Title: Training Lay Healthcare Workers to optimize TB care and improve outcomes in Malawi

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Background/Rationale:

The global shortage of skilled healthcare workers is estimated at 4.2 million, with1.5 million healthcare workers needed in Africa (1). Task shifting of less complex healthcare tasks to LHWs is increasingly employed to address this shortage (2). Despite availability of effective treatment, TB remains an important cause of mortality with 1.3 million lives lost globally to TB in 2012(3). The greatest proportion of new TB cases occurs in Africa and over 95% of TB deaths occur in low income countries (LICs) (3). In response to the high TB burden and severe healthcare worker shortages in these settings, outpatient TB care is among the tasks commonly shifted to LHWs.

LHWs are community members who have received some training but are not healthcare professionals (4). Randomised trials show LHWs improve access to basic health services and TB treatment outcomes by providing care and adherence support in the community (4, 5). However, insufficient training and supervision are recognized barriers to their effectiveness (5). LHW training is typically conducted off-site (6), an approach that is expensive in both direct and opportunity costs due to disruption in care provision, and thus, limits training. Given their relative low cost and proven effectiveness, educational outreach and reminder KT strategies offer a promising solution to addressing LHW training needs by increasing incorporation of best evidence into LHW practice.

Malawi has among the lowest healthcare worker to population ratios with 2 physicians and 34 nurses/midwives per 100,000 people (7). In response, Malawi scaled up its LHW cadre to >10000. As the primary providers of outpatient TB care LHWs have a pivotal role in addressing the high TB burden in Malawi, with over 20000 new TB notifications in 2012 (8). In spite of ongoing efforts, poor treatment adherence remains an important contributor to the high TB burden in Malawi with treatment completion rates ranging from 58 to 70% in our recent study in Zomba district(9).

Despite their critical role, LHWs (termed health surveillance assistants, HSAs, in Malawi) in our recent study identified lack of disease and job-specific training as the key barrier to their role as TB care providers (10). This project aims to address this knowledge-to-action gap by refining, implementing and evaluating a KT strategy designed to improve LHW TB knowledge and counselling skills, and through this improve TB care provided by LHWs and TB outcomes. Based on the findings of our previous study, knowledge users in Malawi are keen to improve and further explore the strategy in preparation for scale up.

Study Goals and Objectives:

Our goal is to improve tuberculosis (TB) care provided by Lay Health Workers (LHWs) in Malawi by refining, implementing and evaluating a knowledge translation (KT) strategy designed to facilitate incorporation of evidence into LHW practice.

Specific objectives:
1. Improve TB outcomes by implementing and evaluating a KT strategy developed and tested by our group to address an identified gap in care provided by LHWs in Malawi.

2. Identify barriers and facilitators to scalability and sustainability of this KT strategy, and its potential to address other gaps in care provided by LHWs.

Research Question(s):
1. Is a KT strategy to improve LHW TB knowledge and skills, effective in improving TB care and outcomes in Malawi?
2. What are the barriers and facilitators to scalability and sustainability of the TB intervention and to the use of KT strategies to address other gaps in care provided by LHWs?

Methods:

Design: This project will employ a mixed methods design. We will conduct a pragmatic cluster (RCT) to evaluate effectiveness and understand how to scale up and sustain the strategy. Qualitative interviews with LHW participants and patients, and document analysis of training logs, quarterly peer trainer meeting and mentorship meeting notes, will be used to gain an understanding of barriers/facilitators to implementation, scalability and sustainability of the program.

Setting, Participants, & Randomization:

Dignitas International works closely with the Malawi MOH to support health system strengthening and build capacity among healthcare workers to improve clinical care and outcomes. This project will include all HCs providing TB care among the 124 HCs in 4 districts in which DI operates, excluding the district included in our preliminary study and 1 district that declined to participate. As TB care is provided at health centers (HCs) on a rotating basis patients receive care from several LHWs during treatment. Given this system of care, a cluster RCT (with allocation at the HC level) was chosen to prevent contamination. HCs will be randomly allocated using a computer-generated random number list prepared by the statistician, stratified by district and HC status as anti-retroviral (ARV) initiation sites. These stratification variables are chosen to address district level variations in operationalization of TB policy and the potential for LHWs at ARV initiation sites to have received additional clinical training relevant to TB care.

