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Contact screening and management in a high-transmission MDR-TB setting in Papua New Guinea: Progress, challenges and future directions

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Daru, South Fly District, Papua New Guinea is a high transmission setting for multidrug-resistant tuberculosis (MDR-TB). An emergency response by the Government in 2014 established a high-quality model for treatment and care. Household contact screening and management commenced in 2016 with TB preventive treatment (TPT) for well young child (<5 years) contacts of people with drug-susceptible TB and later expanded to young child contacts of MDR-TB. The model of care is community-based and led by non-specialist health workers, under supervision. An electronic medical record system supports care, reporting and operational research. Community engagement and education has been central, with a concerted focus on peer-led counselling and patient-centred services to improve TPT uptake and completion. Challenges include the application of households as the unit of intervention for detection of active TB and TPT provision. Our implementation experience in Daru has highlighted significant population mixing dynamics with most transmission likely occurring outside the household. We propose a community-wide screening approach with the provision of TPT based on testing to include older children, adolescents, and young adults. As there is the possibility of MDR-TB infection irrespective of the drug susceptibility of the household index case, a novel option is a combination TPT regimen of 6 months of daily isoniazid and levofloxacin (6HLfx). A sensitive aged-related

algorithm to detect and exclude active TB is being developed. Ongoing community engagement, quality data systems with operational research to evaluate approaches are critical in high transmission MDR-TB settings.

KEYWORDS

tuberculosis, contact management, multidrug-resistant TB (MDR-TB), Papua New Guinea, contact screening, implementation research

Introduction

Tuberculosis (TB) is the leading infectious cause of morbidity and mortality in Papua New Guinea (PNG) (1, 2). The emergence and increasing transmission of multidrug-resistant TB (MDR-TB) is a major challenge (3). On Daru Island in the South Fly District of Western Province, PNG, there is an unprecedented MDR-TB outbreak with a TB notification rate of 2,021 per 100,000 for all TB and 594 per 100,000 for MDR/RR-TB (rifampicin-resistant) in 2015 (4, 5). In 2014, the PNG National Department of Health and Western Provincial Health Authority (WPHA) initiated an emergency response to MDR-TB, which has resulted in the stabilisation of TB notifications, improved treatment outcomes and a reduction in TB-related mortality (5, 6). A description of the geographical, social and demographic context in Daru, which is located in the transboundary region between PNG and the Australian Torres Strait, has been detailed elsewhere (7, 8).

A comprehensive community-based model of care for TB was established through the introduction of evidence-based practice, with significantly improved outcomes and introduction of novel tools including bedaquiline-containing treatment regimens (5, 9, 10). Community engagement and patient-centred support services have been central to delivery of care (11). An electronic patient-level medical record system (EMRS - Bahmni, Thoughtworks) was implemented in 2016 to support quality patient care, program monitoring and operational research (5, 9). The screening and management of household contacts of people with TB commenced in 2016. TB preventive treatment (TPT) for well young child (<5 years) contacts of drug-susceptible (DS) TB index cases was introduced in 2017 and extended to those of MDR-TB index cases in 2019 (12).

In Daru, as in many other high-transmission and resource-limited settings, best practice strategies and tools for TB and MDR-TB are often under-utilised or not prioritised (13). Active case finding through contact screening and TPT for eligible at-risk contacts is a programmatic priority. However, application to high transmission MDR-TB settings presents additional challenges that require specific considerations and novel approaches. Table 1 summarises the current approach, challenges and solutions for contact screening and management in Daru, PNG.

