How to eliminate tuberculosis 1

Data for action: collection and use of local data to end tuberculosis

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This is the first in a Series of four papers about how to eliminate tuberculosis

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Accelerating progress in the fight against tuberculosis will require a drastic shift from a strategy focused on control to one focused on elimination. Successful disease elimination campaigns are characterised by locally tailored responses that are informed by appropriate data. To develop such a response to tuberculosis, we suggest a three-step process that includes improved collection and use of existing programmatic data, collection of additional data (eg, geographic information, drug resistance, and risk factors) to inform tailored responses, and targeted collection of novel data (eg, sequencing data, targeted surveys, and contact investigations) to improve understanding of tuberculosis transmission dynamics. Development of a locally targeted response for tuberculosis will require substantial investment to reconfigure existing systems, coupled with additional empirical data to evaluate the effectiveness of specific approaches. Without adoption of an elimination strategy that uses local data to target hotspots of transmission, ambitious targets to end tuberculosis will almost certainly remain unmet.

Introduction

The fight against tuberculosis is entering a new era, moving from one of control to one of attempting to end the tuberculosis epidemic. The international donor and policy community have embraced targets of 90–95% reductions in incidence and mortality by 2035, relative to 2015.[1] One important component of such so-called epidemic-ending approaches is an increased focus on local-level strategies, which have been instrumental during elimination of infectious diseases ranging from smallpox to polio.[2–5] The successful elimination of disease epidemics has typically involved two important components: systematic reporting of every case and identification of disease clusters or hotspots at the local level where ongoing transmission occurs. These components enable the documentation of disease trends in each community and the subsequent targeting of resources to where they are needed most. Local strategies for tuberculosis could, for example, tailor diagnosis and treatment of infection to subpopulations that are at highest risk of disease progression [6] or target case-finding to stop transmission in high-incidence populations.[7] Some countries are starting to use subnational trends to inform more tailored approaches; however, to end tuberculosis in a 20 year timeframe, this trend must be accelerated and focus increased on local empowerment with centralised (national and global) support.[8,9]

Since the 1993 adoption of a widely accepted approach to tuberculosis treatment known as DOTS (directly observed treatment, short-course), a standard set of clinical, demographic, bacteriological, and treatment outcome data have been collected and aggregated by national tuberculosis programmes and subsequently reported to WHO.[10,11] This approach, although essential to inform country-level and global estimates and to monitor the high-level progress of strategies such as DOTS, has not emphasised the use of existing data (or collection of additional data) to identify sites of ongoing transmission and target local responses accordingly. Local tuberculosis epidemics differ in intensity, drivers, and key characteristics, and approaches that are effective in some hotspots (eg, informal urban settlements) might not work in others (eg, prisons or rural villages with poor access to care). Without high-quality data and infrastructure at the local level (and support from national and global entities) to inform more locally

Key messages

- Tuberculosis epidemics, like those of other infectious diseases, vary largely across different geographical regions; to end epidemics in high-burden areas, control efforts will need to be tailored to local conditions
- To design interventions that effectively combat tuberculosis, national control programmes should shift from a centralised approach in which local data are deposited into national databases for aggregated analyses, to a bidirectional one in which local partners have the capacity to collect and analyse data and then use those data to design locally responsive interventions
- This shift requires local tuberculosis programmes to make better use of existing data, expand routine data collection, and make informed use of targeted surveys
- These efforts also require the modernisation of data collection and storage systems, substantial financial investment in infrastructure and human resources (including the use of mobile technology and social media), and the reallocation of resources to support local decision making
- Programmes will need to develop the necessary analytical and support infrastructure to measure the effect of local interventions and disseminate these findings within the national programme

responsive strategies, the goal of ending tuberculosis worldwide will not be achieved.

Awareness is building of the importance of local data and capacity, but action is not being taken fast enough. WHO has championed the need for national programmes to respond to setting-specific differences, according to the scale of the epidemic in the country.[12] Three specific steps will accelerate this process (figure 1). First, countries must better use existing data on tuberculosis case notifications, risk factors, and treatment outcomes to inform local interventions. Second, national and global systems should augment the set of standard, routinely collected data with additional data elements (eg, geographical information, drug resistance, and risk factors) to target resources better, while ensuring that this additional data collection is feasible. Third, programmes must build capacity for the periodic and focused collection of novel data components (such as targeted surveys), contact investigations, and sequencing data, to inform local policy decisions.

