Protocol: A Surveiallance system Evaluation of EDRWebs ability to measure initiaion rates in the Free-State

Evaluation performed in accordance with the CDC guidelines, and completed as part of the requirments for the SOuth African Field EPidemiology Training Programme.

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**Background:**

**Objectives:**

**Methods:**

**Results:**

**Conclusion:**

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# 1 Background

The World Health Organization’s (WHO) “end TB strategy” has targeted >90% of patients eligible for Tuberculosis (TB) treatment to be treated with appropriate regimens by 20251. An analysis of the South African TB care cascade published in 2017 found that 47% of DR-TB incident cases are initiated on treatment and concluded that significant effort would be required to meet the “end TB strategy” goals2.

Surveillance systems provide “information for action” and inform the planning, resource management, response and effect of health programmes3. Surveillance systems should be evaluated to ensure they are meeting their objectives and uses4. Evaluating the surveillance of DR-TB initiation rates in SA, is an important element to ensure SDG targets are met and to save lives.

Delayed treatment initiation has an acute impact on TB related deaths and increases TB incidence delayed since patients remain contagious for longer.5 In South Africa, the reduction in TB mortality has not been dramatic - HIV coinfection is considered the main driver of increased DR-TB cases and poorer outcomes.6 Early treatment is vital to reduce morbidity and mortality from DR-TB5 and South Africa recommends that DR-TB patients initiate treatment within 5 days of diagnosis. However, a nested trial in SA found that mean time-to-initiation of DR-TB patients was 11 days7.

Without near real-time surveillance, delayed initiation may only be realised once the window for initiation within the 5 days has passed - the opportunity for action is therefore lost. A study in the Cape Town metropole demonstrated that patients with initial loss to follow up were 2.4 times more likely to die compared to those without initial loss to follow up.8 This highlights that timely initiation is critical to patient’s survival and therefore the monitoring and response to such information may save lives.

While recent efforts are being made to SMS TB results to patients, it has been demonstrated that it does not increase initiation rates to 95%, but does decrease the time to initiation to acceptable levels (3-5days).9 As it stands, initiation largely relies on passive initiation and surveillance - patients return to clinics to find out their result and are then initiated at the facility; Active case-finding is implemented in high-risk and vulnerable groups by Community Health Workers, however, these strategies are often hindered by resource-limitations10 making the majority of case-finding and initiation active conditional on a patient presenting to a health facility.

TB and HIV related surveillance systems have been through digital permutations since the early 2000s. In their current forms, Drug Sensitive TB and HIV are recorded in TIER.net (previously ETR) and Drug Resistant TB in EDRWeb. Evaluations of systems related to TB have been published in the following areas: ETR in Western Cape found digital data to be less complete than paper-based records11 TIER.net in Northern parts of SA found good completeness except in treatment outcomes12, ETR in Mpumalanga found over reporting of successful treatment outcomes13 and in Gauteng and KZN EDRWeb was found to under-report treatment outcomes and HIV status14. Furthermore, a study in a paediatric setting in Cape Town found that only 64% of clinically diagnosed DR-TB paediatric cases appeared on EDRWeb15, this finding was reproduced with a nationally representative facility sample on ETR which demonstrated that one-third of incident TB cases were not captured on ETR16 and these results were reproduced using a Paediatric setting in Cape Town which found that only 64% of clinically diagnosed DR-TB paediatric cases appeared on EDRWeb15. It can be noted that statistically speaking, missing out on 33% of cases means that your database needs to increase in size by 50% to be 100% complete since 0.66x 1.5 = 1 and this is important to note when setting targets of improvement.

The Free-State is considered a province with a high burden of HIV and TB [6; @engelbrechtUnsuccessfulTBTreatment2017 ;17] and it has been demonstrated that successful and unsuccessful treatment outcomes18 and factors associated with defaulting17 are affected by HIV coinfection. TB and HIV service delivery however, remain fragmented19. Governance structures have rightly been improved20 yet, their role in surveillance systems seems to be lacking. A position statement on the use of programmatic TB data to inform practice encourages the use of programmatic data, but also advocate the responsible use of data linkage of surveillance systems to measure TB programme’s effect.21

In Free-State, the TB programme meets bi-weekly to discuss initiation rates of both DS and DR-TB. Data is generated from both the TB LINELIST line list and EDRWeb, to create initiation rates of each district based on weekly headcounts from each system after deduplication by district programme coordinators with the support of district epidemiologists. While this effort is promising and has likely resulted in improvements, its methods are not reproducible and the limitations of the system are not documented. Furthermore, its strengths are not documented for adoption in other programmes.

Conducting and documenting the evaluation of the surveillance of TB initiation has important implications in the improvement of DR-TBsurveillance and the fulfilment of the “end TB strategy”. Improvements in the surveillance and fulfilment of the “end TB strategy” form part of providing patient-centred and evidence-based care.

# 2 Research Question

What are the attributes of the EDRWeb surveillance system in the Free-State, specifically as they relate to linkage to care (initiation) of patients with DR-TB and are these attributes associated with DR-TB patient outcomes?