Current approach to household contact screening and management

In Daru, a dedicated public health TB Team consisting of a health extension officer (an auxiliary medical officer), nursing officers, community health workers and health promoters conduct contact screening for all newly detected bacteriologically confirmed pulmonary or extrapulmonary TB under the supervision of a medical officer. Following verbal consent by index cases or their guardian and the household head, contact screening occurs at the household level. Education is provided by trained health promoters to household contacts, who are defined as any person who lives in the same house as the index case within three months prior to diagnosis, including spending time during the day. Contacts with a positive symptom screen are referred to the TB diagnostic clinic for investigation and asymptomatic young child contacts to the TPT clinic. Young children are also screened for malnutrition which is managed according to local guidance and includes empiric treatment for soil transmitted helminths. Screening and management are provided by non-specialist nursing community health worker teams, in a community-based model of care (decentralised clinics) following standard operating procedures.

Detecting active TB in contacts

TB detection with treatment of disease is a critical role of contact screening and management along with determining eligibility for TPT. In Daru, there is a TB diagnostic clinic in the hospital where contacts with TB-related symptoms are referred for further investigation including chest radiography (CXR) and appropriate specimens such as sputum or lymph node aspirate for Xpert Ultra as per PNG and World Health Organisation guidelines (14). If RR-TB is detected, a specimen is

sent to the national laboratory for culture and drug-susceptibility testing and molecular assays for early diagnosis of fluoroquinolone-resistance. Gastric aspirate and/or stool samples for Xpert Ultra are taken from symptomatic child contacts unable to expectorate sputum. Asymptomatic contacts are not routinely referred for investigation, including asymptomatic young child contacts who are eligible for TPT.

TB preventive treatment

The provision of TPT to eligible household contacts is widely recommended but implementation in resource-constrained settings remains limited (1, 15). TPT should be routinely offered to well young child (<5 years) household contacts of people with confirmed or presumptive pulmonary DS-TB (16). The protective efficacy of TPT is well established (17) and the recently recommended shorter regimens are associated with high rates of completion and very few adverse events (16). The program in Daru was the first in PNG to systematically introduce a community-based model of TPT in 2016 using 6 months of daily isoniazid (6H) for young child contacts. A TPT regimen of 3 months of daily rifampicin and isoniazid (3RH) – recommended by WHO in 2018 – has been associated with high uptake, completion and safety in young child contacts under programmatic conditions in resource-limited settings (18). The availability in PNG of dispersible, child-friendly combined formulations for active TB since 2016 (19), led to the

TABLE 1 Contact screening and management – current approach, challenges and solutions in Daru, PNG 2017 - 2022.

Program Area	Approach to date	Challenges and considerations	Solutions and future directions
Model of contact screening and management	• Community-based (decentralised clinics) • Non-specialist public health team • Health promoters and education • Integrated screening for malnutrition and treatment for helminths in children <5 • Standard monthly follow up, including education and counselling if required	• Human resource shortage • Operational interruptions to CXR, laboratory and internet • COVID-19 impacts led to suspension of contact investigation • Large multigenerational households and contact networks (kinship, visitors) – definition of household	• Community-wide screening: detect, treat, prevent approach with evaluation • Task-shifting to nurses and community health workers • Technical partner implementation support • Households as unit of intervention
Detecting active TB	• Referral to hospital, dedicated TB diagnostic service • Gastric aspirate, lymph node aspirates and stool samples performed for mWRD e.g. Xpert Ultra • Chest radiography (CXR)	• Excluding active TB in children and adolescents • Optimal use of CXR – as abnormalities require follow-up	• Excluding active TB in children and adolescents with sputum for mWRD and CXR • Optimal use of CXR, consider in all >10 or >15 • Computer-aided detection of CXR >15
TB Preventive Treatment (TPT)	• TPT to child contacts <5 (and people living with HIV) • Shorter TPT regimens: 3RH • 6Lfx if evidence of infection (TST positive)	• Household exposure may not correlate with resistance of infecting strain as transmission occurring outside the household and multiple index cases • Who to test for TB infection • Optimal TPT for a high MDR-TB setting • Fluoroquinolone resistant exposure	• TPT for TST positive in 5-34 years • TPT for <5 years according to household exposure • Novel combination regimen with 6HLfx • Individualised approach to fluroquinolone resistant exposure
Community education & patient education and support	• Community education and health promotion campaign to explain "sleeping TB" (TB infection) prior to TPT service initiation • Peer counselling model. With family based care • Visual tools and aides (education games) • Child-friendly space in TPT clinic	• TPT for the well • Structural barriers – poverty, low health literacy, overcrowding, food insecurity, • Stigma and trust • Mobile population	• Community advisory group to co-design public health activities and education materials • Engagement of priority populations • Continue peer-led model • Person-centred care
Program monitoring and data systems	• Paper-based household mapping tools for contact investigation • Electronic medical record system for data entry, management, reporting and analysis •Cascade of care indicator set (individual or longitudinal)	• Comprehensive guidance on tools, definitions and processes for contact screening and management not available • Resources required to support EMRS • The need for re-identification across multiple health interactions for care (no ID system)	• Continue EMRS and cascade reporting • Unique identifiers: health book with ID and verbal ID. Biometrics not feasible. • Cascades of care for quality improvement

