Targeting Diseases

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Abstract

Global health has emerged as a core component of global development, and financing for global health has increased dramatically. Yet despite the growing recognition that poor health status is both a cause and an effect of poverty, and that the greatest gains in health can be achieved with relatively low-cost interventions, funding has continued to target infectious diseases. The history and practice of disease targeting is explored to identify lessons from notable examples of targeting, including smallpox, polio, and HIV/AIDS. The targeting of diseases is shown to remain an important development concept, especially for new and emerging health challenges, but one that should be applied appropriately and for long-term results. Invariably, targeted

approaches will require strong and functioning health systems to "walk that last mile" toward lasting impact.

Keywords: targeting, disease, eradication, health systems, global health, smallpox, polio, HIV/AIDS

Introduction

Global health as development

Global health as global development is not a novel idea, but it has taken decades for this concept to crystallize. The past fifty years of health development assistance from rich countries and multilateral institutions to recipient countries has been characterized by philosophical and funding swings that reflect the continuing debates on disease-specific interventions versus strengthening health systems, as well as the need for country ownership of both the problems and the solutions. In 2000 the United Nations Millennium Development Goals (MDGs) included specific health goals focused on maternal and child mortality and infectious disease, as well as other conditions related to health, such as hunger and sanitation.

It was not until the early 2000s that development financing for global health increased dramatically. Even then, donor dollars were motivated by and flowed to specific infectious diseases, namely, HIV/AIDS, tuberculosis (TB), and malaria. For example, funding for HIV/AIDS reached unprecedented levels by 2005. Funding commitments for HIV/AIDS in

low- and middle-income countries increased thirtyfold from 1996 to 2008, from US$ 300 million to US$ 8.7 billion (Kates et al. 2012). Funding flowed through donor-established mechanisms such as the Global Fund for AIDS, TB and Malaria and the U.S. President's Emergency Plan for AIDS Relief (PEPFAR).

Why are development dollars targeting these three infectious diseases? Looking back at development success stories provides some answers to this question, and explains the persistence of this relatively narrow approach despite concerns that such specifically targeted funding may have the unintended consequence of undermining health systems designed to meet a much broader array of public health needs.

Origins of the concept of targeting disease

Even before it was linked to the notion of enhancing development gains and increasing the effectiveness of public health responses to disease, eradication of specific diseases was tantalizing to thinkers and practitioners. This was particularly the aim of work on the ancient scourges of humanity, such as smallpox, typhoid, tuberculosis, plague, and leprosy. The promulgation, proof, and acceptance of germ theory and the subsequent rapid expansion of

medical knowledge since the nineteenth century was accompanied by enormous reductions in disease burden and increases in life expectancy. These reductions occurred even prior to the widespread use of antibiotics in the late 1940s. Levine et al. (2004) estimate that more than half of all improvements in health indices since the nineteenth century were due to social and economic advances, including housing and education.

The adoption of hygienic practices such as hand washing and proper food preparation and storage, coupled with improved public and private sanitation, had an enormous impact on disease prevention and mitigation. With the advent of antibiotics and vaccines, the concept of conquering disease became closer to reality. This was not necessarily seen as a development assistance priority, but as a worldwide cooperative effort that assumed that the entire world shared the dream of eliminating these ancient diseases and the death, disability, fear, and disruption that accompanied them. If diseases were conquered, it was thought, development would inevitably follow.

A review of the literature and current medical knowledge reveals eight requisite conditions for the eradication of an infectious disease. They are:

Biological conditions

1. A completely described natural history and pathophysiology
2. Humans as the sole natural host, with only human-to-human transmission
3. Lack of a carrier state, i.e., the infection manifests as recognizable disease in all or the majority of cases

Medical conditions

4. A safe and effective (and cost-effective) vaccine or treatment intervention that works in almost all cases

Leadership and resource conditions

5. Systems to deliver the vaccine or treatment
6. Surveillance systems that can detect the agent or condition and prove that eradication has been achieved
7. Political will to effect the eradication
8. Resources to effect the eradication

Over the past fifty years, there have been multiple attempts to identify human infectious diseases that possess all the required conditions for eradication. While smallpox is the only human disease that has been eradicated (rinderpest, an economically important disease of livestock, was declared eradicated in 2011) and is explored in greater detail below, other human infectious diseases targeted for eradication include poliomyelitis, dracunculiasis (guinea worm disease), hookworm, malaria, yaws, and yellow fever. Only the first two on this list meet most, but not all, of the conditions set out above for eradication and are still the subject of active international campaigns, notwithstanding enormous challenges in their implementation. Five other common infectious diseases have been tagged as potentially eradicable with current technology: measles, mumps, rubella, lymphatic filariasis, and cysticercosis.

