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Dominique Kyelem
The Task Force for Global Health, Decatur, Georgia

Gautam Biswas

Moses J. Bockarie
Case Western Reserve University School of Medicine

Mark Bradley
Global Community Partnerships

Maged El-Setouhy

See next page for additional authors

Authors
Dominique Kyelem, Gautam Biswas, Moses J. Bockarie, Mark Bradley, Maged El-Setouhy, Peter U. Fischer, Ralph H. Henderson, James W. Kazura, Patrick J. Lammie, Sammy M. Njenga, Eric A. Ottesen, Kapa Ramaiah, Frank O. Richardson, Gary J. Weil, and Steven A. Williams

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Determinants of Success in National Programs to Eliminate Lymphatic Filariasis: A Perspective Identifying Essential Elements and Research Needs

Dominique Kyelem,* Gautam Biswas, Moses J. Bockarie, Mark H. Bradley, Maged El-Setouhy, Peter U. Fischer, Ralph H. Henderson, James W. Kazura, Patrick J. Lammie, Sammy M. Njenga, Eric A. Ottesen,* Kapa D. Ramaiah, Frank O. Richards, Gary J. Weil, and Steven A. Williams

Lymphatic Filariasis Support Center, Task Force for Child Survival and Development, Decatur, Georgia; Department of Control of Neglected Tropical Diseases, World Health Organization, Geneva, Switzerland; Lymphatic Filariasis Support Centre, Liverpool School of Tropical Medicine, Liverpool, United Kingdom; Global Community Partnerships, GlaxoSmithKline, Brentford, United Kingdom; Department of Public Health, Ain Shams University, Cairo, Egypt; School of Medicine, Washington University, St. Louis, Missouri; Center for Global Health & Diseases, Case Western Reserve University, Cleveland, Ohio; Division of Parasitic Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia; Kenya Medical Research Institute, Nairobi, Kenya; Vector Control Research Centre, Indian Council of Medical Research, Pondicherry, India; Carter Center, Atlanta, Georgia; Clark Science Center, Smith College, Northampton, Massachusetts

Abstract. The Global Programme to Eliminate Lymphatic Filariasis (GPELF) was launched in 2000. To understand why some national programs have been more successful than others, a panel of individuals with expertise in LF elimination efforts met to assess available data from programs in 8 countries. The goal was to identify: 1) the factors determining success for national LF elimination programs (defined as the rapid, sustained reduction in microfilaremia/antigenemia after repeated mass drug administration [MDA]); 2) the priorities for operational research to enhance LF elimination efforts.

Of more than 40 factors identified, the most prominent were 1) initial level of LF endemicity; 2) effectiveness of vector mosquitoes; 3) MDA drug regimen; 4) population compliance.

Research important for facilitating program success was identified as either *biologic* (i.e., [1] quantifying differences in vectorial capacity; [2] identifying seasonal variations affecting LF transmission) or *programmatic* (i.e., [1] identifying quantitative thresholds, especially the population compliance levels necessary for success, and the antigenemia or microfilaremia prevalence at which MDA programs can stop with minimal risk of resumption of transmission; [2] defining optimal drug distribution strategies and timing; [3] identifying those individuals who are "persistently non-compliant" during MDAs, the reasons for this non-compliance and approaches to overcoming it).

While addressing these challenges is important, many key determinants of program success are already clearly understood; operationalizing these as soon as possible will greatly increase the potential for national program success.

BACKGROUND AND APPROACH

Since the official launch of the Global Program to Eliminate Lymphatic Filariasis (GPELF) in 2000,[1] almost 2 billion doses of once-yearly anti-filarial drug treatment have been administered to over 570 million people through national programs in 48 of the world's 83 endemic countries.[2] It is not surprising that some of these programs have been more successful than others. Now that a number of the early programs are approaching the point at which they can contemplate stopping the MDA component of their programs, it is possible to look retrospectively to identify factors that have influenced their outcomes. Such evaluation provides an opportunity to guide ongoing and still-to-be-initiated national programs toward adopting more successful strategies, and it identifies key biologic, epidemiologic, and programmatic uncertainties that might be addressed through targeted research.

