Statistical analysis plan (SAP): REDRESS

# Administrative information

Protocol version 0.1

## SAP revisions

### Revision history

### Justification for revision

### Timing in relation to analyses

## Roles and Responsibility

Sally Theobald, Liverpool School of Tropical Medicine, PI REDRESS

Laura Dean, Liverpool School of Tropical Medicine, Research Director REDRESS

Yan Ding, Liverpool School of Tropical Medicine, research fellow evaluation

Lucas Sempé, Queen Margaret University, research fellow evaluation and health finance

## Signatures

### Person writing the SAP

Lucas Sempé

### Reviewers

### Chief investigator

# Introduction

## Background and rationale

Liberia became one of the first countries in the world to adopt and begin the implementation of a national integrated approach to managing severe skin diseases (Buruli Ulcer, lymphoedema, hydrocele, and yaws). This approach seeks to address issues of effectiveness and equity previously overlooked through disjointed approaches while contributing to health systems strengthening1.

Effective systems to support those affected by SSSDs (and their families) rely on training of health care workers, active detection of cases, timely clinical diagnosis, and laboratory confirmation, as well as holistic treatment including mental health support.

Preliminary information and programme knowledge indicate a rise in the numbers of patients receiving care, although there is still an evidence gap regarding the effectiveness of this approach across all relevant actors. REDRESS hopes to fill this gap providing a better understanding and evaluating the different components of Liberia´s SSSD integrated approach.

# Study methods

# Study 1: Effectiveness of an integrated approach case management and REDDESS bundle

The study is a controlled before and after (also known as Difference-in-Differences) divided into 2 sub studies, each with an intervention and a control group. Figure 1 represents both sub studies, where there are two data collection points (baseline and endline).

Figure 1: Visual representation of Study 1

Chart, line chart

Description automatically generated

## Design

### Sub study A

In the sub study A (purple in Figure 1), conducted in counties where case management have been already deployed, we study the effectiveness of the ‘REDRESS intervention bundle’ as a quality improvement to the standard case management already in place.

‘The REDRESS intervention bundle’ includes:

**Pathway 1a: Improved clinical accuracy and quality of case detection, referral, and management for SSSDs at community and clinic level.**

* Developing integrated training manual showcasing clinical algorithm, including mental health screening, and counselling with adaptations for different cadres
* Training of trainers for intervention roll out
* Training of community health volunteers and assistants utilising integrated training manual
* Training of health facility workers utilising integrated training manual
* Establishing referral pathway between community, health facility and tertiary levels and increased case detection

**Pathway 1b: Enhanced laboratory systems for SSSD diagnosis at district and county level.**

* Strengthening of sample collection, storage and transportation procedures at county and district level
* Strengthening of referral laboratory PCR capacity for BU and Yaws confirmation

**Pathway 2: Improved retention and performance of health workers involved in SSSD management.**

* Training mid-level health workers
* Non-cash awards competition for health facilities
* Peer supervision meetings with CHSS once per quarter (TBC)
* Essential package for CHAs & CHVs – backpack, raingear, rainboots, stationaries
* HR management integrated within TOT for national and county trainers

**Pathway 3: Improved mental wellbeing and social participation for people affected by SSSDs.**

* Integration of Basic Psychological Support – NTDs (BPS-N) within mid-level health worker CM training
* Integration of BPS-N within CHA/CHV training
* BPS-N training for faith healers, traditional healers and people affected
* Ongoing screening for patients diagnosed for CM with PHQ 9 by mid-level health workers, with provision basic psychological support/ or referral to MHGAP clinician as appropriate
* Ongoing screening by CHAs and CHVs of patients with CM with PHQ2 with referral to link facility for further assessment
* Faith healer and traditional healer ongoing discussions after initial BPS-N training to identify opportunities for collaboration– expected 4 group discussions with faith healers and TH
* Peer support groups with people affected

Data used is collected from the HMIS system.

