Evidence based interventions and implementation gaps in control of tuberculosis: A systematic review in low and middle-income countries with special focus on India

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A B S T R A C T

We synthesised the findings of intervention studies on Tuberculosis control (TC) in low-and middle-income countries with specific reference to India through a systematic review during the period 2000–2017 in order to identify the implementation gap. The research questions were framed using PICOS (population, intervention, comparison, outcomes and study design) framework and PRISMA (preferred reporting items for systematic reviews and meta-analyses) guidelines were used for study selection. The search was mainly carried out in MEDLINE/PubMed, Web of Knowledge and Cochrane libraries. DOTS was found to be the most effective intervention program for control of Tuberculosis. Lack of utilization of the capacity of various level health staff, accessibility in utilizing health facilities and insufficient community involvement was identified as the major gaps for TC. In the case of India, each state has its own priority and applicability for different TC interventions. Most of the studies on implementation of the TC program supported the encouraging effect of the intervention in the control of Tuberculosis. The specific need of each country is clearly reflected in many of the selected studies. In order to establish the association of intervention and its implementation gaps on TB control, more rigorous evaluation methods are needed including meta-analysis.

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1. **Background**

Tuberculosis (TB) is the ninth leading cause of death in the world. In 2016, among the 10.4 million people with TB and 1.7 million deaths from TB globally, over 95% of TB deaths and cases were in low- and middle-income countries (LMIC). Seven countries accounted for 64% of the total TB cases with the highest percentage seen in India followed by Indonesia, China, Philippines, Pakistan, Nigeria, and South Africa. Both World Health Organization’s (WHO) End TB Strategy and the United Nations’ (UN) Sustainable Development Goals (SDGs) have a common aim to end the global TB epidemic.

India is on the top of first five countries, with 56% of estimated cases of TB in the world. The country accounted for 33% of global TB deaths among HIV-negative people, and for 26% of the combined total TB deaths in HIV-negative and HIV-positive people. Globally the highest burden of both TB and multi-drug-resistant TB (MDR-TB) is reported to be in India. India accounted for an estimated incidence of 2.79 million cases of TB in 2016. In India, TB treatment and care are being provided in the government’s Revised National TB Control Programme (RNTCP). TB treatment is also provided through private sector health providers in the country. RNTCP is one of the vertical programs for TB control that have been initiated by the government in 1997. Now RNTCP has covered all over India, making it the second largest such program in the world. In the five-year National Strategic Plan for 2012–2017, TB free India was the vision of the government through achieving universal access. Implementation of the national strategic plan (NSP) was one of the main areas of RNTCP in this period. In spite of the remarkable achievement of NSP, people seeking care from private sector is a big challenge. So, in NSP 2017, participation of private sector was integrated into the plan in order to ensure quality care and treatment.

TB is a curable and preventable disease. Hence, most deaths from TB could be prevented with early diagnosis and appropriate treatment. So, the interventions in the area of TB control needs special importance as it is the most effective way to control this infectious disease. With this background, this review attempts to synthesize the findings of intervention studies carried out on TB control in LMICs with specific reference to India through a systematic review of literature during the period 2000–2017 from an implementation gap perspective Table 1. This article seeks to address the following review questions:

1. What are the published available interventions on control of TB in LMICs including India?
2. What are the gaps identified in implementation on the intervention for the TB control programs in India?

2. **Methods**

We followed the five-step strategy for conducting this systematic review similar to the one proposed by Khan K et al. 2003. The first step to frame questions for the review was done by all the three authors jointly. In the second step the second author identified the relevant work related to the present study with the help of a research assistant. The quality of the studies based on the objective of this review was assessed by all the authors and we summarized the evidences from the selected studies based on the research question. Narrative approach of data synthesis was adopted. Finally, based on the findings of the studies, conclusions were drawn. The study has been registered in PROSPERO (reg no CRD42018070406).

3. **Search strategy**

3.1. **Study design and data sources**

We systematically reviewed literature published during June 2000 to June 2017 to identify studies on interventions for control of tuberculosis and evaluated the implementation gaps. Our priority was to select studies from LMICs including India. A comprehensive search strategy was used with suitable key words used to identify pertinent literature. The search was carried out in MEDLINE/PubMed, Web of Knowledge and Cochrane libraries. Additional studies were identified by manual search and cross referencing.