mWRD, molecular WHO-recommended rapid diagnostics; DS, drug-susceptible; MDR/R, multidrug-resistant/rifampicin-resistant; RH, rifampicin and isoniazid; Lfx-levofloxacin; TST, tuberculin skin test; CXR, chest radiography; CAD, computer-aided detection; TPTTB, preventive treatment; EMRS, electronic medical record system; ID'identification.

successful implementation of 3RH for young child contacts of DS-TB in Daru from 2019.

In Daru, up to 20% of incident TB is MDR/RR-TB (5). TPT as 3RH or 6H may not be protective for child contacts of MDR-TB and is not recommended in that context (16). Furthermore, known exposure to DS-TB does not necessarily determine that infection is limited to a drug-susceptible strain only (20, 21). The optimal TPT regimen following infection with MDR-TB is unknown. A regimen that includes daily levofloxacin for at least six months (6Lfx) is widely used. Observational evidence from a number of settings suggests that a fluoroquinolone-based TPT regimen in MDR-TB contacts with evidence of TB infection (TBI) can substantially reduce the risk of developing MDR-TB, and with no significant safety concerns (22–26). The findings from two randomised-controlled trials of 6Lfx for MDR-TB contacts are expected in 2023 (27, 28).

The use of TPT in MDR-TB contacts requires an assessment of potential benefit versus risk, and benefit is greatest in contacts with infection (17). In 2019, tuberculin skin test (TST) was introduced in Daru to determine eligibility for 6Lfx as TPT for young child contacts of index cases with bacteriologically confirmed MDR-TB (without fluoroquinolone resistance) as part of a pilot project. This age group was selected as being high risk for disease due to care-giving relationships and high likelihood that exposure occurred in the household of the index case. A similar model of implementation was used as for 3RH for young child contacts of DS-TB, with the addition of TST. An operational research protocol with ethical approval was obtained and following informed consent, young child contacts with a positive TST and no evidence of disease were offered 6Lfx. To date, an effective model of care has been established with high uptake and completion.

Community engagement and patient education

Community engagement and education is critical to support contact screening and management, and especially to support TPT uptake and adherence given that this requires giving medication daily for months to a child or adolescent who is well. In Daru, several approaches are utilised to deliver education to people on treatment, their families and the wider community. An international community-based organisation has been providing TB health promotion and social mobilisation activities since 2011, focussing on enhancing detection and treatment support for active TB (6). A peer counselling model was introduced in 2017 involving People who have been Affected by, Living with or having Survived TB, known as PALS, who are trained and mentored to provide education and counselling support (11). The counselling program initially focused on support for people on treatment for active TB and expanded in 2018 to include families of children on TPT.