## Objectives

We aim to identify the effectiveness of the ‘REDRESS intervention bundle’ in terms of case detection and management.

## Hypotheses

We hypothesize that the ‘REDRESS intervention bundle’ will produce an increase in the detection of SSSD cases:

* Increase of number of cases ~~identified in the community being~~ referred to the health facility

We aim to

* Number of leprosy cases presenting with grade 2 disability (delays in case detection)
* Number of leprosy cases presenting with grade 2 disability (delays in case detection)
* Number of cases of lymphoedema (delays in case detection)
* Number of reported hydrocele (delays in case detection)
* Treatment completion rate (BU/Leprosy)

[Main and secondary outcome hypothesis here for each of the above objectives – i.e. clinical, cost, process]

[Any equity related hypotheses here]

## Sample size

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| County | Randomization | POPULATION | DISTRICTS | TOTAL HF |
| Bomi | 0 (Group One) | 103550 | 4 | 27 |
| Lofa | 1 (Group Two) | 340818 | 6 | 59 |
| Nimba | 0 (Group One) | 568753 | 6 | 79 |

### Eligibility

[Refers to all eligibility – for the counties, for the facilities, health workers etc.]

### Recruitment

[How will participants be recruited?]

### Withdrawal and follow-up

[Can participants withdraw? Will we follow them up?]

## Analysis

### Outcome definitions

Outcome types and definitions as well as time-points at which outcomes are assessed and calculated are provided in Table 2.

Table 2: Outcome types and definitions

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Outcome type | Outcome abbreviation | Outcome type and definition | Population | Time-points assessed | Time-point reported in main trial publication | Calculation |
| Primary |  |  |  |  |  |  |
| Secondary |  |  |  |  |  |  |

### Analysis methods

[Specify both the primary and the secondary]

### Additional analyses

[Equity, sex disaggregation, etc.]

### Statistical interim analyses

**Baseline data**

Participants: We will summarize baseline characteristics of the participant sample at specified time points (pre-intervention and time completion).

Baseline characteristics include: age, gender and socio-economic characteristics of patients enrolled in study; method of TB diagnosis and type of DOT treatment initiated (in person or VOT).

We will provide: the mean, standard deviation and range for continuous, approximately symmetric variables; medians, interquartile range and range for continuous, skewed variables; frequencies and percentages in each category for categorical variables.

### Missing data

[What do you do to examine missingness and when/how will you use imputation?]

# Study 2: Pathway 1b: Enhanced laboratory systems for SSSD diagnosis at district and county level

## Design

Controlled before and after – insert the tables of the study settings here

Note that this is a pragmatic study

## Objectives

REDRESS aims to identify:

Clinical effectiveness of an enhanced intervention package vs. intervention vs. status quo

[Process evaluation outcomes here]

## Hypotheses

[Main and secondary outcome hypothesis here for each of the above objectives – i.e. clinical, cost, process]

[Any equity related hypotheses here]

## Sample size

### Eligibility

[Refers to all eligibility – for the counties, for the facilities, health workers etc.]

### Recruitment

[How will participants be recruited?]

### Withdrawal and follow-up

[Can participants withdraw? Will we follow them up?]

## Analysis

### Outcome definitions

Outcome types and definitions as well as time-points at which outcomes are assessed and calculated are provided in Table 2.

Table 2: Outcome types and definitions

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Outcome type | Outcome abbreviation | Outcome type and definition | Population | Time-points assessed | Time-point reported in main trial publication | Calculation |
| Primary |  |  |  |  |  |  |
| Secondary |  |  |  |  |  |  |

### Analysis methods

[Specify both the primary and the secondary]

### Additional analyses

[Equity, sex disaggregation, etc.]

### Statistical interim analyses

**Baseline data**

Participants: We will summarize baseline characteristics of the participant sample at specified time points (pre-intervention and time completion).

Baseline characteristics include: age, gender and socio-economic characteristics of patients enrolled in study; method of TB diagnosis and type of DOT treatment initiated (in person or VOT).