A detailed search strategy was executed. The following key words were used: “Tuberculosis”, “implementation gaps”, “control programs”, “RNTCP”, “policy evaluation”, “evidence-based policies”, “implementation science”, “interventions”. Key words were combined using Boolean operators and the database specific controlled vocabulary.

3.2. **Methodological quality appraisal**

The methodological quality or risk of bias of the studies included were not appraised in consistent with guidance.

3.3. **Selection criteria**

Based on the objective of the study, inclusion criteria were fixed a priori by the authors. Original full text articles published in English in the above search engines in this particular period were included. As per the inclusion criteria, articles on intervention studies on control of TB and gaps identified in implementation of the intervention programs were included. Studies reporting prevalence and correlates of TB were excluded (Table 2).

3.4. **Data extraction and analysis**

All search results were entered into Zotero and duplicates were removed. The authors reviewed titles and abstracts in order to ensure the selection criteria matching with our objective. A total of 1324 records were screened, and 77 full text articles were extracted and reviewed independently by two authors. Discrepancies in the decisions were resolved with the aid of a third reviewer. For inclusion and exclusion criteria we followed preferred reporting items for systematic reviews and meta-analysis.
(PRISMA) guidelines (See Fig. 1). Of this, 29 articles met our inclusion criteria. From these we categorized the articles into interventions and program implementations. All the articles selected were reviewed by all the authors. Table 3 describes the characteristics of the articles selected for the final review.

**Table 1 – Final search terms used with PICOS framework.**

<table>
<thead>
<tr>
<th>Population</th>
<th>Intervention/Comparator</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults population with tuberculosis in Low and middle-income countries</td>
<td>All interventions targeting control of TB</td>
<td>Major interventions for TB control Major implementation gaps in TB control interventions</td>
</tr>
</tbody>
</table>

PICOS-patient/problem/population, intervention, comparison/control/comparator, outcomes, study type.

**Table 2 – Inclusion and exclusion criteria.**

<table>
<thead>
<tr>
<th>PICOS</th>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>P</td>
<td>Individuals from LMICs with Tuberculosis</td>
<td>Prevalence of TB</td>
</tr>
<tr>
<td>I</td>
<td>All interventions</td>
<td>Correlates of TB</td>
</tr>
<tr>
<td>C</td>
<td>Interventions and implementation gaps</td>
<td>National TB control programs by the governments</td>
</tr>
<tr>
<td>O</td>
<td>Intervention gaps</td>
<td>Government documents</td>
</tr>
<tr>
<td>S</td>
<td>All study types including quantitative and qualitative studies, systematic reviews, meta-analysis etc</td>
<td>Government document</td>
</tr>
<tr>
<td></td>
<td></td>
<td>National TB control program evaluation</td>
</tr>
</tbody>
</table>

PICOS-patient/problem/population, intervention, comparison/control/comparator, outcomes, study type.

Records identified through database searching (n = 6521) Additional records identified through other sources (n = 37)

Records after duplicates removed (n = 1403)

Records screened (n = 1324) Records excluded (n = 1247)

Full-text articles assessed for eligibility (n = 77) Full-text articles excluded (n = 48) (Did not meet inclusion criteria)

Number of studies included in the final qualitative synthesis (n = 29)