TB focused LHWs (TBLHWs) at participating HCs will be contacted through the district health offices. TBLHWs are general LHWs who receive 2 weeks of additional TB training and are responsible for TB care at the HC level. TBLHWs were selected as peer trainers by the MOH given their status and responsibilities as the local head of TB care. Our previous work found TBLHWs effective in this role as they were seen as experts by general LHWs particularly after they were trained and assumed the role of peer trainer. All LHWs routinely providing TB care will be eligible and invited to participate in the training with refusal to participate the only exclusion criteria. Health Centers and TBLHWs will be enrolled by the study coordinator. Given the nature of the intervention blinding is not possible.

Interview participants will include LHWs who have received the intervention and patients/guardians who begin TB treatment on or after the trial start date and who are followed at a participating health center.

Inclusion/Exclusion Criteria:

The trial will include all Health centers providing TB care among the 124 HCs in 4 districts in which DI operates, excluding the district in which the pilot study was conducted and a second district that declined to participate. Health centers will be excluded if they do not routinely provide TB care.

LHWs who have completed the educational outreach training and TB patients of participating health centers who begin TB treatment during the trial period presenting for TB care on days the study research assistant is collecting data will be eligible for participation in the qualitative study. Exclusion criteria for interview participants include: TB patients less than 18 years of age unaccompanied by a parent or guardian, patients/guardians or LHWs unwilling or unable to give informed consent, patient not usually treated at the participating health center, patients deemed by the local healthcare team to be too ill to participate.

Sample Size:

Although 124 health centers are available for participation in the 4 study districts, a small number do not routinely provide TB care. In addition, based on our experience in the preliminary study, where several clusters were lost due to staff shortages necessitating transfer of TB cases or failed to accrue eligible TB cases in small remote health centers, we have estimated the sample size for the present study conservatively as follows. Based on an alpha of .05, power of .80, baseline successful treatment completion of .80 at 1year, ICC of 0.1 based on our pilot study data and an estimated 100 clusters (HCs that provide TB care), a minimum of 6 patients are required per cluster to detect a clinically significant .10 increase in proportion of successful treatment completion.

Interviews will be conducted with LHWs and patients at 2 time points during the trial, with an estimated 10-15 participants from each group required each time to reach saturation and allow for sampling from all participating HCs for a total of 40-60 participants.

KT Intervention:

The current strategy builds on our earlier work, which identified a gap in LHW TB knowledge and job-specific training. The multifaceted KT strategy will employ peer-trainer led educational outreach, a point of care reminder tool, and a peer mentoring network, chosen based on evidence for effectiveness of this approach with mid-level health workers in South Africa (12,13,14) and feedback from our prior study (9). Improved patient TB knowledge and positive patient-provider interactions, two common barriers to adherence (15,16,17,18), are targeted through improved LHW skills in patient education and adherence counselling. Although evidence for communities of practice is poor (19), we include a peer mentorship network based on previous feedback from peer trainers to evaluate its potential role and cost implications.

The educational outreach component will employ on-site training, led by the TBLHWs trained as peer trainers, delivered to small groups of general LHWs (typically 5-10) who provide TB care. Sessions will use both didactic and interactive techniques including case based learning and role playing to convey TB and adherence knowledge, and counselling skills, and to allow for practice with the point of care tool, critical reflection, and exchange of ideas among LHWs. Topics include: TB transmission and treatment; common causes and consequences of non-adherence; approaches to support adherence and address non-adherence while maintaining a positive patient-provider relationship. Based on our previous study two sessions will be added and the training period extended by 1 month to allow more time for each topic, and a reference manual provided in Chichewa.

