

Innovative Strategies for Developing Tuberculosis Implementation Research in Sudan

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Abstract

Introduction: Sudan, especially Eastern States are very poor areas at great risk of endemic and communicable diseases particularly tuberculosis. The reasons for the spread and transmission of this disease include medical, economical and geographical issues, besides Sudan's location in the middle of nine countries in East Africa, its boundaries were affected by free movement, high number of conflicts displaced peoples from boarders' countries, high illiteracy rates, limited financial resources and shortages in medical services.

Objectives: This project is conducted to implement a new developed system for eliminating Tuberculosis infections among eastern Sudanese populations focusing on the eradication of multidrug resistant *Mycobacterium tuberculosis* including novel methods for the targeted delivery of new therapeutic drugs.

Conceptual Methodology: Strategies adopted in this work are proposed to increase access includes to communicable and economic factors. Disease Survey and Laboratorial Investigation for Multi Drug Resistant bacterial strains confirmation. Medical Assessment of TB Patients to facilitate improved efficiencies through metric measurement and enable patients' relationship management. Established a national level policy of treatment, vaccination and prevention. Administering regular evaluation of the disease situation and control.

Results: Implementation outcomes includes the conceptual framework for this project were informed by a combination of the general program logic model, the health system framework of the World Health Organization, WHO, the pillars of the Sudan health agenda, and the framework of the Strategic Elimination Plan. It is assumed that the reduction of TB burden at the national level (long-term output or impact) is preceded by improved case-finding and case-holding practices (short-term output). Impact outcome of the project is derived from the observation that tuberculosis is much more common at the boarders than center of Sudan where no adequate clinical services are available. It is conceivable that, although outbreaks may occur periodically, the control of disease might be easier to overcome than direct medication.

Conclusion: A major success of the project accomplishment, is the stimulation of the implementation strategy development for elimination and eradication of Tuberculosis in Sudan with a view to bring diagnostic and surveillance issues much higher up according to the implementation research agenda especially for those areas explored with similar national and international research projects, reports and technical initiatives.

Contributions To The Literature:

- Africa -with its all conflicts- at great risk of endemic, pan-endemic and epidemic of tuberculosis spread and outbreaks
- Reasons for spread and transmission of these diseases among poor communities are affected by free movement, high number of war displaced peoples beside other demographical issues.

- Poor health systems coverage in Africa make it very important to intervene with emerging **Implementation Research** projects taking into account the proportion of clinical cases with underestimating the burden of tuberculosis.
- Utilizing data on actual burden of tuberculosis is crucial for health authorities to design control programs for developing public health strategies such as surveillance, early warning and quick response system for spread and outbreaks, all can be defined as Implementation Research Conceptual Framework.

Introduction:

Globally, tuberculosis remains one of the top 10 causes of death worldwide. Millions of people continue to fall sick from TB each year(1–3). The huge biodiversity in Sudan, has a great bacterial record showed variable characteristics of infections and antibiotics susceptibility, this gives an excellent opportunity to find the effective intervention system(4). This study emphasizes the implementation systems that control, analyze and characterize TB treatment. In Sudan, especially the Eastern States, there are many areas at great risk of endemic, poverty and communicable diseases particularly tuberculosis (5–7). The reasons for the spread and transmission of the disease in Sudan are attributed to medical, economical and geographical location of the country which is bounded by nine Eastern African countries; free movement, high number of Conflicts displaced peoples from boarders' countries, high illiteracy rates, limited financial resources(8). The human host serves as the only natural reservoir for *Mycobacterium tuberculosis* of majority of tuberculosis but natural disasters such as aridity and geographical inaccessibility of some areas especially during the dry season can affect the circulation of tuberculosis in the Sudan(9). Poor health system coverage makes it very important to conduct a population-based prevalence survey taking in to account the proportion of clinical cases which is always very few as such as a tip of iceberg underestimating the burden of the disease because most of the cases are asymptomatic infections(10–14). b Urban areas have, in general, greater health provider diversity, are socioeconomically and culturally more diverse, and operate under different governmental structures. Furthermore, the transmission pattern and intensity are often different from rural areas. Many of these factors influence health seeking behaviour and perceptions about the disease, as well as case-definition and the epidemiology of tuberculosis, and, in general, methods, points and approaches for potential intervention. Moreover, the symptomatic cases are not adequately reported, so data on the actual burden of the disease is crucial for the public health authorities to design control programs(15–17). The prevalence of risk factors of tuberculosis can be used to ascertain the vulnerable groups and develop public health strategies namely adequate surveillance system and early warning and response body to guard particularly against multi-drug resistant tuberculosis. Principally, the risk of anti-drugs resistant disease is very high; this increases the need to find new low-cost drugs(18–20). One of the more interesting aspects of the present study into new implementation systems may in fact be the sequencing of their outcomes. The most important outcome is the change into how studying the treatment, vaccination and prevention is approached. It is also quite likely that even if the initial research is relatively not costly, the results may have great benefits in poor communities.