Locally tailored education materials including visual tools were developed, tested with community, and guides created for standard counselling sessions scheduled at key points of treatment. A child-friendly space with activities was initiated at the TPT follow-up clinic. Counselling and education are provided in the family's preferred language where possible. Due to the limited health literacy and linguistic diversity (>3 languages) of the people South Fly District, visual tools and aides have been important. The term "sleeping TB" was used to explain the concepts of TBI. Community education and health promotion campaigns to increase understanding of "sleeping TB" and TPT were conducted including promotion from the town mayor and local leaders, public education sessions at churches, schools, sports events, community locations and local radio. The above measures have contributed to high rates of adherence and TPT completion.

Program monitoring and data systems

Monitoring and evaluation of contact screening and management programs are essential. However, comprehensive guidance does not exist regarding tools, data definitions or processes for programs to implement contextually adapted solutions. The WHO has defined minimum data and indicator definitions for TPT and the Zero TB Initiative has outlined a comprehensive set of indicators for the search-treat-prevent approach (29, 30). The EMRS in Daru was adapted to include modules for contact screening and TPT in 2018. A household mapping tool that documents investigation of all close contacts of an index case is used as previously described (12). The public health team records patient data using paper-based records. A data entry team subsequently enters this data into the EMRS. Contact screening and management is monitored using a cascade-of-care framework for TB detection and prevention. The EMRS enables reporting of an individual-level cascade, rather than aggregate. Resources required to support the EMRS, including information technology expertise, programming skills and data entry capacity, are provided through partner support. Despite challenges, implementation has been successful, with the data system monitoring TPT uptake and outcome.

Implementation challenges and considerations

Operational challenges include a chronic shortage of health care workers, interruption of CXR services, laboratory reagents and power and internet outages. The availability of international partner support has been critical to the TB program in Daru since 2011. Adopting a community-based model with mobile

teams and task-shifting from medical and para-medical staff to nurses and community-health workers with training and technical support from partners has helped to address human resource issues. The COVID-19 pandemic has had a major impact on the delivery of TB services. From March 2020 until April 2022, contact screening was suspended initially due to public health restrictions and infection risks and subsequently health workforce shortages. Programmatic focus over this period was active TB treatment and care with case-finding limited to facility-based only (passive). Household contact screening and management restarted in April 2022.

Daru, and South Fly District have significant particular challenges in the social determinants of health which contribute to increased risk of TB transmission, with one of the highest measures of household poverty in the region, low levels of health literacy overcrowding food insecurity and low access to health services due to service availability, remoteness and lack of trust (7) (8). The TB program has had a concerted focus on community engagement, health promotion and patient-centred services. A major challenge has been identifying and reaching households which has been successfully addressed through the engagement of community leaders, household heads and community education. This patient and family-centred approach has built trust. Timely referrals for eligible TPT candidates for pre-initiation counselling also reduced delays in time to initiation of TPT. In the early implementation of TPT for young children, adherence issues were noted prompting an exploration and development of solutions for contributing issues through counsellors.

A Community Advisory Group, self-named TB Nanito Kopia Kodu (the Voice to Kill TB Forever) was formed from community consultations in late 2019 with members representing key stakeholder groups (e.g. churches, schools, businesses, key populations). The group's primary focus is providing community input and co-design for TB public health activities, including the development of community education materials and models to reach key populations such as adolescents and students, working adults (not present at home), prisoners, people with disabilities and the elderly. Accordingly, a comprehensive community education campaign has been developed with a participatory approach involving training of representatives from key populations.

Re-identification of individuals during multiple episodes across the screening and prevention cascades of care has been a particular challenge due to poor civil registration coverage (31). In PNG, people may give different names, age and residence from visit to visit with addresses not specific enough. Paper-based recording at multiple points of care also contributes to the problem by making it difficult to check a patient's details against existing information. The linkage of contacts to multiple index cases needs to be reconciled for reporting. This is currently addressed through local health worker and community knowledge of households and engagement *via* peer counsellors. Biometric systems have been proposed as a solution for patient identification, but cost, complexity and acceptability are barriers to implementing them. An immediate solution is patient-held records, such as health books or a card that can be issued and used to identify patients. However, these may get lost or not brought to patient visits. We have designed a potential solution for re-identification at low cost that supplements patient-held records with a memorisable unique identifier consisting of three common objects, represented with images. Even partial recall of this identifier can aid re-identification.