Collection of detailed analytical data has not been a standard component of most national MDA programs, so the richest source of information for identifying potential determinants that affect program outcome lies with those programs working closely with research teams from either government research institutions or academia. In some instances these collaborating research teams have directly tracked the progress of the national programs, and in others they have made detailed observations at study sites where treatment activities were carried out in parallel to those of the national program.

To capture the experiences of programs that have been closely monitored (epidemiologically, entomologically, and through laboratory studies) in different parts of the world, investigators from programs in 8 countries (Table 1) provided information identifying successes and failures within each program and the likely reasons for these outcomes. Although program "success" can have many dimensions, here the principal measure of success was the decrease in microfilaremia prevalence, a *sine qua non* of LF elimination. The specific factors evaluated in relation to this marker of success—either having a positive influence (i.e., leading toward greater impact or shorter duration of MDA activities) or a negative influence (i.e., leading toward lesser impact or longer duration of MDA activities)—are detailed in Table 2. Some of these factors represent determinants that will have an effect on program *outcome* regardless of how effectively the program itself is carried out (Table 2a), whereas others relate principally to the operational effectiveness of the programs themselves (Table 2b). The conclusions in Table 2 largely reflect the considered assessment and consensus of the investigators themselves after analysis and discussion of, in most instances, published data describing the impact of MDA on

* Address correspondence to Dominique Kyelem or Eric A. Ottesen, Lymphatic Filariasis Support Center, Task Force for Child Survival and Development, Decatur, Georgia. E-mails: dkyelem@taskforce.org and eottesen@taskforce.org

TABLE 1
National LF elimination activities assessed in this perspective

Program country	LF parasite	No. of MDAs
Burkina Faso	*Wuchereria bancrofti*	5
Egypt	*W. bancrofti*	5
Haiti	*W. bancrofti*	5
India	*W. bancrofti*	9
Indonesia	*Brugia timori*	6
Kenya	*W. bancrofti*	2
Nigeria	*W. bancrofti*	6
Papua New Guinea	*W. bancrofti*	7

microfilaria prevalence and transmission[3–19] and, in other cases, less formal reports of LF elimination program activity.[20–22]

DETERMINANTS AFFECTING PROGRAM OUTCOME

More than 40 different determinants affecting program outcome were identified and described as leading to either greater or lesser likelihood of success (defined as the *rapid and sustained fall in the prevalence of microfilaremia*) for the MDA-based LF elimination programs (Table 2).

Among the most prominent factors to affect program outcome were: 1) the initial level of LF endemicity (i.e., prevalence and density of microfilaremia); 2) the competence and vectorial capacity of the local vector; 3) the drug regimen used for the MDAs; and 4) both population coverage* and population compliance.†

Some of the determinants noted in Table 2 are not easily changed—particularly those that are biologic/epidemiologic in nature or those that reflect the underlying socioeconomic and political environments of the endemic areas. Despite their being relatively unchangeable, however, programs do need to recognize their influence when implementation strategies are being developed.

Other determinants are more readily modifiable—such as compliance within the endemic communities and coverage of the target population. These, in turn, are heavily dependent on 1) the *operational effectiveness* of the programs (especially social mobilization, supervision and monitoring), 2) the adequacy of resources (both funding and human), and 3) the political commitment to support the program.

IDENTIFYING RESEARCHABLE ISSUES

Although many of the factors identified in Table 2 are not amenable to research or have been so well documented

* Defined by the proportion of the population targeted by the program that was provided with the appropriate drugs.

† Defined by the proportion of eligible individuals actually ingesting the drugs provided to them.