In this, the first paper in a Series of four about how to eliminate tuberculosis, we describe how existing data and analysis systems could be improved to enable these three steps, highlighting the benefits and challenges in transitioning to a locally focused agenda to end tuberculosis (table 1).[12–16] Combined with strategies to interrupt transmission (see Series paper 2[7]), treat latent tuberculosis (see Series paper 3[6]), and improve social conditions (see Series paper 4[17]), use of local data and infrastructure to target interventions appropriately could form the basis for a coherent strategy to end tuberculosis from both a top-down and a bottom-up direction.

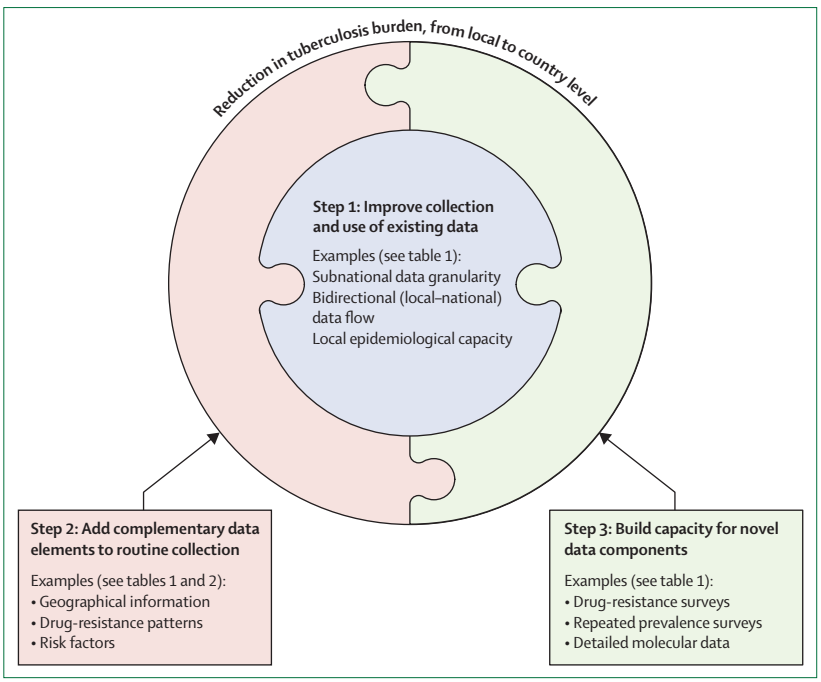

Figure 1: **A three-step approach for leveraging data to end tuberculosis**
To build locally tailored responses to effectively combat tuberculosis, three interlocking categories of activities are required. Effective local tuberculosis responses must start with improving the collection and use of existing data (blue centre), onto which additional data elements can be added (in peach). A third essential component involves building capacity to collect and use novel data at all levels of the health-care system (in green). Employing these three categories of activities in a multi-tiered and bidirectional fashion (as depicted in figure 4) should result in tuberculosis control policies that are more data driven and thus more likely to be effective.

Improving data collection and analysis

Step one: improving the collection and use of existing programmatic data

Routinely collected data for tuberculosis vary substantially in scope and detail between countries. WHO recommends a minimum set of variables, comprising age, sex, geographical region, previous treatment, smear microscopy result, anatomical site (pulmonary or extrapulmonary), and treatment outcome, which are ideally linked to unique patient identifiers.[13,18] In many settings, data for HIV and exposure to high-risk congregate settings are also routinely collected. Although WHO recommends the use of secure, self-contained electronic systems, paper forms are still predominantly used.[13,14] Thus data analysis is often delayed until entry into a central country wide database is completed, reducing its usefulness to inform realtime programmatic decisions.[14] When such data are rapidly incorporated into policy, results can be dramatic. For example, in 2008, the tuberculosis programme in Lesotho found that more than 90% of patients diagnosed with tuberculosis were HIV seropositive.[19] The Ministry of Health, in collaboration with Médecins Sans Frontières, rapidly scaled up and integrated decentralised tuberculosis–HIV care in response. As a result, the number of adults on antiretroviral therapy (ART) in the programme doubled over 4 years, and the incidence of HIV-positive tuberculosis decreased by about 40%.[19,20]

Of particular importance to interrupting transmission is more focus on childhood tuberculosis, which is currently greatly underdetected and can serve as an important marker of ongoing transmission.[21–23] Better systems for the detection of paediatric tuberculosis and rapid notification when childhood cases rise higher than a certain threshold might not only inform specific interventions such as household contact tracing and preventive therapy for children, but could also serve as an early detection system to identify transmission hotspots.[24]

Ultimately, centralised tuberculosis data collection and reporting systems must be designed not only to inform national policy changes, but also to build local capacity to create tailored responses at the community level. Examples exist in other infectious diseases, such as with polio surveillance in India, which showed lower vaccine efficacy in high-population-density districts with poor sanitation, thereby enabling the roll-out of a different vaccine that was better suited to these areas.[25,26] This ultimately contributed to the elimination of polio where national-level policies had failed.[27] Similar targeted approaches, which are often as cost effective as broader,