General Objective:

The general objective of this project is to implement a new developed system for eliminating Tuberculosis infections among Sudanese focusing on the eradication of multidrug resistant Mycobacterium tuberculosis using novel methods for the targeted delivery of new therapeutic drugs.

Specific objectives are to:

1. Manage clinical and diagnosis process inside the endemic area.
2. Control drug delivery to patients through direct channels.
3. Utilize stakeholders outsourcing, networking, and connections for serving patients.
4. Management of surveillance and data collection.
5. Assess conceptual, outcomes and evaluation systems.

Methodology:

Study area/setting

Sudan (1,886,068 km²), has 18 states after separation of South Sudan in 2011. The geostatistical and the socioeconomic model will be an inclusive framework that takes various aspects of the study area, such as economic status, social and the geospatial distribution of TB into consideration. Climate change may have effects in the spread of TB, where the environment can be seen as a biosocial determinant of the diseases, it provides a direct space in which infection can take place, predominantly through increased exposure.

Sample Size:

Sudan population is 32 million according to 2008 census excluding the separated South Sudan. The prevalence of Tuberculosis is very high especially among Eastern states' populations; namely Kassala (2,519,071), Al-Gedarif (2,208,385) and The Red Sea (1,482,053) respectively. These populations were chosen for a survey and/or experiment using World Health Organization recommended Sample Size Calculator and Sampling Spreadsheet (The STEPS) that can assist in first determining the size of sample and then in drawing a sample from sampling frame (<https://www.who.int/ncds/surveillance/steps/resources/sampling/en/>). This will construct a 95% confidence interval with a margin of error of about $\pm 4.4\%$ (for large populations).

Medical intervention for tuberculosis infections:

Onsite clinical testing and investigations

Tuberculin skin test (TST) and/or interferon-gamma release assay (IGRA) were used to test for LTBI, both tests measure immune sensitization (type IV or delayed-type hypersensitivity) to mycobacterial protein antigens that occurs following infection by *M. tuberculosis*. Antibiotic susceptibility testing to isoniazid or rifampicin will be done by using CLSI guidelines and the second-line drugs considered are those listed in the WHO Guidelines for the Management of Drug Resistant Tuberculosis(21).

Medical Assessment of Tuberculosis Patients:

1-Patient Registration: of both healthy and sick patients.

2-Appointment Management: with routine reminders to notify patients about appointments and delays.

3- Reports and Dashboards: To facilitate improved efficiencies through metric measurement. 4-Computer software: To enable patients' relationship management especially for chronic patients who visit the clinics more often.

Inclusion Criteria:

The inclusion criteria included the following: (a) Tuberculosis diagnosis (b) tuberculosis treatment fully conducted at field site during infection pandemic and (c) being African citizens or residents.

