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Data for action: Collecting and using local data to more effectively fight tuberculosis

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INTRODUCTION

The fight against tuberculosis (TB) is entering a new era, from one of control to one of attempting to end the TB epidemic, where the international donor and policy community have embraced targets of 90–95% reductions in TB incidence and mortality by 2050[6]. One important component of such “epidemic-ending” approaches is an increased focus on local-level strategies, which have proved instrumental in eliminating infectious diseases ranging from smallpox to polio[7–10]. The successful elimination of disease epidemics has typically involved two important components: (1) systematic reporting of every case and (2) 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 TB could, for example, tailor diagnosis and treatment of TB infection to subpopulations that are at highest risk of disease progression, or target case finding to stop transmission in high-incidence populations. Some countries are starting to use subnational trends to inform more tailored approaches[12]; however, to end TB in a 20-year time frame, this trend must be

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accelerated along with increased focus on local empowerment with centralized (national and global) support[13].

Since 1993, with the adoption of a widely-accepted approach to TB treatment known as DOTS[14], a standard set of clinical, demographic, bacteriological, and treatment outcome data have been collected and aggregated by national TB programs and subsequently notified to the World Health Organization (WHO)[15]. This approach, while essential for informing country-level and global estimates and monitoring the high-level progress of strategies such as DOTS, has not traditionally emphasized the use of existing data (or collection of additional data) to identify sites of ongoing transmission and target local responses accordingly. Local TB epidemics differ in terms of intensity, drivers, and key characteristics, and approaches that are effective in some “hotspots” (e.g., informal urban settlements) may fail in others (e.g., 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 a tailored response to each individual micro-epidemic, the goal of ending TB globally will not be achieved.

Awareness is building surrounding the importance of local data and capacity, but action is not being taken fast enough. The WHO has championed the need for national programs to respond to setting-specific differences, according to the scale of the epidemic in the country[16]. Three specific steps will accelerate this process. First, countries must better use existing data on TB notifications, risk factors, and treatment outcomes to inform local interventions. Second, national and global systems must augment the set of standard, routinely-collected data with additional data elements to better target resources, while ensuring that this additional data collection is feasible. Examples of additional data include geographic information, drug resistance, and clinical risk factors. Thirdly, programs must build capacity for the periodic, focused collection of novel data components, such as targeted surveys, contact investigations, and sequencing data, to inform local policy decisions.

In this manuscript, 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 TB (Table 1). Combined with strategies to interrupt transmission, treat latent TB, and improve social conditions, empowering the use of local data and infrastructure to target interventions appropriately can form the basis for a coherent strategy to end TB, from both a top-down and a bottom-up direction.

IMPROVING DATA COLLECTION AND ANALYSIS TO END TB: THREE STEPS

Step 1. Bidirectional systems for accessing and linking programmatic data to policy

Routinely collected TB data varies substantially in scope and detail between countries. The WHO recommends a minimum set of variables, comprising age, sex, geographic region, previous treatment, smear microscopy result, anatomic site (pulmonary or extrapulmonary), and treatment outcome[17,18], which are ideally linked to unique patient identifiers. In many settings, data on HIV and exposure to high-risk congregate settings are also routinely

collected. Although the WHO recommends the use of secure, self-contained electronic systems, paper forms are still predominantly used[18,19]. Data analysis is thus often delayed until entry into a central country-wide database is completed[19], reducing its utility to inform real-time programmatic decisions. When such data are rapidly incorporated into policy, results can be dramatic. For example, in 2008 the Lesotho TB program found that >90% of patients diagnosed with TB were HIV seropositive[20]. The Ministry of Health, in collaboration with *Médecins Sans Frontières*, rapidly scaled up and integrated decentralized TB/HIV care[21] in response. As a result, the number of adults on antiretroviral therapy (ART) in the program doubled over four years, and the incidence of HIV-positive TB decreased by approximately 40%[20].

