

Summary of the Twenty-Ninth Meeting of the International Task Force for Disease Eradication (ITFDE) January 15, 2019

The 29th meeting of the International Task Force for Disease Eradication (ITFDE) was convened at The Carter Center, Atlanta, GA, USA on January 15, 2019 to discuss "Strengths and Limitations of Officially Validating Disease Elimination as a Public Health Problem." The Task Force members at the time of this meeting were Dr. Stephen Blount, The Carter Center (Chair); Dr. Peter Figueroa, The University of the West Indies, Jamaica; Dr. Donald Hopkins, The Carter Center; Dr. Hamid Jafari, Centers for Disease Control and Prevention (CDC); Mr. Fernando Lavadenz, The World Bank; Dr. Mwelecele Malecela, World Health Organization (WHO); Professor David Molyneux, Liverpool School of Tropical Medicine; Dr. Stefan Peterson, UNICEF; Dr. David Ross, The Task Force for Global Health; Dr. Nilanthi de Silva, University of Kelaniya, Sri Lanka/WHO Strategic and Technical Advisory Group for Neglected Tropical Diseases (STAG-NTDs); Dr. Dean Sienko, The Carter Center; Dr. Laurence Slutsker, PATH; Dr. Jordan Tappero, Bill & Melinda Gates Foundation; Dr. Ricardo Thompson, National Institute of Health (Mozambique); and Dr. Dyann Wirth, Harvard School of Public Health. Twelve Task Force members (Blount, Figueroa, Hopkins, Lavadenz, Malecela, Molyneux, Ross, Sienko, Slutsker, Tappero, Thompson, Wirth) participated in this meeting, and two were represented by an alternate (Dr. Steve Cochi for Jafari; Dr. Robert Kezaala for Peterson).

Presenters at this meeting included Drs. Gregory Noland, The Carter Center; Jonathan King, WHO; Gary Weil, Washington University in St. Louis; Deborah MacFarland, Emory University; Luis Castellanos, Pan American Health Organization (PAHO); Edwin Michael, University of Notre Dame; and William Schluter, CDC.

Strengths and Limitations of Officially Validating Disease Elimination as a Public Health Problem

The term "elimination" often is defined and used differently by different disease programs and the nomenclature for how events and achievements are evaluated is inconsistent. This has resulted in WHO Member Countries expressing confusion and the desire for WHO to reach internal agreement to provide advice to Member States on how to achieve this goal for the various diseases targeted for elimination. In 1997, WHA resolution 50.29 established the goal of "elimination of lymphatic filariasis (LF) as a public health problem (EPHP)"¹ and in 2000 WHO established the Global Programme to Eliminate LF (GPELF)². At that time, there was no standard definition of EPHP. In our current understanding, achieving EPHP, does not mean that infection has been eliminated and a country is free of the pathogen. It is important to recognize that this achievement is potentially reversible, as transmission of infection could recrudesce whilst residual chronic clinical conditions remain as a public health problem.

¹ Generic Framework for Control, Elimination, and Eradication of Neglected Tropical Diseases. WHO 2016. https://www.who.int/neglected_diseases/resources/WHO_HTM_NTD_2016.6/en/.

² Global Programme to Eliminate Lymphatic Filariasis: Progress Report 2017. Wkly Epidemiol Rec 93(44): 589-601.

In 2016, WHO published a generic framework for neglected tropical diseases (NTDs) to standardize the definitions of the targets and processes by which it would assess and acknowledge the claimed achievements among the NTDs. EPHP is achievement of global targets set by WHO for a specific infection and/or disease and when achieved requires continued action to maintain the target or to advance to the interruption of transmission. Countries claiming to have met the targets follow a process called *validation* to document EPHP. Elimination of transmission (EOT) or interruption of transmission is the reduction to zero of the incidences of infection in a defined geographical area with minimal risk of reintroduction where continued actions to prevent re-establishment of transmission may be required, but on-going interventions (such as mass drug administration (MDA)) can be suspended. The process to document EOT is *verification*. Eradication is the permanent reduction to zero of a specific pathogen globally, with no more risk of reintroduction; the process of documenting eradication is *certification*. The amount of evidence and effort required to document these achievements increases from EPHP to EOT to eradication, the latter of which can be proclaimed only at the global level.³ WHO has not yet defined the pathway, milestones and standardized criteria to verify EOT of LF, for example, and Member States have urgently requested assistance from WHO to do so.

