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LSHTM, NHM

“Feasibility of interrupting STH transmission: the DeWorm3 Project”
April 4th, 2019
London, UK
The NTD context

- Launched in 2012, the London Declaration on Neglected Tropical Diseases is a collaborative effort bringing together pharmaceutical companies, donors, endemic countries and NGOs.

- The WHO Roadmap on NTDs set out a comprehensive plan for control and elimination of various NTDs by 2020.

- Mass Drug Administration (MDA) is the cornerstone strategy for helminthic NTD control & elimination
Why attempt to break transmission?

Comparison of 2016 coverage for PC NTDs with the WHO target and the UHC coverage target (over 1 billion people reached with PC in 2016)

- Push to accelerate impact; MDA delivered through STH programs does not meet global demand

- To allow Ministries to shift attention and resources to other pressing health needs
Populations targeted for treatment

- Many of those in need of STH treatment are reached through the LF programme.

- Opportunities exist to leverage established momentum and the infrastructure of community-wide drug distribution, as LF programmes wind down.

- WHO 2017 guidelines greatly expand the target population for treatment to include 12-24mos and non-pregnant adolescent girls and women of reproductive age.
To mitigate potential drug resistance that may result from continued, long-term drug pressure

**Albendazole** - Unlimited supply for as long as needed from GSK for LF worldwide and up to 400 million doses per year for STH for school-age children worldwide; donations made through WHO

Since 2000, they have donated 8 billion tablets to WHO and reached >850 million people. The total commitment is ~1 billion tablets per year (as of 2018).

**Mebendazole** - 200 million tablets annually from Johnson & Johnson for STH control programmes for children

- Current donations cannot extend indefinitely. Need to reach a point when these can scale down
- To mitigate development of potential drug resistance that may result from long-term pressures
To ensure that generous drug donations associated with the London Declaration commitments have maximum impact.
DeWorm3 Objectives

1. Define STH elimination
2. Demonstrate the feasibility of interrupting STH transmission
3. Develop an implementation plan for scale-up

Evidence generation:
- Benin
- Malawi
- India

Informing policies:

<table>
<thead>
<tr>
<th>Intermuption Status</th>
<th>Policy Recommendation</th>
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<tbody>
<tr>
<td>All sites</td>
<td>Community-wide MDA should be included in the global guidelines to interrupt STH transmission.</td>
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<tr>
<td>Some sites only</td>
<td>MDA should be adjusted according to given characteristics.</td>
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<tr>
<td>Not feasible</td>
<td>Continue MDA targeting high risk groups.</td>
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Policy recommendation:
Interruption of STH transmission is feasible at all DeWorm3 trial sites.

Policy recommendation: Community-wide MDA should be included in the global guidelines to interrupt STH transmission.

Policy recommendation: MDA should be adjusted according to given characteristics.

Policy recommendation: Continue MDA targeting high risk groups.
Malawi
- Lead institutions:
  - Blantyre Institute for Community Outreach
  - London School of Hygiene and Tropical Medicine
  - Ministry of Public Health, Education, Malawi
- Trial Site: Namwera, Mangochi

Benin
- Lead institutions:
  - Institut de Recherche Clinique du Bénin
  - Institut de Recherche pour le Développement
  - Ministry of Public Health, Education, Benin
- Trial Site: Come, Mono

India
- Lead institutions:
  - Christian Medical College, Vellore
  - Imperial College London
- Trial Site: Timiri and Jawadhu Hills, Vellore, Tamil Nadu

Malawi
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Defining STH Transmission Interruption

STH transmission models suggest reaching a prevalence of 2% measured by quantitative PCR (for any species) 24 months after stopping MDA reliably predicts transmission interruption.
DeWorm3 Study Design

Objectives

1. Define STH elimination
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Intervention Years

<table>
<thead>
<tr>
<th>Year 1</th>
<th>Year 2</th>
<th>Year 3</th>
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<tbody>
<tr>
<td>Q1</td>
<td>Q2</td>
<td>Q3</td>
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Surveillance Years

<table>
<thead>
<tr>
<th>Year 4</th>
<th>Year 5</th>
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<tbody>
<tr>
<td>Q1</td>
<td>Q2</td>
</tr>
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</table>

Data collection

- C: Census
- SAC: SAC- and PSAC-targeted MDA
- PSAC: Post-MDA coverage validation survey

Mass drug administration

- Q1: Mass drug administration
- Q2: Q3: Q4: Mass drug administration

Surveillance Years

C: Community-wide MDA

Stool collection

- Cross-Sectional Survey
- Longitudinal Monitoring Cohort
Possible Resulting Scenarios

Scenario 1
Prevalence never falls below the threshold

Scenario 2: BOUNCEBACK
Prevalence falls below \( \leq 2\% \) six months post-MDA, but then increases above the threshold over two years of surveillance

Scenario 3: TRANSMISSION INTERRUPTION
Prevalence does not fall below the threshold six months post-MDA, but falls below the threshold over two years of surveillance

Scenario 4: TRANSMISSION INTERRUPTION
Prevalence falls below the threshold six months post-MDA, and maintains or continues to decrease over two years of surveillance
## Baseline Census

### INDIA

- **Households enumerated:** 36,536
- **Individuals enumerated:** 140,932
- **Infants (<1yr):** 1,750 (1.2%)
- **Pre-SAC (0-4):** 8,482 (6.0%)
- **SAC (5-14):** 21,839 (15.5%)
- **Adult (15+):** 108,861 (77.2%)

- **No access to latrine:** 65.6%
- **Natural floor:** 12.4%

### MALAWI

- **Households enumerated:** 27,750
- **Individuals enumerated:** 121,819
- **Infants:** 4,368 (3.6%)
- **Pre-SAC:** 17,455 (14.3%)
- **SAC:** 37,652 (30.9%)
- **Adult:** 62,161 (51.0%)