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	Current capacity	Potential improvements	Key challenges
Programmatic data	Strong systems for collection of aggregate data in many countries WHO guidance is available for surveillance and other systems[12-14]	Stronger systems for disaggregation of data at the subnational level Building internal capacity for epidemiological analysis and reporting to subnational tuberculosis authorities	Current incentive structures that prioritise national-level reporting Human resource constraints Infrastructure constraints (eg, reporting systems for surveillance) Little consistent data quality
Additional data that could be collected programmatically	Many clinics already informally collect additional data for internal quality control purposes	Routine data collection could expand to include patients' location, key risk factors, interactions with congregate settings, etc Increased autonomy and decision making capability at local clinics to decide data collection priorities Local stakeholders, who might have a better idea of interventions that are locally important, can be consulted in order to expand additional data collection	Standardised notification systems must be preserved in some form, but must balance the need for national reporting with local flexibility Local tuberculosis officials currently have little experience in collecting or using additional data Additional data must be able to be fed into large-scale tuberculosis elimination projects and compatible with national databases Routine (rather than targeted or time-limited) collection of additional data can be expensive and might compromise data quality
Specific surveys	Capacity to perform surveys for drug-resistant tuberculosis is increasing National prevalence surveys are being increasingly done WHO guidance is available for certain types of surveys[13,15]	Repeated surveys to better inform longitudinal analyses Routine surveillance systems that could feed back to national and subnational authorities Inclusion of data and reporting systems (eg, geographical data on drug-resistant cases) to inform local policies	Surveys can be very expensive, politically motivated, and not well integrated into existing routine tuberculosis efforts In-country capacity to do surveys without outside technical assistance is small Infrastructure for surveillance systems is often poor
Novel data	Some reference or academic laboratories can collect and analyse novel forms of data, such as the genetic distance between strains, to identify transmission events WHO guidance is available for some types of novel data[12]	Creation or adaptation of existing systems to allow for inputting of novel data Establishment of mechanisms for internal and external quality control Co-collection of other types of data (eg, social network data) must be improved to maximise the potential of novel data such as strain genotyping	IT (eg, data capturing and storage), laboratory (eg, infrastructure for culture, DST, and strain genotyping), and human resource capacity challenges need to be overcome to generate new types of data Storage and reporting of some types of novel data (eg, whole-genome sequence data) is not standardised
Systems for reporting and analysing data	Strong systems for reporting clinical laboratory data often exist, and could be adapted for epidemiological data BRICS and other middle-income countries have skilled (but highly centralised) capacity to perform epidemiological analyses Countries are increasingly moving towards individual-based electronic systems	Formal frameworks and how-to guides are needed to analyse data at a local level Better access to data and analytical support staff at the subnational or local level Better, automated systems for capturing new data on the ground in clinics (eg, electronic forms) Better integration of analytical expertise with other in-country disease control programmes Better systems for data sharing between local tuberculosis control programmes	Linkage of disparate IT systems (eg, for laboratory and patient data) Lack of human resource capacity to clean data and perform analyses, especially at the subnational level Lack of clear political, economic, or financial incentives to develop such capacity within countries
Empirical evidence to support local approaches	Reasonably strong evidence exists that tuberculosis incidence (including drug resistance) is heterogeneous at the local level Mathematical models suggest that local approaches might be more effective and efficient[16]	Programmatic evaluations and research studies could help to compare the effectiveness of locally targeted strategies against nationally standardised ones Cost-effectiveness analyses could evaluate whether the additional cost of local targeting provides sufficient health value to be justified	Generalisability of data from one epidemic and intervention to another is difficult Infrastructure and incentives (both organisational and financial) to collect such data are deficient outside of existing academic centres

IT=information technology. DST=drug-susceptibility testing. BRICS=Brazil, Russia, India, China, and South Africa.

Table 1: **Key elements of a data-driven, locally tailored approach to tuberculosis elimination**

untargeted interventions, will be needed to end epidemics of tuberculosis.[28–30]

Step two: routine collection of additional data to inform targeted responses

Although challenging in many settings, expansion of the minimum set of routinely collected tuberculosis data is essential to empower more locally responsive strategies.[12] Additional data include geographical information (eg, to assist with community-based follow-up, panel 1,[31] figure 2; or transmission-hotspot mapping, figure 3[32,33]), drug-resistance patterns (eg, for region-specific drug susceptibility testing algorithms and localised treatment regimens), and risk factors such as diabetes, smoking, or previous hospitalisation or imprisonment (eg, to inform local screening strategies).[34–36] For example, a surveillance study in Japan found high diabetes mellitus rates in some populations of elderly or homeless people with tuberculosis, thereby enabling clinics serving these individuals to do targeted screening.[37] Similarly, data from China showed a dramatic increase in the proportion of patients with tuberculosis that had recently migrated into Beijing, and that these patients rarely completed treatment.[38] This led to targeted case-finding and counselling to be carried out by clinics serving these communities. In table 2, we provide an illustrative list of