Despite the clear value of the phrase EPHP early in the drive toward global elimination of LF, for example, the recent experience of some Member States is instructive of its limitations, including Sri Lanka, which was validated by WHO as achieving EPHP for LF. Following this achievement, but before EOT was achieved, there was subtle pressure to downplay continued problem areas with persistent LF. Sri Lanka's donor support declined dramatically, including for drug donations, diagnostic kits and operational activities. Recrudescence of LF then was documented in some communities.⁴ The ITFDE learned of similar premature loss of support by leprosy programs after that disease was declared to have achieved EPHP. Having EPHP as a target, however, has enabled substantial improved control of onchocerciasis, trachoma, leprosy and human African trypanosomiasis, as well as LF. For some diseases, effective tools and strategies are available to establish clear criteria and practical quantitative targets to document EOT, but for others research is needed to define which indicators and what tools provide the measurable evidence of zero transmission. Consideration should be given to "re-branding or "re-titling" the current validation target as "the first elimination milestone," defining the other milestones, and stating that posttreatment surveillance, outbreak investigation and response activities, and social mobilization campaigns will still be needed until EOT is achieved, to protect the earlier investment. Despite its limitations, some WHO Regional Offices, including PAHO, which has established a regional elimination agenda, feel strongly that EPHP represents a useful intermediate goal and regional bodies should maintain the freedom to establish and pursue region-specific goals.⁵

Efforts to eradicate/eliminate vaccine-preventable diseases (VPDs) provide important lessons to countries working to end the scourge of other pathogens by, among other activities, strengthening primary health care services. ⁶ Strengthening primary health care service delivery and disease surveillance systems will play an important role in achieving and sustaining VPD eradication/elimination goals. Some specific examples where disease eradication/elimination efforts will likely depend on a strong primary health care service delivery system includes: (1) preventing the emergence of circulating vaccine-derived

https://www.who.int/lymphatic_filariasis/resources/9789241511957/en/.

³ Validation of elimination of lymphatic filariasis as a public health problem. WHO 2017.

⁴ Rao RU, Samarasekera SD, Nagodavithana KC, Dassanayaka TDM, Punchihewa MW, Ranasinghe USB, et al. (2017) Reassessment of Areas with Persistent Lymphatic Filariasis Nine Years After Cessation of Mass Drug Administration in Sri Lanka. *PLoS Negl Trop Dis* 11(10): e0006066. https://doi.org/10.1371/journal.pntd.0006066.

⁵ Castellanos' oral presentation on "PAHO Elimination Initiative for the Americas" at the 29th meeting of the International Task Force for Disease Eradication, January 15, 2019.

⁶ Rohde J, Cousens S, Chopra M, Tangcharoensathien V, Black R, Bhutta ZA, Lawn JE. 30 Years After Alma-Ata: Has Primary Health Care Worked in Countries? *Lancet*. 2008 Sep 13;372(9642):950-61. doi: 10.1016/S0140-6736(08)61405-1.

polioviruses; (2) sustaining polio eradication activities with inactivated polio vaccine; (3) achieving and sustaining measles and rubella elimination; and (4) increasing the acceptance of vertical eradication/elimination interventions among the most marginalized populations.⁷

Economic studies have in the past few years increasingly demonstrated their value in gaining the attention of decision makers, particularly those involved in making investment choices. The most significant messages from a review of economic studies of the elimination of NTDs are that methods and estimates should be consistent across NTDs. There are resource requirements that often have not been carefully considered when technical and operational changes are proposed or made in eradication/elimination strategies. Making the investment case for an individual eradication/elimination strategy is notably problematic for domestic financing as countries confront the challenge of providing universal health care; and there are few tools available for economic appraisal at the country level.⁸

Mathematical models have been found to be increasingly useful in recent years to investigate the potential to eradicate/eliminate parasitic infections and disease. Such models help to characterize complex dynamical systems and facilitate study of their transmission, persistence and spread. For eradication/ elimination programs, they allow quantification of critical transition thresholds that shift parasitic systems to their null states and can facilitate assessment of the potential impact of any proposed intervention or combination of interventions to achieve elimination of parasite transmission.⁹

Elimination of Malaria and Lymphatic Filariasis on Hispaniola

The island of Hispaniola, shared by Haiti and the Dominican Republic, remains the only Caribbean island with endemic *Plasmodium falciparum* malaria transmission and accounts for 95% of the LF burden in the Americas. In 2009, the countries announced a bi-national plan to eliminate malaria and LF by 2020.