Of particular importance to interrupting transmission is better detection of childhood TB, which is currently grossly under-detected[22,23] and can serve as an important marker of ongoing transmission[24]. Better systems for the detection of pediatric TB and rapid notification when childhood cases rise above a certain level might inform not only specific interventions such as household contact tracing and preventive therapy for children[25] but can also serve as an early detection system for identifying transmission hotspots more broadly.

Ultimately, centralized TB data collection and reporting systems must be designed not only to inform national policy changes but also for building local capacity to create tailored responses at the community level. Examples exist in other infectious diseases: polio surveillance in India demonstrated lower vaccine efficacy in high population density districts with poor sanitation[26]; thereby enabling the roll-out of a different vaccine that was better suited to these districts[27]. This ultimately contributed to the elimination of polio where national-level policies had failed[28]. Similar targeted approaches, which are often as cost-effective as broader, untargeted interventions[29–31], will be required to end epidemics of TB.

Step 2. Collection of additional routine data to inform targeted responses

Though challenging in many settings, expanding the minimum set of routinely collected TB data is essential to empower more locally responsive strategies[16]. Additional data may include geographic information [e.g., to assist with community-based follow-up (Box 1) or transmission hotspot mapping (Figure 1)], drug resistance patterns (e.g., for region-specific drug susceptibility testing algorithms and localized treatment regimens), and risk factors such as diabetes, smoking, or previous hospitalization or imprisonment[32–34] (e.g., to inform local screening strategies). For example, Japan found high diabetes mellitus rates in certain populations of elderly or homeless TB patients, thereby enabling clinics serving these individuals to perform targeted screening[35]. Similarly, data from China showed a dramatic increase in the proportion of patients that had recently migrated into Beijing, and that these patients rarely completed treatment[36]. 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 additional data that could be collected and used for local decision-making.

In routine practice, TB programs must weigh data quantity against quality and may therefore focus additional data collection in particular patient groups or during the roll-out of new

initiatives. To encourage the collection and use of relevant data, policymakers and TB programs could promote new frameworks that use local data collection as benchmarks for clinic performance. Local clinics must have sufficient autonomy, funding, and also oversight to collect the data and implement interventions that will be most responsive to their unique epidemics. Examples of strategies for additional TB data collection and linkage to tailored interventions are multi-country projects such as ENGAGE-TB[37] and TB-REACH[38]. Importantly, the implementation of local interventions may reveal other issues (e.g., comorbidities) that traditionally would have been centrally managed. Thus, the better collection of local data will likely drive organizational and operational changes within healthcare systems, which can be facilitated by better integration of care.

Step 3: Targeted collection of novel data: surveys, spatial data, and strains/sequences

Routine data will always be limited to elements that can be collected during busy clinical practice, with limited programmatic budgets, and from patients who actually present to care. To take a more comprehensive step toward ending TB, 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 TB in a representative population sample[13]. Between 2009 and 2015, 23 countries are expected to have conducted TB prevalence surveys[39]. These surveys, with WHO guidance[40], can produce national (or occasionally subnational) estimates of the fraction of new cases with drug resistance[17], characterize broader patterns of transmission, and identify gaps in current control efforts[41]. Because surveys are expensive, logistically complex, and have relatively small sample sizes at the sub-national level, they generally lack the 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)[42,43]. LQAS can classify the risk of drug resistance among TB patients at a sub-national level using pre-defined thresholds of TB drug resistance[44]. Unlike traditional national-level drug resistance surveys, LQAS surveys do not attempt to precisely estimate the prevalence of resistance. 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 appear to have low MDR-TB prevalence amongst new cases[45,46] nationally, Vietnam may have considerably more subnational heterogeneity[44]. In particular, one province (Tay Ninh) was classified as having high MDR-TB prevalence, focusing attention on areas closer to Cambodia, where MDR-TB is more prevalent. Targeted surveys have also shown unusually high rates of MDR-TB in certain ART clinics and Tibetan refugee communities in India[47,48]. Similar methods, such as sentinel surveillance, have identified large numbers of MDR-TB patients from Somalia seeking treatment in Kenya[49].

