parasitic infection that strikes 120 million individuals in over 80 countries. Also known as elephantiasis, the parasite causes massive, painful swelling of the limbs, breasts, and genitals, which can lead to permanent disfigurement and severe social stigmatisation. Over the last decade The Carter Center, GlaxoSmithKline, the World Health Organization (WHO) and their partners have made great strides in fighting LF through drug donation, education and technical assistance programmes. To date, the initiative has helped these countries prevent infection in nearly 6.6 million newborns that would have otherwise acquired the disease.

Meeting attendees brought a wide range of expertise to the conversation, and included representatives from, the World Bank, Unicef, the International AIDS Society, the U.S. Centers for Disease Control and Prevention, the Bill & Melinda Gates Foundation, the Sabin Vaccine Institute, the Global Alliance to Eliminate Lymphatic Filariasis, The Carter Center, GlaxoSmithKline, and Merck & Co., Inc. John Hardman M.D. (The Carter Center) and Duncan Learmouth (GlaxoSmithKline) gave the opening remarks. Susan Dentzer (Health Affairs, PBS NewsHour, Global Health Council) and Chris Elias M.D., M.P.H. (PATH) moderated the panels, while former U.S. President Jimmy Carter, founder of The Carter Center and GlaxoSmithKline CEO Andrew Witty delivered closing remarks.

INTRODUCTION: ERADICATING AND ELIMINATING INFECTIOUS DISEASES

Infectious diseases take the lives of more than fourteen million people each year, the vast majority of whom live in poor countries in the developing world. Many of these deaths are caused by the “big three” infectious diseases–HIV/AIDS, tuberculosis, and malaria–but others can be attributed to a less well-known class of diseases.

These so-called “neglected diseases” cause systemic and pervasive disability, disfigurement, and mortality, striking a total of one billion individuals worldwide and driving poverty in developing countries. The WHO has identified fourteen of these diseases. They include afflictions such as LF, Guinea worm, onchocerciasis (river blindness), and Chagas disease, illnesses largely unknown beyond the global public health community and the world’s poorest citizens. Efforts to combat them are underfunded, and the health systems they affect are overwhelmed.

The impact of these diseases on the world’s poor is staggering, but many of them can be fought with relatively simple and cost-effective health interventions. Some, such as LF or Guinea worm, may even be eliminated or eradicated over the next several decades. Smallpox remains the only disease that has been successfully eradicated, and there is no shortage of cautionary tales to remind us of what happens when eradication and elimination efforts fail. Still, there is cause for optimism. The global public health community has engineered some remarkable programmes that are paving the way toward these long-term goals. There may even soon be breakthroughs in the fight against the “big three,” with the prospect of a malaria vaccine on the horizon and the personal, full-throated call for malaria eradication by Bill and Melinda Gates.

6 Guinea worm is a parasitic disease that is contracted through the consumption of stagnant water containing the parasite’s larvae. Once inside the human host, the worm matures and a year later forces its way out of the host's body. This removal process can take up to a month, and causes the extreme burning sensation that gave the disease its Latin name, dracunculiasis: affliction with fiery dragons. Definition adapted from: The Carter Center. Guinea Worm Eradication Program. Available at: http://www.cartercenter.org/health/guinea worm/index.html. Accessed 7 December 2008.
7 Onchocerciasis, also known as river blindness, is a parasitic disease transmitted by the bites of black flies found in areas around streams and rivers. If the parasitic worms transmitted by the bites enter into the eyes of the human host, they can cause reduced vision and blindness. Definition adapted from: The Carter Center. The Carter Center River Blindness (Onchocerciasis) Program. Available at: http://www.cartercenter.org/health/river_blindness/index.html. Accessed 7 December 2008.
As the global health community looks to the future, there are lessons to be learnt from past elimination and eradication efforts. Successes have often resulted not from major scientific breakthroughs but rather from simple, smart public health: a combination of the right approach with the right partnership. Given enough political will, donor funding and country and community-level involvement, the global public health community may soon turn many of these diseases into things of the past.