![Fig. 1 – Prisma flow diagram.](image-url)
<table>
<thead>
<tr>
<th>Ref No</th>
<th>Author &amp; year</th>
<th>Title of the study &amp; Journal</th>
<th>Country</th>
<th>Type of study</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>Wingfield T et al, 2015</td>
<td>Designing and implementing a socioeconomic intervention to enhance TB control: operational evidence from the CRESIPT project in Peru; BMC Public Health</td>
<td>Peru</td>
<td>Randomized Controlled Trial</td>
</tr>
<tr>
<td>11</td>
<td>Tola HH et al, 2016</td>
<td>Psychological and Educational Intervention to improve Tuberculosis Treatment Adherence in Ethiopia Based on Health Belief Model: A cluster Randomized Control Trial; PLOS ONE</td>
<td>Ethiopia</td>
<td>Randomized Controlled Trial</td>
</tr>
<tr>
<td>12</td>
<td>Colvin C et al, 2014</td>
<td>Evaluation of community-based interventions to improve TB case detection in a rural district of Tanzania; Global health: Science and Practice</td>
<td>Tanzania</td>
<td>Cross sectional pre-post evaluation</td>
</tr>
<tr>
<td>13</td>
<td>Kironde S et al, 2002</td>
<td>Community participation in primary health care (PHC) programmes: Lessons from tuberculosis treatment delivery in South Africa; African Health Sciences</td>
<td>South Africa</td>
<td>Prospective quantitative study</td>
</tr>
<tr>
<td>14</td>
<td>Tulloch O et al, 2015</td>
<td>Patient and community experiences of tuberculosis diagnosis and care within a community-based intervention in Ethiopia: a qualitative study; BMC Public Health</td>
<td>Ethiopia</td>
<td>Qualitative</td>
</tr>
<tr>
<td>15</td>
<td>Ollé-Goig JE et al, 2001</td>
<td>Treatment of tuberculosis in a rural area of Haiti directly observed and non-observed regimens. The experience of Hospital Schweitzer; The International Journal of Tuberculosis and Lung Disease</td>
<td>Haiti</td>
<td>Retrospective study based on clinical records</td>
</tr>
<tr>
<td>16</td>
<td>Das M et al, 2014</td>
<td>Directly-Observed and Self-Administered Tuberculosis Treatment in a Chronic, Low-Intensity Conflict Setting in India; PLOS ONE</td>
<td>India</td>
<td>Retrospective observational cohort study</td>
</tr>
<tr>
<td>17</td>
<td>Heller RF et al, 2006</td>
<td>Prioritising between direct observation of therapy and case-finding interventions for tuberculosis: use of population impact measures; BMC Medicine</td>
<td>India</td>
<td>Comparative study of two interventions</td>
</tr>
<tr>
<td>18</td>
<td>Frieden TR et al, 2003</td>
<td>Impact of national consultants on successful expansion of effective tuberculosis control in India; The International Journal of Tuberculosis and Lung Disease</td>
<td>India</td>
<td>Pre-post evaluation using medical records</td>
</tr>
</tbody>
</table>

(continued on next page)
<table>
<thead>
<tr>
<th>Ref No</th>
<th>Author &amp; year</th>
<th>Title of the study &amp; Journal</th>
<th>Country</th>
<th>Type of study</th>
</tr>
</thead>
<tbody>
<tr>
<td>19</td>
<td>Venugopal K et al, 2008</td>
<td>Treatment Outcome of Neuro Tuberculosis Patients Put on Dots-an Observation Study from the Field; Indian Journal of Tuberculosis.</td>
<td>India</td>
<td>Hospital based cohort study</td>
</tr>
<tr>
<td>20</td>
<td>Hadley M et al, 2000</td>
<td>Community involvement in tuberculosis control: lessons from other health care programmes; The International Journal of Tuberculosis and Lung Disease</td>
<td>Developing countries</td>
<td>Review</td>
</tr>
<tr>
<td>21</td>
<td>Borgdorff MW et al, 2002</td>
<td>Interventions to reduce tuberculosis mortality and transmission in low-and middle-income countries; Bulletin of World Health Organization</td>
<td>LMIC</td>
<td>Literature Review</td>
</tr>
<tr>
<td>22</td>
<td>Arshad A et al, 2014</td>
<td>community based interventions for the prevention and control of tuberculosis; Infectious diseases of Poverty</td>
<td>NA</td>
<td>Systematic Review</td>
</tr>
<tr>
<td>23</td>
<td>Adams LV et al, 2014</td>
<td>Interventions to improve delivery of isoniazid preventive therapy: an overview of systematic reviews; BMC Infectious Diseases</td>
<td>NA</td>
<td>Systematic Review</td>
</tr>
<tr>
<td>24</td>
<td>Cobelens F et al, 2012</td>
<td>Research on implementation of interventions in Tuberculosis control in Low-and middle-income countries: A systematic review; PLOS Medicine</td>
<td>LMIC</td>
<td>Systematic Review</td>
</tr>
<tr>
<td>25</td>
<td>Jeyashree K, e al, 2016</td>
<td>Smoking cessation interventions for pulmonary tuberculosis treatment outcomes (Review); Cochrane Review</td>
<td>NA</td>
<td>Cochrane Review</td>
</tr>
<tr>
<td>26</td>
<td>Awaisu A et al, 2011</td>
<td>The SCIDOTS Project: Evidence of Benefits of an Integrated Tobacco Cessation Intervention in Tuberculosis Care on Treatment Outcomes; Substance Abuse Treatment, Prevention and Policy</td>
<td>Malaysia</td>
<td>Quasi experimental</td>
</tr>
</tbody>
</table>

