Comparing Measles with Previous Eradication Programs: Enabling and Constraining Factors

Introduction

More than 22 years have passed since the launching of the polio eradication initiative by the World Health Assembly in 1988, the last of five major eradication activities in the second half of the twentieth century. Given that only one of these disease eradication programs has been completed successfully, serious consideration of a global measles eradication initiative merits a comparison of the present enabling and constraining political, social, economic, and technical factors for measles eradication with those of the previous global disease eradication programs. This analysis may be helpful to decision-makers weighing the evidence for or against the establishment of a measles eradication initiative. Also, it may illuminate opportunities to build on factors that facilitate success and to mitigate factors that might threaten success if a global measles eradication initiative were launched at a future date.

The malaria, smallpox, and polio eradication initiatives were formally launched by the World Health Assembly in 1955, 1959, and 1988 respectively (table 1). The yaws eradication program also had its formal beginning in 1955 at the Second International Conference on the Control of Yaws, although it was never formally launched as an eradication initiative by WHO (i.e., no WHA resolution was ever passed). Guinea Worm (dracunculiasis) eradication was made a sub-goal of the Water and Sanitation Decade in 1981. In 1986, the WHA resolved to eliminate dracunculiasis, and passed a resolution for eradication in 1991. Other large public health programs launched in the twentieth century and continuing today, including programs to eliminate neonatal tetanus and tuberculosis, do not have eradication as the objective and are not considered in this paper.

The table below summarizes these five eradication programs:

<table>
<thead>
<tr>
<th>Disease</th>
<th>Date started/ended</th>
<th>Primary intervention</th>
<th>Results</th>
<th>Reasons for delay or failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yaws</td>
<td>1955/1967</td>
<td>Penicillin treatment of cases &amp; contacts</td>
<td>95% case reduction&lt;br&gt;5</td>
<td>Inadequate strategy for latent disease, inadequate surveillance and funding</td>
</tr>
<tr>
<td>Malaria</td>
<td>1955/1969</td>
<td>Insecticide treatment</td>
<td>Reduced cases by more than 100 million/yr</td>
<td>Insecticide resistance, outside biting/sheltering, inadequate funding, GMEP* not implemented in many African countries</td>
</tr>
<tr>
<td>Smallpox</td>
<td>1959/1979</td>
<td>Vaccine</td>
<td>Succeeded; last case in 1977</td>
<td>Inadequate funding and vaccine supply/quality delayed progress</td>
</tr>
<tr>
<td>Guinea worm</td>
<td>1981/ongoing</td>
<td>Safe drinking water (filters, wells, larvicide)</td>
<td>99% reduction; 5 endemic countries remain</td>
<td>Inadequate funding and war in Sudan</td>
</tr>
<tr>
<td>Polio</td>
<td>1988/ongoing</td>
<td>Vaccine</td>
<td>99% case reduction, 4 endemic plus 12 re-infected countries remain</td>
<td>Inadequate funding, operational gaps in reaching high coverage, reduced vaccine efficacy in India, and wars/civil conflicts.</td>
</tr>
</tbody>
</table>
Methods

We reviewed the literature of the yaws, malaria, smallpox, guinea worm, and polio eradication programs and compared enabling and constraining factors for each of the prior eradication programs to the same factors that might facilitate or hinder global measles eradication in 2010. These programs were selected because they were the only global disease eradication programs initiated in the last half of the twentieth century. These programs were deliberate efforts to end disease transmission and to obviate the need for further control measures, thus meeting the definition of eradication of the International Task Force for Disease Eradication in 1993.6

From the literature, we developed a list of political social, economic and technical factors perceived to be important in considering the feasibility of candidate diseases for eradication and ultimately, for the success of the program. We focused our analysis on the following specific factors:

Political factors

- Wars and armed conflicts affecting endemic areas
- Population displacement or migration to or from endemic areas
- Endemic country political support for eradication

Wars and armed conflicts have an adverse effect on disease control and eradication activities. They cause large displacement of populations, reduce access to health facilities, reduce the priority given to health care, and reduce national funds available for health care, including eradication activities.7 Population displacement and migration may be the result of armed conflicts or may occur in response to economic or social conditions, or natural disasters such as floods and droughts. Population displacement and migration often result in large populations moving from endemic areas, carrying disease with them. Politically stable governments with strong central and peripheral health systems tend to have more success with eradication than governments in which control is weak or fragmented.8

Social factors

- Perception of disease burden and risk; motivation/acceptance of intervention
- Competition from other health programs and disease control/elimination/eradication initiatives
- Social/economic inequality
- Level of information and communications technology

The perception that an endemic country government and its people have about the risk of a given disease affects political and financial support, and acceptance of recommended disease eradication interventions. These perceptions may vary within a country, especially in larger countries. In general, greater perceptions of risk are associated with higher levels of acceptance of interventions. In addition to weighing risks (e.g., risk of disease vs. risks associated with the intervention), affected populations also may hold cultural and religious beliefs that affect acceptability of the intervention.

Competition from other health programs affects the degree to which endemic country governments, health workers, and donors support and implement eradication strategies. This is especially true in developing countries that depend on donor support and expertise to fully implement recommended strategies. Government health priorities may be influenced by donor priorities and funding.

Social/economic inequality is associated with less access to health care services by the poor and sometimes, the frustration caused by this inequality is expressed through isolated or coordinated acts of non-compliance with eradication interventions.9 However, if eradication programs can market themselves as a “force for greater equity,” this factor may be mitigated.
Effective communications and information systems are enabling factors in eradication programs, allowing a greater degree of efficiency and completeness in disseminating and receiving information and compiling and analyzing surveillance and intervention data. However, the new technology may also enable the voices of unsatisfied “resisters” and the anti-vaccine movement to a much greater degree than was possible in the twentieth century.