The primary challenge in Daru is the application of the household as the unit of intervention for contact screening and to deliver post-exposure management including detection of active TB and TPT. This is both from an implementation perspective and the fact that households may not be the optimal unit of intervention for timely detection of active TB and identifying those at risk of recent exposure for TPT (32, 33). The socio-cultural context in Daru, as elsewhere in PNG, involves large multi-generational family structures based on kinship. However, there are some unique features with significant overcrowding in settlements and frequent travel between mainland villages and Daru Island, often for extended periods of time. This results in large "households" with complex family structures and population movement. Therefore, the operational household contact definition used is broad and includes those who have spent more than one night in the household.

Our experience in Daru is that most transmission is likely occurring outside the household, as noted even in children in other high-incidence settings (32). The likelihood of exposure and infection occurring outside of the household increases with age. Adolescence is a peak age for close and casual social contact and so in a highly endemic setting such as Daru, the majority of the population may be infected by adulthood (34). TST testing in MDR-TB household contacts in Daru has demonstrated a high prevalence of infection similar to reported elsewhere (35). The majority of TB and MDR-TBnotifications are in older adolescents and young adults, with around 70% of TB notified in those 15-34 years (5). Furthermore, with large household sizes and a very mobile population, an individual can be exposed to multiple index cases concurrently, including DS and MDR-TB. Therefore, consideration of alternative approaches in Daru to household contact management are warranted.

Future directions – moving beyond household contact screening and management

Until recently in high TB transmission settings, recommendations for TPT have been limited to specific high-

risk groups for disease such as young child contacts and people living with HIV (16). Whilst important in reducing tuberculosis-related morbidity and mortality in these groups, the impact of TPT on community transmission by preventing new cases is small, likely negligible for young child contacts (32, 36). Therefore, a community-wide strategy has been considered in the design of an enhanced public health intervention and model of care that aims to increase TB detection and treatment while providing TPT to a broader population to reduce transmission in addition to TB morbidity and mortality (37, 38). Figure 1 outlines our considerations for a comprehensive detect-treat-prevent strategy in a high TB transmission setting by age.

First, programmatic scaling-up of contact screening and management that includes older children, adolescents and young adults in the community is planned. The 2020 WHO recommendations include a wider age range of TPT options for HIV-uninfected contacts (16). We therefore propose community-wide TST testing for Daru residents aged 5-34 years irrespective of household contact, with TPT provided to those with infection and no evidence of active TB, as part of a comprehensive approach to complement active case-finding. The model of community engagement and implementation described above will be applied and the household will be the unit of intervention. The application of a community-wide systematic screening for case detection aligns with recent WHO recommendations for settings with a TB prevalence of 0.5% such as Daru, and is based on new evidence of public health benefit (39). The decision to provide TPT for 5-34 years with infection is based on the following considerations: high-risk age group for active TB; high risk age group for transmission in the community; and lower risk of isoniazid-related toxicity due to TPT compared 35 years and older.

Second, in high transmission MDR-TB settings, consideration of a TPT regimen for older children, adolescents and adults that considers the possibility of infection with an MDR-TB strain irrespective of the index case is needed. A novel option is a combination TPT regimen of 6 months of daily isoniazid and levofloxacin (6HLfx) for 5–34 year-olds with evidence of infection and no active TB. This TPT regimen is chosen to effectively treat infection with either DS or MDR-TB as a positive TST cannot determine drug susceptibility. Whilst exposure to both is common, the majority (>80%) of TB in Daru is DS-TB. Isoniazid or rifampicin may not effectively treat infection with an MDR-TB strain. While it is plausible that levofloxacin alone may cover treatment of DS in addition to MDR infection, there is no definitive evidence of efficacy at present. There is circumstantial evidence that isoniazid may also be effective in the treatment of MDR infection (20). Rifapentine is currently not available in PNG and a three-drug regimen may have additional adverse effects over two. Therefore, isoniazid is included in the proposed regimen. Young child (<5 years) contacts can be managed as per the strain of the index case. The optimal approach for management of fluoroquinolone-resistant TB infection is uncertain and should be individualised.