Panel 1: Data for action in Karachi, Pakistan

Interactive Research and Development, a local research organisation in Karachi, Pakistan, has used a range of electronic recording and reporting systems to improve access to and reporting from diagnostic and treatment sites.[31] For example, global positioning system (GPS) data have been used to identify the exact coordinates of private family practitioner clinics, public and private national tuberculosis programme (NTP) reporting centres, private laboratories, and pharmacies. All patients with drug-resistant tuberculosis or at high risk of loss to follow-up are mapped to approximate home locations with GPS-enabled phones, to inform assignment of community treatment supporters and to facilitate follow-up. For most of these patients, private clinics (red boxes in figure 2) are more accessible than the NTP reporting centre (NTP in figure 2) for scheduling of follow-up visits. These data have informed key programme decisions for targeted intensified case-finding, location of digital radiograph systems and GeneXpert machines, and recruitment of treatment supporters.

Figure 2: **GPS map of facilities and patient homes in Karachi, Pakistan (May, 2009)**
Illustrative example discussed in panel 2 showing coordinates of private family practitioner clinics, public and private national tuberculosis programme (NTP) reporting centres, and people with TB. GPS=geographical positioning system. NTP=national tuberculosis programme. TB=tuberculosis. Map data from Google, DigitalGlobe.

additional data that could be collected and used for local decision making.

In routine practice, tuberculosis programmes must weigh data quantity against quality and might therefore focus additional data collection on particular patient groups or during the roll-out of new initiatives. To encourage the collection and use of relevant data, policy makers and tuberculosis programmes should promote new frameworks that use local data collection as benchmarks for clinic performance. Local tuberculosis control authorities must have sufficient autonomy, funding, and oversight to obtain data and implement interventions that will be most responsive to their unique epidemics. Examples of strategies that collect additional tuberculosis data and link these to tailored interventions are multicountry projects such as ENGAGE-TB and TB-REACH.[39,40] Importantly, local data collection can reveal other issues (eg, comorbidities such as diabetes and malnutrition) that are important for tuberculosis control and will also need to be addressed in a targeted fashion. Better integration of care is needed to address these factors; targeting them can also help to drive organisational and operational changes to strengthen local health systems.

Step three: targeted collection of novel data

Routine data will always be limited to elements that can be collected during busy clinical practice, with tight programmatic budgets, and from patients who actually present to care. To take a more comprehensive step toward ending tuberculosis, these data must be occasionally augmented by additional investment in collecting non-routine information that can improve understanding of transmission and drug-resistance patterns.

Prevalence surveys estimate how many people have tuberculosis in a representative population sample.[9] Between 2009 and 2015, 23 countries are expected to have carried out tuberculosis prevalence surveys.[41] These surveys, with WHO guidance, can produce national (or occasionally subnational) estimates of the fraction of new cases with drug resistance, characterise broader patterns of transmission, and identify gaps in current control efforts.[13,15,42] Because surveys are expensive, logistically complex, and have relatively small sample sizes at the subnational level, they generally do not have resolution to inform local decisions. Innovative approaches to representative survey designs must therefore be considered.

One example of an alternative design in the case of drug resistance surveys is lot quality assurance sampling (LQAS).[43,44] LQAS can classify the risk of drug resistance among patients with tuberculosis at a subnational level with use of predefined thresholds of drug resistance.[45] Unlike traditional national-level drug-resistance surveys, LQAS surveys do not attempt to estimate the prevalence of resistance precisely. Instead, LQAS surveys classify areas as likely being above or below a threshold selected to guide local interventions. LQAS has shown, for example, that although Tanzania and Vietnam seem to have low multidrug-resistant (MDR) prevalence among new tuberculosis cases nationally, Vietnam has considerably subnational heterogeneity.[45–47] In particular, one province (Tây Ninh) had high MDR tuberculosis prevalence, which focused attention on areas closer to Cambodia, where MDR tuberculosis is more prevalent. Targeted surveys have also shown unusually high rates of MDR tuberculosis in some ART clinics and Tibetan refugee communities in India.[48,49] Similar methods, such as sentinel surveillance, have identified many patients with MDR tuberculosis from Somalia seeking treatment in Kenya.[50]