Economic factors

- Cost of eradication activities
- Cost-effectiveness and potential cost savings
- Ability and willingness of endemic governments to self-fund
- Funds potentially available from governmental and non-governmental donors

Although high cost is not an insurmountable problem, programs requiring large amounts of funds for extended periods of time have a high risk of having funding gaps. Programs documented or perceived to be cost effective if the cost benefit ratio is perceived as being advantageous, it may engender support from endemic countries and donors. Potential cost savings from a reduced level of control activities after eradication may serve as an incentive to governments to support eradication. A higher degree of self-funding by endemic countries may increase chances of success. This is particularly true for China and India. The need to raise funds from external sources, such as donor governments and non governmental agencies (NGO), makes it more likely that funding will be erratic.

Technical factors

- Properties of the agent (infectiousness, duration of infectious period, genetic stability, host preference/reservoirs)
- Level of disease control already achieved; number of cases/endemic countries
- Demonstration of success of eradication strategy in large geographic area or region
- Surveillance factors
  - Relative ease/difficulty in clinical case identification
  - Existence of sub-clinical cases
  - Availability, ease, and cost of diagnostic tests; availability of field diagnostics
- Quality of intervention tools
  - Effectiveness; number of doses required, duration of protection
  - Safety
  - Ease of administration; use by non-technical staff/volunteers
  - Heat stability; cold chain requirements
- Existence of a quality research program before and during the eradication initiative

Less infectious diseases may be easier to eradicate, possibly permitting transmission to be interrupted with less intense application of the interventions. Genetic stability of the disease-causing agent makes it more likely that the interventions will remain effective until eradication is achieved. The effectiveness and ease of use of the intervention(s), and the ability to easily establish effective surveillance directly affect the ability to eradicate a disease. Additional enabling technical factors are the level and quality of disease control prior to eradication, and demonstrated success of the eradication strategies in a large geographic area.

Eradication programs may benefit from robust research programs that can identify new tools or strategies as the agent, host, and environment may change over time. Past failures of some eradication programs have been in part due to failure of the interventions or strategies. Insecticide resistance became increasingly more problematic for the GMEP, and inadequate strategies to address latent yaws disease proved to be the Achilles heal for yaws eradication. Interventions that were effective in one country may not always work adequately in other countries, especially if extreme differences of climate, population density, sanitation, and competing disease priorities exist.
Other key factors

Strong health systems were identified as a key factor in enabling disease eradication. Disease eradication is facilitated in countries which have a functioning network of urban and rural health clinics staffed by trained health workers, effective administrative systems, and adequate supplies.

Effective management was also identified as a key factor in the success of eradication programs. Disease eradication is facilitated by strong management through which clear and measurable objectives are established, appropriate strategies are developed and modified, qualified and dedicated staff are deployed and held accountable, and for whom adequate resources are made available. Effective management is needed at global headquarters, and regional and national levels.

Analysis

Political factors

Wars and armed conflicts in endemic areas: The 1950s, when the yaws, malaria, and smallpox programs were launched, was a period of relative global tranquility. The Korean War ended in 1953 and the First Indochina War ended in 1954.\(^\text{11}\) The remaining few conflicts, e.g. Algeria, Cuba, Suez, Laos, were comparatively small and caused relatively little displacement of populations. The onset of the civil war in Sudan in 1955 would cause the greatest adverse impact on eradication initiatives among the wars from this era. The colonial empires of England, France, Spain, and Portugal were still largely intact in Africa during the 1950s. Although population movement still continued in the 1950s following World War II, it did not pose a serious threat to eradication.

The 1980s, when the polio and the Guinea worm eradication program were launched, was a more violent era than the 1950s. The Iran-Iraq war was the most significant, but conflicts also occurred in Afghanistan, Angola, El Salvador, Eritrea, Ethiopia, Lebanon, Liberia, Peru, Uganda, and Somalia.\(^\text{12}\) From a political perspective, global eradication programs launched in the 1980s were at a comparative disadvantage with programs launched in the 1950s. The conflict in southern Sudan continued into the 1980s, 1990s, and 2000s, delaying for many years the eradication of Guinea Worm. Insecurity in Afghanistan in the 1990s and the war in Afghanistan since 2001 have caused grave obstacles and delays in stopping polio transmission both in Afghanistan and Pakistan.

By comparison with earlier eradication programs, a potential measles eradication initiative would likely be at a disadvantage from a political/security perspective. Wars are ongoing in Afghanistan, Pakistan, Iraq, and Somalia with smaller conflicts continuing in Southern Sudan, Chad, DR Congo and other countries. Terrorism and threats of terrorism in 2010, rare events in the 1950s and 1980s, pose a challenge to the success of eradication programs and raise costs significantly. The continued growth of arms in all countries, including in the smallest tribal villages of Africa and Asia, increases the impact of insurgency movements and creates a historically high incendiary environment.

Population displacement and migration: Population displacement was a challenge for the smallpox program, especially in Bangladesh, India, Ethiopia, Nigeria, and Somalia. The GPEI has also faced challenges in achieving or maintaining polio eradication in the face of population displacement in Afghanistan, Pakistan, China, and various countries in Africa. Additionally, the GPEI has been frustrated by the cross-border transmission of polio associated with annual pilgrimages to Saudi Arabia by religious travelers. The yaws and Guinea worm programs have been comparatively less affected by population displacement due both to the smaller size of the endemic populations and the rural foci of disease.

A measles eradication initiative would also face challenges from population displacement and migration. Currently, there are large displaced populations in Pakistan, economic migrants in China, India, and numerous other countries. The UN has predicted that migration will increase in the future as a result of climate changes, including changes in sea level.\(^\text{13}\) As a result of exponential increases in air travel for tourism and business, the measles program may face greater challenges than eradication programs
launched earlier. However, some of his threat may be mitigated by faster communication facilitated by information technology.