Third, it is critical to exclude active disease especially in adolescents and adults. An optimal age-related contact management algorithm is required to mitigate the risk – individual and public health – of generating resistance including to fluoroquinolones. This risk needs to be negligible, similar to isoniazid and rifampicin (40, 41). In addition to symptom screening, the inclusion of CXR and sputum Xpert Ultra in the algorithm will provide high sensitivity for detection. The optimal age-related use of chest-radiography in asymptomatic, HIV-uninfected people aged 5–34 years to rule out active TB before TPT is unclear. WHO guidelines recommend that asymptomatic young child contacts or PLHIV do not require CXR before TPT initiation. It is likely that the same approach could be applied to all well children (<10 years) with infection without risk of not detecting sub-clinical disease. This is the approach that is being considered in Daru. In addition to a negative symptom screen, CXR will be routinely included in screening adolescents and adults (≥10 years), as it is

	< 5 years	5-14 years	15-34 years	35-54 years	55 years +
Potential impact on transmission	Minimal +/-	+	+++	++	+
Symptom screen	For all ages				
CXR if symptom screen negative	Not recommended	**Uncertain**	Recommended		
Test (sputum) for active TB and resistance with mWRD	For symptomatic and abnormal CXR		For all – symptomatic, CXR abnormal and consider in asymptomatic if able to provide sputum		
Test for infection for TPT initiation	Not required	Recommended			
TPT indicated	If TB-exposed and asymptomatic	If evidence of TB infection		Uncertain	
TPT regimen	**3RH if DS-TB exposure 6Lfx if MDR/RR-TB exposure**	**Consider combination regimen in high MDR setting: 6HLfx**			
TPT safety	+++	+++	++	+	+

FIGURE 1
Considerations for a comprehensive detect-treat-prevent strategy in a high MDR-TB transmission setting by age. mWRD, molecular WHO-recommended rapid diagnostics; DS-TB, drug-susceptible tuberculosis; MDR/RR, multidrug-resistant/rifampicin-resistant tuberculosis; RH, rifampicin and isoniazid; Lfx, levofloxacin; CXR, chest. NB. Different considerations apply in high HIV transmission settings and special populations.

important to exclude active TB with a sensitive algorithm prior to TPT initiation. Computer-aided detection of CXR is recommended for TB screening in people ≥15 and this will also be used for screening young adolescents (10-14 years). This is because adolescents with TB commonly present with adult-type disease such as with cavitation, most critical to rule-out before initiating TPT.

The significant health individual and health system burden of ongoing MDR-TB transmission is a compelling argument for the potential benefit of the community-wide approach to detect, treat and prevent DS and MDR-TB and likely outweighs potential individual treatment risks with 6HLfx (13, 42). Operational mixed-methods research will evaluate the impact, acceptability, feasibility and cost-effectiveness. The intervention will build on the local leadership, programmatic experience and platform of innovation that has been established in Daru. Ongoing engagement and placing the affected community at the centre of the response remains critical to success and towards ending tuberculosis in high-transmission settings.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material. Further inquiries can be directed to the corresponding author.

Author contributions

SM, SG and GKH contributed to conception and design of the study. GD, SB, TK, GC, SF, AM, JG, CM, TM, SU, SG and SM developed sections of the manuscript. SM wrote the first draft of the manuscript. All authors contributed to manuscript revision and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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