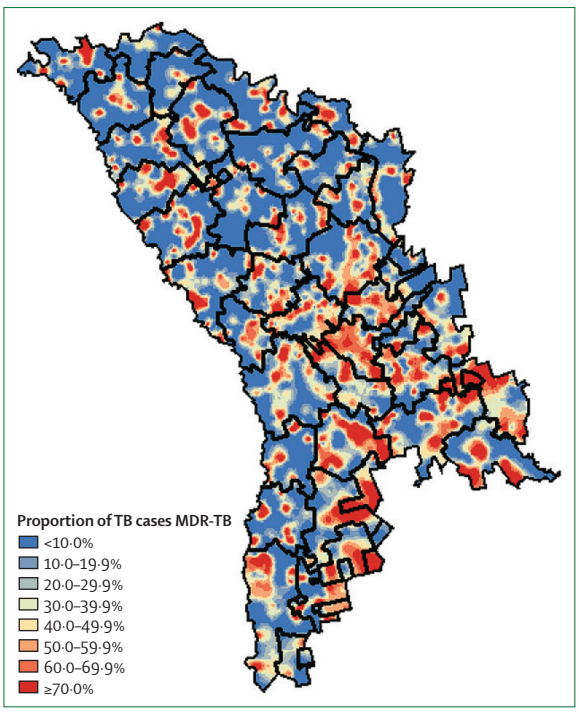

Figure 3: **Geographical hotspots of MDR-TB risk in Moldova**
Colours represent the proportion of previously treated TB cases with drug susceptibility testing data that are MDR-TB by location of residence. Maps such as this, which can help target intervention efforts and direct future research, represent the product of strengthening multiple aspects of the TB surveillance system. In the early 2000s, Moldova's TB programme updated the laboratory network, revised guidelines, and improved training to ensure universal drug susceptibility testing. Standardised reporting systems enabled more complete and accurate reporting of incidence, outcomes, and drug resistance, and a nationwide online database was introduced with access at every national TB facility.[32] Physicians and laboratory staff enter data (including routinely collecting location of residence) for individual patients with TB in realtime at the relevant points of contact. Data can then be synthesised into detailed maps of TB and drug-resistant TB, such as the one presented here, which can in turn be used to focus resources and efforts on regions of likely high ongoing transmission of drug-resistant TB (eg, see southeast represented in red). TB=tuberculosis. MDR=multidrug resistant. Reproduced with permission of the European Respiratory Society.[33]

Other potentially useful data sources are molecular data for strain types, transmission, and drug resistance.[51] Currently, such data are only collected broadly and systematically in resource-rich settings. For example, an analysis of US national surveillance identified which racial minorities are most likely to develop tuberculosis from recent transmission and a service in the UK has used molecular typing prospectively since 2010 to identify outbreaks and estimate the proportion and identity of MDR tuberculosis cases attributable to transmission.[52–54] Locally, such data can also be used to improve both contact investigations (which might be complemented by online social network data) and the laboratory methods used to diagnose drug-resistant tuberculosis (panel 2).[60] Newer technologies, such as whole-genome sequencing (WGS), can identify strains responsible for major outbreaks, uncover highly infectious super-spreaders, and help to understand the completeness of contact investigations.[51,61–63] Although not widely implemented, BRICS countries (Brazil, Russia, India, China, and South Africa) and other middle-income countries have capacity to collect and analyse molecular data, and WHO guidance exists about strain genotyping for tuberculosis surveillance.[12] Although WGS might be more challenging to implement, it can inform the development of simpler tests, which have been used in preliminary studies to infer transmission patterns.[64] Mobile technology can also help the collection of novel geospatial information. For example, human movement (measured via mobile phone towers) has been combined with high-resolution prevalence data for malaria in Kenya to show that migration from less-developed residential areas accounts for most new cases of malaria within urban centres.[65] Importantly, the usefulness of these additional data will always be small if they cannot also be easily captured and integrated into existing data systems.

Enhancing data systems

Systems for reporting and analysing data

An investment in surveillance systems for tuberculosis, including strengthening of WHO-supported electronic data collection systems, is needed to achieve greater local control of tuberculosis.[12,14] Maintaining a system that is sufficiently agile to be useful for heterogeneous patient populations and the levels of resource availability (eg, internet access) across all localities can be difficult. This difficulty is compounded by the long-term use of proprietary systems for which support might have ceased and the requirement by governments for a lengthy public tender process.[66] Implementation of flexible systems for a locally tailored tuberculosis response—especially in high-burden countries that often have extreme resource limitations, little political will, and the highest need for such systems among disenfranchised populations—will be no easier.