**Endemic country support:** Pre-eradication political support for disease eradication programs has been a major challenge historically. Public health programs, including disease eradication, are rarely among the priorities of the highest level politicians and eradication programs have not had adequate political support at the onset of the respective initiatives. The smallpox, Guinea worm, and polio eradication programs went years with limited progress due to gross shortages of funding and limited advocacy. The yaws program never enjoyed the support of a WHA resolution and yaws funding ended pre-maturely as the program was shuffled off to become part of inadequate general health systems. A WHA malaria resolution was passed, but most endemic African countries had no vote, being represented by the colonial powers, and the malaria program was never fully operational in many endemic countries of Africa. Although the malaria and polio programs enjoyed the greatest overall political support at their inception, much of this was generated by donor countries. The smallpox program had significant political support in the late 1960s and throughout the 1970s, but support at the time of the first WHA resolution in 1959 was weak.

A measles eradication initiative will likely benefit from the comparatively exhaustive process being undertaken to evaluate the appropriateness of an eradication initiative compared with what was done before embarking on previous eradication initiatives. Further, the Member States of five of six WHO regions have already endorsed regional elimination initiatives. However, we expect that a measles eradication initiative would face challenges in engendering political support. The European Region is unlikely to complete regional measles eradication by 2010, as resolved in 1998. Thirty of the 53 EURO Member States comprising two thirds of the regional population will likely miss their target. Various western European governments lack urgency about measles elimination, in part due to perceptions that the disease is not serious, and because of the comparatively low priority given to immunizations in the process of health care reform. Until recently, India has been unwilling to conduct a catch-up campaign to reduce measles mortality, unlike the other 46 high priority countries targeted by the Measles Initiative. India is now planning to introduce a second dose of measles vaccine through either routine immunization system (in high performing states) or through SIAs (in low performing states). Countries in the African region have been highly supportive of measles mortality reduction and mortality has been reduced sharply in the last decade. However, progress in AFRO has slowed with evidence of resurgence in 2009-2010, partly due to waning political and financial support. Competition from the GPEI may continue to hamper the political support which a measles initiative could engender, especially in the remaining polio-endemic countries.

### Comparison of Political Factors

<table>
<thead>
<tr>
<th>Disease</th>
<th>Security risks due to war/civil unrest</th>
<th>Population displacement &amp; migration</th>
<th>Endemic &amp; donor govt political support for eradication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yaws</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>Malaria</td>
<td>Low</td>
<td>Low</td>
<td>Variable</td>
</tr>
<tr>
<td>Smallpox</td>
<td>Low</td>
<td>Low-medium</td>
<td>Variable</td>
</tr>
<tr>
<td>Guinea worm</td>
<td>Medium</td>
<td>Low</td>
<td>Variable</td>
</tr>
<tr>
<td>Polio</td>
<td>Medium-high</td>
<td>Medium-high</td>
<td>Variable</td>
</tr>
<tr>
<td>Measles</td>
<td>High</td>
<td>High</td>
<td>Variable</td>
</tr>
</tbody>
</table>
Social factors

Perception of disease burden and risk; acceptance of intervention: Smallpox and malaria were broadly perceived as deadly threats in the endemic countries during the pre-eradication era. Yaws, although a disfiguring disease, affected comparatively few people and caused little mortality. Similarly, Guinea worm disease can be disabling during the months of worm emergence, but mortality is very low and even within endemic countries the disease is focused in remote areas with little political influence. Polio, despite the existence of safe and effective vaccines, had an “aura” of threat and engendered fear, especially in industrialized countries, as a result of the large and well-publicized epidemics in the pre-vaccine era. Polio infections are usually asymptomatic and the number of serious cases is relatively low compared to other diseases, even prior to the launching of the eradication initiative. Although the perception of threat varied among the five diseases in the pre-eradication era, all of the programs had widespread acceptance of their principal interventions. However, the polio program in Nigeria suffered a severe setback in 2003 when organized resistance to polio vaccine and SIAs led to a large outbreak that spread widely internationally.17

By comparison, measles has been a disease of high burden historically, and as recently as 2000, an estimated 733,000 persons, mainly children, died from measles complications. However, recent progress in reducing measles mortality (an estimated 78% decrease in the year 2008 compared to 2000) may have reduced the perception of “threat” from measles. Also, measles seldom causes mortality in developed countries, many of which have not stopped measles transmission and don’t consider it a high priority. In western Europe, where deaths from measles are rare, there exist pockets of resistance to immunizations, especially measles vaccine, as a result of the efforts of anti-vaccine groups and highly publicized and unfounded vaccine safety concerns. Despite varying perceptions of threat, measles vaccine is generally well accepted and there has been no widespread rejection of measles vaccine based on safety, religious, or cultural grounds outside of Europe.

Competition from other health programs: In the 1950s and 1960s, there were few large health programs competing with the yaws, malaria, and smallpox eradication initiatives. Routine immunization programs had not been started in most developing countries and health care systems were weak. The polio and Guinea worm programs in the 1980s had to compete with HIV/AIDS and the Expanded Programme on Immunizations for political and financial support.

Pressure to do more to “strengthen health systems” has been a constant challenge for eradication programs as advocates push for policies, funds, and other resources for infrastructure development rather than targeted disease control programs. All of the eradication programs have shared this challenge, perhaps none more than the GPEI due to its great size and costs over an extended period of more than 20 years.

