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


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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 if 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
microfilaria prevalence and transmission\textsuperscript{3-19} and, in other cases, less formal reports of LF elimination program activity.\textsuperscript{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 \textit{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\textsuperscript{*} and population compliance.\textsuperscript{†}

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 unchanged, 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 \textit{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

\begin{table}[h]
\centering
\begin{tabular}{|l|l|l|}
\hline
\textbf{Program country} & \textbf{W. bancrofti} & \textbf{No. of MDAs} \\
\hline
Burkina Faso & \textit{Wuchereria bancrofti} & 5 \\
Egypt & \textit{W. bancrofti} & 5 \\
Haiti & \textit{W. bancrofti} & 5 \\
India & \textit{W. bancrofti} & 9 \\
Indonesia & \textit{Brugia timori} & 6 \\
Kenya & \textit{W. bancrofti} & 2 \\
Nigeria & \textit{W. bancrofti} & 6 \\
Papua New Guinea & \textit{W. bancrofti} & 7 \\
\hline
\end{tabular}
\caption{National LF elimination activities assessed in this perspective}
\end{table}

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

\textsuperscript{*} Defined by the proportion of eligible individuals actually ingesting the drugs provided to them.
\textsuperscript{†} Defined by the proportion of the population targeted by the program that was provided with the appropriate drugs.

\textsuperscript{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

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

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 antigen-emia 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.

Received June 16, 2008. Accepted for publication August 20, 2008.

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