Peer Trainers will be trained over 5 days off-site by Lisa Puchalski Ritchie in English with the help of a socio-linguistic level interpreter. Training will include content and techniques for peer-training and supportive supervision. Peer trainers will be mentored by DI clinical staff during regular field visits conducted at HCs they provide support to. Based on knowledge user feedback from our earlier work, development of a peer-support network will be encouraged through quarterly in-person meetings bringing together peer trainers in each district, to share experience, offer peer-support and provide an additional opportunity for mentorship from the implementation team. To encourage development of the network, peer trainers will receive monthly phone credit throughout the study period. If effective this credit may be sustainable by the MOH particularly during the initial roll out, which is the most challenging time for new peer trainers.

Training

Peer trainers will provide a minimum of 8 sessions each lasting 60-90 minutes over a 4-month period, on-site during regular work hours, with all general LHWs providing TB care invited to participate. Extra sessions as refreshers or to train new staff will be left to the discretion of the peer trainers. Training materials and certificates of completion will be provided in English and Chichewa. Incentives will not be provided as training of general LHWs to assist with TB care is part of the TBLHWs job description, training will occur during regular work hours, and providing incentives would limit sustainability.

The point of care tool provided in Chichewa (English version attached), is a two-sided laminated flip chart point of care tool, that can stand on a desk or be carried during field visits. The patient side uses simple pictorials to illustrate a patient and TB bacterium's course through treatment and acts as an aid to LHWs in providing patient education and adherence counselling. The LHW side provides a reminder to trigger an adherence discussion during patient interactions and supports side-effect management and constructive approaches to addressing non-adherence. Based on our earlier work, a drug dosing reference will be added to the tool.

Control Group

LHWs in control sites will receive usual training at the discretion of the HCs' TBLHW; the content, format, and duration of which varies considerably and ranges from a 1-2 hour briefing on medication dispensing and form completion to a few days working alongside the TBLHW as they provide patient care. They will not receive access to the point of care tool or the peer network.

Outcomes:

The primary trial outcome of interest is proportion of cases successfully treated, defined according to the World Health Organization criteria (20), as the total number of cases cured and completing treatment. Secondary trial outcomes include: proportion of default cases (treatment interrupted >= 2 consecutive months) and proportion of successes among HIV co-infected cases.

Qualitative outcomes of interest include barriers and facilitators to implementation, scalability, sustainability, and to identify potential program improvements.

Participant Recruitment/Consent:

Two to four participants from each group (LHWs and Patients) will be selected in each data collection period from each district and a maximum of 2 from any one HC.

LHWs will be selected for interviews using mixed purposeful sampling. A list of trained LHWs compiled by the peer trainers will provide the initial sampling frame. LHWs will be selected from the list to represent the range of LHW characteristics in terms of gender, age, years of experience and HC characteristics (rural/urban). Three LHWs chosen to reflect the range of responses (positive to negative) in the first round of interviews will be selected to be interviewed at both study onset and conclusion. The study and research assistant will be introduced to the general LHWs by the peer trainers. LHWs will then be approached in person or by telephone if the selected LHW is not present on site at the time of the health center visit by the study RA using the recruitment script (appendix C).

Convenience sampling will be used to select patients/guardians for interviews. . Patients will be selected to represent the range of characteristics in terms of age, gender, and TB characteristics (new/recurrent, pulmonary/non-pulmonary). A research assistant will attend HCs on days identified by HC staff as typically busy. The research assistant will be introduced to patients by the LHWs working in the health center during health center visits. After being introduced the RA will approach patients in person using the recruitment script (appendix D).

LHW participants in the educational intervention are health center personnel, who receive routine training and supervision. LHWs in intervention sites routinely involved in care of TB patients will be encouraged but not required to attend training sessions. The educational intervention and point of care tool will be revised in collaboration with and approved by the National TB program (NTP) to ensure consistency with National TB treatment guidelines. As undergoing training is a routine expectation of health center staff and the training will be approved by the NTP, individual consent is not required for participation in the intervention.