Measles eradication would likely face stiff competition for political and financial support from the existing GPEI, the introduction of newer vaccines against diarrhoea, pneumonia, and cervical cancer, as well as from the other large, ongoing health initiatives. Some donors have already expressed a specific interest in building health systems rather than focusing on measles eradication. However, a measles eradication initiative may benefit from efforts to merge with one or more other programs (e.g., through campaign-style delivery of multiple interventions like bed nets, micronutrients, de-worming medicines, etc.), thus avoiding the competition which can be detrimental to resource mobilization and implementation. The existence of combination measles-rubella vaccines creates an effective synergy between prevention of congenital rubella syndrome and measles eradication and raises the possibility of a combined eradication program.18

Social/economic inequality: Globalization has helped bring many of the poor above the poverty line in Asian countries, especially in India and China. However, per capita income growth in Sub Sahara Africa actually declined between 1980 and 2000.19 Although it is difficult to definitively show a specific cause and effect relationship between inequality and resistance in the eradication programs, various programs have encountered resistance among socially and economically disadvantaged groups. The malaria program experienced problems with resistance to indoor insecticide spraying. Underlying causes for the 2003 polio outbreak in Nigeria included issues of social/economic inequality.20 It is likely that a measles
eradication program would face some of these same kinds of social/economic challenges, especially as fear of the disease wanes following reductions in measles mortality.

Information technology has burst forth in the last 20 years with new developments happening nearly on a weekly basis. The existence of computers, hand held digital assistants, I-Pads, internet, email, etc., are potentially game changing in their ability to organize and analyze data, and facilitate communications. None of this technology existed at the time the yaws, malaria, and smallpox programs were launched in the 1950s. At the time the polio and Guinea worm eradication programs were initiated, some of this technology existed but it was comparatively primitive. If launched today, a measles eradication initiative would greatly benefit from the many technological advances, enabling strengthened surveillance, monitoring, evaluation, and information activities.

### Comparison of Social Factors

<table>
<thead>
<tr>
<th>Disease</th>
<th>Perception of disease burden and threat</th>
<th>Acceptance of intervention</th>
<th>Competition from other health programs</th>
<th>Social and economic inequality</th>
<th>Level of information &amp; communication technology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yaws</td>
<td>Low</td>
<td>High</td>
<td>Low</td>
<td>Medium</td>
<td>Low</td>
</tr>
<tr>
<td>Malaria</td>
<td>High</td>
<td>High</td>
<td>Low</td>
<td>Medium</td>
<td>Low</td>
</tr>
<tr>
<td>Smallpox</td>
<td>High</td>
<td>High</td>
<td>Low</td>
<td>Medium</td>
<td>Low</td>
</tr>
<tr>
<td>Guinea worm</td>
<td>Medium</td>
<td>Medium</td>
<td>Medium</td>
<td>High</td>
<td>Medium</td>
</tr>
<tr>
<td>Polio 1988</td>
<td>Variable</td>
<td>High</td>
<td>High</td>
<td>High</td>
<td>Medium</td>
</tr>
<tr>
<td>Measles</td>
<td>Variable</td>
<td>High</td>
<td>Very high</td>
<td>High</td>
<td>High</td>
</tr>
</tbody>
</table>

### Economic factors

**Cost**

The smallpox eradication program is estimated to have cost some $300 million from endemic and donor governments combined. The yaws program and Guinea worm eradication programs, at $9 million and $250 million respectively, also cost comparatively small amounts. The comparatively small number of endemic countries for these three diseases helped keep costs low. The GPEI has already spent more than $7 billion and the malaria program spent an estimated $2-3 billion, both in real dollars. The malaria program is estimated to have cost more than $14 billion in inflation-adjusted dollars.

Cost estimates for measles eradication prepared by each region in 2010 total under $5 billion globally. Including costs for program implementation by WHO and UNICEF headquarters, and accounting for differences by the WHO Regions, we anticipate that measles eradication would cost between $5-8 billion. We predict that measles eradication costs would be less than for polio and malaria (measured in 2010 dollars), but higher than the yaws, smallpox, and Guinea worm eradication programs.

**Cost-effectiveness and potential cost savings**

Despite the obvious benefits of preventing disease and death through eradication programs, an analysis of costs, cost-effectiveness, and cost savings is considered essential by some experts and decision-makers. Cost savings are a selling point, although for some diseases, these savings are more likely to accrue to industrialized countries where health care is comparatively expensive. There are surprisingly few data available about cost and cost-effectiveness prior to the start of prior eradication programs. Most eradication programs were initiated based primarily on technical issues, e.g., availability of effective, inexpensive interventions rather than based on an analysis of economic issues. Also, the potential financial benefits of vaccine preventable disease eradication programs have changed significantly
because some countries will continue vaccination after eradication due to the perceived threat of bio-terrorism.

A cost-effectiveness analysis of measles eradication in 6 countries was prepared for this meeting and concludes that in the countries studied, measles eradication is highly cost effective and is cost saving in countries which have already eliminated measles (Brazil and Colombia). Results on cost effectiveness are expected to be published in 2010.

**Funding by governments of endemic countries**

Most of the eradication programs have suffered funding problems, especially in their early years. The smallpox eradication program made relatively little progress from 1959 to 1966. Only four Guinea worm endemic countries undertook the recommended eradication activities from 1981-1990. Although polio eradication in the American Region and in China was largely funded by the endemic governments, the GPEI waited 7 years before initiating significant activities in Africa and Southeast Asia, largely because of funding gaps. The first polio SIAs were conducted in India in 1995, 7 years after the WHA polio eradication resolution. Although this was also due to political resistance, adequate funding may have helped soften that resistance. By contrast, the yaws and malaria program received substantial early funding from USAID, UNICEF, and other donors that allowed faster initial progress, although later funding gaps contributed to program failures.