TABLE 2a
Determinants influencing *outcome* of LF elimination programs

Factor	Positive influence*	Negative influence†	Readily changeable	Important/ researchable
Biologic/epidemiologic/therapeutic				
Endemicity (prevalence/density)	Low	High	No	✓
Human population	Small	Large	No	
Endemic areas	1) Easily accessed 2) Rural	1) Remote 2) Urban	No	
Vector density	Low	high	Yes	✓
Vector species	Anopheles (? some better than others)	*Aedes* or *Culex*	No	✓
Transmission	Seasonal	Year-round	No	✓
Parasite species	Anthropophilic *Brugia*	*W. bancrofti*	No	
MDA treatment regimen	DEC (diethylcarbamazine) + albendazole	Ivermectin + albendazole	+/–	✓
Ivermectin dosage in regimen	400 mcg/kg	150–200 mcg/kg	Yes	✓
Parasite responsiveness to treatment	Excellent	Residual mf/ag-emia	No	
Contiguous endemic areas	Under MDA treatment	Untreated	Yes	✓
Sympatric *Loa loa*	No	Yes	No	
Sympatric zoophilic *Brugia*	No	Yes	No	✓
Economic/political/social				
Economic development of endemic area	High (including housing, roads)	Low, with poor physical infrastructure	No	
Administrative development of endemic area	High overall performance	Low performance record	No	
Health system infrastructure	Good (including local health units)	Poor, with weak national MOH	No	
Urban population: socio-economic status	Lower (more difficult to reach, easier to treat)	Higher (easier to reach, more difficult to treat)	No	✓
Political stability, security	Good	Poor, high security risk	No	
Political commitment for NPELF	Strong	Minimal	Yes	
Compliance (people *taking* the drugs)	High compliance rate; no persistent non-compliance	Persistent non-compliance or poor compliance rate	Yes	✓
Evident morbidity in population	High (leads to perception of importance)	Low (inhibits recognition of importance)	No	
Past experience of population with LF or other MDA programs	Good results, minimal inconvenience	Poor quality drugs, adverse reactions	No	
Migration from other endemic areas	Minimal	Extensive	No	✓

* Leading to greater impact or shorter duration of MDA activities.
† Leading to lesser impact or longer duration of MDA activities.
MDA = mass drug administration; NPELF = National Program to Eliminate Lymphatic Filariasis; MOH = Ministry of Health.

TABLE 2b
Factors affecting *operational effectiveness* of LF elimination programs

Factor	Positive influence	Negative influence	Readily changeable	Important/ researchable
Global program guidelines	Detailed, comprehensive	Imprecisely defined goals, tools, strategies (compliance, # MDAs, monitoring tools, sampling strategies, stopping criteria)	Yes	
Mapping of LF and other NTDs	Complete	Incomplete	Yes	
Program management, leadership	Strong	Weak	Yes	
Advocacy and fund-raising	Active and effective	Poor or non-existent	Yes	
"Personpower"	Sufficient, well-trained, conscientious	Shortage, unskilled or untrained	Yes	
Drug distributors	Well trained, well informed, compensated	Poorly motivated and trained	Yes	
Social mobilization	Strong (IEC/COMBI), with involvement of village leaders	Inadequate	Yes	✓
Drug quality	High and consistent	Uncertain or poor	Yes	
Drug supply/delivery	Timely and coordinated for 2-drug delivery	Unreliable, uncoordinated	Yes	
MDA organization	Well timed (dates, duration)	Shifting dates, conflicting dates	Yes	
Drug administration	By Directly Observed Treatment	Not DOT	Yes	✓
Treatment "coverage" (tablets *distributed*)	High (estimated > 70% *total* population)	Low	Yes	✓
Treatment of "side reactions"	Provision for rapid, effective management (medical and "political")	Inadequate response to person and community needs	Yes	
Morbidity management	Strong program in place for lymphedema management and hydrocoele surgery	Minimal attention to morbidity issues	Yes	
Monitoring	Independent, routine; following process indicators, using good sampling strategies	Insufficient frequency or attention to detail	Yes	
Evaluation	Baseline mf- or ag-emia and reassessment at defined intervals or potential program end-point, using good sampling strategies	No baseline values; poor sampling strategy	Yes	✓
Adjunctive tools to eliminate LF	Vector control, twice-yearly MDA or DEC-salt supplements in place	No adjunctive measures	Yes	✓
LF's relation to other NTD Programs	Integration or strong coordination in place	National program operates independently	Yes	✓
Community understanding	Recognizes multiple benefits of MDA (on LF, on intestinal parasites etc.)	Inadequate information on program's full benefits to the population	Yes	✓
Partnering organizations	Multiple and coordinated	Few or uncoordinated	Yes	
Funding for LF program	Sufficient (best from national budget line)	Inadequate, without ensured continuity	Yes	
Link between national program and research community	Good collaboration; shared responsibility	Competition, distrust	Yes	