No doubt increasing knowledge of disease causation, transmission, pathophysiology, and epidemiology will allow multilateral health agencies to set targets for additional candidates for disease eradication, though the above eight conditions are not expected to change significantly. What is likely to evolve is the continued improvement in population health indices in greater numbers of countries, particularly for childhood diseases. The resulting "health and wellness space" may be rapidly filled by non-communicable chronic diseases that are becoming more

prevalent worldwide. Both the demand for and supply of modern health practice are becoming significant indicators of social and economic progress in emerging economies. Meeting the MDGs now occupies governments in meaningful ways not seen in the past. At the same time, health goals have become a significant component of development assistance, albeit not always the preeminent one.

A milestone in the evolution of current health and development assistance was the set of conditions that fell into place for smallpox eradication. This was built on over two hundred years of experience with vaccination, predicated on the notion that science held the answers to major health problems and that these solutions could be applied worldwide with international collaboration. Such conditions may prove difficult to reproduce for polio and other diseases, because many countries are not willing or able to guarantee the collaboration and security necessary for such a global campaign.

What follows is a discussion of the targeting of three diseases: smallpox, polio, and HIV/AIDS. These examples illustrate the advantages and limitations of focusing on a single disease, and the accompanying need for political stability, security, and a functioning health system.

Cases of targeted disease approaches

Smallpox, the only example of successful total eradication, was eradicated using a targeted vertical approach that depended on cooperation with local health authorities and surveillance systems. The effort was coordinated through a newly created nerve center at the World Health Organization (WHO) with technical assistance from the U.S. Centers for Disease Control (CDC). The fight against polio is very advanced. However, the need for all susceptible children to receive three doses of oral vaccine maintained in cold chain has hampered the campaign's implementation. Finally, the global HIV/AIDS response, initiated as an "emergency" vertical approach, has of necessity switched toward systems strengthening and country ownership to consolidate the gains made in treatment and prevention of mother-to-child transmission and the potential for similar gains in preventing sexual and intravenous HIV transmission.

Smallpox: mission accomplished

> "If a house is on fire, no one wastes time putting water on nearby houses just in case the fire spreads. They rush to pour the water where it will do the most good—on the burning

> house. The same strategy turned out to be effective in eradicating smallpox." (Foege 2011)

All relevant global organizations enthusiastically adopted the global smallpox eradication campaign within a relatively short time span in the 1960s, prompted by the 1959 12th World Health Assembly's endorsement of eradication as a goal. At that time, it is estimated that there were approximately 10 to 15 million cases of smallpox in more than 50 countries, and that 1.5 million to 2 million people died from the disease each year. The success of the two-decade eradication campaign was preceded by more than two hundred years of accumulated knowledge and experience with vaccination.

The World Health Assembly declared smallpox eradicated in 1980. Globally coordinated efforts had rid the world of a disease that had once killed up to a third of its victims and left others scarred or blind for life. The last case of indigenous smallpox was diagnosed on October 26, 1977 in a hospital cook in Merca, Somalia. Subsequently, independent experts certified each country was free from smallpox for at least two years, and that the surveillance systems were in place capable of detecting outbreaks.

The smallpox eradication effort started by supporting national country programs to vaccinate people who were susceptible and assuring a supply chain of the vaccine was available where needed. Regional organizations such as the Pan American Health Organization (PAHO) led the effort. A special WHO unit created in 1967 by Donald Henderson, an American from CDC, provided technical support. WHO established a network of consultants who assisted countries in setting up surveillance and containment activities. Production of vaccine was shifted from the United States and then USSR to multiple sites in developing countries to assure the supply chain.

As case numbers fell, focus shifted to a combination of enhanced and focused surveillance—rapidly identifying new clinical smallpox cases—and vaccination of all contacts of such cases. This "ring vaccination" meant that anyone who could have been exposed to a smallpox patient was tracked down and vaccinated as quickly as possible, effectively isolating the disease and preventing its further spread. The campaign focused resources where they were needed and provided a stimulus to develop local health delivery systems. According to Levine et al. (2004), "This helped develop immunization services more generally—health staff helping with the campaign received training in vaccination and search and containment. This training was especially important for hospital-based health systems that had no experience in setting up preventive campaigns."

Smallpox was a prime candidate for eradication for several reasons. First, the disease is highly visible in all clinical cases: smallpox patients develop a rash (pox) that is easily recognized. Photographs of the typical rash were used by field workers in case identification. Second, the time from exposure to the initial appearance of symptoms is fairly short, so the disease usually doesn't spread very far before it is first noticed. Third, only humans can transmit and contract smallpox. People who survived smallpox developed lifelong immunity against future infection. For everyone else, vaccination was highly effective. WHO trained and deployed vaccinators quickly, and they could immunize large groups of people in a short time. While logistically difficult, it was operationally possible and manageable as a program.