Other potentially useful data sources include molecular data on strain types, transmission, and drug resistance[50]. Currently, such data are only collected broadly and systematically in resource-rich settings. For example, an analysis of United States national surveillance identified which racial minorities are most likely to develop TB from recent transmission,[51]

and the United Kingdom has used molecular typing prospectively since 2010 to identify outbreaks[52] and to estimate the proportion and identity of MDR-TB cases attributable to transmission[53]. Locally, such data can also be used to improve both contact investigations (which may be complemented by online social network data[54]) and the laboratory methods used to diagnose drug-resistant TB (Box 2). Newer technologies, such as whole genome sequencing (WGS), can identify strains responsible for major outbreaks[50,55–57], uncover highly infectious "super-spreaders"[50], and help understand the completeness of contact investigations[58].

Although not widely implemented, the BRICS and other middle income countries have capacity to collect and analyze molecular data, and guidance exists regarding strain genotyping for TB surveillance[16]. While WGS may be more challenging to implement, it can inform the development of simpler tests, which have been used in preliminary studies to infer transmission patterns[59]. Mobile technology may also facilitate the collection of novel geospatial information. For example, human movement (measured via cellphone towers) has been combined with high resolution malaria prevalence data in Kenya to show that migration from less-developed residential areas accounts for the majority of malaria within urban centres[60]. Importantly, the usefulness of these additional data will always be limited if it cannot also be easily captured and integrated into existing data systems.

ENHANCING DATA SYSTEMS

Systems for reporting and analyzing data

Achieving more local control requires an investment in TB surveillance systems, including a strengthening of WHO-supported electronic data collection systems[16,19]. Maintaining a system that is sufficiently agile to be useful for heterogeneous patient populations and levels of resource availability (e.g., internet access) across all localities can be difficult. This is compounded by the long-term use of proprietary systems for which support may have ceased[61], and the requirement by governments for a lengthy public tender process. Implementing similarly flexible systems for a locally tailored TB 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 standardized data and identification of surveillance gaps[16,18,19]. These benchmarks encourage TB programs to assess the consistency of case definitions and national data in interactive workshops with stakeholders. Such benchmarks can be internal (e.g., subtotals by age group equal the total number of reported cases) or external (e.g., the percentage of new TB cases in subgroups, such as children, is comparable to similar countries). Although linking data across disparate electronic databases (e.g., laboratory results and treatment information) is challenging, guidelines for the development of national electronic TB data systems[19] are potentially useful for local system development.

Potential improvements to existing systems

Existing systems may be improved by: (a) incorporating more local data, (b) facilitating the easy capture of additional setting-specific data, (c) integrating with other disease databases, and (d) implementing features that facilitate rapid data analysis and linkage to intervention.

Systems incorporating local data should permit the timely collection, reporting, and analysis of those data at all levels of the healthcare system (Figure 2). Critically, this must be done while maintaining the capacity of existing systems to facilitate country-level reporting. This will require substantial new investments into human resource capacity (particularly epidemiological expertise) and IT infrastructure. These data can be inputted directly using mobile devices. Countries[62] and cities[63,64] are increasingly developing individual-based electronic data systems. Mobile technology can also be combined with innovative methods to maximize case finding by reimbursing TB control officers promptly or providing appropriate incentives for finding additional cases[62].

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 from national to local level and between local control programs. 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 healthcare information[65], which supplements the surveillance of non-communicable diseases in high burden countries and are subsequently fed into national databases[66]. Including data from both public and private sectors is also an important consideration[67].

If locally important data are to be effectively analyzed, improved quality control and standardized “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[68], or detect drug resistance mutations from WGS data[69]. Wider availability and adoption of such tools could encourage the collection of local data and improve the analytical capacity of TB programs; however, data might also need to be analyzed at a more centralized level where analytical capacity is likely to be greater.