### PANEL 1: TODAY’S VISION FOR ELIMINATION AND ERADICATION

**Opening Remarks**

Moderated by Susan Dentzer | Health Affairs, PBS NewsHour

Steven Ault | Pan American Health Organization
David Molyneux, M.A., Ph.D, D.Sc, Hon F.R.C.P. | Global Alliance to Eliminate LF
Frank O. Richards Jr., M.D. | The Carter Center
Tadataka Yamada, M.D. | Bill & Melinda Gates Foundation

Ms. Dentzer opened the panel by welcoming the participants and stating the purpose of the discussion: to explore lessons learnt from past and present disease elimination and eradication programmes. Due to time constraints and the broad remit of the panel, Ms. Dentzer requested that the experts avoid dwelling upon the academic distinction between eradication and elimination, and rather focus on the ways in which these programmes have radically reduced human suffering and death.<sup>8</sup>

### Successes and Challenges in Elimination and Eradication

The panelists began the session by discussing key elements of current disease elimination and eradication programmes. These included the greatest programmatic successes seen over the past decade, the biggest unmet challenges, and the success factors that have moved these efforts forward.

Dr. Molyneux pointed to the increased awareness of neglected diseases as the greatest success of the last decade. There is now widespread recognition that these illnesses are key drivers of poverty, and therefore major impediments to achieving the targets of the Millennium Development Goals—especially the primary target of cutting global poverty by 50 percent<sup>9</sup>. Understanding how high the stakes are has given new impetus to the success of eradication and elimination programmes. The sheer number of countries that have embraced the elimination of LF as a public health goal provides a clear example of this increased attention, and the greatest hallmark of success may be the significant resources that developing countries are drawing from their own health budgets to combat neglected diseases. The LF programme has been scaled up faster than any public health programme in history, and nearly two billion doses of anti-parasitic medication have been administered to at-risk individuals since its inception<sup>10</sup>. The challenge moving forward will be to increase advocacy efforts for LF and other neglected diseases, since advocacy has clearly been a key success factor in maximising the impact of elimination and eradication programmes.

The case of Guinea worm was championed by Dr. Richards as a paramount success in the history of disease eradication. Current programmes have dramatically reduced the global burden of disease from 3.5 million cases annually in 1986 to just 4,410 cases today<sup>11</sup>. This success has not been brought about by a vaccine, a cure, or even a diagnostic test. Instead, the drastic reduction in incidence is a result of other interventions. Widespread health education and behaviour modification have played a crucial role, as affected communities have learnt how to interrupt transmission by using simple filters and ensuring affected individuals stay away from bodies of water where the

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<sup>8</sup> **Elimination** is the reduction to zero of the incidence of a disease or infection, in a defined geographical area, as a result of deliberate efforts. Continued interventions to prevent resurgence are required. **Eradication** is the permanent reduction to zero of the worldwide incidence of disease or infection as a result of deliberate efforts. No further interventions are needed to prevent resurgence. Definitions adapted from: Dowdle W. The Principles of Disease Elimination and Eradication. MMWR. 1999;48(SU01):23-7


adult worms can release their larvae. Strong disease surveillance systems are also extremely important. Robust data monitoring has allowed eradication programmes to combat pockets of infection wherever they appear and successfully eliminate the disease.

The Guinea worm effort has clearly demonstrated that scientific breakthroughs are not always necessary to make an impact. Sometimes, all that's needed for success is a long-term plan, a strong technical approach, and dedicated partnerships to ensure a necessary flow of funds and other resources. But success can often bring its own challenges. As Guinea worm incidence is dramatically reduced and health workers experience diminishing returns on their efforts, it will become more difficult to sustain the necessary political will to combat the final few cases and halt transmission once and for all. This “end-game” phenomenon is not restricted to Guinea worm; panelists noted that all eradication efforts, when successfully prosecuted, can reach the point where the final cases are much more difficult to find and more expensive to treat.

This challenge can also be seen in the case of polio transmission in Nigeria, where there is little political will to mount programmes that will interrupt transmission. India on the other hand has enough political will to fight the final cases of polio, but not the right resources—the oral polio vaccine is no longer working well enough to halt infections in the country.