The campaign proceeded in stops and starts over the 1960s and 1970s, and intensified in 1967. At that time, smallpox was still endemic in twelve countries or territories in eastern and southern Africa, eleven in western and central Africa, seven in Asia, and in Brazil in the Americas. The WHO eradication plan included mass vaccinations using freeze-dried vaccine material, and the development of a system to detect, monitor, and investigate smallpox cases and contain outbreaks. Three principles were vital to the WHO program: participation of all countries,

flexibility in implementing national programs, and ongoing research to evaluate progress and deal with problems that arose.

The campaign was not without its detractors, who did not see the eradication of an already waning disease as a shared global objective. WHO came under criticism from some health workers and human rights advocates who objected to the search and quarantine aspects of the program, in particular charging that campaign workers at times bent WHO and local regulations to use police-type tactics. Later, some critics claimed that physicians used coercion to ensure vaccination of quarantined individuals (Henderson 2009).

Despite its success, the campaign to eradicate smallpox would be difficult to replicate today. In fact, Levine and Oomman (2009) point out that at the time, "No two national campaigns were alike, which points to . . . the need for a flexible approach." One reason is the change in the development paradigm: the "donor-driven," single-minded focus on smallpox would likely face resistance today given the current development approach that emphasizes factors such as country ownership, sustainability of effort, and relative impact on domestic health priorities. For example, it is unlikely that the smallpox eradication campaign could have taken place in the current global environment, with instability and conflict in the countries where the virus proved

most difficult to overcome. In an era where infectious diseases co-exist with chronic diseases, hard decisions will have to be made for such success to be replicated: evidence-based allocation of resources, setting health priorities, and maximizing coverage without sacrificing quality of services.

At the same time, smallpox eradication still offers lessons for global health priorities. The disease had loomed large in human history, having killed more than 300 million people in the twentieth century (Henderson 2009). The campaign also exercised a powerful influence on the human imagination, having demonstrated a potential for a one-time monumental effort of collective global will to reach a common goal. Finally, the smallpox campaign left behind a number of important legacies, including the beginning of infectious disease surveillance systems in many countries and an expanded program of immunization for childhood vaccinations against common diseases.

Polio: the challenge of the "last mile"

> "We are so close, but we have to finish the last leg of the journey. We need to bring the cases down to zero, maintain careful surveillance to ensure the virus is truly gone, and keep defenses up with polio vaccines until we've confirmed success." (Gates 2011)

The polio virus was first identified in 1908 in Vienna, Austria, although the disease had struck children all over the world in the late 1800s. Despite advances in medical knowledge, polio persists more than a century later. In the 1980s, PAHO set a goal to eradicate polio in the Americas within ten years, and the World Health Assembly signed on to global polio eradication by the year 2000. Neither of these goals was reached, but the job is almost done. In 1988, polio was endemic in 125 countries and as many as 350,000 children were paralyzed every year. Today, all but three countries—Afghanistan, Pakistan, and Nigeria—have managed to eliminate polio, and just about 200 cases were reported worldwide in 2012. In most countries, the answer lay in routine immunization efforts and mass vaccination campaigns. But why has it taken so long to eliminate polio in these three countries? A review of the conditions for eradication outlined above offers a few suggestions.

Like smallpox, the natural history and pathophysiology of polio is well known, and there are safe and effective vaccines that work in almost all cases. The live attenuated Sabin vaccine is preferred for population vaccination programs because of its high levels of immune response and low incidence of secondary infection. However, polio differs from smallpox in three ways. First, the polio virus can survive outside the human host, circulating in wastewater. Second, infection is not always recognized, with a small proportion of people infected suffering atypical symptoms such as gastrointestinal illness, and 1 in 100 suffering paralysis. Third, at least three oral doses of the vaccine are required to confer full immunity to a child, so a functioning health system is needed for ongoing vaccine delivery.

All of the above suggests that the "last mile" to eradicate the polio virus is challenging, but not impossible. Consider the case of India, which despite its high poverty and low demand for vaccines in some areas did not shy away from its eradication efforts. Its last reported case of polio was in January 2011, and the country is expected to be declared polio-free in 2014. Recent interviews with practitioners suggest that this success was due to several factors, including political leadership, public-private partnerships to enable delivery of vaccines to hard-to-reach locations (e.g., Bihar and Uttar Pradesh), the use of new technology to identify outbreaks and

track the vaccination history of newborns, and the use of community health workers to explain the benefits of childhood immunization to parents (Raina 2012).