Benchmarks and performance indicators can facilitate the collection of standardised data and identification of surveillance gaps.[12–14] These benchmarks encourage tuberculosis programmes to assess the consistency of case definitions and national data in interactive workshops with stakeholders. Such benchmarks can be internal (eg, subtotals by age group equal the total number of reported cases) or external (eg, the percentage of new cases in subgroups, such as children, is comparable with similar countries). Although linking data across disparate electronic databases (eg, laboratory results and treatment information) is challenging, guidelines for the development of national electronic tuberculosis data systems are potentially useful for local system development.[14]

Potential improvements to existing systems

Existing systems might be improved by: incorporation of more local data; enabling the easy capture of additional setting-specific data; integrating with other disease

databases; and implementing features that enable rapid data analysis and linkage to intervention. Systems incorporating local data should permit the timely collection, reporting, and analysis of these data at all levels of the health-care system (figure 4). Crucially, these steps must be done while maintaining the capacity of existing systems to enable country-level reporting. This effort will require substantial new investments in human resource capacity (particularly epidemiological expertise) and technological infrastructure. Countries and cities are increasingly developing individual-based electronic data systems.[67–69] Mobile technology can also be combined with innovative methods to maximise case-finding by reimbursing tuberculosis control officers promptly or providing appropriate incentives to find additional cases.[67]

Importantly, these improved systems for local data should not only integrate with national systems but also allow for bidirectional data flow, facilitating the direct transfer of data between national to local level and control programmes. This information can also link into systems used in other sectors. For example, the INDEPTH Network provides support and guidance for the collection of community-level demographic and health-care information, which supplement the surveillance of non-communicable diseases in high-burden countries and is subsequently fed into national databases.[70,71] Data from both public and private sectors should also be considered for inclusion.[72]

If locally important data are to be analysed effectively, improved quality control and standardised best practice guidelines are required, especially for new types of data. Open-source tools are available to assist in the analysis of these data, whether, for example, it is to project the local impact and cost of diagnostic tests or to detect drug-resistance mutations from WGS data.[73,74] Wider availability and adoption of such methods could encourage the collection of local data and improve the analytical capacity of tuberculosis programmes; however, data might also need to be analysed at a more centralised level, at which analytical capacity is likely to be greater.

Unique patient identifiers are essential. Without these, linkage of routine clinical and laboratory data to those from targeted surveys, sentinel surveillance systems, and other novel data collection efforts will be challenging. This data linkage can facilitate pragmatic studies of the impact of interventions at a subdistrict level. In Brazil, data collected before and after the roll-out of Xpert MTB/RIF (a molecular test for tuberculosis and rifampin resistance) allowed for Xpert's effect on local case notification rates to be quantified and for poor-performing sites to be identified and targeted for further strengthening.[75] However, because the laboratory and treatment databases used their own internal identifiers, linking specific laboratory results with specific treatment outcomes was a challenge. Weak existing data structures have also made it difficult to generate empirical evidence for locally targeted approaches to tuberculosis control.

	Items
Drug resistance surveys	
Drug resistance diagnoses	Genotypic (eg, Xpert MTB/RIF) and phenotypic (eg, liquid culture) drug-susceptibility testing results, mutational analyses
Monitoring of disease severity	
Bacterial load	Smear grade, culture time-to-positivity, Xpert MTB/RIF cycle threshold values, LAM strip grade
Clinical test data	Chest radiograph, BMI, haemoglobin concentrations
Transmission mapping	
Strain genotype	MIRU-VNTR, spoligotype, RFLP pattern, WGS
Geospatial, location, and contact data	Administrative region (eg, district, city, and suburb), residential address, or GPS coordinates of residence; recent hospital admissions (name of hospital, duration, and reason for treatment); incarcerations or known tuberculous contacts
Risk factor analysis	
Comorbidities	HIV, diabetes, chronic obstructive pulmonary disease, pneumonia, diabetes
Occupational exposure	Health-care workers, miners
Substance use	Cigarette pack-years, AUDIT alcohol use scores, illicit narcotic usage

LAM=lipoarabinomannan. BMI=body-mass index. MIRU-VNTR=mycobacterial interspersed repetitive units–variable number of tandem repeats. RFLP=restriction fragment length polymorphism. WGS=whole-genome sequencing. GPS=global positioning system. AUDIT=alcohol use disorders identification test.