Exclusion Criteria:

The exclusion criteria included the following: (a) death within the first 15 days of treatment, (b) treatment default during the first 30 days after treatment initiation, (c) change of Tuberculosis diagnosis during treatment, (d) transfer to other health unit, or (e) unknown treatment outcome. The project also will provide information on socio-demographic variables, presence of comorbidities, tuberculosis features and treatment, which we included as covariates.

Management of Mobile Emergency health intervention:

Using well equipped mobile clinics, labs and pharmacies for emergency intervention is essential especially in those areas who lack for regular health facilities, outreach clinic mobiles aim to provide primary and emergency health care services for poor communities.

Data Collection methods, instruments used, measurements:

Networking and media and communication:

Data that has been collected and analyzed must be passed on to decision makers, the staff involved, and partners. This communication aspect is an essential component of a surveillance system and includes:

feedback, dissemination of information, specific communications.

Surveillance data collection

Public health surveillance in points of care for communities/migrants operates inside camps with daily collection of epidemiological data for selected syndromes/health conditions that are important from a public health point of view. Data recorded refer to consultations for each syndrome/condition under surveillance in primary health care facilities in community/migrant reception centers. Data are sent daily to the Department of Surveillance and Intervention of communities by doctors, nurses and other health professionals from services and NGOs staffing primary care facilities.

Data quality assurance methods, data management and analysis plans:

All official statistical activities shall be conducted in accordance with a Data Quality Framework that shall be developed by the National Centre for Statistics and Information in consultation with other government units that conduct official statistical activities. Once developed, the Data Quality Framework will be promulgated by Regulation/Government Decree (need to specify the legal process involved)"

Developing the national level policy of treatment, vaccination and prevention:

- 1-Developing drug delivery to lower levels and the cost of supervision of the communities.
- 2- Community based TB care developed together with implementing partners (Conduct situational analysis, establish partnership & coordination mechanism and Developing surveys).
- 3- Conducting a needs analysis, administering surveys, conducting interviews and developing curriculum.

Administering regular evaluation of the disease situation

- 1- Organize community base and multidisciplinary teams.
- 2- Regular Survey and Monitoring
- 3- Quarterly Review Meeting.
- 4-Dissemination of training materials.
- 5-Infection Control.

Strategies to increase community access:

- 1-Education: Patient consulting, social marketing,
- 2-Management: Financial management, business management.
- 3-Regulation: Standards development, task-shifting.
- 4-Economic: Insurance plans, pooled procurement.

Major workplan and Budget

The work plan identified tasks, time and period of the activity took place and executive responsible person as scheduled in appendix (B). An outline of the financial costs involved in implementing the proposed study and any other essential resources was declared in appendix (C).

Results And Outcomes:

The prevalence of tuberculosis among population

The disease total estimations in Sudan were 200,000 cases with 200 new infections annually include 1.9% Multi-Drug-Resistant *Mycobacterium tuberculosis* and 20.0% of them were previous treated patients (Fig. 1). Using World Health Organization Sample Size Calculator, the final sample size = 0.015 for all Eastern States (Appendix A 1,2).

Management of mobile health intervention:

Management of mobile clinic

Clinic Management Systems to give complete end to end solutions to clinics that are looking for administrative support along with Record Management. The Clinic Management System is focused on bringing in efficiencies into the mobile clinics by streamlining Appointment management, Registration and follow up along with maintaining electronic records for all TB patients. The system was ensuring collection of appropriate data to be able to present dashboards to the key users with a focus on improving clinical and operational efficiencies and reducing costs.

B) Management of mobile laboratory:

Simple laboratory tests such as microscopy, ICTs blood tests, hemoglobin estimation and urine examination are carried out at camps by regular moving of laboratory with its technicians. The clinics received referrals from the laboratory technicians for the management of medical and surgical emergencies and making etiological diagnosis quick and correct.

C) Management of mobile Pharmacy:

Quick delivery of health services including treatment and vaccinations attuned to the needs of patients in different area. Monitoring of patients' health and their outcomes: An important benefit of the project drug delivery is derived from observations that tuberculosis patients at the boarders are suffering from lack of medical services than others.