MDA = mass drug administration; LF = lymphatic filariasis; NTD = neglected tropical diseases; IEC/COMBI = information education communication/communication for behavioral impact; DOT = directly observed treatment; DEC = diethylcarbamazine.

previously as to require little or no further study, the effects of almost one-third of the identified determinants are poorly understood, and they require further study. Some reflect current uncertainties in the biology of the parasite and vector (including their interactions with each other and the human host); others reflect uncertainties about how best to design national programs to ensure success; and still others indicate uncertainties in the way people respond to MDAs.

"Biologic" research priorities. Two vector/parasite biologic issues, if more well defined, could have particular impact on program success: 1) quantifying the differences in vector competence (microfilaria uptake, L3 production) among the different vector species, particularly the anophelines in Africa—as this would better define the "force of infection" that individual programs must confront and would affect decisions about the frequency and duration of MDAs required to interrupt LF transmission; 2) identifying potential seasonal variations of relevance to LF transmission (microfilaremia in humans, biting patterns in mosquitoes) in different endemic regions—as this might open opportunities to tailor the timing of MDAs to maximize their impact toward interrupting LF transmission.

"Programmatic" research priorities. A better *quantitative* understanding of the operational factors essential for program success would be particularly valuable for improving program outcome. Specifically, these factors would include: 1) the levels of population compliance required during MDAs to achieve interruption of transmission (and the levels of non-compliance or systematic non-compliance that still permit LF elimination); 2) the levels of microfilaria (mf)-positivity or antigen-positivity at which the MDA component of programs can safely be stopped (i.e., an understanding of the "natural history" and programmatic implications of persistent antigenemia in mf-negative individuals and of low-level microfilaremia prevalence in communities after multiple rounds of MDA); 3) the number of rounds of MDA required for success in different epidemiologic situations—perhaps fewer in low endemicity areas and more, even with supplemental measures including vector control and enhanced drug regimens, in other epidemiologic settings.

Resolving programmatic uncertainties related to conduct of the MDAs themselves could also greatly increase the likelihood of individual program success. Particularly important are 1) defining the optimal drug distribution methods and strategies (Directly Observed Treatment [DOT] being the

"gold standard") for use in different settings—including "problem settings" such as refugee, migrant, or urban areas; 2) determining the importance of interruptions in the planned yearly implementation of MDAs; 3) identifying the importance of conducting the MDAs in relation to transmission seasonality; and 4) understanding whether the effectiveness of MDA-based programs in *Brugia* endemic areas is affected by sympatric zoonotic *Brugia* infections.

"Community-focused" research priorities. The most important community-related uncertainty is the issue of compliance. It will be valuable to develop "compliance profiles" of communities to identify those groups of individuals who remain "persistently non-compliant" during MDAs (e.g., children, upper socioeconomic classes, young men, older ages), and then to determine the causes of this non-compliance and effective approaches to overcoming it.

WAY FORWARD

It is unlikely that studies will be carried out, or answers found, for *all* of these researchable questions in the near future. There are financial constraints, limitations in available study opportunities, and the fact that for some of these questions the essential research tools to address them are not yet in hand. However, because *each* issue is important and because answers to *any* can certainly lead to improvements in program design or execution, every opportunity to address them should be taken.