**Studies on implementation gaps**

<table>
<thead>
<tr>
<th>Ref No</th>
<th>Author &amp; year</th>
<th>Title of the study &amp; Journal</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>27</td>
<td>Essa SA et al, 2017</td>
<td>Assessment of the participation of primary care services in national tuberculosis control program in Gharbia Governorate; Egyptian Journal of Chest Diseases and Tuberculosis</td>
<td>Gharbia Governorate</td>
</tr>
<tr>
<td>28</td>
<td>Khan AH, 2017</td>
<td>Tuberculosis Control in Sindh, Pakistan: Critical Analysis of its Implementation; Journal of Infection and Public Health</td>
<td>Pakistan</td>
</tr>
<tr>
<td>29</td>
<td>Seddiq K et al, 2014</td>
<td>Implementing a successful tuberculosis programme within primary care services in a conflict area using the stop TB Strategy: Afghanistan case study; Conflict and Health</td>
<td>Afghanistan</td>
</tr>
<tr>
<td>30</td>
<td>Roy TK et al, 2015</td>
<td>Bridging Gaps in Revised National Tuberculosis Control Program at Bankura District, West Bengal State, India; American Journal of Public Health Research</td>
<td>India</td>
</tr>
</tbody>
</table>
4. Results

4.1. Study selection

Finally, we identified a total of 29 original articles for final synthesis. In this manuscript, the synthesis is presented theme wise into two: studies on interventions in TB control programs and studies on implementation gaps. There were 17 studies in the first category including five systematic reviews and 12 studies in the second category including two systematic reviews.

4.2. Studies on interventions in TB control programs

The review in this section rests on interventions in TB control across LMICs. We used WHO criteria for the selection of LMICs. The following section provides the main findings of the selected intervention studies.

4.2.1. Randomized Controlled Trials

Two were Randomized Controlled Trials (RCTs): one from Peru and the other from Ethiopia. Socio-economic intervention was delivered along with the national TB control program to the intervention group against the normal standard of care from the National TB program in a study from Peru as part of a large project on Community Randomized Evaluation of a Socioeconomic Intervention to Prevent TB (CRESIFT). The economic support included cash transfer to patient’s households. Social interventions were household visit, participatory community meetings, mutual support including stigma reduction and community empowerment. Even with logistic difficulties, socio-economic intervention played a major role in control of TB in similar settings. The study from Ethiopia was a hospital based RCT conducted among 698 TB patients based on health belief model. The four months intervention included several sessions of psychological counselling and educational intervention. The pre-post evaluation findings indicated significant improvement in the intervention group with regard to adherence level compared to control group.

4.2.2. Community based studies

A cross sectional survey was conducted in Tanzania to determine effectiveness of community-based intervention on TB case detection. Sensitizing regional and district TB co-ordinators, community leaders, and community-based organizations, training pharmacists and traditional healers, training, deployment, and supervision of two sputum fixers and training to eight current TB patients were done as part of the intervention. Two years after the intervention, the case notification rate for smear-positive TB increased by 68%. The findings of the study indicated the importance of community-based interventions on improved TB case notification. The primary focus of a community-based study in South Africa was the feasibility of community participation in a high burden TB program in a resource limited setting. The adult TB patients in this study were given options to choose community-based treatment, clinic-based treatment and self-administered treatment. Volunteers supervised the patients...
who opted community-based Directly Observed Therapy (DOT). The study established the important role of lay volunteers in TB treatment supervision compared to other methods of TB treatment delivery. After a year, no significant difference was seen between the treatment options regarding the outcome among new patients. However, for re-treatment of patients, community-based supervision was found to be superior to self-therapy. A high level of female patient participation was another major finding of the study.