Table 2: **Possible data items to be collected on individual tuberculosis cases, in addition to the WHO minimum set of variables,[13] by purpose and data type**

Panel 2: Strain typing to inform the local scale-up of drug susceptibility testing (DST) in South Africa

The Western Cape province in South Africa, which has relatively strong drug-resistant tuberculosis surveillance infrastructure, has seen a change in drug-resistant tuberculosis strain diversity. Strains with an atypical Beijing genotype, which are historically scarce, have become dominant among patients with drug-resistant tuberculosis and are associated with clustered outbreaks of extensively drug-resistant (XDR) tuberculosis.[55] A series of molecular epidemiological studies[56–58] showed that these strains likely originated from an adjacent province (Eastern Cape), which has relatively weak DST surveillance infrastructure. These atypical Beijing strains in the Eastern Cape had an unusually high prevalence of inhA promoter mutations which, in addition to conferring low-level resistance to isoniazid (a key drug in the first-line regimen), also confer resistance to ethionamide (a key drug in the second-line regimen used to treat multidrug-resistant tuberculosis, but for which resistance was not routinely tested). The effectiveness of the second-line drug regimen was thus substantially weakened, and atypical Beijing strains were programmatically selected to evolve into XDR tuberculosis, which subsequently entered the Western Cape, likely via the large migrant population. Molecular tests are now used to identify inhA promoter mutations in the Eastern Cape. An alternative drug can thus potentially be substituted for ethionamide to limit the emergence of XDR tuberculosis; however, in practice, this is not yet widely adopted.[59]

Despite their clear benefits and potential cost savings, improvements to these systems need substantial investment.[76–78] To justify such investment, strengthening of the empirical evidence base is essential.

Empirical evidence for local approaches

Little evidence has been provided for the effectiveness of the types of locally targeted approaches described above for tuberculosis control. Nevertheless, targeting of

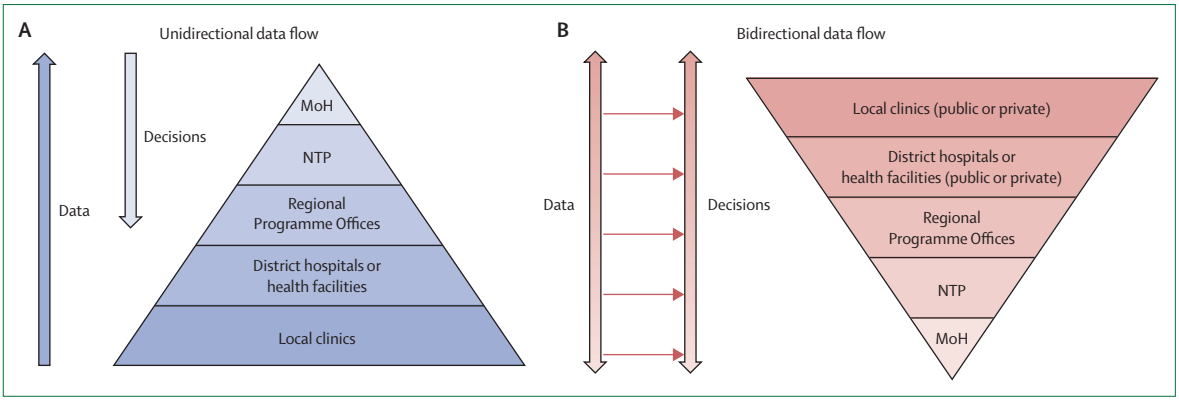

Figure 4: **Structuring data and decision making for tuberculosis elimination**
In existing systems, data is largely sent from the local level and aggregated at the central level for reporting and broad target-setting, with decisions made in top-down fashion and rarely involving individuals below the regional or district level (A). To achieve tuberculosis elimination, data structures, and decision making should arguably be centred around activities at the local level, which is the level at which tuberculosis transmission occurs. Such structures should support data and decision making that is bidirectional and mutually informative in nature, involving all levels of the tuberculosis control system (B). This flow of information should not only occur between health-care system tiers, but also between localities, to disseminate information about what works in different settings. NTP=National Tuberculosis Programme. MoH=Ministry of Health.

	Examples of potential benchmarks*	Improvements in data systems and structures required to assess progress
High HIV rate, low MDR, urban setting (eg, African city)	Percent decline in notified tuberculosis incidence in the five highest-incidence neighbourhoods	Ability to measure tuberculosis incidence by neighbourhood or postal code
Diffuse, private-sector driven, periurban setting (eg, Indian informal settlement)	Percent increase in patients notified and successfully treated (including referrals) among those diagnosed with tuberculosis in the private sector	Integration of private care notification data with routine public systems
Low HIV, moderate incidence, high MDR (eg, town in former Soviet Union)	Absolute decline in incidence of MDR tuberculosis among treatment-naive individuals	Repeat, targeted surveys to measure and stratify MDR tuberculosis according to previous tuberculosis history
Rural subdistrict with poor access to laboratory testing facilities (eg, in southeast Asia)	Absolute reductions in average time to diagnosis and the proportion of patients who test positive but do not start treatment	Integration of laboratory results with treatment initiation (yes/no, and date-stamped) data
Well resourced city with large migrant community (eg, in western Europe)	Absolute reduction in proportion of new cases due to recent infection, informed by molecular epidemiology	Inclusion of strain type data into routine notification systems

MDR=multidrug resistance. *The specific change targeted, and the duration of time provided to meet the benchmark, would depend on the current rate of tuberculosis, existing trends, and anticipated costs.