In describing what he believed had been the biggest success in global disease elimination and eradication efforts, Dr. Yamada pointed to the formation of partnerships among private industries, international agencies, and developing nations. These partners have brought different resources and skills to the table for a host of diseases, and have often given elimination and eradication programmes the tools needed to relieve the suffering of the world's poorest citizens. For example, the pharmaceutical industry has shared solutions for both LF and onchocerciasis at essentially no cost, and worked with international agencies, NGOs, and developing countries to implement drug distribution programmes.

**Elements of Successful Programmes and Partnerships**

Building on the discussion of partnerships, the panelists went on to compare and contrast the key elements of the most effective disease elimination and eradication partnerships. Some key themes began to emerge. The successful partnerships are flexible, relying constantly on rigorous scientific inquiry and operational research while adapting their strategies and tactics as they go. They work closely with the communities they serve, and they assign clear roles that align with each partner’s comparative advantage. They build on core commitments from the affected countries themselves—commitments that include the funding and political will needed to get the job done. The lessons of smallpox—the only major disease to have been eradicated from the planet—are instructive even nearly forty years later, said Dr. Richards. At the time that the goal of eradicating smallpox was set in 1959, two million people per year were dying from the condition worldwide and millions more survivors were left disfigured or blind. The twenty-year eradication effort that followed would not have succeeded unless each country involved had devoted substantial resources and commitment to the effort. On top of that, Richards said, flexibility of the programme was an evolutionary step forward. This flexibility was grounded on a strong system of operational research to which 15-20 percent of the programme budget was dedicated. Based on the results of this research, the eradication programme evolved from the idea of mass vaccination to the notion of “ring vaccination”—identifying persons with smallpox and the people around them, and vaccinating those persons in order to break the cycle of transmission. This change in overall strategy, together with a willingness to adapt individual country eradication programmes to address specific operational challenges, paved the way for the eradication effort's ultimate success.

Partnerships with industry also played a key role in this effort. Among the technical innovations that led to the success of the eradication programme were the development of a new freeze-dried smallpox vaccine and a special two-pronged needle to deliver it. This “bifurcated” needle was developed by Wyeth, and was combined with a new vaccination technique in which sharp and shallow multiple punctures were made in the skin. Realising that the bifurcated needle was integral to a successful vaccination strategy, Wyeth gave up its patent rights so

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The global health community could quickly and cheaply mass produce the tool and enable “ring” vaccination to be carried out far more quickly and efficiently.

The Global Alliance to Eliminate LF has taken a similarly flexible approach to its elimination effort, and has also been made possible by donations from industry. GlaxoSmithKline and Merck have donated nearly two billion doses of the drugs albendazole and Mectizan® to interrupt transmission of the disease-causing parasite. Dr. Molyneux also pointed out the Alliance is characterised by another proven practice: a “free and nonrestrictive partnership” that manages to maintain clearly defined roles for partners, but is also flexible enough that the Alliance can act quickly and efficiently when opportunities arise. Even more important, the Alliance fully represents all the constituencies involved in the programme, including the developing countries served by the elimination efforts.

The Bill & Melinda Gates Foundation’s new drive to eradicate malaria, a disease which kills close to a million people a year, also adheres to some of these guiding principles. This effort is also built on partnerships. For example, PATH’s Malaria Control and Evaluation Partnership for Africa (MACEPA), which is a Foundation grantee, has been offering technical assistance on malaria control to the government of Zambia for the last two and a half years. The initiative utilises a comprehensive control approach that includes insecticide-treated bed-nets; indoor residual spraying; a strong disease surveillance system; rapid response protocols for disease outbreaks; and prompt treatments with artemisinin combination drug therapy for those who fall ill. The impact has already been dramatic: recent results show that the initiative has been able to reduce incidence of malaria by a full 50 percent, and produce a substantial reduction in child mortality as well13.

The next step toward malaria eradication will be developing a long-term plan and new tools to reach the goal. Research and development partnerships will play a key role in this endeavour. The Gates Foundation is currently in the process of forming a new research and development coalition with other research funders, such as the U.S. National Institutes of Health and the U.K.-based Wellcome Trust, as well as the WHO and other entities, to set an agenda for malaria eradication and maximise the impact of the community’s limited resources.