Management of communication network

include coordinate with others. Interagency and interectoral coordination should be established to ensure comprehensive care for community.

Conduct orientation meetings with community leaders; include representatives of social and community services, protection, the police or legal justice system, and security. Depending on the services available in the particular setting, others may need to be included. As a multi-sectoral team, establish referral networks, communication systems, coordination mechanisms, and follow-up strategies as shown in (Table-1).

Table 1
Formal and Informal Communication Channels Matrix in a typical Sudanese community

Communication channel	Perceived Effectiveness
Announcements at mosque by Sheik	Very effective
Public address system by partners	Very effective
Community leaders meeting then information dissemination	Very effective
Community meeting	Very effective
Community radio	Effective
Role Plays	Effective
Mobile phones	Effective
Health education at facility level	Effective
Printed materials	Less effective

Implementation of service delivery plan

Implement solutions determined in the Improve stage. Comprehend both technical as well as any business process related changes. Implement a comprehensive 'Change Management' plan to ensure that all stakeholders are appropriately trained.

Data Control Measurement

Verify at periodic intervals that the data is consistent with the business goals and the data rules specified in the Definition Step. Communicate the Data Quality metrics and current status to all stakeholders on a regular basis to ensure that Data Quality discipline is maintained on an ongoing basis across the organization as declared in (Table-2).

Table 2
Data Quality & Assurance for implementation of service delivery plan

Activity	Responsible Organization/ Person
Conduct situational analysis	Implementing Partners
Establish partnership & coordination mechanism	Township health committee & Implementing Partners and/all stakeholders
Capacity building	
Dissemination of training materials	National Tuberculosis Program at Region/State level
Training	NGOs, Township health staff with technical support from National Tuberculosis Program
Infection Control	All health workers
Advocacy, Communication and Social	Key stakeholders, National Tuberculosis Program and Implementing Partners
Mobilization	
Supervision	
Organize community base and multidisciplinary teams	Led by Implementing Partners and local authorities
Regular Survey and Monitoring	Joint supervision, National Tuberculosis Program, and Implementing Partners
Quarterly Review Meeting	TMO, BHS, TB Coordinators, Volunteers, focal from IPs and local authorities

* Data Quality is not a onetime project but a continuous process and requires the entire organization to be data-driven and data-focused. With appropriate focus from the top, Data Quality Management can reap rich dividends to organizations.

Implementation Research Outcomes

The conceptual framework for this project was informed by a combination of the general program logic model, the health system framework of the World Health Organization, the pillars of the Sudan health agenda, and the framework of the Strategic Elimination Plan. It is posited that the reduction of TB burden at the national level (long-term output or impact) is preceded by improved case-finding and case-holding practices (short-term output).

Medical intervention and quick response:

These, in turn, require the following inputs and activities: (i) delivery of health services that are consistent with accepted standards, but are also attuned to the needs of the local population; (ii) availability of human, material and financial resources to support program implementation; (iii) evidence-informed decision making; (iv) exercise of administrative oversight, and presence of support from policy-makers and local stakeholders; and (v) effective partnerships that harness contribution from the other government agencies, private sector and civil society.

Acceptability

Perception of local policy-makers and decision-makers on their agreement to the TB prevention and control program as cascaded by the national government (and development partners, as applicable).

Appropriateness

Perception of local policy-makers and decision-makers on the relevance to their local context of the TB prevention and control program as cascaded by the national government (and development partners, as applicable).

Fidelity

The consistency and quality of the intervention's implementation was implemented as intended due to major plan and conceptual framework (Figures-2, 3)

Feasibility

Perception of local policy-makers and decision-makers on the practicality of implementing the TB prevention and control program as cascaded by the national government (and development partners, as applicable). For purposes of the implementation research, the acceptability, appropriateness and feasibility of the package of interventions for TB prevention and control as provided by the national government from the local policy-makers shall be considered as among these potential driving or restraining forces.