Written informed consent will be obtained in person by the study RA prior to beginning the interview (appendix E and F). In order to ensure participant understanding, in addition to providing the consent form in Chichewa, the study RA will read through the consent form out loud. Participants will then be given an opportunity to read the consent form and to have any questions they may have answered by the study team. Once all questions are answered to the

participants' satisfaction, they will be asked if they wish to participate, and the form signed and witnessed. For patients under 18 years of age, consent will be obtained from their parent or guardian using the same process, and assent (appendix H) obtained for children old enough to participate in interviews after parental consent has been obtained

A copy of the consent form which includes contact information for the co-principal investigators, Dr. Sharon Straus and Dr. Puchalski Ritchie, and local Co-PI Dr. Monique van Lettow, both the St. Michaels' Hospital ethics review board and Malawi National Health Sciences Research Committee. Participants are free not to answer any question or to withdraw from the study at any time without penalty.

Data Collection:

Trial data will be collected at the end of the 1 year trial period. A digital copy will be made of TB registers from all included health centers at the end of the 1 year trial period. Digital copies will be password protected and stored on a secure server accessible only to the study team. Once double data entry and verification of the database is complete the digital copies will be destroyed.

Interviews will be conducted with LHWs and patients at 2 time points; in the first 3 months after training and in the last 3 months of the trial to assess barriers to implementation and sustainability. 2-3 LHWs will be interviewed both times, in order to capture change within and across individuals over time. Participants will be interviewed by a trained research assistant fluent in English and Chichewa, using a semi-structured interview guide (Appendix A and B) to ensure key areas of interest are addressed and to allow for emergence of novel themes. Interviews will be conducted in a private location (at or near the participants' health center) at a time convenient to participants, with interviews expected to last 30 to 60 minutes. Interviews will be audio recorded digitally using unique numeric identifiers only.

Training logs, quarterly peer trainer and mentorship meeting notes will be collected by the RA for analysis. No identifying data will be collected during the document review, with documents identified by unique numeric codes only.

Data Management:
No paper copies of the recruitment list will be maintained. The electronic copy of the recruitment list will be password protected and stored on an encrypted USB and secure server, maintained separate from the unique numeric identifier list, and accessible only to the principal investigators, a study co-ordinator and research assistant. The recruitment list will be destroyed once the study is complete.

Digitized health center TB registers will be password protected and stored on an encrypted USB and secure server. Identifying data (name, village name, and TB number) will be used to verify records from double data entry only. Once verified name, village name and TB number will be removed from the database, and records maintained using a unique ID number only. No personal identifiers will be collected from interview participants. Only unique numeric identifiers will be

utilized for audio recordings and transcripts. Audio recordings will be destroyed by the principal investigator once analysis is complete.

Consent forms, training logs, quarterly peer trainer and mentorship meeting notes will be stored in a locked cabinet in a locked room in dignitas international Malawi until transferred to li ka shing, and accessible only by (Co-PIs, study coordinator and research assistant). No identifying data will be released at any time, with results reported in aggregate form only. Electronic records including the trial outcome database, transcripts, training logs, quarterly peer trainer and mentorship meeting notes will be destroyed after 10 years.

Analysis Plan:

The primary outcome of interest is proportion of treatment successes at 1 year. Multilevel modeling will be used to compare proportion of treatment successes among control and intervention groups with analysis adjusted for correlation due to clustering and stratification. Multilevel modeling will also allow us to examine similarity and differences between and within district (strata) and healthcare center (cluster) outcomes. Analysis will be conducted on an intention to treat basis and performed using SAS and R statistical software.

Interviews will be conducted by a trained Malawian research assistant (RA) fluent in both English and Chichewa, and functioning at the level of a socio-linguistic translator (21). Interviews will be audio taped, transcribed verbatim, and translated by the RA who conducted the interview. Twenty percent of transcripts will be re-translated by a second RA as a quality check. Should discrepancies in conceptual equivalence be observed, all transcripts will be translated by a second interpreter and discrepancies resolved by consensus. Interviews and training log entries will be analyzed using qualitative content analysis. Two study team members will read and code the transcripts, training logs, and meeting reports, independently with discrepancies resolved through consensus. Nvivo 10 will be used to code and organize data into themes. Themes will be sought within and across individuals, participant groups, and data collection periods, to allow for assessment of change and emergence of themes over time. Results from qualitative data sources will be triangulated using the technique of integration, with data from all sources considered in detail to provide a more comprehensive understanding of the barriers and facilitators of sustainability and scalability of the intervention, and to use of the approach to address other gaps in care provided by LHWs.