Unique patient identifiers are essential. Without these, it will be challenging to link routine clinical and laboratory data with those from targeted surveys, sentinel surveillance systems, and other novel data collection efforts. This data linkage can facilitate pragmatic studies on the impact of interventions at a sub-district-level. In Brazil, data collected before and after the roll-out of Xpert MTB/RIF (a molecular test for TB and rifampin resistance) allowed for Xpert MTB/RIF’s effect on local case notification rates to be quantified and for poor-performing sites to be identified and targeted for further strengthening[70]. However, because the laboratory and treatment databases used their own internal identifiers, linking specific results with specific outcomes was a challenge. Weak existing data structures have also made it difficult to generate empirical evidence for locally targeted approaches to TB control.

Despite their clear benefits and potential cost savings[71–73], improvements to these systems will require substantial investment. To justify such investment, it is essential to strengthen the empirical evidence base to support locally tailored approaches to ending TB.

EMPIRICAL EVIDENCE FOR LOCAL APPROACHES TO END TB

At present, there is limited evidence describing the effectiveness of the types of locally targeted approaches described above. Nevertheless, targeting high-risk populations (e.g., homeless populations, HIV-infected people, or drug users) has been a critical component of nearly every major success in TB control[74,75]. Mathematical models based on empirical data provide indirect support for targeted TB elimination strategies. Data from Rio de Janeiro suggest that, as with other diseases[8,31,76,77], targeting hotspots containing 6% of the population on a district level (identified from local notification rates) could reduce city-wide TB incidence to a similar degree as an intervention of equal intensity covering the remaining 94% of the population[78].

Local control officials undoubtedly target high-risk patient groups intuitively, but to demonstrate the effectiveness of these approaches, data must be collected and compared against standardized benchmarks. Ideally, these benchmarks should be agreed upon at the local and national level, accounting for local epidemiology and existing trends (Panel). Guidance regarding these measures of success could come from global agencies such as the WHO, and implementation of these standards could drive the improvement of local data collection efforts. Targeted approaches become increasingly important as TB incidence declines and TB becomes more concentrated within specific subpopulations[79]; thus, collection of empirical evidence to inform such approaches against standardized benchmarks should become a higher priority.

Encouraging parallels exist for other diseases. The Tanzanian ART program'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[80]. After data for each clinic were reviewed in conjunction with local staff, site-specific interventions were implemented that involved addressing administrative and laboratories barriers, strengthening staff training, and educating 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 using pragmatic trials embedded within the implementation of locally tailored responses, or before-after comparisons of communities that adopt tailored strategies for TB control. A study in Karachi showed that when community members screened patients in private healthcare facilities, the number of detected TB cases doubled, compared to areas without the intervention[1].

PANEL

Examples of settings and potential benchmarks for success of locally targeted strategies or interventions to end TB.

Illustrative Setting	Examples of potential benchmarks*	Improvements in data systems and structures required to assess progress
High HIV, low MDR, urban setting (e.g., African city)	Percent decline in notified TB incidence in the five highest-incidence neighborhoods	Ability to measure TB incidence by neighborhood or postal code
Diffuse, private-sector driven, peri-urban setting (e.g., Indian informal settlement)	Percent increase in patients notified and successfully treated (including referrals) among patients diagnosed with TB in the private sector	Integration of private care notification data with routine public systems
Low HIV, moderate incidence, high MDR (e.g., town in Former Soviet Union)	Absolute decline in incidence of MDR-TB among treatment-naive individuals	Repeat, targeted surveys to measure and stratify MDR-TB according to previous TB history
Rural sub-district with poor access to laboratory testing facilities (e.g., 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 (e.g., 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