Program improvement, moreover, need not await the outcome of more research. The extensive programmatic experience summarized in Table 2 clearly identifies situations where specific steps can be taken immediately to improve the likelihood of success for LF elimination programs. Key determinants of successful outcomes have already been identified; the challenge for the Global Program now is to support national program managers in taking the *right* steps as quickly as possible.

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Authors' addresses: Dominique Kyelem, Task Force for Child Survival and Development, 325 Swanton Way, Decatur, GA 30030, E-mail: dkyelem@taskforce.org. Gautam Biswas, World Health Organization, Avenue Appia 20, 1211 Geneva 27, Switzerland, Tel: +41-22-791-21-11, Fax: +41-22-791-31-11, E-mail: biswasg@who.int. Moses J. Bockarie, Case Western Reserve University, Center for Global Health and Diseases, Wolstein Research Building Rm. 4129, 2103 Cornell Road, Cleveland, OH 44106, Tel: (216) 368-6285, Fax: (216) 368-4825, E-mail: mbockarie@gmail.com. Mark H. Bradley, GlaxoSmithKline, Global Community Partnerships, 980 Great West Road, Brentford, Middlesex TW8 9GS, United Kingdom, E-mail: mark.h.bradley@gsk.com. Maged El-Setouhy, Professor, Department of Community, Environmental and Occupational Medicine, Faculty of Medicine, Ain Shams University, Abbasia, Cairo, Egypt, Tel: +(202) 2685-3276, Fax: +(202) 2483-7888, E-mails: maged_elsetouhy@yahoo.com and maged.elsetouhy@gmail.com. Peter U. Fischer, Washington University School of Medicine, Infectious Disease Division, Campus Mailbox 8051, 660 S. Euclid Ave., St. Louis, MO 63110, Tel: 314-454-7876, Fax: 314-454-5293; E-mail: PUfische@im.wustl.edu. Ralph H. Henderson, Task Force for Child Survival and Development, 325 Swanton Way, Decatur, GA 30030, E-mail: rafeh@bellsouth.net. James W. Kazura, Case Western Reserve University, Center for Global Health and Diseases, Wolstein Research Building Rm. 4129, 2103 Cornell Road, Cleveland, OH 44106, Tel: (216) 368-4810, Fax: (216) 368-4825, E-mail: james.kazura@case.edu. Patrick J. Lammie, U.S. Centers for Disease Control and Prevention, DPD/NCID/CCID, 4770 Buford Hwy NE, MS F-13, Atlanta, GA 30342-3742, Tel: 001-770-488-4054, E-mail: pjl1@cdc.gov. Sammy M. Njenga, Kenya Medical Research Institute, P.O. Box 54840, 00200 Nairobi, Kenya, Tel: +254-20-2722541, Fax: +254-20-2720030, E-mail: snjenga@kemri-nuitm.or.ke. Eric A. Ottesen, Task Force for Child Survival and Development, 325 Swanton Way, Decatur, GA 30030, E-mail: eottesen@taskforce.org. Kapa D. Ramaiah, VCRC, No: 12, Bhaktavatsalam Street, Tagore Nagar, Lawspet, Pondicherry—605 008, India, E-mail: ramaiahk@yahoo.com. Frank O. Richards, The Carter Center, One Copenhill, 453 Freedom Parkway, Atlanta, GA 30307, Tel: 404-420-5100, E-mail: fxr1@cdc.gov. Gary J. Weil, Washington University School of Medicine, Infectious Disease Division, Campus Mailbox 8051, 660 S. Euclid Ave., St. Louis, MO 63110, Tel: 314-454-7782, Fax: 314-454-5293, E-mail: GWEIL@im.wustl.edu. Steven A. Williams, Smith College, Clark Science Center, 44 College Lane, Northampton, MA 01063, Tel: 413-585-3857 ext. 3826, Fax: 413-585-3786, E-mail: swilliam@email.smith.edu.

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