A measles eradication initiative, if launched, would likely benefit from substantial funding from endemic countries, especially China and India, the Middle East, and countries of the European Region. However, substantial external funding would be required for countries in Africa, south Asia, and the poorest countries of southeast Asia.

**Funding by donor governments and NGOs**

Non-endemic governments may be motivated to support disease eradication programs based on altruism or self-interest. For smallpox eradication, governments were motivated by a desire to stop smallpox vaccination due to the severe side effects. The business community and non-endemic governments had an interest in malaria eradication due to the adverse impact of malaria on international and national staff. The GPEI was both motivated by, and benefited from, an early commitment of $220 million from Rotary International. Countries in the Americas have an interest in measles eradication so they can stop SIAs and save on costs due to importations and outbreak response.

Donor funding is difficult to predict and the 2010 environment is a challenging one in which to raise funds due to the global financial crisis. However, compared to the 1950s and the 1980s, there now exists a stronger culture of donating to immunization programs from which a measles initiative may benefit. The existing Measles Initiative is well-positioned to take advantage of this, especially if they build on fund-raising ideas developed by the GPEI. Continuing support from CDC, the UN Foundation, American Red Cross, and new support from the Bill and Melinda Gates Foundation, suggests that fund-raising targets might be achievable by a well-managed measles eradication program.
Comparison of Economic Factors

<table>
<thead>
<tr>
<th>Disease</th>
<th>Funds expended</th>
<th>Cost-effectiveness &amp; savings</th>
<th>Potential endemic govt funding</th>
<th>Donor govt or NGO/private donor funding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yaws</td>
<td>$9+ million spent²¹</td>
<td>Not done</td>
<td>Mixed</td>
<td>Low</td>
</tr>
<tr>
<td>Malaria</td>
<td>$2-3 billion spent²²</td>
<td>Global study not done</td>
<td>Mixed</td>
<td>Medium</td>
</tr>
<tr>
<td>Smallpox</td>
<td>$300 million spent²³</td>
<td>Not done</td>
<td>Mixed</td>
<td>Low</td>
</tr>
<tr>
<td>Guinea Worm</td>
<td>$250 million spent²⁴</td>
<td>Cost benefit study done 1997</td>
<td>Mixed</td>
<td>Low</td>
</tr>
<tr>
<td>Polio</td>
<td>$7.13 billion spent to date²⁵</td>
<td>CE study published in 1993</td>
<td>Mixed</td>
<td>High</td>
</tr>
<tr>
<td>Measles</td>
<td>$5-6 billion (rough estimate)</td>
<td>To be published 2010</td>
<td>Mixed</td>
<td>Medium</td>
</tr>
</tbody>
</table>

Technical factors

Properties of the agent

The smallpox virus was comparatively easy to eradicate because it was not very infectious, with only 3 - 5 cases spread from each index case despite an infectious period lasting up to four weeks. The virus was genetically stable and a single dose provides long-lasting immunity, allowing the vaccine to remain efficacious for the duration of the program. The yaws bacteria was also genetically stable but yaws patients remained infectious throughout multiple periods of symptomatic disease lasting weeks or longer. Polio, with 3-5 infections spread from each case (10-12 in tropical developing countries)²⁶, is also infectious for some 4-6 weeks, increasing the challenge of stopping transmission. The polio virus has been sufficiently stable such that the vaccine has remained efficacious throughout the program. However, the live virus vaccine itself is on rare occasions the cause of disease and may be spread to others. Comparisons with malaria and Guinea worm are more difficult because their spread involves a vector. However, the density of infectious anopheles mosquitoes can make it very difficult to stop malaria transmission. Although drinking contaminated water is necessary to become infected with Guinea worm disease, one case in Mali led to 84 subsequent cases.²⁷

The measles virus is highly infectious with an average of 12-18 cases spread from each index case in a fully susceptible population.²⁸ This challenge is mitigated considerably by the short period of infectiousness lasting just 8 days on average. Further, the measles virus is genetically very stable. The measles vaccine has remained efficacious and although it is a live virus vaccine, does not appear to cause significant disease in recipients. The risk of current vaccine viruses reverting to wild-type transmissibility is thought to be extremely low. As is the case for smallpox and polio, humans are the only reservoir for measles virus. In terms of transmission factors, with the exception of greater infectiousness, measles virus behaves more like the smallpox virus than the polio virus. However, due to the high infectiousness of measles, a high level of population immunity will be required to achieve herd immunity.

Comparison of properties of the agent

<table>
<thead>
<tr>
<th>Disease</th>
<th>Infectiousness</th>
<th>Duration of infectiousness</th>
<th>Genetic stability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yaws</td>
<td>?</td>
<td>During presence of moist yaws lesions</td>
<td>Stable</td>
</tr>
<tr>
<td>Malaria</td>
<td>Variable (vector required)</td>
<td>Infectious to mosquitoes 1 – 5 years (if untreated)</td>
<td>Resistance to insecticides and chloroquine</td>
</tr>
<tr>
<td>Disease</td>
<td>$Ro = 3 - 5$</td>
<td>Presence of Rash</td>
<td>Infectious Duration</td>
</tr>
<tr>
<td>------------------</td>
<td>-------------</td>
<td>------------------</td>
<td>---------------------</td>
</tr>
<tr>
<td>Smallpox</td>
<td></td>
<td>During presence of rash, about 3 weeks</td>
<td>&quot;Infectious&quot; during worm emergence – 8 weeks</td>
</tr>
<tr>
<td>Guinea worm</td>
<td>Variable (vector required)</td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td>Polio</td>
<td>Ro = 3-5 US 10 – 12 in tropical countries</td>
<td>4 – 6 weeks</td>
<td>Stable, but cVDPV risk</td>
</tr>
<tr>
<td>Measles</td>
<td>Ro = 12 - 18</td>
<td>8 – 10 days</td>
<td></td>
</tr>
</tbody>
</table>