We will provide: the mean, standard deviation and range for continuous, approximately symmetric variables; medians, interquartile range and range for continuous, skewed variables; frequencies and percentages in each category for categorical variables.

### Missing data

[What do you do to examine missingness and when/how will you use imputation?]

# Study 3: Improved retention and performance of health workers involved in SSSD management

## Design

Controlled before and after – insert the tables of the study settings here

Note that this is a pragmatic study

## Objectives

REDRESS aims to identify:

Clinical effectiveness of an enhanced intervention package vs. intervention vs. status quo

[Process evaluation outcomes here]

## Hypotheses

[Main and secondary outcome hypothesis here for each of the above objectives – i.e. clinical, cost, process]

[Any equity related hypotheses here]

## Sample size

### Eligibility

[Refers to all eligibility – for the counties, for the facilities, health workers etc.]

### Recruitment

[How will participants be recruited?]

### Withdrawal and follow-up

[Can participants withdraw? Will we follow them up?]

## Analysis

### Outcome definitions

Outcome types and definitions as well as time-points at which outcomes are assessed and calculated are provided in Table 2.

Table 2: Outcome types and definitions

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Outcome type | Outcome abbreviation | Outcome type and definition | Population | Time-points assessed | Time-point reported in main trial publication | Calculation |
| Primary |  |  |  |  |  |  |
| Secondary |  |  |  |  |  |  |

### Analysis methods

[Specify both the primary and the secondary]

### Additional analyses

[Equity, sex disaggregation, etc.]

### Statistical interim analyses

**Baseline data**

Participants: We will summarize baseline characteristics of the participant sample at specified time points (pre-intervention and time completion).

Baseline characteristics include: age, gender and socio-economic characteristics of patients enrolled in study; method of TB diagnosis and type of DOT treatment initiated (in person or VOT).

We will provide: the mean, standard deviation and range for continuous, approximately symmetric variables; medians, interquartile range and range for continuous, skewed variables; frequencies and percentages in each category for categorical variables.

### Missing data

[What do you do to examine missingness and when/how will you use imputation?]

# Study 4: Pathway 3: Improved mental wellbeing and social participation for people affected by SSSDs.

## Design

Controlled before and after – insert the tables of the study settings here

Note that this is a pragmatic study

## Objectives

REDRESS aims to identify:

Clinical effectiveness of an enhanced intervention package vs. intervention vs. status quo

[Process evaluation outcomes here]

## Hypotheses

[Main and secondary outcome hypothesis here for each of the above objectives – i.e. clinical, cost, process]

[Any equity related hypotheses here]

## Sample size

### Eligibility

[Refers to all eligibility – for the counties, for the facilities, health workers etc.]

### Recruitment

[How will participants be recruited?]

### Withdrawal and follow-up

[Can participants withdraw? Will we follow them up?]

## Analysis

### Outcome definitions

Outcome types and definitions as well as time-points at which outcomes are assessed and calculated are provided in Table 2.

Table 2: Outcome types and definitions

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Outcome type | Outcome abbreviation | Outcome type and definition | Population | Time-points assessed | Time-point reported in main trial publication | Calculation |
| Primary |  |  |  |  |  |  |
| Secondary |  |  |  |  |  |  |

### Analysis methods

[Specify both the primary and the secondary]

### Additional analyses

[Equity, sex disaggregation, etc.]

### Statistical interim analyses

**Baseline data**

Participants: We will summarize baseline characteristics of the participant sample at specified time points (pre-intervention and time completion).

Baseline characteristics include: age, gender and socio-economic characteristics of patients enrolled in study; method of TB diagnosis and type of DOT treatment initiated (in person or VOT).

We will provide: the mean, standard deviation and range for continuous, approximately symmetric variables; medians, interquartile range and range for continuous, skewed variables; frequencies and percentages in each category for categorical variables.

### Missing data

[What do you do to examine missingness and when/how will you use imputation?]

