Global Programme to Eliminate Lymphatic Filariasis
fundamentals towards successful NTD elimination

courtesy of Nepal and GSK
Lymphatic filariasis

- NTD caused by three species of nematodes that nest in the lymphatic vessels
- Transmitted by mosquitoes
- Infection impairs function of lymphatic system by vessel dilatation

Image source: www.dpd.cdc.gov/dpdx
LF Morbidity— a leading cause of global disability

Chronic manifestations
• Lymphoedema
• Elephantiasis
• Hydrocele

Acute manifestations
• Adenolymphangitis (ADL) ‘acute attacks’
Social and Economic burden of LF

- Disfigurement, pain & disability
- Stigma
- Depressive illness
- Economic loss
- Causes and aggravates poverty

courtesy of Nepal and Kiribati
Endemic in 72 countries; 856 million people require mass treatment.
Transmission to Elimination

What are the fundamentals needed to move from transmission towards successful elimination?
1. *Global commitment* – WHA 50.29

Elimination of LF as a public health problem

Global Programme to Eliminate Lymphatic Filariasis (GPELF) was launched in 2000

1. **Stop transmission**
   - Mass drug administration (**MDA**)

2. **Reduce suffering and improve quality of life**
   - Morbidity management and disability prevention (**MMDP**)
2. **Effective strategies** – Mass Drug Administration

- Annual mass treatment with antihelminthic medicine (treating both infected and uninfected)
- 100% geographical coverage = **ALL** endemic districts
- Effective (≥65%) coverage of the **total** population ≥5 rounds
How MDA works

1. Partially damages and reduces reproductive capability of adult worms

2. Reduces circulating microfilaria in the blood

**MDA**
- Medicine ingested

**L3 larvae**
- Partially damages and reduces reproductive capability of adult worms

**Adult worms in lymphatic vessels**
- Temporary reduction of transmission

**Microfilariae**
- Reduces circulating microfilaria in the blood

**Microfilariae in blood**
- Ingested MDA medicine

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**Slide 10**
WHO recommends the following MDA regimens:

- **New** triple-drug therapy for annual MDA in special settings
  - Ivermectin + diethycarbamazine + albendazole (IDA or *triple therapy*)

- Annual two-drug therapy for all other areas
  - diethycarbamazine + albendazole
  - ivermectin + albendazole

- Biannual albendazole alone in loiasis co-endemic areas
Efficacy of IDA

DEC+ALB x 2

DEC+ALB x 1

IVM+DEC+ALB x 1

Microfilaria per ml

Years Post-Treatment

N=61, 56, 55

N=61, 59, 56

N=60, 57, 54

34% 76%

34% 56%

97% 96%

N=61, 56, 55

N=61, 59, 56

N=60, 57, 54

Efficacy of IDA

Courtesy of Chris King 2017 DOLF PNG
2. **Effective strategies**

Morbidity Management and Disability Prevention

Health facilities must be able to provide minimum package of care in every district with known *patients*

- surgery for hydrocele
- management of lymphedema
- treatment of acute attacks
- treatment of patients with LF infection

*courtesy India and GSK*
3. **Integration:** where feasible for broad impact

- **MDA/PC**
  - Blinding trachoma
  - Schistosomiasis
  - Onchocerciasis
  - Soil-transmitted helminthiases

- **VC/IVM**
  - Dengue
  - Malaria

- **GPELF**

- **MMDP**
  - Leprosy
  - Buruli ulcer
  - Podoconiosis

PC – preventive chemotherapy
VC – vector control
IVM – integrated vector management;
MMDP – morbidity management and disability prevention
### 4. *Standardized tools*: Recommended diagnostic tests

<table>
<thead>
<tr>
<th>Field assay</th>
<th>Detection target</th>
<th>Recommended for use during</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood film</td>
<td>Microfilariae</td>
<td>Mapping, Sentinel site and Spot-check site monitoring</td>
</tr>
<tr>
<td><strong>Alere Filariasis Test Strip (FTS)</strong></td>
<td>Filarial <em>antigen</em> (Ag)</td>
<td>Mapping, Sentinel site and Spot-check site monitoring, and Transmission Assessment Survey (TAS)</td>
</tr>
<tr>
<td>Brugia Rapid™ test</td>
<td>Antifilarial <em>antibody</em> (Ab)</td>
<td>TAS</td>
</tr>
</tbody>
</table>
4. *Standardized tools: Transmission Assessment Survey*

- Decision making tool, **tells when to stop MDA**
- Standardized survey with robust, yet practical statistical design
- Uses children as an indicator of incident infection
- Measures whether prevalence of infection is **below a threshold** (critical cut-off) at which transmission is assumed no longer sustainable, even in the absence of MDA
5. **Strategic Framework**

1. MDA
   - Mapping
   - MDA
   - Post-treatment surveillance

2. MMDP
   - Situation analysis
   - Plan
   - Minimum package of MMDP care

**Integrated Vector Management**

Pre-TAS

TAS1  TAS2  TAS3

Dossier development

Post-validation surveillance

**VALIDATION**

**MMDP and rehabilitation integrated into health services**
6. **Measurable progress**: proportion of implementation units that have completed TAS and no longer require MDA*

*Percent of all known endemic implementation units (IU) in countries by region that have completed TAS1 or previous stop-MDA surveys and reported meeting criterion for stopping MDA. IUs where endemicity is unknown have not been included.