The pressure to replicate India's model is high, but different contextual challenges in Afghanistan, Pakistan, and Nigeria do not guarantee success in the short term. Even where health systems may be functional enough to deliver the vaccine to all children in need, issues of insecurity and conflict as well as local misconceptions about and fear of vaccinations complicate the rollout of immunization programs. In all likelihood polio will be eradicated, but unlike smallpox, eradication requires an ongoing effort that depends on strong health delivery and surveillance systems. Some locations, including China and West Africa, have experienced recent outbreaks of polio, brought in from Pakistan and Nigeria, respectively. This highlights the continued threat of resurgence when every child has not been protected against the virus.

HIV/AIDS: from emergency to mainstream

> "Let me begin by defining what we mean by an AIDS-free generation. It is a time when . . . virtually no child anywhere will be born with the virus . . . as teenagers become adults, they will be at significantly lower risk of ever becoming infected. . . . So yes, HIV

> may be with us into the future until we finally achieve a cure, a vaccine, but the disease that HIV causes need not be with us." (Clinton 2012)

The emergence of AIDS as a global political and scientific target was prompted by the potential for the epidemic to reverse hard-won health gains. Longer life expectancies in sub-Saharan Africa, which took decades to achieve, were being reversed in the 1980s and 1990s. From the first description of the syndrome in 1981 to the recognition of high population prevalence rates in sub-Saharan Africa, the response to the epidemic has been characterized by high and low points: elegant science, social confusion, paranoia and discrimination, heroism, and hard work.

As a disease caused by a newly described human retrovirus, HIV/AIDS has catalyzed an intense biomedical response to find drugs to reverse the effects of immunodeficiency and a vaccine to prevent infection. The former took more than fifteen years of effort before azidothymidine was licensed in 1996, and by 2012 there were more than thirty-five approved pharmacologic agents and combinations of agents to treat AIDS. The search for an effective vaccine continues and has been beset with numerous setbacks, chief among them the elusive search for a durable correlate of immunity to HIV.

But the biggest challenges are not biomedical. More than 36 million people were estimated to be living with HIV in 2011, the majority in sub-Saharan Africa. Almost half of these people (16 million) are eligible for antiretroviral therapy (ART) under current guidelines, and of those, about half (8 million) have access to such treatment. Enormous global investment in this biomedical model over the past decade has enabled this progress to happen as an "emergency." Given the fact that almost all transmission is via sexual exposure, the challenge before us is to sustain this investment by reducing sexual transmission.

The continuing world financial crisis that began in 2008 has prompted the U.S. government to take a much closer look at the costs of PEPFAR, its flagship program to assist the most affected countries in their progress against AIDS. The Global Fund has also signaled interest in managing program costs and rooting out corruption in grant management. Cost benefit and cost effectiveness are the new buzzwords of the global AIDS response, and clearly money is expected to be in short supply for the foreseeable future even as recipient countries are expected to increase their own contributions to the effort.

Yet the unmet need for antiretroviral therapy and awareness-raising about effective prevention is still enormous. Even with full funding, many countries face structural and systemic limitations,

from inadequate human resources to losses from corruption and poorly functioning health systems. It takes time and commitment to build systems and operate them for impact.

Much of this effort has focused on establishing country-led systems to deliver and disseminate treatment. Tremendous progress has been made, but treatment needs to be coupled with effective prevention efforts. The latter require both medical technology to ensure safe blood supply and medical procedures, and an integration of health and education into daily social and work life, including HIV testing and counseling.

Prevention also requires targeting young people before and as they become sexually active, equipping them with knowledge of proven approaches (such as barrier methods), promoting behavioral and medical interventions (such as male circumcision), and providing pre- and post-exposure prophylaxis. Yet such efforts often are undermined by the stigma surrounding social taboos around sex in general, and sexually transmitted infections in particular.

Combination prevention programs must be based on current data about transmission, and they must reach people where they live and interact in their communities. Finally, the costs of such

programs must fit within the resources available and be able to integrate into country, region, and local health priorities that compete for available resources.

HIV/AIDS donor assistance has been transformative in providing ART to halt and reverse the immune sequelae of HIV and return people to health so that they can resume productive lives. The impact of these interventions is still growing as systems are strengthened to deliver ART successfully and meet the additional needs of patients (for food, water, shelter, etc.). Notwithstanding the debate surrounding the questions of sustainability of and attribution to specific programs, the short-term impact of more widely available treatment has been to extend life and increase hope for millions of affected and infected people. The key development that enabled this transformation was highly active antiretroviral therapy as defined by iterative clinical trials in the United States and Europe and which mandated a comprehensive package of services (e.g., clinical, social, laboratory) to deliver drugs according to best practice that could permanently suppress HIV replication.