Table 3: **Examples of potential benchmarks for success of locally targeted strategies to end tuberculosis in five emblematic settings**

high-risk populations (eg, homeless people, HIV-infected people, or drug users) has been a crucial component of most major successes in tuberculosis control.[79,80] Mathematical models based on empirical data provide indirect support for targeted tuberculosis elimination strategies, as has been demonstrated for other diseases.[3,16,81,82] Data from Rio de Janeiro, Brazil, suggest that, as with other diseases, targeting hotspots containing 6% of the population on a district level (identified from local notification rates) could reduce city wide incidence to a similar degree as an intervention of equal intensity covering the remaining 94% of the population.[30]

Local control officials undoubtedly target high-risk patient groups intuitively, but to show the effectiveness of these approaches, data must be collected and compared against standardised benchmarks. Ideally, these benchmarks should be agreed upon at the local and national level, accounting for local epidemiology and existing trends (table 3). Guidance about these measures of success could come from global agencies such as WHO and implementation of these standards could drive the improvement of local data collection efforts. Targeted approaches become increasingly important as tuberculosis incidence declines and becomes more concentrated within specific subpopulations; thus, collection of empirical evidence against standardised benchmarks to inform such approaches should become a higher priority.[83]

Encouraging parallels exist for other diseases. The Tanzanian ART programme's "Know your CD4 count" campaign used a consultation process to identify clinic, patient, and infrastructural factors that limited the number of HIV-infected patients with a known CD4 count.[84] After data for each clinic were reviewed in conjunction with local staff, site-specific interventions were implemented to address administrative and laboratory barriers, strengthen staff training, and educate patients. After the roll-out of the intervention, ART enrolment increased by an average of 62% at each clinic.

Evidence for the effectiveness of local interventions could also be collected with pragmatic trials embedded within the implementation of locally tailored responses, or before–after comparisons of communities that adopt tailored strategies for tuberculosis control. A study in Karachi showed that when community members screened patients in private health-care facilities, the number of detected tuberculosis cases doubled, compared with areas without the intervention.[31]

Ethical considerations

When designing targeted approaches to end tuberculosis locally, ethical considerations are an important challenge. Tuberculosis programmes collect anonymised data routinely and are working increasingly closely with patient advocacy groups, but local-level collection requires additional engagement with the targeted communities. Tuberculosis officers might therefore wish to consult with community organisations to ensure that data are used to address local public health priorities. For example, community consultation is a core component of the Reaching Every District approach for childhood vaccination, and many countries with the most successful vaccination programmes also have high outreach and community engagement.[85,86] Ethical considerations should also be considered when prioritising interventions such as ART to specific groups; targeting of one region or population over another might be perceived as inequitable.[28] Finally, with regard to security, data can be anonymised, but sufficient technological infrastructure is still required to protect patient privacy, especially in resource-limited settings, in which such systems might be weaker. However, systems to protect privacy do not need to be specific to tuberculosis, and cross-sector initiatives should be encouraged.

Conclusion

Traditionally, interventions to control tuberculosis have focused on providing a basic level of care to a large number of people. As global priorities shift from controlling tuberculosis to ending tuberculosis, we must rapidly develop new systems that empower interventions tailored to heterogeneous epidemics. Locally targeted approaches have been successful in other diseases, but need routine collection of local data, bidirectional flow of information and capacity between local and central level, augmentation of existing data collection efforts, and investment in the systems needed to collect and analyse disaggregated data.

In many settings, the focus of data collection is already shifting from national reporting to informing local strategy. Accelerating this expansion will require stronger links between local clinics, national tuberculosis programmes, in-country and regional institutions with specialised expertise, and global organisations such as WHO. A political commitment to increase human and information technology resources at all levels, and to collect empirical data to show the effectiveness of locally targeted strategies, will also be essential. To stop tuberculosis worldwide, variation in epidemics locally must be addressed, meaning that we must modernise data, systems, and ethical structures at all levels to empower communities to understand tuberculosis epidemics better, and ultimately to end them.

Contributors

GT, HEJ, TC, and DWD conceived the idea for this manuscript. GT and HEJ wrote the first draft, and all authors revised it for important intellectual content. All authors approved the final version as submitted for publication.

Declaration of interests

The authors declare no competing interests.

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