- **African**: 18.4%
- **Americas**: 47.3%
- **Eastern Mediterranean**: 77.8%
- **South-East Asia**: 55.5%
- **Western Pacific**: 74.0%

* prior to 2015
** 2015
*** 2016

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World Health Organization

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### 6. Measurable progress: MDA status of countries

<table>
<thead>
<tr>
<th>MDA not started</th>
<th>MDA started but not at scale</th>
<th>MDA scaled to all endemic IUs</th>
<th>Post-MDA Surveillance</th>
<th>Elimination as a Public Health Problem</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gabon, Sao Tome and Principe, South Sudan</td>
<td>Comoros, Eritrea, Madagascar, Guyana, Indonesia, Papua New Guinea</td>
<td>Dominican Republic, Haiti</td>
<td>Egypt, Yemen, Bangladesh</td>
<td>Cambodia, Cook Islands, Marshall Islands, Niue, Tonga, Vanuatu</td>
</tr>
</tbody>
</table>

- **MDA not started:** 5 (7%)
- **MDA started but not at scale:** 16 (22%)
- **MDA scaled to all endemic IUs:** 31 (43%)
- **Post-MDA Surveillance:** 10 (14%)
- **Elimination as a Public Health Problem:** 10 (14%)
Cumulative treatments administered during MDA in 67 countries

6,700,000,000

499,400,000

Population no longer requiring MDA in 44 countries
Prevented or cured more than 97 million cases
(Ramaiah, Ottesen 2014 PLoS NTD)

Forecasted to avert >US $100 billion in economic loss
(Turner et al 2016 Infect Dis Pov)
7. **Partnerships**

- **WHO**: Policy and guidelines
- **GAELF**: Advocacy / fundraising
- **Pharma**: Drug donation
- **Donor**: Financial assistance
- **National Govt**: Coordinating / implementing
- **Academic**: Operational research and evidence
- **NGO**: Assistance to MoH

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NPELF – national programmes to eliminate LF
GAELF – Global Alliance to Eliminate Lymphatic Filariasis
7. **Partnerships**: Government Leadership
### 7. Partnerships: Donations - medicines

<table>
<thead>
<tr>
<th></th>
<th>Ivermectin</th>
<th>Diethylcarbamazine (DEC)</th>
<th>Albendazole</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dosage</strong></td>
<td>150-200 µg/kg</td>
<td>6mg/kg</td>
<td>400mg</td>
</tr>
<tr>
<td><strong>Manufacturer</strong></td>
<td>Merck Sharp &amp; Dohme (MSD)</td>
<td>Eisai</td>
<td>GSK</td>
</tr>
</tbody>
</table>
| **Commitment**   | a. Since 1997  
  b. 2017-2025 | 2014-2020              | Since 2009 until elimination is achieved |
| **Donation**     | a. Needed amount for LF elimination in oncho-coendemic countries | Up to 2.2 billion tablets | Up to 600 million tablets annually  
  b. Up to 280 million tablets per year for IDA |
7. **Partnerships: Operational research**

- Research that directly contributes to the achievement of GPELF aims
  - raises level of awareness and directs investments
  - develops more effective strategies
  - identifies programme challenges and solutions
  - facilitates costing, forecasting and planning
Conclusion

What are the fundamentals driving GPELF towards success?

1. Global commitment
2. Effective strategies
3. Integrated approach
4. Standardized tools
5. Strategic framework
6. Measurable progress
7. Partnerships
WHO Guideline development group meeting

Systematic Review: alternative MDA strategies for the elimination of lymphatic filariasis

Xavier Bosch-Capblanch, Peter Steinmann, Amanda Ross, Heather Ames, Meike Zuske

Geneva, 17-19 May 2017

http://www.who.int/lymphatic_filariasis/resources/9789241550161/en
Current obstacles to success

- MDA has not started in all endemic districts
- Sustaining effective coverage for ≥5 MDA rounds
- Sub-optimal results of impact surveys
  - 10% of TAS have failed across 14 countries
- Persistent transmission in certain settings
  - *Aedes* vector
  - Zoonotic *Brugia malayi*
- Need more sensitive tools/responsive targets for measuring impact of better regimens
Thank you
Swiss TPH!
courtesy of Zanzibar and GSK