Once it became clear that the efficacy of highly active combination treatment for AIDS was so unequivocal and sustained even in low-resource environments, the barriers to widespread treatment of people in the developing world, including cost of ART, began to fall and in effect, a

best practice model was exported around the world. For example, in 2003–04 the average annual cost of delivering ART to a patient in the United States was $12,000–$15,000. These high costs were met by federally funded entitlement programs administered by states. Through advocates, activists, and donors such as PEPFAR and the Global Fund, by 2008 the cost had fallen to less than $1,000 per patient per year, and fell further to $200–$300 as the program reached a greater number of patients. Even then, costs were shared by recipient governments, donors, and others, including the patients themselves.

Paradoxically, the resounding success of life-prolonging treatment through effective and affordable ART presents a setback in combating the pandemic, in that treatment success is masking the still urgent need to focus on prevention. Under any given program of expanding AIDS treatment, a predictable result is escalating program costs as average survival lengthens (the initial PEPFAR models were computed with an overall five- to seven-year gain in life expectancy, but the need for ART is permanent so long as the patient is alive) and patients eventually need to switch to more expensive second- and third-line drug combinations. This leads to the sobering conclusion that the models for delivering ART assistance are not sustainable in the long term without concomitant prevention successes to ensure a diminished need for treatment over time. South Africa, a middle income country, is a case in point: the

country now has the largest ART program in the world, with more than two million people on treatment. However, the long-term costs of AIDS there are unsustainable unless further gains are made in HIV prevention.

Given the sum total of knowledge about how to prevent and treat HIV, is it likely that epidemic control will be achieved within the next generation? From our framework it is clear that HIV does not fit the criteria established for eradication: there is no vaccine or preventive technology that works in all circumstances, transmission is primarily sexual, and successful treatment requires daily medication and extends the period when infected persons may transmit HIV. Problems abound in HIV prevention. Unlike treatment, which is fairly standard whether the patient is a poor woman or a rich man, a heterosexual or a homosexual, an injecting drug user, or a combination of all of these (that is, the same drugs are used in the same combinations to achieve the same effect, all else being equal), an effective prevention approach depends on risk matrix, demography, geography, and other factors.

Some approaches can be broadly targeted. For example, sexual health education can build demand for prevention services, though attaining consensus on what this means is a contentious process. Other approaches require a narrow focus on so-called key populations, such as

interventions for young gay men or needle exchange programs for injecting drug users, both of which are evidence-based but neither of which garners much support among recipient governments or even donors. Demand for prevention programs, especially among key populations, still needs to be built and sustained in governments and communities; and like drugs for treatment, once started, supply should not be interrupted. As with treatment, there are severe policy, demand, and resource constraints. However, unlike treatment, achieving consensus on the approach and scale of prevention programs is highly elusive and subject to political interference, normative confusion about what works and for whom, and lack of understanding of what constitutes effective prevention. To even start this discussion requires expending political capital and making tough policy and resource allocations. No wonder the task is so daunting. People and politicians may listen to the doctor when it comes to treatment but everyone is an expert when it comes to prevention.

It is also clear that to build on and consolidate the gains of the "emergency" and targeted response to the global AIDS epidemic, the approach needs to change to a more sustainable and systems strengthening one. This change shifts the locus of control to the country, both government and non-government entities, and relieves the donors and their agencies of some of the management burden. This shift has to be a gradual but clear process that spells out roles and

responsibilities and does not allow patients and their lives to "slip through the cracks" during the transition. This also shifts the focus from service delivery to technical assistance in building local capacity to manage disease prevention and treatment.

In summary, the continuing global struggle against HIV/AIDS has entered a new phase where there is widespread agreement about the policy goal of an AIDS-free generation. However, given that there is no cure for AIDS, no effective vaccine, and no way to eradicate HIV, determining what it takes to get there and how to finance the inexorably growing commitments to services for people living with HIV, particularly in sub-Saharan Africa, is going to occupy development experts for the foreseeable future. The urgent need to match the treatment success with prevention success, and the fact that the well- articulated AIDS medical treatment model does not impact sexual transmission, point to the need for a new model operating beyond just health and embracing social, education, and financing systems if eradication is to be a real possibility.

Key debates

In the last decade two key debates have emerged around the practice of targeting a disease. One is whether such intensive focus on one disease comes at the cost of neglecting others, or exceptionalization. The other is whether efforts that target a specific disease strengthen the ability of health systems to respond to a range of priorities. The extraordinary financial and implementation focus on AIDS in the last decade has heightened these tensions in development discourse.

"Exceptionalizing" a disease

The thirtieth anniversary of the first description of AIDS occurred in 2011. In those three decades, much has changed in the global history of the HIV/AIDS epidemic, with global access to appropriate therapy increasing exponentially. Yet numerous obstacles to controlling the epidemic persist, including lack of widespread access to effective prevention programs that directly address major modes of transmission, including sexual activity and injection drug use.

