**Trachoma surveys and alternative interventions/surveillance scenarios.**

Key criteria for elimination of trachoma as a public health problem (EPHP) which is tracked in the model is prevalence of trachomatous inflammation-follicular (TF) in children aged 1-9 years of less than 5% (TF1-9<5%).

This is in the model output as: ***True\_Prev\_Disease\_children\_1\_9***

WHO MDA guidelines recommend:

5 rounds of MDA following baseline survey TF1-9 >30%

3 rounds of MDA following baseline survey TF1-9 10-30%

1 round of MDA following baseline survey TF1-9 5 5-10%

MDA is always community wide

**Impact survey is carried out 6-12 months after the final planned round of MDA**

If impact survey is TF1-9 <5%, stop MDA, wait 2 years for surveillance survey

If impact survey is TF1-9 5 5-10% one further round of MDA then repeat impact survey

If impact survey is TF1-9 10-30% 3 rounds of MDA then repeat impact survey

If impact survey is TF1-9 >30% 5 rounds of MDA then repeat impact survey

Surveillance survey 2 years after impact survey (can then either enter pre-validation phase if TF<5% or re-instigate MDA if TF>5%, with most recent survey result determining number of rounds as before).

Diagram

Description automatically generated

**Survey Design**

**WHO recommended sampling:**

Currently recommended sampling design is a two-stage cluster in which 20-30 villages (clusters) are selected in the first stage of sampling, and approximately 25-30 households are selected within each cluster in the second stage.

Only children ages 1-9 are surveyed

**Test:** Diagnosis is currently a clinical examination by a trained grader to detect TF.

**The model:**

Model population size is 2500

The timestep is 1 week. For each individual in the model population, there are 11 values given in “vals” which are updated at each timestep.

The individual’s infection and disease status, which are tracked as positive or negative (1,0, Boolean) and correspond to the compartment of the model each individual is in:

|  |  |  |
| --- | --- | --- |
|  | **IndI** | **IndD** |
| S | 0 | 0 |
| I | 1 | 0 |
| ID | 1 | 1 |
| D | 0 | 1 |

**IndI**=Individual infection status

**IndD**=Individual disease status



Through the “***sim\_Ind\_MDA***” function, we also track total number of children aged 1-9 years (***N\_children\_ages\_1\_9***) and number of diseased children aged 1-9 years (***N\_True\_Diseased\_children\_1\_9***) and number of infected children aged 1-9 years (***N\_True\_Infected\_children\_1\_9***) as well as “true” prevalence of disease and infection in both children 1-9 and the whole population (***True\_Prev\_Infection\_children\_1\_9***, ***True\_Prev\_Disease\_children\_1\_9***, ***True\_Prev\_Disease*** and ***True\_Prev\_Infection***)

**Simulating sampling:**

Impact survey: If(time==max(MDA\_times)+26 or 52 (6-12 months after last MDA)

Surveillance survey:If(time==Impact survey+52 or 104) (12-24 months after impact survey)

**Suggest a simulated sample size of 250 children aged 1-9** to capture the uncertainty within each simulation (assume treat each simulation as a survey, rather than a cluster within a survey, i.e. we are not simulating the two-stage nature of the survey design). Then compare “survey” prevalence for different diagnostics to “true” prevalence of TF in children aged 1-9 years.

**Suggest keep sample children aged 1-9**, these are generally the core group for transmission, (with testing babies practically difficult).

Performance of clinical grading as a diagnostic has an inherent degree of subjectivity, and “grader drift” (decreasing performance of graders as prevalence decreases) is documented in a range of settings.

Main alternative strategies are:

* **Improved use of TF grading (e.g. smartphone technology, machine learning)**
* **Survey for infection rather than disease (e.g. PCR or novel point-of-care molecular diagnostic)**

Sensitivity and specificity estimates from the literature for these and the standard diagnostic are in file: “Trachoma\_diagnostics\_summary”.

Incorporating the potential utility of serological tests into the current model will require additional data relating to seroconversion/reversion given number of infections and age at infection. We are not currently in a position to incorporate this (may be possible with analysis of longitudinal serological data).

To simulate survey aimed at detected disease (TF) suggest:

draw 250 from children aged 1-9: ***which(vals[[11]]<10\*52 & vals[[11]]>=52)***

Probability observed (true) positive= ***IndD\*Se\_CE***

Probability observed (false) positive= ***-1\*(IndD-1)\*(1-Sp\_CE))***

With survey prevalence then sum of true positives and false positives over sample size.

Where Se\_Test is test sensitivity and Sp\_Test is test specificity.

Suggested value for Se\_CE: 0.96 (based on Grassly et al., 2008, PLOS NTDS)

Suggested value for Sp\_CE: 0.93 (based on Grassly et al., 2008 PLOS NTDS)

Then for detecting infection (e.g. PCR):

Probability observed (true) positive= ***IndI\*Se\_PCR***

Probability observed (false) positive= ***-1\*(IndI-1)\*(1-Sp\_PCR))***

Suggested value for Se\_PCR: 0.95(based on Solomon et al., 2004, Clin Micr Rev)

Suggested value for Sp\_PCR: 1 (based on Keenan et al., 2012 Invest Opth)

HOWEVER, FOR THE INITIAL COMPARISON, SUGGEST PLOT OBSERVED DISEASED (TF) vs TRUE INFECTION (i.e. Both Se\_PCR and Sp\_PCR set to 1).

**Scenarios for simulations:**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Scenario** | **MDA coverage** | **MDA protocol** | **Systematic non-compliance assumptions** | **Survey** |
| **Scenario 1** | **0.8** | **Annual treatment of whole community** | **Rho=0.3** | **TF in children aged 1-9 years, (based on individual “D” status)**  **Sensitivity 0.96, and Specificity 0.93** |
| **Scenario 2i)** | **0.85** | **Biannual:**  **Round 1:Treat whole community**  **Round 2: One month later treat children aged 1-9 years** | **Rho=0.3** | **As in Scenario 1** |
| **Scenario 2ii)** | **0.85** | **Biannual:**  **Round 1: Treat whole community**  **Round 2: 1 month later treat whole community again** | **Rho=0.3** | **As in Scenario 1** |
| **Scenario 2iii)** | **0.85** | **Biannual:**  **Round 1:Treat whole community**  **Round 2: One month later treat children aged 1-9 years**  **Round 3: One month after round 2 treat children aged 1-9** | **Rho=0.3** | **As in Scenario 1** |