Building on the close relationship MACEPA shares with local stakeholders, Mr. Ault pointed out that the most fruitful partnerships are with affected communities. Although many regions affected by neglected diseases may lack strong health systems, affected communities are often organised—through municipal bodies, local NGOs, churches, and other groupings—in ways that can be utilised to address disease transmission. These organisations are critical components of community outreach efforts, and can provide much-needed local structures to frame elimination and eradication programmes.

Encouraging multi-disease collaborations that link efforts across conditions is another largely untapped opportunity found on the local or national level. For example, the different parasites that cause malaria and LF are both transmitted by common mosquito vectors. Thus, interventions such as bed-nets and spraying will fight both conditions. Similarly, anti-parasitic medications such as GlaxoSmithKline’s albendazole and Merck’s Mectizan® can prevent onchocerciasis, or river blindness, as well as LF. More can be done at the individual country level to link disease-fighting efforts that attack these conditions vertically and maximise the return on investment of limited resources. In addition, special opportunities for collaboration exist in regions where elimination is particularly feasible. An example is the island of Hispaniola – where on the eastern side, LF remains a problem in the Dominican Republic, while malaria continues to afflict populations on the western side of the island in Haiti.

**Lessons Learnt From Past Efforts**

At the close of the panel, the speakers each offered a key lesson learnt from past programmes, the kind of insight or principle that must guide future elimination and eradication efforts.

Dr. Yamada echoed the point that flexibility is central to these efforts, but offered the takeaway message that the global public health community needs to focus on the ultimate goals and outcomes—in other words, to “keep the eye on the prize.” Activities can’t be funded

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indefinitely, and eradication and elimination partnerships should aim seriously to put themselves out of business. If current approaches aren’t yielding the desired results, it’s time to rethink the approach. This is especially true in the realm of scientific discovery and innovation. It may be unthinkable as yet to set a goal of eliminating HIV/AIDS, but in order to make any progress, the global community undoubtedly must develop new vaccine strategies that will represent a radical departure from current ones that haven’t worked.

Dr. Richards underscored the importance of a comprehensive long-term plan that includes strong technical teams and “enduring” support from politicians, policymakers and donors. Another key component is maintaining optimism in the face of setbacks or difficult circumstances—especially as the “end-game” approaches in disease eradication efforts, as is now the case in Guinea worm.

Even as the world needs new tools to fight malaria and HIV/AIDS, Dr. Molyneux stressed that the global health community already has the tools needed to eradicate a number of diseases by 2015 or 2020. These include LF, Guinea worm, and onchocerciasis, all of which are being controlled or eliminated with existing drugs or basic public health interventions. The underlying biology of the parasites involved in these conditions make them an easy target compared to fast-reproducing and fast-changing pathogens like malaria or HIV/AIDS. There’s no sign that parasites are developing any resistance to drugs like Mectizan®, for example, whereas there are already concerns about drug resistance to the artemisinin combination therapies used to treat malaria. All of this means that success could truly be achieved in eradicating LF, onchocerciasis, and Guinea worm over roughly the next decade, given the appropriate partnerships and approaches that employ the tools at hand.

Finally, Mr. Ault highlighted the importance of “inter-sectoral approaches” at the national level, which can involve multiple ministries working with the private sector. He also emphasised the potential of teaming up with new foundations, charities and faith-based groups at the national or local levels, and offered the example of Fundación Mundo Sano (Healthy World Foundation), an Argentina-based foundation now fighting conditions like Chagas disease, dengue fever and Hantavirus.

Panel 2: Lessons Learnt and Application for Future Programmes

Opening Remarks

Moderated by Chris Elias, M.D., M.P.H | PATH

Joe Cohen, Ph.D | GlaxoSmithKline Biologicals
Alan Court | United Nations
Mwele Malecela, Ph.D | Tanzania Ministry of Health and Global Alliance to Eliminate Lymphatic Filariasis
Steven Phillips, M.D. | Exxon Mobil

Dr. Elias opened the second panel by welcoming the participants and stating the purpose of the discussion—to apply the lessons and key points from the first panel to future eradication and elimination efforts. The panelists then took questions from the audience, and engaged in two lively debates on HIV/AIDS funding and health systems strengthening.