# Study 5: Health finance

## Design

Controlled before and after – insert the tables of the study settings here

Note that this is a pragmatic study

## Objectives

REDRESS aims to identify:

Costs of the enhanced intervention and intervention package vs. status quo from societal perspective

[Process evaluation outcomes here]

## Hypotheses

[Main and secondary outcome hypothesis here for each of the above objectives – i.e. clinical, cost, process]

[Any equity related hypotheses here]

## Sample size

### Eligibility

[Refers to all eligibility – for the counties, for the facilities, health workers etc.]

### Recruitment

[How will participants be recruited?]

### Withdrawal and follow-up

[Can participants withdraw? Will we follow them up?]

## Analysis

### Outcome definitions

Outcome types and definitions as well as time-points at which outcomes are assessed and calculated are provided in Table 2.

Table 2: Outcome types and definitions

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Outcome type | Outcome abbreviation | Outcome type and definition | Population | Time-points assessed | Time-point reported in main trial publication | Calculation |
| Primary |  |  |  |  |  |  |
| Secondary |  |  |  |  |  |  |

### Analysis methods

[Specify both the primary and the secondary]

### Additional analyses

[Equity, sex disaggregation, etc.]

### Statistical interim analyses

**Baseline data**

Participants: We will summarize baseline characteristics of the participant sample at specified time points (pre-intervention and time completion).

Baseline characteristics include: age, gender and socio-economic characteristics of patients enrolled in study; method of TB diagnosis and type of DOT treatment initiated (in person or VOT).

We will provide: the mean, standard deviation and range for continuous, approximately symmetric variables; medians, interquartile range and range for continuous, skewed variables; frequencies and percentages in each category for categorical variables.

### Missing data

[What do you do to examine missingness and when/how will you use imputation?]

# Study 6: Comparison scales different instruments

## Design

Controlled before and after – insert the tables of the study settings here

Note that this is a pragmatic study

## Objectives

REDRESS aims to identify:

Costs of the enhanced intervention and intervention package vs. status quo from societal perspective

[Process evaluation outcomes here]

## Hypotheses

[Main and secondary outcome hypothesis here for each of the above objectives – i.e. clinical, cost, process]

[Any equity related hypotheses here]

## Sample size

### Eligibility

[Refers to all eligibility – for the counties, for the facilities, health workers etc.]

### Recruitment

[How will participants be recruited?]

### Withdrawal and follow-up

[Can participants withdraw? Will we follow them up?]

## Analysis

### Outcome definitions

Outcome types and definitions as well as time-points at which outcomes are assessed and calculated are provided in Table 2.

Table 2: Outcome types and definitions

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Outcome type | Outcome abbreviation | Outcome type and definition | Population | Time-points assessed | Time-point reported in main trial publication | Calculation |
| Primary |  |  |  |  |  |  |
| Secondary |  |  |  |  |  |  |

### Analysis methods

[Specify both the primary and the secondary]

### Additional analyses

[Equity, sex disaggregation, etc.]

### Statistical interim analyses

**Baseline data**

Participants: We will summarize baseline characteristics of the participant sample at specified time points (pre-intervention and time completion).

Baseline characteristics include: age, gender and socio-economic characteristics of patients enrolled in study; method of TB diagnosis and type of DOT treatment initiated (in person or VOT).

We will provide: the mean, standard deviation and range for continuous, approximately symmetric variables; medians, interquartile range and range for continuous, skewed variables; frequencies and percentages in each category for categorical variables.

### Missing data

[What do you do to examine missingness and when/how will you use imputation?]

# Statistical principles

## Confidence intervals and p values

### Level of statistical significance

### Adjustment for multiplicity

### Confidence intervals

## Adherence to protocol deviations

## Analysis populations

[For each analysis you are running who is or not included in the analysis]

## Analyses for primary outcome

[What is the analysis for your primary outcomes? Specify in detail – e.g. difference in difference?]

# References