Malaria cases have significantly declined in both countries since a peak following the 2010 earthquake in Haiti. In Haiti, reported cases declined 90% between 2010 and 2018 from 84,153 to 8,426 (provisional) cases, with a 56% decline observed between 2017 and 2018 alone. In the Dominican Republic, there was an 81% decline between 2010 and 2018, from 2,482 to 480 reported cases. A total of 7 malaria deaths, 6 in Haiti and 1 in the Dominican Republic, were reported in 2018. Geographically, Grande Anse and Sud departments in the southwest of Haiti have accounted for at least two-thirds of all cases nationwide since 2016. In the Dominican Republic, transmission in urban and peri-urban areas of Santo Domingo has accounted for at least half of all cases nationwide since the emergence of an outbreak in the Los Tres Brazos area of Santo Domingo beginning in 2014.

Similar progress against LF has been achieved also. In Haiti, 118 (84%) of the 140 communes have met criteria to stop annual MDA with diethylcarbamazine (donated by Eisai) and albendazole (donated by GSK). Of these, 72 have passed the stop-MDA transmission assessment survey (TAS-1), while 42 have

⁷ 16th Report of the Independent Monitoring Board of the Global Polio Eradication Initiative, October 2018 at http://polioeradication.org/wp-content/uploads/2018/11/20181105-16th-IMB-Report-FINAL.pdf.

⁷ A Report Commissioned by the Independent Monitoring Board of the Global Polio Eradication Initiative on Progress in Afghanistan, Nigeria and Pakistan: Review of Polio Endemic Countries, September 2018 at <u>http://polioeradication.org/wp-content/uploads/2018/10/Review-of-Polio-Endemic-Countries-2018.pdf</u>.

⁸ Redekop WK, Lenk EJ, Luyendijk M, Fitzpatrick C, Niessen L, Stolk WA, et al. (2017) The Socioeconomic Benefit to Individuals of Achieving the 2020 Targets for Five Preventive Chemotherapy Neglected Tropical Diseases. *PLoS Negl Trop Dis* 11(1): e0005289. https://doi.org/10.1371/journal.pntd.0005289

⁹ Michael E, Madon S. (2017) Socio-Ecological Dynamics and Challenges to the Governance of Neglected Tropical Disease Control. *Infectious Diseases of Poverty* 6:35.

passed both TAS-1 and TAS-2, which WHO recommends two or three years following TAS-1 as part of post-treatment surveillance. Concerningly, one Haitian commune, Dondon, met stop-MDA criteria of antigen prevalence less than 2% at the 95% confidence level during TAS-1, yet failed TAS-2. This area requires at least two additional rounds of MDA and warrants further investigation to determine whether this was the result of imported cases leading to local transmission, undetected transmission, or a limitation in the TAS-1 survey design of only testing school-aged children 6-7 years old. In the Dominican Republic, LF transmission was restricted to 19 municipalities (12% of national total) in three distinct foci: the Southwest, La Cienaga in Santo Domingo, and the East. In 2018, the Southwest and La Cienaga passed TAS-3 surveys, while the East region passed TAS-1, meaning that all previously endemic areas qualify to stop MDA in the Dominican Republic. The national program plans to conduct a nationwide re-mapping survey in 2019 to confirm that there is no evidence of transmission in other parts of the country.

Conclusions and Recommendations

- 1. The ITFDE commends WHO Member States for progress toward eradicating/eliminating several diseases targeted for eradication/ elimination, including Guinea worm disease, polio, LF, onchocerciasis, trachoma, leprosy and human African trypanosomiasis. The ITFDE also commends WHO for its leadership in assisting Member States to pursue eradication and elimination targets. More attention should be paid to the precise definitions and rigorous use of accepted nomenclature to focus on measurable events to document progress.
- 2. WHA Resolution 50.29 in 1997 was an important early step toward elimination of LF by introducing the phrase "elimination as a public health problem" (EPHP). The ITFDE recommends that WHO further assist Member States by accelerating its work to define the pathway, milestones and standardized criteria to verify elimination of transmission of diseases currently targeted for EPHP. However, the recent experiences of some Member States are instructive. Effective tools and strategies are available to establish clear criteria and practical numerical targets to document elimination of transmission. Consideration should be given to "re-branding" or "re-titling" the current validation target, perhaps as "the first elimination milestone", defining the other milestones and clearly stating that post-validation surveillance, outbreak investigation and response, and public education campaigns will still be needed. Despite limitations, EPHP represents a useful intermediate goal and regional bodies should maintain the latitude to pursue region-specific goals. If used in future, resolutions for EPHP should include a measurable objective and specific target date and acknowledge the need for ongoing effort to preserve the accomplishment after it is achieved, by strengthening and integrating surveillance system into the primary health care services.
- 3. For diseases currently targeted for EPHP, research leading to the establishment of standardized criteria is an urgent priority. To eliminate transmission of LF it will be necessary to establish the quantitative level to which the infection must be reduced; set a target date; specify the type and level of surveillance needed to document change; and, while recognizing the role of political-economic issues, respond to the needs of program managers. The ITFDE also recommends that greater emphasis be placed in national LF elimination programs on morbidity management and disability prevention.
- 4. The ITFDE recommends that WHO work with the World Bank and other development agencies to develop tools for ministries of health and finance to use to: (a) estimate the cost and benefits of NTD elimination at the country level, including the cost of the "end game;" and (b) establish an investment case for morbidity management/disability prevention activities to be included in a package of essential health services. In calling attention to this area, Task Force members expressed a strong sense of