Dr. Phillips began the discussion by highlighting a point from the first panel—that as of yet, no major disease has been eradicated since smallpox. Taking into account the lessons from that effort, he underscored that any serious eradication schemes have to be based on aggressive control strategies in every place that the disease-causing organism exists. He also emphasised the importance of what he described as “externalities”—the factors that have nothing to do with the underlying biology of an organism, but that can pose equally large obstacles to eradication or elimination efforts. These include inadequate human resources or institutional infrastructure; religious and cultural factors; and natural or man-made disasters such as wars and population migrations. All of these can and do interfere with biological models of disease eradication. Up against these powerful forces, the types of partnerships discussed in the first panel are critical—as is making sure that the right partners are involved in them.
Building on this last point, Dr. Cohen said that arranging the appropriate partnerships will be a key challenge in the roll-out of GlaxoSmithKline’s malaria vaccine candidate RTS,S/AS, assuming that the Phase III trials scheduled to begin in 2009 prove the vaccine’s efficacy. Many stakeholders will have to be involved, including global agencies like Unicef, global health authorities like the WHO, national health ministries and malaria control programmes, and the international donors who will help to pay for the vaccine. This will be an even larger effort than the impressive research and development partnership that produced the vaccine in the first place—which included the Walter Reed Army Institute of Research, the PATH Malaria Vaccine Initiative (supported by the Bill & Melinda Gates Foundation) and academic and clinical partners from around the globe.

“In 2009 GSK will start Phase III trials of our malaria vaccine candidate. We will need to go beyond research and development partnerships, and form new partnerships to distribute and implement the vaccine in the near future.”
– Joe Cohen

Building on the critical importance of flexibility in disease eradication and elimination efforts, Dr. Malecela spoke about the importance of countries being able to tailor their control efforts to varying conditions in different regions and even different health districts. For example, an elimination programme in the business district of Dar es Salaam will require a very different approach from one taking place in that city’s slums. She further emphasised the point from the first panel that operational research was critical to being able to adapt strategies and tactics, and noted that it was sometimes difficult at the country level to maintain adequate operational research budgets in the face of the reality that limited resources are available for the implementation of programmes.

Mr. Court spoke of the importance of maintaining national and international support for eradication and elimination programmes and forestalling flagging attention at all levels. He argued for highlighting the success stories in global health, such as the enormous benefits that have flowed from the invention of long lasting insecticide-treated bed-nets. Virtually in one stroke, this development overcame the logistical challenge of repeatedly distributing or re-treating bed-nets across vast stretches of sub-Saharan Africa. Keeping these developments in the public eye will be key during the long effort that surely lies ahead in the fight against malaria.

HIV/AIDS and Resources for the Future

The conversation turned to HIV/AIDS as Craig McClure, Director of the International AIDS Society, raised the ongoing controversy over whether HIV/AIDS receives too much donor funding compared to other diseases. He asked for the panel’s thoughts on whether HIV/AIDS was getting too much of the funding “pie,” and whether the battle against the disease was evolving, or should evolve, into a broader movement for global health.

The panelists broadly agreed with a statement by Mr. McClure: that, given deteriorating global economic conditions, it was unlikely the total amount of money devoted to disease-fighting efforts in developing countries would increase in the short-term. As a result, they said, it would be optimal to look for ways not necessarily to reduce the size of the “pie” devoted to HIV/AIDS, but to make better use of those resources to fight multiple diseases. Dr. Malecela noted that there are already some examples of this; in Tanzania for example, home-care workers who visit patients with HIV/AIDS could also provide lymphoedema care and education to LF patients if funders were open to more pragmatic approaches.

All of the panelists agreed that the considerable advocacy around HIV/AIDS was evolving into a broader movement for global health. Dr. Malecela mentioned that a recently formed group of LF sufferers has borrowed a leaf from AIDS activists and begun to work on an advocacy agenda for fighting their disease. The group’s members have made appearances on local television and have since generated much interest from other LF patients who want to speak out about their experiences. Residents in Tanzanian districts without an elimination programme have also begun to openly ask their parliamentarians why they don’t have access to interventions against LF, and when the elimination programme might reach them.