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

ETHICAL CONSIDERATIONS

In designing targeted approaches to ending TB locally, ethical considerations are an important challenge. TB programs routinely collect anonymized data and are working increasingly closely with patient advocacy groups, but local-level collection requires additional engagement with the targeted communities. TB officers may therefore wish to consult with community organizations 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,[81] and many countries with the most successful vaccination programs also have high levels of outreach and community engagment[82]. There are also ethical considerations when prioritizing interventions such as ART[83] to specific groups; targeting one region or population over another may be perceived as inequitable. Finally, with regard to security, data can be anonymized, but sufficient IT infrastructure is still required to protect patient privacy, especially in high-burden settings where such systems may be weaker. Systems to protect privacy need not be TB-specific, however, and cross-sector initiatives should be encouraged.

CONCLUSION

Traditionally, interventions to control TB have focused on providing a basic level of care to a large number of people. As global priorities shift from controlling to ending TB, we must rapidly develop new systems that empower interventions tailored to heterogeneous epidemics. Locally targeted approaches have been successful in other diseases but require

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 analyze 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 TB programs, in-country and regional institutions with specialized expertise, and global bodies such as the WHO. A political commitment to increase human and information technology resources at all levels, and to collect empiric data to demonstrate the effectiveness of locally targeted strategies, will also be essential. To stop TB globally, we must address variation in TB epidemics locally – meaning that we must modernize data, systems, and ethical structures at all levels to empower communities to better understand their TB epidemics, and ultimately to end them.

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Box 1: Data for Action in Karachi, Pakistan

Interactive Research and Development has used a range of electronic recording and reporting systems to improve access to and reporting from diagnostic and treatment sites[1]. For example, Geographical Positioning System (GPS) data have been used to identify the exact coordinates of private family practitioner clinics, public and private NTP reporting centers, private laboratories and pharmacies. All patients with drug-resistant tuberculosis or a high risk of loss to follow-up are mapped to approximate home locations using GPS-enabled phones, in order to inform assignment of community treatment supporters and to facilitate follow-up. For the majority of these patients, private clinics (red boxes in the Figure) are more accessible than the National TB Programme Reporting Centre ("NTP" in the Figure) for scheduling of follow-up visits. These data have informed key program decisions with regards to targeting intensified case finding, location of digital X-ray systems and GeneXpert machines, and recruitment of treatment supporters.

Box 2: Illustrative Example: 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 TB surveillance infrastructure, has seen a change in DR-TB strain diversity. Historically scarce atypical Beijing genotype strains have become dominant and are associated with clustered outbreaks of extensively drug-resistant TB (XDR-TB)[2]. A series of molecular epidemiological studies demonstrated that these strains likely originated from an adjacent province (Eastern Cape), which has relatively weak DST surveillance infrastructure[3–5]. These atypical Beijing strains 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 MDR-TB, 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-TB, which subsequently entered the Western Cape, likely via the large migrant work population. Molecular tests are now used to identify inhA promoter mutations in the Eastern Cape. An alternative drug can thus be potentially be substituted for ethionamide in order to limit the emergence of XDR-TB, however, in practice, this is not yet widely adopted[11].

KEY MESSAGES

- TB epidemics, like those of other infectious diseases, vary dramatically across different geographical regions; to end TB epidemics in high-burden areas, control efforts will need to be tailored to local conditions.
- To design interventions that effectively combat TB, national control programs should shift from a centralized approach where local data is deposited into national databases for aggregated analyses, to a bidirectional one in which local partners have the capacity to collect and analyse data, using those data to design locally-responsive interventions.
- This shift requires local TB programs to make better use of existing data, expand routine data collection, and make informed use of targeted surveys.
- These efforts also require the modernization 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.
- TB control programs will need to develop the necessary analytical and support infrastructure to measure the impact of local interventions and disseminate these findings within the national program.