The idea that HIV is an exceptional disease under a set of exceptional conditions and therefore requires an exceptional and emergency response characterizes only the past ten years of global public health and the pandemic. It is important to recall that this apparent exceptionalism, with its accompanying high levels of attention and funding, represents a hard-won public policy debate in the rich donor countries. In fact, in the first twenty years of the AIDS epidemic the response was not exceptional. AIDS was initially characterized in the West, specifically the United States, as a disease of homosexuals, hemophiliacs, heroin addicts, and Haitians (the infamous "four H's"), none of whom had the clout to marshal the resources required for an adequate response from a skeptical political class cloaked in moral superiority. Most activists would posit that not one iota of the AIDS response was achieved easily, and that it took more than half a million deaths from AIDS in the United States before the first specific treatment was approved.

The sudden global prominence of HIV/AIDS conferred a number of lasting benefits that went beyond simply addressing the epidemic. This new and unique syndrome brought together unlikely allies as it allowed activists to challenge the scientific establishment's control of the public health enterprise and called for an agreement that recognized the role of the individual and the community and the rights and responsibilities of sexual minorities. It advanced the cause of

gay rights in the West and called for a new approach to health promotion and disease control. It advanced the rights of women and young girls in Africa and Asia and focused attention on the needs of children and orphans. It helped drive the notion that the entire world's population had the right to expect to participate in the gains of social progress and medical knowledge. And finally, it was the awesome potential of the global AIDS pandemic to cause suffering and death that most marked it for global attention and resources.

A key question is whether the global AIDS response encourages neglect of other health problems. A related question is whether the singular focus on HIV/AIDS is resulting in missed opportunities for synergy with other health-related policies, programming, and resources. In terms of the volume of scientific and social outputs, the level of funding, the scale and openness of attention, and the contentiousness of the discussion, HIV/AIDS is without precedent. Some criticize the continued growth of the global HIV/AIDS enterprise: the entrenched multilateral agencies such as UNAIDS and the Global Fund, the global research establishments where lifetime careers can be spent, the international organizations that provide technical assistance and support program implementation in beneficiary countries. From a recipient country perspective, one negative outcome of the massive HIV response is the siphoning off of much available talent

and resources, sometimes leaving little capacity and resources to address other health priorities in most affected countries.

Articulate arguments can be made that AIDS funding is disproportionate to its impact. For example, some argue that these resources can be better applied to childhood diseases and generate greater gains in life expectancy in beneficiary populations (Over 2012). There are proposals to redirect some donor agencies' missions to more health generalist entities. All these developments should be seen as inevitable given the substantial gains made against AIDS. Broadening the response could not have been contemplated back in 2000 when AIDS treatment emerged as a best practice.

Have there been losers in the singling out of HIV/AIDS for special attention? One could argue that attention, and consequently funding, to maternal/child health and family planning, in terms of both priority and funding, decreased in the age of the expanded global AIDS response. For example, all available analyses of the U.S. government's PEPFAR program, which was criticized in its initial phase for taking an emergency approach, suggest that the only potential downside was the crowding out of family planning and broader maternal/child health in the USG resource envelope, an issue that is being addressed in phase II.

Diseases and health systems

As funding for AIDS increased exponentially in the last decade, a polarized debate began to emerge about whether donor financing for HIV/AIDS programs was strengthening or weakening national health systems (Oomman et al. 2008). This concern was not new, but amplified because of the sheer scale of AIDS programs. Many observers have examined the potential impact of the magnitude of funding on weak health systems, asking if AIDS money was in fact making governments and the private sector better able to deliver a broad range of high-quality health services, or if it was weakening health systems by establishing AIDS-specific systems that were intensely focused on combating a single disease.

A pioneering set of country case studies examined the interaction between AIDS programs and the health system (Oomman et al. 2008). They suggested that large funding inflows were perhaps shifting components of the health system, diverting attention and resources from existing programs to AIDS programs. Skilled health workers and managers who otherwise would be deployed managing and implementing other types of health programs were attracted to AIDS programs by salary ‘‘top-ups’’ and better working conditions. Supply chains that bring

antiretrovirals (ARVs) and other AIDS program supplies were prioritized over those for other essential drugs. Information was systematically provided to donors, but not necessarily to national health information systems or local governments. Soon, others heavily involved with the scale-up of HIV/AIDS programs in Africa challenged these early observations. Over time, as the evidence base grew, researchers reported more positive observations about HIV/AIDS funding and its effects on the health system (De Cock et al. 2011).