**Level of disease control already achieved; elimination from large geographic areas**

The task of eradication is made easier when the disease is endemic in fewer areas, has already been eliminated from large geographic areas and/or is well controlled in endemic areas. The yaws, smallpox, and Guinea worm programs were much smaller and involved far fewer endemic countries than the malaria and polio efforts. (See Table xx.) Each of the eradication efforts gained momentum from earlier efforts to eliminate the targeted disease. For example, malaria was cleared from the southeastern United States, and yaws was eliminated from Haiti. Smallpox had been eliminated from the majority of countries before the eradication effort began in 1959. However, later experience showed that neither yaws nor malaria eradication was feasible with the interventions and strategies used. Further, the temperate climate zones in which malaria transmission was stopped may well have happened due to environmental factors as much as to use of insecticide treatments. Several of the programs, especially polio, have had problems in India. Despite success in large geographic areas, it may not be prudent to presume feasibility in India until after the fact.

Population growth adds to the cost and complexity of implementing strategies, especially if the strategies cannot be narrowly targeted. Four billion more people are alive in 2010 compared to 1950. Most of the population growth has occurred in measles endemic countries. The size of the population living in measles endemic countries in 2010 is estimated to be more than 5 billion, some 1 billion higher than the polio-endemic population in 1988, and far larger than the endemic populations for the other programs.

Urbanization and population density can make it more difficult to break transmission chains. In the second half of the twentieth century, and continuing today, there has been a steady shift of people from rural areas to cities. In the 1950s, New York was the only city with an urban area population of more than 10 million. In 2010, there are 25-30 such urban areas in the world. Since the early 1950s, an additional 1.3 billion people are living in cities with a population of ≥ 1 million. Urbanization and greater population density likely will make measles eradication more difficult in comparison with 20th century eradication programs.

By comparison with earlier eradication efforts, measles eradication would benefit from the large demonstration of success in the Americas, including in large cities such as Mexico City, Rio de Janeiro, and Sao Paulo, providing strong evidence that the measles eradication strategies would work throughout the world. Elimination of measles in other European, Asian, and island countries, combined with high levels of control in many countries, bode well for the success of measles eradication. However, the large size of the measles endemic population and increasing urbanization, combined with the greater infectiousness of measles, will make measles eradication very challenging. The increases in air travel and migration during the last half century will also make it difficult to prevent measles importations from endemic countries.
Comparison of levels of control at onset of eradication programs

<table>
<thead>
<tr>
<th>Disease</th>
<th>Estimated Incidence</th>
<th>Size Endemic Population</th>
<th>Number of Endemic Countries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yaws</td>
<td>2 - 5 million cases</td>
<td>0.4 billion</td>
<td>46</td>
</tr>
<tr>
<td>Malaria</td>
<td>150 million cases</td>
<td>1.1 billion</td>
<td>143 (1950)</td>
</tr>
<tr>
<td>Smallpox</td>
<td>20+ million cases</td>
<td>1.5 billion</td>
<td>59</td>
</tr>
<tr>
<td>Guinea Worm</td>
<td>3.5 million cases (1986)</td>
<td>0.14 billion</td>
<td>19</td>
</tr>
<tr>
<td>Polio</td>
<td>0.35 million cases</td>
<td>70+ million infections</td>
<td>125</td>
</tr>
<tr>
<td>Measles</td>
<td>12 million cases</td>
<td>5.2 billion</td>
<td>125</td>
</tr>
</tbody>
</table>

World population and urbanization, 1955–2010

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Population (billions)</td>
<td>2.80</td>
<td>3.04</td>
<td>3.71</td>
<td>4.45</td>
<td>5.29</td>
<td>6.09</td>
<td>6.85</td>
</tr>
<tr>
<td>Urban pop billions (%)</td>
<td>0.75 (27%)</td>
<td>0.99 (33%)</td>
<td>1.33 (35%)</td>
<td>1.74 (40%)</td>
<td>2.27 (43%)</td>
<td>2.85 (48%)</td>
<td>3.49 (51%)</td>
</tr>
</tbody>
</table>

Surveillance factors

Symptomatic cases and asymptomatic disease: Smallpox eradication was facilitated by the relative ease of case identification and the absence of asymptomatic cases. Similarly, yaws and Guinea worm have easily recognizable symptoms, although lab testing is useful to confirm a yaws diagnosis. Malaria surveillance was difficult because diagnostic tests were essential to distinguish malaria from other febrile illnesses. An adequate global network for malaria surveillance was never established. Polio surveillance has been made more challenging because the majority of infections are asymptomatic or cause only minor illness. Further complicating surveillance in the GPEI, the paralysis of polio is often mimicked by other diseases, causing an abundance of necessary work investigating non-polio acute flaccid paralysis cases.

The smallpox and Guinea worm programs did/do not require extensive laboratory networks to complement case-based surveillance, thus facilitating eradication. By contrast the yaws and malaria programs needed more laboratory support although it was not available in many countries. The polio program has developed an impressive network of 147 laboratories. There is a global measles laboratory network encompassing 679 laboratories.

Measles surveillance would be facilitated by the relative ease of case identification since virtually all cases have a rash. Distinguishing a measles rash from other rash illness, especially rubella, often requires laboratory testing. Although some asymptomatic measles cases have been documented, transmission from such cases is likely to be very rare, if it occurs at all, and is unlikely to be efficient enough to sustain transmission. Measles outbreaks are relatively easy to detect, facilitating more rapid responses.