# 3 Aims

To describe the attributes of EDRWeb and see whether some of these attributes may have an effect on DR-TB patient outcomes.

# 4 Objectives

1. To descibe the current trends of DR-TB in Free-State
2. To compare three common data linkage methods for linking TB line list data and EDRWeb data.
3. To report the attributes of EDRWeb as defined by the CDC guidelines. These can be further conceptualised in Table 1 under methodology.
4. To determine whether the time to initiation of DR-TB treatment has an effect on mortality.
5. To determine whether the timeliness of EDRWeb data has an effect on mortality.

Look at table @ref(tbl\_objectives)

# 5 Methodology

## 5.1 Outline

Due to the nature of the evaluation, different methods will be used depending on the objective. Broadly speaking there are qualitative and quantitative methodologies. Detailed methodology, per objective can be viewed in Tables 1-3. The following sub-headings provide a general overview.

## 5.2 Design

Qualitative methods will use open-ended and close-ended questionnaires directed at personell involved in TB surveillance within the FS TB programme such as programme co-ordinators, managers and epidemiologists. Results will be presented as a narrative. Quantitative methods will use cross-sectional type designs from data collected on EDRWeb and from laboratory testing data. Details on the approach for each objective will be described in more detail.

## 5.3 Setting and population

Qualitative methods will be aimed at stakeholders of the TB programme, such as programme directors and TB coordinators in Free-State department of Health. For quantitative methods, routinely collected data of DR-TB patients who access health facilities that utilise NHLS laboratories and/or their treatment being recorded on EDRWeb. Therefore, all patients who have accessed diagnostics and/or treatment provided by the Free-State department of health may be included in the evaluation.

## 5.4 Data sources

Relevant datasets will be requested from the TB programme, namely A dataset of EDRWeb may be exported and transferred to the authors laptop. In addition, historical laboratory testing data, sent to the TB programme to supplement surveillance activities, may be transferred to the author’s computer.

## 5.5 Data management

Data will be collected on RedCap which is end-to-end encrypted. Only the author will have access to the responses. Data will be analysed using the latest version of Rstudio.

## 5.6 Data protection

The author’s laptop is protected by an alphanumeric password and can be remotely shutdown and formatted in the event it is stolen. Regarding data linkage, linkage is already happening at facility level, the more formal type of linkage in this report will pose no increased risk to what is already being conducted under programmatic conditions.

Table 5.1: EDRWeb Surveillance Evaluation Research Objectives and Methods:

|  |  |
| --- | --- |
| Objectives | Methods |
| To describe the current trends of DR-TB in Free-State | Analyse routinely collected DR-TB data from the Free-State Department of Health. |
| To compare three common data linkage methods for linking TB line list data and EDRWeb data. | Explore the strengths and weaknesses of deterministic, probabilistic (Jaro-Winkler), and fuzzy matching approaches. |
| To report the attributes of EDRWeb as defined by the CDC guidelines. | Review the CDC guidelines and collect inforamtion on each attributes as pertains to the EDRWeb system in the Free-State context. More detailed infromation on each attribute can be found in Table 2 |
| To determine whether the time to initiation of DR-TB treatment has an effect on mortality. | The association between the time to initiation of DR-TB patinets and treatment outcomes will be analyzed using appropriate statistical methods, such as the chi-squared test and logistic regression analysis. Adjustments will be made for potential confounding variables, such as sociodemographics and clinical factors. |
| To determine whether the timeliness of EDRWeb data has an effect on mortality. | The association between the timeliness of EDRweb and DR-TB treatment outcomes will be analyzed using appropriate statistical methods, such as the chi-squared test and logistic regression analysis. Adjustments will be made for potential confounding variables, such as sociodemographics and clinical factors. Timeliness can be defined as the length of time between the submission of the patient's sample for drug susceptibility testing and the reporting of the results via EDRweb |
| To create simple dashboards for the surveillance of EDRWeb using the same anlyses and measures produced by the evaluation. | Develop the dashboards using RMarkdown, Shinydashboard, and flexdashboard packages which can be made available via a private internet link to the TB programme.The analyses for timeliness, sensitivity, time to initiation, incidence and patient outcomes will be automatically reproduced when data is updated. |