urgency, that "clouds are on the horizon" and that all matters should be seen through the lens of efforts to achieve universal health coverage.

- 5. To distill and use lessons drawn from rapidly progressing advances outside of the health arena, WHO was recommended to draw on experiences in the fields of education and agriculture. The ITFDE recommends that countries, NGOs, WHO, and donor organizations more fully consider the use of mathematical models of parasite transmission, which offer a powerful tool to help assess the potential to eliminate/eradicate a parasite and consequently the derivation of options to reduce variability and increase the feasibility of elimination of transmission.
- 6. The ITFDE recommends that WHO, in its assistance to Member States, prioritize the importance of working at the community level "from the bottom up," to support strategies formed by local cultural context in which eradication/elimination activities take place.
- 7. The ITFDE recommends that WHO learn from the lessons of regional bodies that have established a regional elimination agenda, as did PAHO, the WHO Regional Office in the Americas, whose leaders meet frequently with leaders of the Inter-American Development Bank to advocate for investments. Increased and reinvigorated advocacy to decision makers (including Member States, NGO partners, donors and development banks) is needed urgently to strengthen political commitments, perhaps under the rubric of "Protecting the Investment" or "Sustaining the Gains." Words matter, and WHO is recommended to strengthen the capacity within its Member States to use the modern tools of media and communications, particularly about the economic impact of preventable diseases to maintain political commitment and garner needed resources. WHO also is urged to intensify its efforts to distill the experiences of its Member States to more appropriately and carefully align eradication/elimination programs with VPDs, education, Water, Sanitation and Hygiene, and Integrated Disease Surveillance, a village-based system.
- 8. The ITFDE recognizes that one of the most urgent issues facing WHO Member States is governance, including helping to improve donor coordination. It urges WHO to work more closely with Member States, donors and implementing NGO partners to develop tools, approaches and training materials to improve skills at national and local levels in priority-setting, communication, decision making, monitoring and evaluation.
- 9. The Dominican Republic and Haiti have made substantial progress against malaria and lymphatic filariasis in recent years. The national programs are encouraged to publish evidence of these gains, and the LF Elimination programs in both countries should begin preparing their elimination dossier. The Task Force is encouraged by recent investments for malaria and LF elimination in both Haiti and the Dominican Republic. However, additional external resources, as well as domestic financing, are needed to consolidate gains and achieve elimination. As 2020 approaches, both countries should recommit to bi-national malaria elimination with a revised target date and budget.
- 10. The Dominican Republic's Ministry of Public Health should continue to implement active surveillance and vector control measures to respond to malaria outbreaks in Santo Domingo. Additionally, studies are recommended to understand risk factors for transmission in the urban and peri-urban environments, as well as evaluation of effectiveness of community-outreach activities by the Ministry.
- 11. The Haitian LF Elimination Program should introduce triple-drug (IDA) in areas still requiring MDA as warranted according to WHO recommendations. The national strategic plan needs to be updated to enable this option. The LF Programs in both Haiti and the Dominican Republic need to scale-up morbidity management and disability prevention services in accordance with WHO guidelines. The program displayed a pair of combined maps showing the distribution and intensity of LF infections on the whole island at the beginning of the bi-national initiative and as of 2018, which demonstrated the

purpose and progress of the fight against that disease very effectively and succinctly. Unfortunately, a similar pair of maps for malaria was not available.