



ParaDrug: an E-tool to analyze and report drug efficacy data in preventive chemotherapy programs targeting schistosomiasis and soil-transmitted helminthiasis

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Goals of ParaDrug

- Standardize reporting and interpretation of the anthelmintic drug efficacy data obtained during preventive chemotherapy (PC) programs against soil-transmitted helminths (STH).
- Support program managers in **analysing, interpreting and summarizing drug efficacy data** according to WHO guidelines

User interface – www.starworms.org/tools

Side panel

Main panel

ParaDrug 1.0

Upload data
Choose Excel file to upload
Upload complete

General Information
Disease: Schistosomiasis
Anthelmintic drug: Praziquantel (1x 40 mg/kg)

Baseline Information
S. haematobium eggs per 10 ml of urine
S. mansoni eggs per gram of stool
S. japonicum eggs per gram of stool

Introduction | My data | Baseline statistics | Drug efficacy | Report | Parameters

Background
The most prevalent neglected tropical diseases (NTDs) include schistosomiasis (Schistosoma haematobium, S. mansoni and S. japonicum) and soil-transmitted helminthiasis (Soil-transmitted helminths, Strongyloides, and the hookworms Ancylostoma duodenale and Necator americanus). The main strategy for controlling the morbidity caused by these diseases are preventive chemotherapy (PC) programs, in which anthelmintic drugs (mebendazole or albendazole, and praziquantel or ivermectin) for soil-transmitted helminthiasis are periodically administered to children (WHO et al., 2013). Followed by the United Nations on WTD, the coverage of children in PC programs has substantially increased (WHO et al., 2013), and an update is underway with the ultimate goal to include at least 75% of the children in all endemic countries by 2020 (WHO et al., 2013). However, a major concern is that the high drug pressure will cause anthelmintic drug resistance, and hence will reduce the impact of the PC programs. Therefore, thoroughly designed monitoring systems are needed, allowing to detect changes in anthelmintic drug efficacy that may arise through the evolution of drug resistance in these worms.

Currently, the reduction in egg counts following drug administration, the egg reduction rate (ERR), is the recommended method for monitoring the efficacy of anthelmintic drugs against both schistosomes and soil-transmitted helminths. However, the efficacy data available have been obtained through a variety of single offering study protocols, which impedes drawing healthy conclusions on the emergence of anthelmintic resistance (Vercruysse et al., 2013). As a response to the lack of organization, World Health Organization (WHO) has developed guidelines on how to assess drug efficacy of anthelmintic drug used in PC programs against both schistosomes and soil-transmitted helminthiasis (WHO et al., 2013). This WHO document provides guidance on when and how to assess the efficacy of anthelmintic drugs, including detailed recommendations on the indicators of efficacy, the sample size, the follow-up period, the laboratory method, the statistical analysis and the final interpretation of the data collected.

Goal of ParaDrug 1.0
ParaDrug 1.0 aims to further standardize reporting and interpreting the anthelmintic drug efficacy data obtained during PC programs, to support program managers in analysing, interpreting and summarizing drug efficacy data as recommended by the WHO, and this without the need of any prior knowledge on statistical software.

- 4 sections
 - upload data; general information; baseline and follow-up information
 - Drop down lists
- 6 tabs
 - background; my data; baseline statistics; drug efficacy; report; parameters
 - Built-in links to WHO documents
 - Reactive analysis/reporting of data

Output parameters

- Number of subjects
 - number of subjects enrolled
 - number of cases per worm species
 - number of mixed infections
 - number of complete cases
- Intensity of infections
 - mean egg count at baseline per species
 - spread of egg count at baseline per species
 - number of low, moderate and high intensity infections per species
- Spread of follow-up period
- Egg reduction rate + 95% confidence intervals
- Interpretation according to WHO guidelines

Software

- ParaDrug was developed using the *Shiny* package of R studio
- R studio is an open source software for R

Work with ParaDrug

Step 1: Check data requirements – my data tab

- Required data
 - egg counts
 - Follow-up period
 - Missing data
 - impossible value (e.g., -1)
- Required format
 - xlsx-file
 - first worksheet
 - unique headers
 - integer numbers

Step 2: Upload data – side panel



Upload data

Choose Excel file to upload

Choose File | ParaDrugData.xls

Upload complete

Step 3: Provide information on the trial – side panel

General Information

Disease:

- Schistosomiasis
- Schistosomiasis
- Soil-transmitted helminthiasis

Anthelmintic drug:

- Praziquantel (1x 40 mg/kg)
- Praziquantel (1x 40 mg/kg)
- Other

- Albendazole (1x 400 mg)
- Albendazole (1x 400 mg)
- Mebendazole (1x 500 mg)
- Other

Step 4: Match your data – side panel

S. mansoni eggs per gram of stool:

Not recorded

Not recorded

Subject ID

preSM

postSM

	A	B	C
1	Subject ID	preSM	postSM
2	102	434	2
3	158	0	0
4	185	0	15
5	220	5	0

Step 5: Press *calculate baseline statistics*

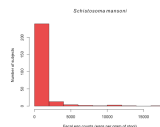
Calculate baseline statistics

Number of subjects

In total, 500 subjects were enrolled in this drug efficacy trial. Schistosoma mansoni infections were observed in 294 subjects (58.8%). Complete data were available for 264 subjects.

Intensity of infections

The distribution of the baseline egg counts across the subjects who completed the trial is illustrated in the figure below. The mean (25th quantile; 75th quantile) S. mansoni egg count equaled 793.2 (10; 738) eggs per gram of stool. Low, moderate and high-intensity S. mansoni infections were observed in 144 (54.5%), 35 (13.3%) and 85 (32.2%) subjects, respectively.

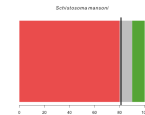


Step 6: Press *calculate drug efficacy*

Calculate drug efficacy

Egg reduction rate

The egg reduction rate (ERR; 95% confidence intervals) of the drug against S. mansoni equaled 81.1% (87; 91.3). The figure below classifies the ERR estimate according to the WHO thresholds (WHO et al., 2013). Any ERR estimate in the green zone indicates that the efficacy of the drug is satisfactory, any value in the grey zone indicates that the efficacy is doubtful and any value in the red zone indicates that the efficacy is reduced. The black vertical line represents the ERR estimate of the drug administered in this trial.



Conclusions

The efficacy of the drug administered is below the expected drug efficacy of 90 percent S. mansoni infections. Please inform the local authorities (e.g., Ministry of Health) about this finding. In addition, it is recommended to contact World Health Organization (wormcontrol@who.int) or Antonio Montresor (montresora@who.int) and its collaborating center (Bruno Levecke: bruno.levecke@ugent.be) to exclude any possible confounding factors that may explain this poor drug efficacy and to discuss further actions.

Step 7: Customize and download report – report tab

Customize report

To further customize please complete the gaps below.

The name of your institution

Ghent University

Country in which the trial was conducted

Belgium

District/province in which the trial was conducted

Flanders

Download report

Download



The efficacy of praziquantel (40 mg/kg) against schistosomiasis in Belgium (Flanders)

A ParaDrug 1.0 drug efficacy report

by Clive Traverso

The developer of ParaDrug 1.0 was funded by the Bill and Melinda Gates Foundation