Measles eradication would be further facilitated by the extensive network of measles laboratories already developed, although further development work would be needed if eradication were undertaken. New laboratory tests, including rapid field tests, may become available, making it easier to confirm measles cases promptly. The surveillance system, including laboratory network, that would be required for measles eradication would likely be easier than that for polio and the failed malaria eradication program.
However, it would be more difficult than the surveillance needed for smallpox and Guinea worm eradication.

### Comparison of Surveillance Factors

<table>
<thead>
<tr>
<th>Disease</th>
<th>Easily identifiable symptoms</th>
<th>Existence of asymptomatic cases</th>
<th>Simple diagnostic tests</th>
<th>Lab network required/developed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yaws</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes/no</td>
</tr>
<tr>
<td>Malaria</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes/no</td>
</tr>
<tr>
<td>Smallpox</td>
<td>Yes</td>
<td>Rare</td>
<td>Not needed</td>
<td>No/no</td>
</tr>
<tr>
<td>Guinea Worm</td>
<td>Yes</td>
<td>No</td>
<td>Not needed</td>
<td>No/no</td>
</tr>
<tr>
<td>Polio</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes/yes</td>
</tr>
<tr>
<td>Measles</td>
<td>Yes</td>
<td>Extremely rare</td>
<td>Yes</td>
<td>Yes/yes</td>
</tr>
</tbody>
</table>

### Quality of interventions

Almost all of the eradication programs have relied heavily on one key intervention to achieve eradication. Interventions which are effective in a single dose, can be administered safely by volunteers, and that can be stored at ambient temperatures offer the greatest advantages. The enabling factors for each are summarized in the table above. However, the risk from primary reliance on a single intervention is that if it proves inadequate in one or more countries or epidemiologic situations due to resistance or inadequate effectiveness, the program may be left without an alternate strategy. Supply problems also become more critical in the absence of alternate tools. Resistance to malaria insecticides hindered success. Vaccine supply problems have affected the smallpox and polio eradication programs. Trivalent OPV proved inadequate to eradicate polio in northern India despite high coverage.

Measles vaccine, the only available intervention for eradication, is safe and highly effective. Measles vaccine is safer than the smallpox (vaccinia) and polio (OPV) vaccines, has excellent immunogenicity after just 2 doses, and is widely accepted. However, measles vaccine is not highly immunogenic for children less than 9 months of age. The current measles elimination strategies require one time catch up campaigns for children up to age 15, and all high priority countries except India have completed these campaigns. Additional challenges with the measles vaccine include the need for trained vaccinators, and cold chain and safe administration/disposal requirements.
## Comparison of Interventions

<table>
<thead>
<tr>
<th>Disease</th>
<th>Simple, effective intervention</th>
<th>Safety risks</th>
<th>Single dose or administration</th>
<th>Cold chain required</th>
<th>Demonstrated effectiveness in large geographic area</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yaws</td>
<td>Yes (penicillin)</td>
<td>Unsafe needle use and adverse reactions</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Malaria</td>
<td>Yes initially (insecticides)</td>
<td>Risks from insecticides</td>
<td>Yes (conventional wisdom at time – later proved false)</td>
<td>No</td>
<td>Yes, but in temperate zones only</td>
</tr>
<tr>
<td>Smallpox</td>
<td>Yes (vaccine)</td>
<td>Risks from adverse events</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Guinea Worm</td>
<td>Yes (clean water, filters &amp; larvicides)</td>
<td>Low risk</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Polio</td>
<td>Yes (vaccine)</td>
<td>Rare risk VAPP*</td>
<td>No (multiple doses required)</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Measles</td>
<td>Yes (vaccine)</td>
<td>Low risk from unsafe vaccine handling</td>
<td>No (2 doses only)</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

*Vaccine Associated Paralytic Polio

### Existence of quality research program

Some of the earlier eradication programs suffered from inadequate research and product development activities. A complaint made about the malaria eradication program is that it eradicated a generation of malariologists but not malaria, setting back future efforts.\(^{36}\) When insecticide resistance was identified, efforts to identify second line insecticides were inadequate. Operational research to identify best practices for identifying and treating latent yaws infections may have prevented program failure. The polio program benefited from efforts to develop vaccine vial monitors, but suspended early efforts to examine a potential role for IPV in the program, and delayed research on monovalent and bivalent vaccine products for years. By contrast, the smallpox program benefited from development of the bifurcated needle, and a strategy of case containment rather than universal vaccination.

The present measles program has a robust program of research work, especially in the areas of needle-free approaches to vaccine delivery and laboratory technology. Development of rapid field tests for measles and other diagnostics could facilitate surveillance and outbreak response. However, the current program of research work could be improved, especially by conducting research that would provide information on the level of effort required to stop transmission in key states of India. In addition, operational research is needed on methods for monitoring and assuring homogeneous high vaccination coverage (≥95%) is achieved, particularly in challenging settings.

### Other key factors

**Effective health systems:** All of the previous eradication programs struggled to implement their respective strategies in countries and localities where health systems are weak.\(^{37}\) The yaws program suffered loss of momentum when the eradication program was integrated into weak health systems in many countries. The recommended measures for malaria eradication were never implemented in some sub-Saharan countries of Africa. The smallpox eradication program had only faltering progress from 1959
to 1966 until supplemental personnel were assigned to countries with ineffective health systems. The polio program has assigned thousands of dedicated staff to compensate for weak health systems in some countries.

By comparison with the 1950s and 1980s, measles should benefit from stronger health systems, especially the routine immunization system and existing SIA and surveillance infrastructure from the MI and GPEI. However, given the large number of endemic countries, a potential measles eradication program would also face serious difficulties in the many remaining areas with weak health systems.