In fact, evidence now suggests that targeting HIV/AIDS for specific development assistance has had positive spillover effects on other health priorities and systems. Country health systems have been strengthened, not weakened, by the AIDS effort, with procurement and supply chain, laboratory and surveillance infrastructure, and clinical services benefiting most. El–Sadr (2012) argues that PEPFAR investments have catalyzed improvements in health systems in recipient countries. Moving forward, these gains can be expanded as the HIV response matures and directs efforts to embed HIV within the agreed health priorities of countries and states. This longer-term vision should occupy the next five to ten years and see country governments assume greater fiscal control of their country health portfolios and focus on long-term gains.

The definitive answer to the question of whether HIV/AIDS has had an overall positive or negative impact on health systems will remain elusive until rigorous cost benefit and impact evaluations are conducted. In the meantime, program implementers are acutely aware of the benefits they have seen from AIDS financing; yet key questions remain about the cost and sustainability of vertically funded programs, and the choices that countries make as donor funding commitments for AIDS and global health shrink.

Future of health as development

This chapter developed a historical understanding of the concept and practice of "targeting disease" to shape investments in health. We did this by looking back at three key diseases targeted for intervention—smallpox, polio, and HIV—and the heated debates that ensue when a disease appears to be prioritized over other important health conditions and other equitable, sustainable development priorities. Three issues emerge from this reflection that will be important for the future of global health as development.

Finite resources and critical choices

Clearly, communicable diseases like HIV, TB, and malaria are here to stay and will continue to demand a major portion of resources for global health into the future. At the same time, new and emerging infections will require global cooperation, often as emergency responses, as for example with H1N1 influenza and severe acute respiratory syndrome (SARS). In an era of climate change and growing population we are seeing the creation of a global incubator for the rapid emergence of previously rare global health events, including highly pathogenic influenzas, zoonoses, and resistant bacterial infections. New infectious diseases will often require a targeted globally cooperative response, particularly when the biology and transmission of the infectious agent have not been fully described. As all three cases above show, the response to new and important human infections will almost certainly require a targeted response early in the life cycle of the disease, transitioning to a health systems and more sustainable response as more is learned about the disease and how to manage it. Occasionally a new disease can be controlled or eradicated early in its emergence, like SARS, which is unlikely to have more than a sporadic incidence in the future. Yet given the conditions necessary, eradication will be the exception rather than the norm.

The world is also facing a global pandemic of non-communicable chronic diseases (NCDs), such as heart disease, diabetes, and cancer, the collective burden of which now threatens to exceed the impact of infectious diseases for the first time. In 2011, the United Nations General Assembly convened a special session on NCDs. Just as the previous special session on HIV/AIDS helped spur global response, advocates are working toward a similar movement to fight the impact of NCDs, capturing the attention of the very same players who championed the fight against HIV/AIDS.

Resources for global health are unlikely to grow even as the list of priorities gets longer and advocates get louder. Critical decisions about how to prioritize a long list of health challenges will dominate the next decade of health. Policy-makers struggle with a finite amount of available resources and face diminishing gains from efficiencies in health spending. They must weigh competing criteria for decision making, including considerations of cost effectiveness, ethics, equity, politics, and diplomacy. Meanwhile practitioners face demands to integrate programs meaningfully to achieve greater synergies among, and greater efficiency and effectiveness within, health interventions. In addition, there is increasing pressure to consider the health impacts of environmental degradation, climate change, and increasing population density in the least resourced parts of the world.

In an era of continuing economic slowdown and uncertainty, there is little appetite for grand schemes and investments, particularly in health, which is often seen by governments as a net consumer of resources. The cancellation of Round 11 by the Global Fund to Fight AIDS, Tuberculosis and Malaria is a resounding example of pulling back of prior commitments by donor countries as their own economies contract and hard choices need to be made. Yet the lesson of smallpox eradication is that investments in health abroad can be in the enlightened self-interest of developed countries. Though the campaign's success was not guaranteed, stakeholders and country partners still invested heavily and the payback was incalculable. It is estimated that the United States recouped its investment in the global smallpox campaign within two years as vaccination of its own population became unnecessary (Levine et al. 2004). This argument will be easier to make for polio, but much harder for HIV/AIDS or NCDs. Without eradication in sight for the latter two, global cooperation agencies and country governments, both donors and recipients of development assistance, are faced with growing and unsustainable costs.

Long-term impact on health systems

Taking responses to scale for maximum impact for existing health priorities often requires transitioning from a targeted approach to a health system response and sometimes even a multi-sectoral response, as demonstrated by the polio and AIDS scenarios. Targeted approaches can lead to eradication, as for smallpox, if all conditions needed for disease eradication are fulfilled. However, the confluence of all requisite conditions is unlikely for most diseases today. Nonetheless, a targeted approach can still have short-term successes for diseases like polio and HIV, but this requires a shift from donor-led to country-led management of a health systems approach (for example, routine immunization for polio, management of chronic disease for AIDS) for even greater impact in the long term.