Implementation research outcomes

Socio-(economic, politics, cultural) impact outcome

An important benefit of the project is derived from the observation that tuberculosis is much more common in boarders than center of Sudan where no clinical services. It is conceivable that, although outbreaks may occur periodically, the control of disease might be easier to overcome than direct medication.

Direct health impact outcome

Changing the regular health policies and the prevention approach have great benefits in poor communities. Another obvious outcome is the increase of patient's outreach, treatment and vaccination from 25% up to 75% in Dordabe locality Eastern Sudan

Beneficial impact outcome

Developing implementation strategy for elimination and eradication of Tuberculosis has stimulated funds from national and (expected international) relevant organizations and academia.

Future Prospects

- Development of future management systems could offer powerful tools for disease management within wider strategies of control
- The Project is an attempted a grand challenge to identify future risks from tuberculosis across Sudan and neighborhood.
- Implementation of a new research study and technology that might reduce such risks.
- Development of alternative therapeutics technology platform against MDR tuberculosis using novel methods for the targeted delivery of Bacteriophage Therapy

Discussion:

Tuberculosis is well-considered as an endemic and economic related disease in many countries as a result of poverty(22, 23). Many health systems in the Globe depend on clinical, official and governmental efforts without considering other implementation research settings against tuberculosis defeating(24). Although the recent health managerial policies of disease control were successful in the treatment of the disease but they failed in eradication (particularly the MDR tuberculosis) due to the lack of effective implementation research studies and trials(25–27). The present study showed the impact of a new empirical, managerial and integrated system for tuberculosis treatment in Sudan using innovative strategies of implementation research and how it is suitable for other countries who have similar conditions of disease epidemiologic. The risk of tuberculosis outbreaks among people fleeing hardship for poor, war's victims and refugees in Sudan is heightened by the description of the local health response

to outbreak of tuberculosis among all those patients (28). Conflict and war have long been recognized as determinants of infectious disease risk, re-emergence of epidemic tuberculosis and also has coincided with extensive civil conflict in affected regions(29). The needs of Implementation Research are very important for the critical health situation in Eastern Sudan, where the population has been suffering for long time from the endemic TB, beside poverty and long distant has stimulate the need of mobile combo-clinic for patients' outreach. This emergency facility has been used in many countries as stated by (30–33). The success of such implemented research is obviously seen in the reduction of the disease among the selected populations, this is in agreement with(34) who outlined the implementation challenges around the diagnosis and treatment of TB and described how current TB preventive therapy activities have been shaped and managed. The triangular conceptual framework (World Health Organization, local health authorities, and our innovative Strategic Plan) was implemented as an urgent responded action to eliminate the disease spreading (Figure – 2)(35). The conceptual framework's inner settings (health services) and outer settings (the financial and sociopolitical environment of local health services) were combined to obtain the highest level of the program perfection(36). This novel framework highlighted the morbidity, disability and heightened mortality that persist after successful treatment completion, in order to appreciate the importance of TB preventive therapy in the overall context of ending the MDR-TB epidemic and ensuring healthy lives(37). The Medical intervention combination (laboratory investigations, patient's assessment, drug delivery and vaccination) all together triggered an immediate quick response to tuberculosis emerging by implementing new strategies based on acceptability of a functional public network composed of specialist, stakeholders, community leaders who have been informed and connected via different means of media including social media(Table-1)this was previously stated by (38, 39). The appropriateness of the program was simplified to local communities by intensive training, lectures and meetings for better understanding, assessment and control of collected data (Table-2). A well-prepared budget for project feasibility was included in the two years plan which has been found it is the minimum period to implement such a project (40). The fidelity transition from input to impact is influenced by the presence of antecedent factors (i.e., elements that the program starts out with, usually forming part of the local milieu) and the emergence of mediating factors (i.e., influences that arise as the program unfolds) (35). Borrowing from force field analysis, inputs, antecedent factors and mediating factors can be classified into two: driving forces (i.e., facilitators, or factors, which, when increased, support attainment of the desired output), and restraining forces (i. e., barriers, or factors, which, when increased, support the status quo or detract from attainment of the desired results)(41–43). It is noteworthy to mention that a restraining force can be the absence of a particular input or contextual factor(44). Our implementation research outcomes were clearly divided into direct and indirect categories, this agreed (45) where the direct health impacted outcome was attenuated by changing regular health policies and prevention approached that have great benefits for poor communities resulted in their life hood enhancement as indirect outcomes(46). One major outcome is the increasing of patient's outreach, treatment and vaccination from 25% up to 75% obviously seen in Dordabe locality Eastern Sudan (Figure-3). The indirect outcomes were assembled in one category contains (economic, politics, cultural outcomes) which highlighted the importance of such approaches that have been credited by stakeholders with leading to greater acceptance of the need to integrate natural and social sciences in disease-related