**Strong management:** All of the prior eradication programs were made more challenging by management problems. The yaws program didn’t adjust strategies to effectively address surveillance problems and the difficulties of eradication in latent cases. The malaria program faced numerous obstacles in strategy development, supplies and logistics and allowed research to lag behind program needs. The smallpox and polio programs struggled to overcome bureaucratic obstacles, both within endemic country governments and within UN and partner agencies. The GPEI only began an effective fund-raising effort 10 years into the initiative.

By contrast with earlier eradication initiatives, a measles eradication program will have the advantage of the many lessons available from which to learn. The MI provides a strong foundation from which to build the management structures that will be needed. However, some management structures that are needed now, including much stronger fund-raising and communications/advocacy units, will certainly need to be developed for an eradication initiative.

**Discussion**

There is increasing recognition that political, societal, economic, and management issues are at least as important as biological ones in assessing the feasibility of a disease eradication initiative. A potential measles eradication program would enjoy distinct advantages in comparison with earlier eradication programs. Perhaps the most important are those below:

- Virtually all countries have indicated strong support for accelerated measles control activities, and five of six WHO regions have announced measles elimination initiatives. This “de facto” eradication program, in the absence of a global resolution for eradication, suggests a strong current of governmental interest that should benefit measles eradication.
- The feasibility of measles eradication is being evaluated more carefully than any of the prior eradication initiatives. These evaluations and discussions likely will pay dividends in engendering greater support should an eradication initiative be launched.
- Global advancements in information and communications technology, and laboratory technology, are exponentially better than in the 1950s and 1980s.
- Measles eradication, estimated to cost about $5-8 billion, would likely cost less than the GPEI in real dollars and result in far greater impact on morbidity and mortality than GPEI. Measles eradication would probably cost less than the failed malaria eradication program in inflation-adjusted dollars. China and India could be expected to largely self-fund. Although more expensive than the yaws, smallpox, and Guinea worm program, the burden of measles disease and the size of the measles endemic population could easily justify an initiative. Past experience with the malaria, polio, and HIV/AIDS programs suggest that the cost of measles eradication is affordable.
- Surveillance for measles eradication would be made comparatively easy because nearly all measles infections are clinically manifested by a characteristic syndrome of fever and rash, the absence of asymptomatic or latent disease, existence of simple laboratory tests for confirmation of cases, and an extensive laboratory network.
- The measles vaccine is highly effective with just 2 doses protecting >99% of vaccinated persons, and is very safe when administered according to recommendations.
- The successful elimination of measles from the Americas provides a good model of the strategies needed for measles eradication globally.
The most daunting challenges for global measles eradication likely would include the following:

- Key measles endemic countries are at war in 2010 including Afghanistan, Iraq, and Pakistan. Further, the world is more heavily armed than ever. Terrorism, both real and perceived, adds to the complexity of challenges from civil unrest. Reaching high coverage in conflict-affected areas will be extremely difficult and dangerous.
- The very high infectiousness of measles will require homogeneous vaccination coverage of >=95%. The resulting population immunity will be continuously challenged by population movements (urbanization, economic migrants, trade, tourism and international travel).
- Measles is not perceived as a very serious problem in some countries, in part because the development of effective health services in wealthy and middle income countries has reduced the mortality rate to low levels. The European Region, a comparatively wealthy region, has not eliminated measles. Although changes appear imminent, India, the country with the largest estimated number of measles cases, has not fully embraced existing measles control and mortality reduction strategies.
- The resistance of the anti-vaccination lobby in Europe must be overcome.
- The challenges of measles eradication in India may not be fully understood. India was extremely challenging for the smallpox program and India has yet to stop transmission of yaws, malaria, or polio. It remains unclear what level of coverage will be required to stop transmission in Uttar Pradesh and Bihar or the level of effort required to achieve it. For example, if house-to-house campaigns proved necessary in Uttar Pradesh and India, this would be an immense and unprecedented undertaking.
- The co-existence of the polio program could create an unhealthy competition for political and financial resources globally, and for priority and technical staffing in key countries, particularly India, Pakistan, and Nigeria. New vaccine programs against diarrhea, pneumonia and cervical cancer will provide stiff competition for limited immunization dollars.

**Recommendations**

The following recommendations derive from lessons learned from analyzing the success and failures of the previous eradication programs:

- Obtain meaningful political and financial commitments, including advance multi-year funding commitments from endemic countries, non-endemic donor countries, and NGOs before launching eradication. A WHA resolution alone does not represent adequate political commitment.
- Consider either delaying measles eradication until polio transmission has been interrupted in both India and Nigeria, or forming a partnership that promotes fighting both diseases simultaneously.
- Consider strengthening partnerships in selected countries with other targeted health programs such as polio eradication and malaria control. A joint measles/rubella eradication initiative may provide greater efficiency and engender more support from some governments and donors.
- Accelerate research and development efforts to increase vaccine and delivery options for eradication. Specifically, a vaccine patch, use of other needle-less injection devices, and use of intra-dermal administration with lower dosing would all increase the chances of achieving eradication.
- Conduct specific research in India, preferably by Indian researchers, to gather data demonstrating that the eradication strategies are effective, or that they need to be modified, in India. India has proven to be an extreme challenge for most of the previous eradication programs. A firm scientific basis in support of the feasibility of measles eradication in India with existing tools is desirable.
- Begin implementation of eradication strategies early on in the most challenging countries rather than leaving them until later in the program.
Conclusions

Compared with disease eradication programs launched in the last half of the 20th century, measles eradication would be very challenging, but probably not as difficult as malaria or polio eradication. Although enormous progress has been made by the Measles Initiative, measles eradication would be a very different kind of challenge requiring an exponential increase in resources and commitment. Measles eradication should be undertaken only if the commitments and resources will be adequate to meet the political, social, economic, and technical challenges.
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