A qualitative study was reported from Ethiopia on the community members treatment seeking behaviour and their perceptions of the intervention based on 36 in-depth interviews with TB patients who were on treatment or screened negative for TB. A community intervention as part of the Ethiopia Health Extension Program appointed female health extension workers (HEW) and volunteer Community Health Promoters (CHP). These workers were giving advocacy, communication and social mobilization activities identifying symptomatic individuals, collecting sputum and preparing smears at community level. The intervention was very much acceptable, especially for poor men and women and those who had difficulty in traveling. A high level of appreciation was seen in case of giving sputum samples and receiving results from within their home communities.

A retrospective study based on clinical records in Haiti compared two strategies for TB treatment: usual standard treatment regime and supervision by former TB patients at home for DOTS (DOT group) and non-observed treatment (non-DOT group). The area was known for its extreme poverty and high rates of HIV infection. Medication together with free food for a complete one-day diet and fuels for cooking were brought to the patients home twice weekly for DOTS group along with former TB patient supervision. For non-dots only, medicine was given. The successful outcome was significantly higher for DOTS than non-DOTS (87% vs 58%) and this difference was also seen among HIV infected patients.

4.2.3. Indian studies

Among the four studies from India, one was a retrospective observational cohort study which compared two treatment methods: DOTS and SAT (self-administered therapy). The study was conducted in the border of Chhattisgarh, Andhra Pradesh and Odisha states in India. Because of the conflict situation in these regions, the accessibility to primary and secondary health care was poor. The success rate was 69% among those who treated under intermittent DOTS compared to 53% under SAT. The duration of treatment for patients under DOTS was shorter than under SAT. Though not superior, SAT can be a feasible option to be adopted in conflict situations where as DOTS is difficult to be implemented.

A study by Heller et al estimated the population impact measures of two interventions using published literature based on national data. The study compared the direct observation of therapy and increasing case-finding. The study estimated that increasing case finding for TB saves nearly 10 times more lives than with the use of the directly observed component of DOTS in India.

Another study was on the impact of national consultants on TB control programs. The study compared areas with and without consultants and individual areas before and after consultation. The study finding indicated that DOTS delivery as well as treatment success was significantly higher in areas with medical consultants. However, the study identified that there were so many difficulties in appointing consultants in all the areas.

The research study conducted in the Indian state of Kerala assessed effectiveness of Revised National TB Control Program among adult neuro tuberculosis patients. After the routine RNTCP program monitoring along with the supervision of drug intake a treatment completion rate of 81% was seen.

4.2.4. Literature reviews

Six selected studies were literature reviews. Among them three were systematic reviews; one Cochrane review and two studies on literature review on LMICs.

Hadley and Maher in 2000 published a review on community-based health care initiatives for TB control in developing countries. The main areas identified were informal community involvement like delivery of messages to encourage TB suspects to encourage treatment, psychological and logistic support to complete the treatment and in case of formal community involvement like ensuring programs for accessibility of treatment by disseminating messages to increase awareness and encourage adherence, identifying the following those who break treatment, identify adverse effect and case detection.

A literature review on interventions to reduce TB mortality and transmission in LMICs specified the available TB interventions as part of the TB control programs such as diagnosis and treatment of smear-positive tuberculosis, BCG immunization, diagnosis and treatment of smear-negative tuberculosis, active case finding and treatment of smear positive tuberculosis, preventive therapy in people with HIV infection and preventive therapy for contacts of tuberculosis patients and adults in the general population. Amongst these, DOTS was found to be the most cost-effective intervention.

A systematic review using 41 studies on community-based interventions for the prevention and control of TB reported that community-based interventions showed significant increase with risk ratio 3.1 in TB detection rates and a non-significant impact on TB incidence. Treatment success rate was also high in case of community-based interventions and the involvement of community health workers further improved access and service utilization.