Table 5.2: CDC Guidelines for a Surveillance Evaluation

|  |  |  |
| --- | --- | --- |
| Usefulness | The extent to which surveillance data provide useful information that can be used for public health decision making | Conduct surveys or focus groups with stakeholders to assess usefulness of surveillance data and identify areas for improvement |
| Simplicity | The extent to which surveillance data are easy to understand, analyze, interpret and communicate | Provide training or user guides with practical examples on how to use and analyze surveillance data |
| Flexibility | The degree to which surveillance data systems can be modified or enhanced to meet evolving public health data needs | Design the system to be modular with clear data standards that allow data entry, sharing and reporting to be flexible and scalable |
| Acceptability | The extent to which the surveillance system is acceptable to stakeholders and the population under surveillance | Conduct regular outreach and communication with stakeholders to ensure their needs are being met |
| Timeliness | The extent to which surveillance data are available in a timely manner and can be used for timely public health action | Implement automated systems for data collection, cleaning, analysis and dissemination that can be updated frequently in real-time |
| Data quality | The extent to which the data collected by the system is accurate, complete and valid | Develop data validation and quality control protocols to ensure data is of high quality and accuracy |
| Sensitivity | The ability of the system to accurately detect changes in health status, behavior or risk factors over time | Use statistical methods to calculate sensitivity and positive predictive value, and use variance estimates to establish confidence intervals |
| Positive Predictive Value | The proportion of reported cases or events that are truly positive | Implement gold standard laboratory confirmation tests when appropriate, and calculate proportion of test results that are positive |
| Representativeness | The extent to which the surveillance system provides an accurate representation of the population under surveillance | Conduct population-based surveys or use statistical weighting to adjust for sampling or other bias |
| Timeliness | The ability of the surveillance system to provide data in a timely manner | Establish a timeline for data collection, cleaning, analysis, and dissemination, and monitor system performance against established benchmarks |

# 6 Limitations

A significant limitation of the comparisons of these surveillance systems is that EDRWeb does not capture the outcomes of patients before they begin treatment. For instance, some patients may demise prior to starting treatment and therefore, they will appear on TB linelist data and not on EDRWeb. This is a limitation of both the research and of the surveillance system under question and may already form part of the recommendations. The laboratory linelist and EDRWeb may not account for the private, military, and mining sectors. Further ethical permissions and significant harmonisation and data cleaning would be required to include these sectors which, for the purposes of this report, is unfeasible.

# 7 Potential Benefits

This evaluation can provide insight into how well the EDRWeb is linked to patient testing. It may be able to identify patients who are at risk of not initiating or initiating late. Furthermore, this evaluation may identify whether timely reporting of initiation rates effect patient outcomes. This evaluation may provide evidence to how EDRWeb may be improved. The analyses developed through this report can be reproduced as part of a dashboard which can be used for readily available and reproducible digital surveillance tools by the TB programme in Free-State.

# 8 Dissemination

The findings of this report will be provided to the TB programme. Surveillance tools will be made available to the TB programme in the form of an on-line application. Findings may be presented at local and national conferences. The report is formulated with the intent to publish in a peer-reviewed journal.

# 9 Ethical considerations

This protocol will undergo ethical submission at the Human Research ethics committee at the University of Free-State after which permission to data will be sought with the Free-State Department of Health.

## 9.1

# 10 To do

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Tuberculosis is one of the leading causes of death worldwide, with drug-resistant tuberculosis (DR-TB) posing a major threat to global health. South Africa is among the countries with high prevalence of DR-TB, and effective surveillance is essential in managing the condition. According to a study by Streicher et al. (2014), DR-TB cases in South Africa have been increasing since 2002, with a higher prevalence among patients who have previously been treated for TB. The study highlights the need for enhanced surveillance to identify and monitor cases of DR-TB, as well as to track treatment outcomes.

In addition to active surveillance, there is a need for periodic evaluation of DR-TB programs in South Africa. A study by National Institute for Communicable Diseases (NICD) (2018) recommends such evaluations to identify gaps in the system and inform improvements. The study emphasizes the importance of assessing programmatic factors that contribute to poor outcomes, such as delays in diagnosis, poor adherence to treatment, and inadequate infection control measures. Evaluation of DR-TB programs can also help identify challenges in the implementation of new treatment regimens, such as bedaquiline and delamanid, which have been introduced in South Africa in recent years.

Finally, surveillance evaluation of DR-TB in South Africa can facilitate the development of evidence-based policies and guidelines. As highlighted by Cox et al. (2018), surveillance data can inform decision-making in TB control programs, guiding the allocation of resources and the implementation of targeted interventions. Evaluation can also help to identify areas where research is needed, such as the development of improved diagnostic tools and the optimization of treatment regimens. Ultimately, comprehensive surveillance and evaluation of DR-TB in South Africa are necessary to achieve better health outcomes for patients and reduce the burden of the disease on the population.

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# 11 from chatcpt

To determine the effect of timeliness of EDRweb on DR-TB patient outcomes, the following methodology can be used:

1. Study design: A retrospective cohort study design can be used to examine the association between timeliness of EDRweb and DR-TB patient outcomes.

2. Data collection: Data will be collected from the EDRweb database for all DR-TB patients who have received treatment. The data will include patient demographics, treatment regimen, treatment outcomes, and timeliness of EDRweb.

3. Exposure assessment: The exposure of interest is the timeliness of EDRweb. Timeliness can be defined as the length of time between the submission of the patient’s sample for drug susceptibility testing and the reporting of the results via EDRweb.

4. Outcome assessment: The primary outcome of interest is DR-TB treatment outcome, which will be classified as cured, treatment completed, treatment failed, died, lost to follow-up, or not evaluated.

5. Data analysis: The association between the timeliness of EDRweb and DR-TB treatment outcomes will be analyzed using appropriate statistical methods, such as the chi-squared test and logistic regression analysis. Adjustments will be made for potential confounding variables, such as age, gender, and treatment

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