Health Systems Strengthening

Another question from the audience touched on the issue of health systems strengthening, and specifically whether the Global Fund to Fight AIDS, Tuberculosis and Malaria, or some other financing mechanism, could provide better coordination among a range of elimination and eradication programmes while strengthening health systems and empowering countries. It’s important to note that the Global Fund has had
so much success in generating quality proposals from developing countries that it has had to scale back its commitments. This was partly caused by the fact that countries were encouraged to apply for the amount of funds they actually needed, rather than what they thought they could get.

There seemed to be a general agreement that, given the right conditions, the Global Fund could expand its mandate more broadly to serve as a Global Fund for Health. Given the global financial crisis and the relative youth of the organisation, the conditions may not be right for a full-fledged expansion. However, as Dr. Malecela and Dr. Molyneux pointed out, the Global Fund might be able to provide better support for health systems and other interventions, specifically in cases where an intervention aimed at one of the neglected diseases also showed efficacy in fighting one of the “big three” diseases of HIV/AIDS, tuberculosis and malaria. An example cited by Dr. Molyneux is the drug praziquantel, or Biltricide, the primary treatment for schistosomiasis. He noted that one recently published study has shown that treatment with the drug in women with urinary schistosomiasis reduces vaginal and cervical lesions, which in turn decreases the risk of transmission for HIV/AIDS.

**CLOSING REMARKS**

In closing comments, Dr. Elias and Ms. Dentzer emphasised several points. Many lessons can be learnt from past and present eradication and elimination efforts—from smallpox to Chagas, onchocerciasis, LF and Guinea worm. The partnerships that have succeeded or made progress in fighting these conditions have been wide-ranging, involving participants in the public, private and nonprofit sectors at the global, national, regional and local levels. They have employed a variety of interventions and tools—in some instances, comparatively low-tech ones such as behaviour change initiatives, and in others, effective drugs donated by pharmaceutical companies like GlaxoSmithKline and Merck. The most successful eradication and elimination efforts to date have been based in large part on strong science, operations research and disease surveillance. They have been flexible—constantly adapting to new information suggesting that new strategies and tactics need to be employed. Their success depends utterly on the commitment of individual countries and the efforts of communities to fighting the conditions that impoverish, kill or cause the extreme suffering of their own citizens.

Going forward, eradication and elimination efforts are at various stages. Some programmes are close to completion, such as those for polio and Guinea worm. But the “end-game” will be difficult, and won’t be accomplished without sustained attention to eliminating the underlying organism or sharply reducing the disease burden it causes, wherever it exists. Advocacy at all levels—global, regional, national and local—will be critical. In many instances, maximum use must be made of the tools and treatments that already exist. Other eradication and elimination efforts, such as in malaria, have much further to go, and may depend on new tools in the pipeline, such as vaccines. Partnerships will be critical in making certain these interventions, if successful, can be taken to scale. It will be critical to maintain a focus on outcomes—for example, sharply reducing rates of death from severe malaria, especially among children.

As panelist Dr. Steven Phillips said during the day’s second panel, it may be a form of hubris to expect that diseases like LF, Guinea worm and onchocerciasis could actually be eliminated or eradicated from the planet by 2020. Given the obstacles and setbacks that are likely to still lie ahead, maintaining optimism will be critical. To that end, it will be important to keep in mind the victories achieved to date:

- That 6.6 million newborn babies have been protected from contracting LF.
- That Guinea worm cases worldwide now total fewer than 4,410 annually, down from 3.5 million cases a year when the World Health Assembly called for eradication in 1986.

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• That 25 million hectares of land previously infested with black flies that cause onchocerciasis are now available for resettlement and cultivation16.

• And that, in countries like Zambia, Rwanda, Zanzibar, and part of Tanzania, child deaths from malaria are already sharply declining based on the comprehensive adoption of tools and control strategies already in hand17.

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