In order to compare different organizational interventions to improve isoniazid preventive therapy (IPT), a systematic review was conducted by Adams et al in 2014. IPT delivery was measured by treatment completion among those at higher risk for the development of TB disease like child contacts or HIV-infected individuals. This review could not find out studies which can demonstrate that interventions improved treatment completion.

The systematic review of research on implementation of interventions in TB control in LMIC is comparable to the present review. This manuscript analysed the interventions from the five WHO recommendations of interventions for TB control. The review identified 73 studies among which 59 were on isoniazid preventive therapy and HIV infection. There were
substantial evidences for scale up of the five interventions at country level. And the studies available had limitation regarding design, geographic distribution and the setting of the study.

A Cochrane Review analysed the effect of tobacco smoking cessation interventions on the treatment outcomes of people with adult pulmonary TB and found a limited high-quality evidence on randomised controlled trails testing the effectiveness of smoking cessation interventions in improving TB treatment outcomes. The authors concluded that short and long-term trials were needed to assess the effect of smoking cessation interventions on TB treatment.

Another study from Malaysia evaluating the additional impact of smoking cessation intervention to conventional DOTS for TB control was reported specifically for LMICs. The study was conducted among 120 samples who were smokers at the time of TB diagnosis. The main intervention given was smoking cessation intervention with DOTS. The TB cure and treatment success rate was 97.5% in the integrated intervention group, which was significantly higher than that of 78.3% in the comparison group.

4.3. Studies on implementation gaps in TB control interventions

This section discusses the major gaps in implementation of intervention for TB control. There were 13 studies finally selected in this category. The studies are from different LMICs including India, Israel, South Africa, Ethiopia, Bolivia, Ecuador and Paraguay, China, Greenland, Afghanistan, Africa, Gharbia Governorate and Pakistan.

In a study from Egypt reported the findings of the evaluation of the Primary Health Care (PHC) service performance in National Tuberculosis Control Program in Gharbia Governorate. The major gap identified in this study was that PHC physician’s lack proper knowledge about TB and their units lack proper equipment. So, there was a need for training and equipment for better performance of the health system in order to control TB program in the country.

In Pakistan, lack of access to TB services was a barrier for empowering TB patients. Partnership between public, private and government sectors in treating TB as well as in improving the quality of the health care system is urgently needed in the country. The main gap identified was the lack of private sector involvement is the National TB Control program in Pakistan.

Using the review of program evaluation and the in-depth interview with key informants Siddiq et al studied the national TB control program in Afghanistan. Along with the high commitment from the government, strong leadership of the program, effective partnership and coordination among stakeholders and adequate technical and financial support from the development partners, co-ordination and service delivery issues in remote areas, lack of trained staff, donor dependence were the sustainable issues identified in the program.

An observational descriptive cross-sectional study was reported from India to find out the gaps at the level of patients, or health providers in implementing RNTCP and find out the reasons. In this quantitative study 106 outpatients enrolled as pulmonary tuberculosis cases in the selected medical college. The service issues identified were, first contact with unqualified local practitioner with delay in advising sputum examination in Government health facility, long distances from facility, non-availability of drugs and staffs with refusal to supply drug, inconvenient timing of clinic, fear from social stigma and fear of side effects of drugs with long duration of treatment were cited as negative factors in treatment. Other gaps identified were the significant association of socio-economic status with delay in diagnosis and initiation of treatment.

With the objective to explore barriers and facilitators to health seeking and adherence to treatment, Mabunda JT et al published a community based participatory study from South Africa. Both Focus group discussions (FGGDs) and workshops were conducted. In the workshops with the planning groups, the planning people review and analyse the existing programs followed by development of a practical application. In FGDs, professional nurses, DOTS supporters, community members, and patients and the agenda for FGDs was discussed in the planning people workshops.