Dissemination Plan:
Study findings will be submitted for peer reviewed publication and for presentation at appropriate international conferences. In addition, study findings will be disseminated to participants and stakeholders through presentation at a local meeting and a one page lay to be made available to participants and to be posted in the TB clinic of participating health centers.

Ethical Considerations:

Risks/Benefits:

There are no known risks to participation in this study. It is possible that LHWs may view the training sessions as an additional burden. However, we think this unlikely as training will occur

onsite during regular work hours, LHWs will be encouraged but not required to attend, and given the positive perceptions of the intervention in the pilot study and expressed need for additional training found in our formative qualitative study. It is possible that participants may be distressed by interview questions. In order to minimize this risk, interviews will be conducted at a time and location convenient to the participant. In the unlikely event that participants are distressed by the interview questions the interview will be immediately terminated.

Potential benefits to LHWs participating in the intervention include additional training and an opportunity to provide input into improving the intervention to better suit their needs. There are no direct benefits to patients participating in interviews, although they may appreciate the opportunity to provide input to allow for improvement of the intervention for the benefit of future TB patients.

Confidentiality:

No paper copies of the recruitment list will be maintained. The electronic copy of the recruitment list and digitized copy of the TB register will be password protected and stored on an encrypted USB and secure server, maintained separate from the unique numeric identifier list, and accessible only to the principal investigators, a study co-ordinator and research assistant. Digitized TB register records will be destroyed once data entry has been verified and the recruitment list destroyed at the completion of the study. Consent forms and training logs, meeting reports and mentorship notes, will be stored in a locked cabinet in a locked room. No identifying data will be released at any time, with results reported in aggregate form only.

Ethical Approval:

Ethical approval for this study will be obtained from the St. Michael's Hospital, and the Malawi National Health Science Committee.

Timeline:

The project will take approximately 24 months from start to finish including local dissemination. Based on our experience with the preliminary study we have scaled back the frequency of data collection for the present study and amended the timeline outlined below accordingly.

Timeline (month) & Deliverable
1-4 Finalize revisions, pilot new tool, train study team and peer trainers, randomize HCs
5-8 LHW training
9-18 Data collection, 4 quarterly meetings, initial qualitative data analysis
19-24 Finalize qualitative, quantitative and economic analysis; report and manuscript preparation; dissemination meetings

Potential Challenges/Solutions:

Staff turnover can present a challenge in Malawi. For this reason peer trainers will be empowered to provide extra training sessions as needed, new peer trainers trained by DI mentors if needed, and multiple knowledge users (KUs) have been engaged at all levels of the ministry of health, to ensure continuity and facilitate engagement of new KUs as necessary. As staff shortages resulted in a loss of clusters in our previous study we have estimated our sample size conservatively based on a lower number of clusters than we anticipate will begin the study. As providing stipends is common in Malawi, not doing so may represent a challenge. But as this was a minor issue in our preliminary study and is in keeping with recent policy changes in Malawi we do not anticipate this will be a significant issue.

Significance of Results:

Despite availability of effective treatment, TB has a substantial impact on mortality in Malawi and other LICs. LHWs provide a potential solution to addressing the severe healthcare worker shortages and high TB burdens in these settings. However, to date expansion of the LHW cadre and task shifting of outpatient TB care in Malawi, has failed to achieve the desired impact. Our project aims to refine, implement and evaluate a knowledge translation intervention previously piloted in a single district in Malawi, designed to improve uptake of evidence into routine practice of LHWs providing TB care in Malawi. Given the increasing role of LHW in LICs, approaches to addressing knowledge gaps among LHWs through adequate training and supervision are essential to improving health outcomes.

The results of this project will inform the efforts of the Malawi Ministry of Health's National TB control program who are keen to implement the program nationally if proven effective. In addition, this project has potential to generate principles that will inform programs to improve practice in other areas of care provided by LHWs in Malawi and in other LICs.

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