work, where a barrel research projects at the economics explicitly should be continued to explore this link(41, 42). A number of the experts that worked on the Project have to continue to research the issues raised during the Project and help lead initiatives and organizations that work on associated areas. The study further assesses some of the implementation challenges of TB preventive therapy and propose how activities can be improved and enhanced through research and innovative strategies for future prospects and increasement of beneficial impact outcomes obtained by developing implementation research for elimination and eradication of Tuberculosis, this in agreement with (47),where the backbone of the project has remained as an enduring point of reference for the 'One Health' Agenda. The project also emphasis on the importance of detecting disease and promoting a joined up One Health approach to be reflected in the creation of some new collaborative networks regionally and globally (48). The establishments of an Inter-departmental and coordination group for high containment facilities is highly needed to develop and have global approach to the procurement of evidence for tuberculosis as stated by(49). The Project also can be credited with the importance that issues concerning the emergence of tuberculosis in Africa should be seen as a global public good, therefore, the extension of the project into Africa was a novel and previously unexplored idea, which in turn will lead to the support and creation of African Centre for Tuberculosis Surveillance directed by African Project team members(50, 51).

Conclusion:

A major success of the project accomplishment, is the stimulation of the implementation strategy development for elimination and eradication of Tuberculosis in Sudan with a view to bring diagnostic and surveillance issues much higher up according to the research agenda especially for those areas explored with similar national and international research projects, reports and technical initiatives. The Project also highlighted the importance of economic, social and communicable approaches that have been credited by stakeholders with leading to greater acceptance of the need to integrate natural and social sciences in disease –related work. The annual and Mid-term review showed that further and- in some cases- impressive progress which has been made in affecting change and influencing policy. The project successfully stimulated the development of the implementation strategy for elimination and eradication of Tuberculosis in Sudan with a view to bring diagnostic and surveillance issues much higher up than the research agenda expectations, with the area explored in similar national and international research projects, reports and technical initiatives.

Declarations

- Ethics approval and consent to participate:**

Can be found as separate attachments

1- Ethical approval in English was issued from Elbarkal research committee

2- Consent to participate in Arabic was issued for patients' participation

• Consent for publication:

An attached license agreement has been signed.

• Availability of data and materials:

All data and materials are available upon request

• Competing interests:

Authors have no competing interests

• Funding:

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• Authors' contributions:

A. A. E. (Principle Investigator), manuscript preparation, coordinated and carried out the study, O.A. N. (Social and Economic Evaluator) and A.A. E. Y. (Director) planned and designed the strategies of the project, performed the statistical analysis and participated in drafting the paper. N. M. A. carried out laboratory investigations, literature review and data analysis. K. M. S. designed patient assessment protocols, medical workshops and manuscript methodology arrangement, A. S. A. designed stakeholders training, locals' lectures, public orientations, paper's results interpretation and validation. All authors contribute manuscript preparation, read and approved the final draft.