A qualitative study from Ethiopia aimed to investigate the experiences from both TB patients and health care providers’ perspective of implementing DOT for the full course of TB treatment using in-depth interviews and focus group discussions. The major implementation gap identified were: the difficulty in making a daily visit to health facility for DOT due to the distance of the facilities from their place of residences and difficult in terms of their work and social lives. Lack of transportation and high transportation cost were also found to be the main implementation gaps of DOTS in Ethiopia.

Rensburg et al in 2004 discussed social research as an intervention tool in tuberculosis control. This study was done in South Africa targeting TB patients visiting PHC and hospitalised patients, DOTS supporters and TB coordinators and health care workers. Information generated by social research was used as an intervention. The findings of the study indicated that the mode of intervention was crucial in influencing TB health policy. The role of social scientist was often ignored even though they were playing major positions and roles in the health system. This was a major gap in the implementation of TB control programs.

Another study from Ethiopia to assess the impact of the DOTs strategy on TB case findings and treatment outcome was a quantitative study based on 136,572 cases in the selected medical college. The service issues identified were, first contact with unqualified local practitioner with delay in advising sputum examination in Government health facility, long distances from facility, non-availability of drugs and staffs with refusal to supply drug, inconvenient timing of clinic, fear from social stigma and fear of side effects of drugs with long duration of treatment were cited as negative factors in treatment. Other gaps identified were the significant association of socio-economic status with delay in diagnosis and initiation of treatment.

A qualitative study to describe the methods, results, and lessons of rapid expansion of DOTS in India was published by Khatri and Frieden in 2002. The main finding indicated that appropriately designed and effectively managed DOTS...
programmes can achieve high case-detection and cure rates even with suboptimal technology and a suboptimal public health infrastructure. The first challenge identified was the difficulty in expanding the program in other parts of the country where it is already not covered mainly due to comparatively poor health infrastructure facilities. The second challenge was to increase the reach of the programme in areas where it was already functioning by ensuring that a greater proportion of patients was treated. The third challenge was to ensure the sustainability of the programme. The fourth challenge was to establish patient-centred services, one of the essential ingredients of successful DOTS implementation. The fifth challenge was to confront MDR-TB, which was present in 1–3.3% of new patients in the districts that have been surveyed. The sixth and most serious challenge was that presented by the epidemic of human immunodeficiency virus (HIV) infection.

An article by Waisbord assessed the challenges in reducing TB in prisons in Bolivia, Ecuador, and Paraguay and propose ways to address them through communication interventions. The main challenges identified were stigmatizing attitudes and low knowledge about TB among inmates and key prison personnel discouraged people living in prisons from seeking diagnosis and treatment. Systemic problems in prison health services, along with squalid living conditions, lack of coordination between national TB programs and prison health systems, and insufficient allocation of resources to health prevented the provision of adequate TB prevention and care.

Two systematic reviews were identified. One was the summary data on the implementation of the DOTS strategy in China in terms of actual observation and treatment adherence, and to review the effectiveness of quality improvement interventions for tuberculosis (TB) control in China. The main interventions identified were patient health education, regular follow-up, personal training and improved drug management, establishment of personal records, electronic information management, communication using the internet, use of telephone reminders and various management and transport subsidies and psychological counselling and fee for DOT. The findings of the review indicated that treatment effects of the different types of care providers and quality improvement interventions did not differ significantly. The results of the meta-analysis suggest that community involvement was effective in terms of patient outcome. The main gap in implementation identified was the need for community level participation in TB control since the DOTS program in China mainly focussed on setting up drug distribution points. Inadequate financial incentive offered to DOT observers was another key barrier identified for the implementation of DOTS.

Another systematic review based on 75 studies, 18,294 patients across 31 countries identified strategies for reducing treatment default. Lower default through the use of community health workers, standardised regimens/systems and combination of adherence interventions provide effective for reducing TB. The need for comparative prospective studies to strengthen the evidence base to allow better decision making in practice and policy where resources are limited to achieve the goal of universal access to effective MDR-TB treatment was identified as the major challenge in published work.

5. Discussions

Even though almost all interventions manuscripts we got presented positive effect of intervention on TB control, generally we found limited evidences to demonstrate the best interventions for the control of TB in low and middle-income countries. Therefore, the present study failed to prioritize the ideal type of intervention applicable to LMICs. However, based on the available findings, effective interventions were more or less regional specific and not generalizable.