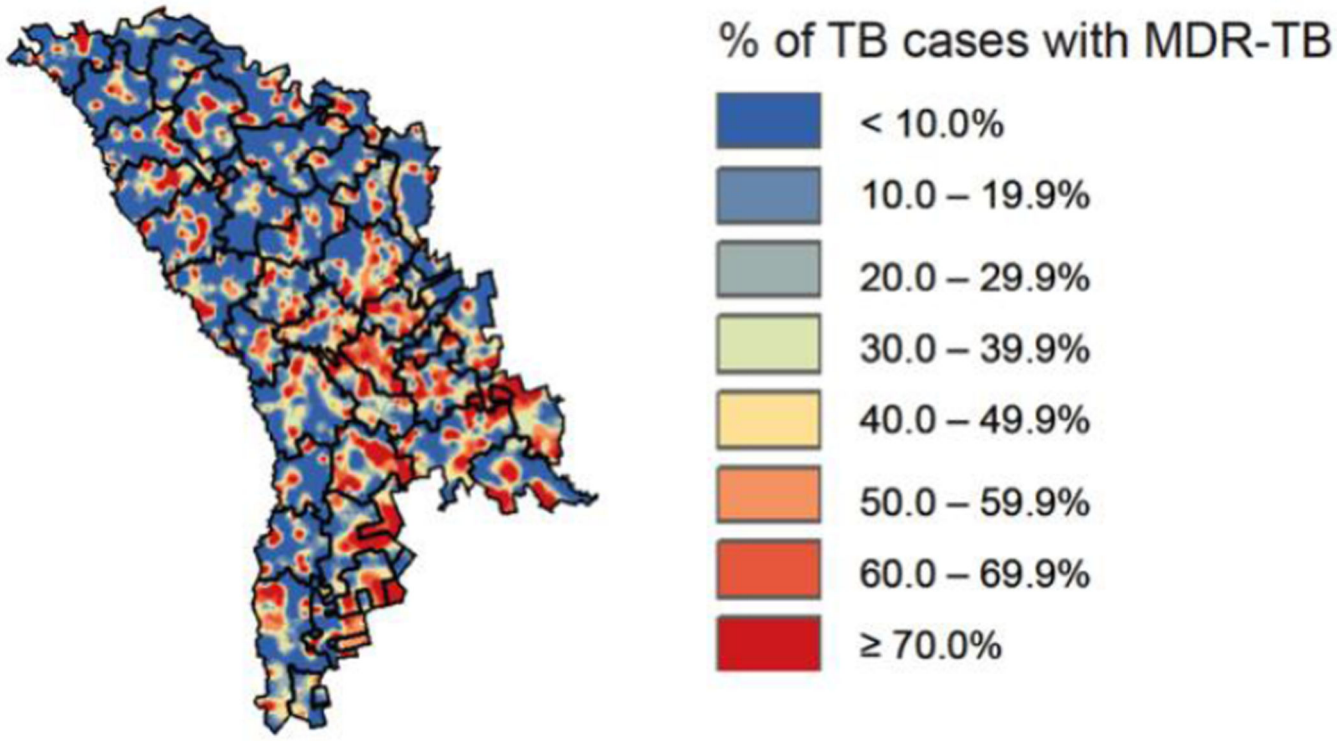

Figure 1. Geographic hot-spots of MDR-TB risk in the Republic of Moldova

Colors represent the proportion of previously treated TB cases with drug susceptibility testing data that are multidrug-resistant 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 program updated the laboratory network, revised guidelines and improved training to ensure universal drug susceptibility testing. Standardized reporting systems facilitated more complete and accurate reporting of TB incidence, outcomes and drug resistance[84], and a nationwide online database was introduced with access at every national TB facility. Physicians and laboratory staff enter data on individual TB patients (including routinely collecting location of residence) in real time at the relevant points of contact. Data are then synthesized 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 (such as certain locales in the southeast represented in orange and red).