- **No access to latrine:** 2.4%
- **Natural floor:** 79.5%

### BENIN

- **Households enumerated:** 24,378
- **Individuals enumerated:** 94,969
- **Infants:** 2,616 (2.8%)
- **Pre-SAC:** 11,188 (11.8%)
- **SAC:** 26,043 (27.4%)
- **Adult:** 54,882 (57.8%)

- **No access to latrine:** 37.0%
- **Natural floor:** 17.3%

Ages missing for 183 and 240 individuals in Malawi and Benin respectively.
## Baseline Surveys

### INDIA

**Baseline Cross-Sectional Survey**
- 19,706 samples collected
- 58,916 aliquots stored

**Baseline Longitudinal monitoring cohort**
- 6,503 individuals enrolled
- 6,089 samples tested by Kato-Katz

**Hookworm prevalence*:** 20.8%

**Ascaris prevalence*:** 0.1%

**Trichuris prevalence*:** 0.3%

### MALAWI

**Baseline CSS**
- 14,289 samples collected
- 42,978 aliquots stored

**Baseline LMC**
- 6,844 individuals enrolled
- 6,136 samples tested by KK

**Hookworm*:** 7.3%

**Ascaris*:** 0.1%

**Trichuris*:** 0.2%

### BENIN

**Baseline CSS**
- 19,298 samples collected
- 56,602 aliquots stored

**Baseline LMC**
- 6,814 individuals enrolled
- 6,139 samples tested by KK

**Hookworm*:** 3.6%

**Ascaris*:** 1.9%

**Trichuris*:** 0.1%

* Weighted KK prevalence from stratified sample of 30 PSAC, 30 SAC and 90 adults in each cluster
Prevalence estimates are weighted to account for the sampling stratification by age and cluster.
The intervention: MDA

- Training
- Sensitisation
- House to house delivery
Steps involved in all activities
MDA Coverage Measures

**Individual treatment logs**
- Recorded by drug distributors
- Intervention arm only

**Coverage survey**
- Self report
- Both arms

**Urine assay**

- 5 coverage survey participants per cluster

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- Reached
- Eligible
- Recent history of deworming
- Consented
- Directly observed therapy

- Present during MDA → Visited by DeWorm3
- → Offered treatment → Accepted treatment → Ingested albendazole
- Reasons for participation/ non-participation

- Validated ingestion of albendazole within 72 hours

- 50 households per cluster

- All censused individuals

- 5 coverage survey participants per cluster

- 50 households per cluster
MDA Coverage

Coverage according to treatment registers

Coverage according to self report (coverage surveys)

Transparent colours represent all recorded treatment. Solid colours represent directly observed treatment.
Primary DeWorm3 implementation science objective:

To develop and evaluate a community-wide STH MDA model that is sustainable and scalable in endemic areas

Methods used to evaluate implementation facilitators and barriers:

- Stakeholder mapping
- Organizational readiness surveys
- Qualitative research (individual interviews and FGDs)
- Process mapping (in-depth and routine)
- Economic evaluation

Hybrid Trial With Embedded Implementation Research
In-depth Process Mapping

- Average of 77 separate activities required to deliver MDA in a cluster
- Over 62% of activities reported to leverage LF infrastructure
- Average of 35% of activities deviate from planned timelines and delivery benchmarks
**Economic Evaluation**

**Capturing and estimating cost of DeWorm3 interventions**

- **Data collection from trial sites**
- **Analytical allocation and estimation**
- **DeWorm3 Trial Costs**
  - **Financial costs**
  - **Economic costs**

**Running costs module**

**Activity costs modules**

**Policy relevant strategies to model**

1. **Different delivery strategies:**
   - Biannual and annual community-wide MDA
   - Biannual and annual SAC / PSAC targeted MDA, in communities and in school
   - WASH scale-up
   - New technologies

2. **Different geographies:**
   - Generic transmission profiles, country specific profiles, and global

3. **Dimensions of heterogeneity**
   - Transmission intensity, age distribution, coverage, population density, compliance, etc.
Some Numbers…

77,673 stool samples collected

85,405 people included in baseline survey

24,341 Kato-Katz tests

230,905 aliquots prepared and stored

396,787 albendazole doses distributed

28 field supervisors

221 enumerators

40 HSAs

16 lab supervisors

40 lab technicians

280 Community drug distributors
Selected Publications To Date

Prospects for elimination of soil-transmitted helminths
Krisjana H. Astholoménsa, Arianna R. Meana, Marko Werkman, and Jüdi L. Watson

Identifying optimal threshold statistics for elimination of hookworm using a stochastic simulation model
James E. Truscott, Marko Werkman, James E. Wright, Sam H. Fare, Raji Satar, Krisjana Astholoménsa, and Roy M. Anderson

Assessing the feasibility of interrupting the transmission of soil-transmitted helminths through mass drug administration: The DeWorm3 cluster randomized trial protocol

Evaluating the sustainability, scalability, and replicability of an STH transmission interruption intervention: The DeWorm3 implementation science protocol

Strategies to improve treatment coverage in community-based public health programs: A systematic review of the literature
Katrine S. Daasbjerg, Arianna Rubin Meana, Krisjana H. Astholménsa, and Jüdi L. Watson

Assessment of serum pharmacokinetics and urinary excretion of albendazole and its metabolites in human volunteers
Laura Gabitoulina, Alejandro Krystewicz-Desjardins, Marisa Juárez, Luisa M_enabled, Paloma Schönen, Luisa Alvarado, Ruben Corzino, Jüdi L. Watson, Carlos F. Lanusse

http://collections.plos.org/deworm3
Thank-you