The three RCTs implemented three types of intervention; socio-economic, psychological and educational interventions to the patients as well as the TB supporting staff. There was no common component in these three studies. However, the important point from the findings of the RCTs in this review was the positive outcome of interventions on TB control and management. In India, most of the TB intervention research concentrated on studies to assess the role of national program on TB control. The National TB control program in the country was the most widespread and effective one in Indian situation. The community-based studies on interventions in TB control carefully indicated the area-based needs of different interventions for control of TB. So, the implications of the study findings are applicable to similar setting and cannot be generalizable.

The findings from Haiti indicated better outcome of TB control by delivering treatment in patient’s homes with direct observation by former TB patients even in areas with poverty and HIV infection. Role of smoking cessation on TB control was established based on some individual study findings. Even though isoniazid preventive therapy is a main category of health intervention on TB control, we could not find a clear evidence on the effect of such intervention on TB control outcome. Findings from South Africa, which is an examples of high TB burden country doing relatively well in terms of some of the indicators associated with TB incidence, showed relative role of community-based interventions in TB control. Implementation of some joint interventions were seen only in a few studies. Our search showed that some of the studies were pilot studies and long term follow up studies were limited.

Most of the review-based studies focussed on LMICs. Role of informal community movements and other participatory approach was found to be important for the success of TB control programs. Among the different type of the interventions, DOTS was found to be the most effective program for control of TB. We found a weak association for the role of isoniazid preventive therapy (IPT) on TB control.

According to WHO, more than 20%of the global TB burden was attributable to smoking tobacco. However, TB control strategies have paid relatively less attention to smoking cessation activities as a means of TB control strategy. It was also interesting to note that countries with high level of smoking also had high burden of TB. Smoking cessation was not addressed well as an intervention to control TB. This might happen at the stage of title screening since most of the study connecting smoking and TB did not include intervention as a usage in their study titles.

Health system strengthening was a main area identified as a gap in the implementation of TB control programs. Capacity
of various level health staff were not utilized properly in most of the health systems in LMICs. Lack of accessibility in utilizing health facilities for TB treatment was another major gap identified in most of the LMICs. Insufficient community involvement was identified as the main gap in the effective implementation of TB control programs in most of the countries. Study findings from different countries indicated the heterogeneity of different interventions and the applicability of it in each geographic area. In case of India as indicated, each state has its own priority and applicability for different TB control interventions.

6. Limitations

One of the major limitations of this review was our inability to identify studies which help to prioritise the best practising interventions in TB control in LMICs. Since we have included all study designs, neither could a pooled analysis nor a meta-analysis be conducted due to heterogeneity, nor could summary measures like effect size be calculated. Apart from our efforts to include relevant studies in this systematic review, there is a chance for missing of some related studies.

Heterogeneity of studies in this review makes conclusion difficult and thus the findings of this review are tentative and propose the need for further research in this area. Another limitation of this study was that we have included full text manuscripts published in English. Finally, this study is a subjective summarization of the literature on the specific subject under consideration rather than a scientific outcome.

7. Conclusion

This systematic review provides evidences over a period of more than 15 years on intervention and implementation gaps in interventions for TB control programs in LMICs. Most of the studies on implementation of TB control program supported the encouraging effect of intervention in the control of TB. The specific need of each country is clearly reflected in many of the selected studies. Even though smoking cessation was considered to be a key element of TB control, we could find limited number of published intervention trials in this area which was a major gap found in this study. To address the association of intervention and its implementation gaps, more rigorous evaluation methods are needed including meta-analysis.

Declarations

Ethics approval and consent to participate

Formal ethical approval is not required as primary data will not be collected.

Consent for publication

All authors agreed to read the final manuscript and agreed to participate.

Availability of data and material

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

Competing interests

The authors have none to declare

Authors’ contributions

AIK, MGK conceived the idea, planned and designed the study protocol. MGK designed the figure and wrote the first draft; ALR planned and done the data extraction. MGK and AIK analysed and interpreted the studies. All authors have approved and contributed to the final written manuscript.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijtb.2019.04.006.

References