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Figures

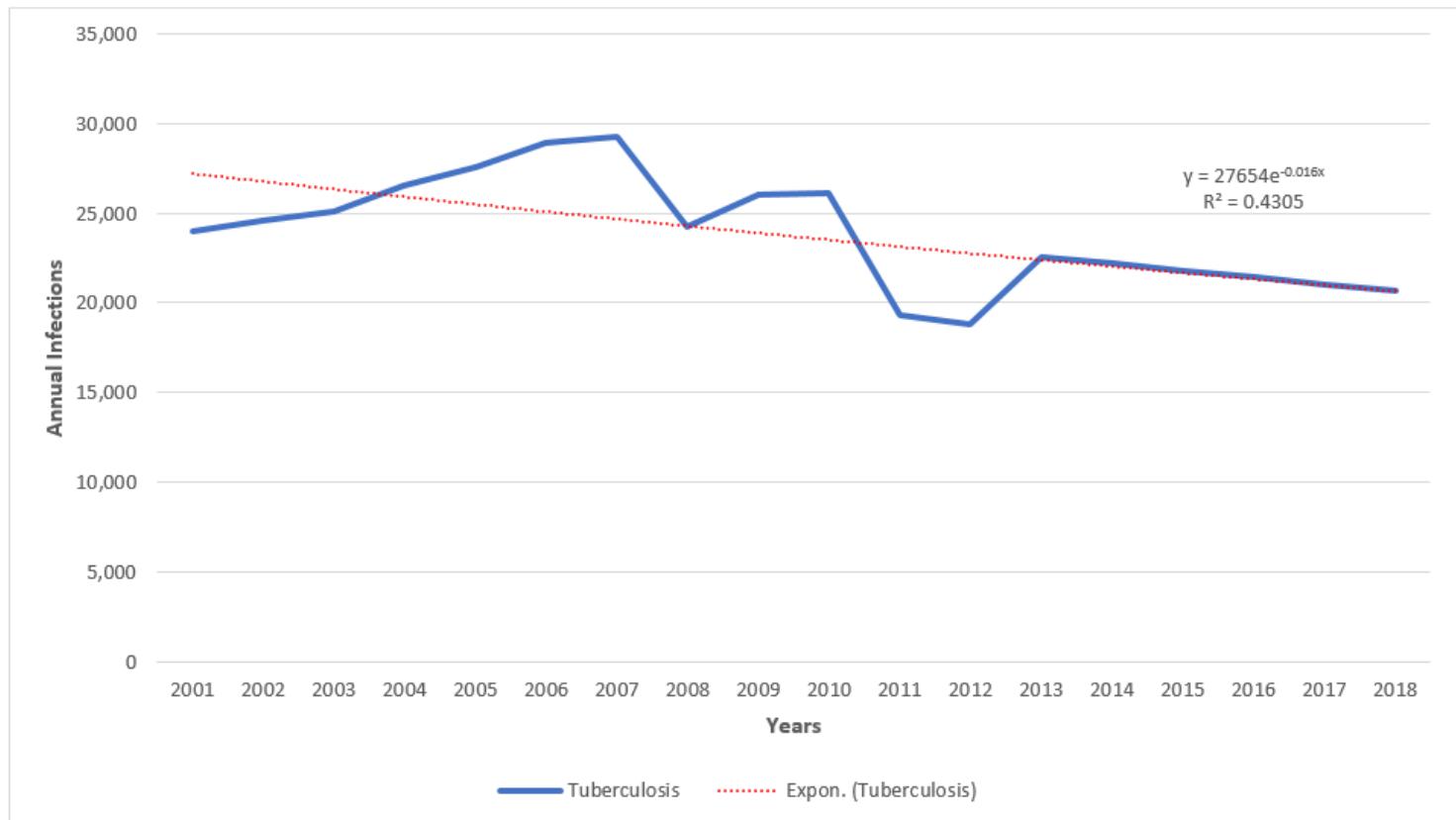


Figure 1

National tuberculosis infections baseline



Figure 2

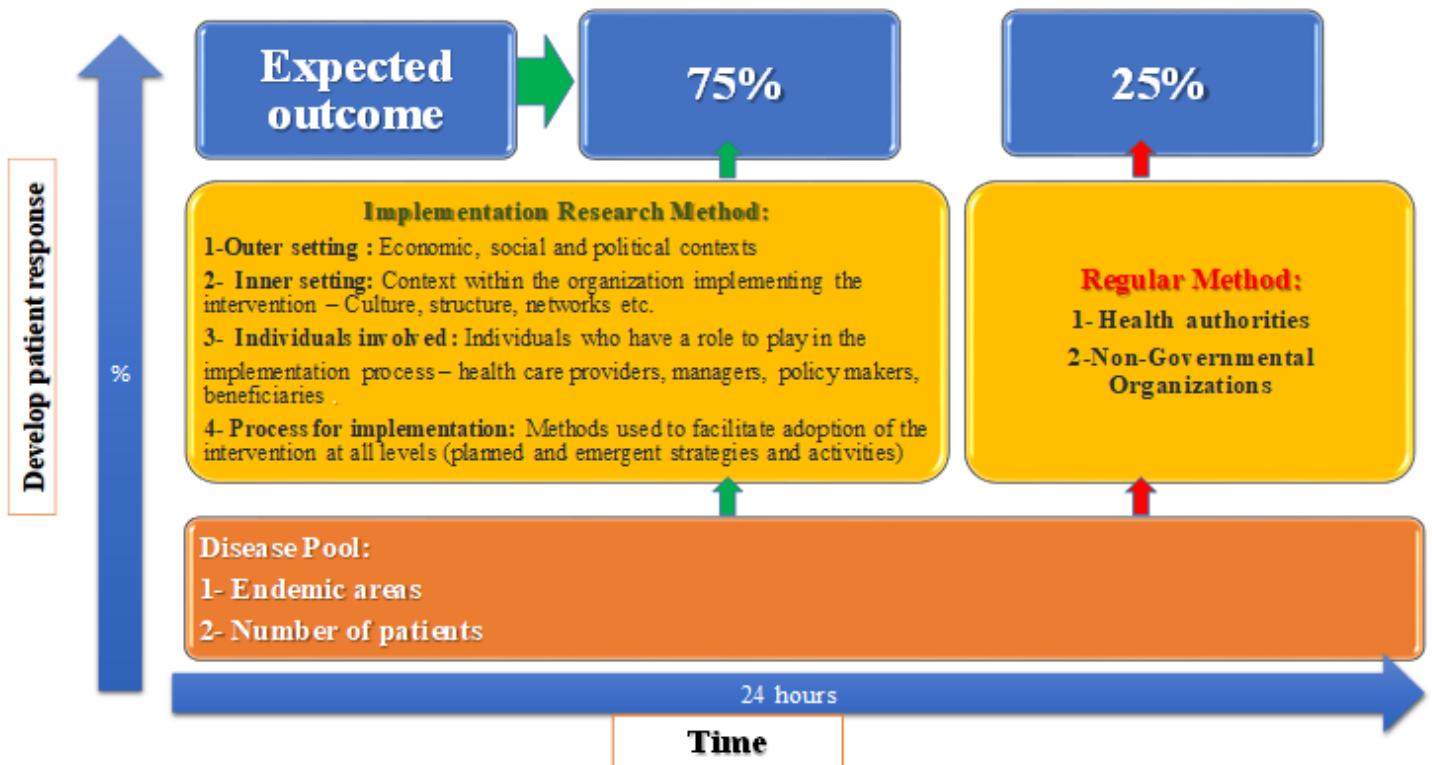


Figure 3

Conceptual Diagram ©Elshayeb 2018

Supplementary Files

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- AppendixD.TIDieRChecklistWord.docx
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