The cases above show that targeted programs can have significant positive effects on health systems in a country and leave behind more robust surveillance systems and laboratories, as well as improved clinical skills and training of health care personnel. These positive effects may initially appear to benefit the disease they are targeting, such as an AIDS-specific health information system or supply chain. A future challenge is to identify and measure whether these early disease-specific effects also provide "hidden" benefits for the health system at large to

respond to other priorities. In the case of the smallpox campaign, for example, the expanded program of immunization for childhood vaccinations certainly benefited countries well beyond the eradication of the disease. Such learning will be critical for decision-makers who take calculated risks as they address emerging health challenges.

The broadening of global health priorities (existing and emerging infectious diseases including HIV and non-communicable chronic diseases, maternal and child health, nutrition, reproductive health, and family planning) and the responses they require will pose enormous challenges that go beyond single diseases, sectors, governments, or single-issue agencies such as UNAIDS. Major constraints exist, including resource, market, and demand constraints, to bringing programmatic responses to scale in response to current and emerging health priorities requiring expensive investments in systems for health, as well as other sectors such as education and finance.

Agendas, accountability, and ownership

In 2012, as countries and donors debate how to reach universal health coverage goals (*The Lancet* 2012), it is unclear how this effort will help build the response structure required to

tackle a range of existing global health challenges and establish responsive systems for threat reduction.

At the outset of this chapter we asked why it is that, even today, donors' development dollars largely target the "big three" infectious diseases: HIV, TB, and malaria. Even when donors attempt to put a unifying overlay on a disjointed health assistance portfolio, it may not work. Consider the recent case of the United States Global Health Initiative (GHI). Despite a visionary strategy to build a streamlined approach guided by key principles of country ownership and programmatic integration, the GHI has met with spectacular failure (Oomman 2012). Examining the conditions that led to this reveals several complex problems: the tension between political and program accountability, funding silos, disease-specific offices, warring implementing agencies, and a failure of health diplomacy. But the biggest impediment to the systemic response is the U.S. accountability structures for foreign assistance that force targeted programming in global health even when it isn't necessarily the most efficient and effective approach.

Similarly, for the next largest health donor, the United Kingdom, the pendulum swings with every funding cycle or change of government between more basket funding and sector-wide approaches, to project-based implementation seeking "value for money." The fact is that most

international aid provided by donors is heavily influenced by political decisions (at home and in receiving countries) and not necessarily by evidence of need or burden of disease. If aid were always expected to succeed (and this is increasingly the pressure on several donors because of the global financial crisis), then only countries with good policies and robust systems would receive aid in the first place, and this is clearly not the case. When a donor would like to strengthen its ties with recipient countries that have weak or dysfunctional health service delivery systems, it makes sense for the donor to target specific diseases through multilateral and bilateral efforts to produce short-term results, push for value-for-money decisions, and ultimately maximize aid effectiveness for health. This push for greater donor accountability creates a tension with the increasing rhetoric about country ownership and how countries must begin to contribute domestic resources for health and take charge of their health delivery systems.

Country ownership of health services delivery is vital. Ideally, donors are helping to support the aims and objectives of countries that have articulated and are implementing plans to address their health priority conditions and commitments. Country ownership is seen as a requisite for sustainability and for delivering results. This does seem to be axiomatic, but begs the question of precisely what is being owned. Even if all service delivery is left to country mechanisms, enormous analytical gaps exist in recipient countries in the design and formulation of health

programs based on evidence, understanding the roles of the public and private markets in health, building demand and assuring supply, and maintaining quality and equitable distribution of services. Such gaps should form the basis for ongoing technical assistance from donors, yet servicing long-term objectives seems beyond the scope of donor support focused on implementing projects focused on attributing short-term results. Donors may well be nostalgic for the promotion of targeted approaches to emergencies like HIV/AIDS, where donor accountability and attribution are easier to report back to political operatives.

While this chapter has primarily focused on health and development from a donors' perspective, countries that are beginning to take charge of their health systems will increasingly turn to countries like Brazil as a role model. No longer a recipient of donor assistance, Brazil has strategically targeted diseases (both infectious and chronic) as a component of a larger decentralized entitlement health system funded by federal, state, and local taxes. Looking ahead, global health will continue to be a core component of development. Similarly, targeting diseases will remain an important development concept, especially for new and emerging health challenges, but one that should be applied appropriately and for lasting impact. Invariably, targeted approaches require strong and functioning health systems to "walk that last mile" toward lasting development impact.

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