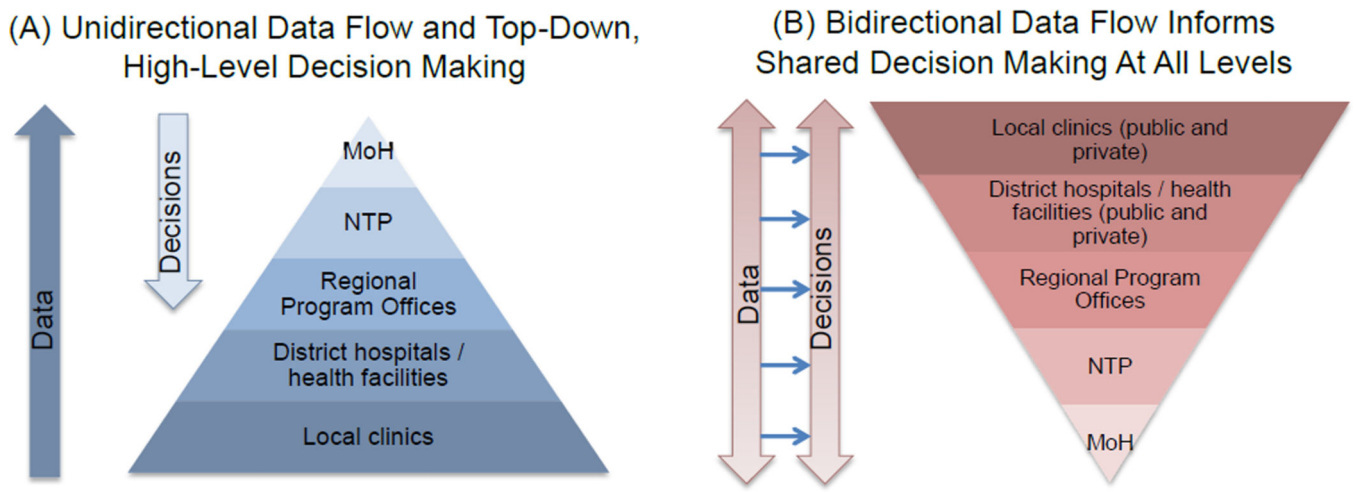

Figure 2. Structuring Data and Decision Making for TB Elimination

Existing structures largely consist of data that are sent from the local level and aggregated at the central level for purposes of reporting and broad target-setting, with decisions made in top-down fashion and rarely involving individuals below the regional or district level (Panel A). In order to achieve TB elimination, data structures and decision-making should arguably be centered on activities the local level, which is the level at which TB transmission occurs. Such structures should support data and decision-making that is bidirectional and mutually informative in nature, involving all levels of the TB control system (Panel B). This flow of information should not only occur between healthcare system tiers, but also between localities, in order to disseminate information about what works in different settings. NTP = National Tuberculosis Program, MoH = Ministry of Health.

Table 1

Key elements of a data-driven, locally tailored approach to TB elimination

Element	Current capacity	Potential improvements	Key challenges
Programmatic data	- Strong systems for collection of aggregate data in many countries - WHO guidance available for surveillance and other systems[16,18,19]	- Stronger systems for disaggregation of data at the subnational level - Building internal capacity for epidemiological analysis and reporting to subnational TB authorities	- Current incentive structures to prioritize national-level reporting - Human resource constraints - Infrastructure constraints (e.g., reporting systems for surveillance) - Lack of consistent data quality
Additional data that could be collected programmatically	- Many clinics already informally collect additional data for internal quality control purposes - Local stakeholders may have a better idea of interventions being considered and which data would help decide between them	- Routine data collection could expand to include TB patients' location, key risk factors, interactions with congregate settings, etc. - Increased autonomy and decision making capability at local clinics to decide data collection priorities	- Standardized notification systems must be preserved in some form but must balance the need for national reporting with local flexibility. - Local TB officials currently have limited experience in collecting or using additional data - Additional data must be able to be fed into large-scale TB elimination projects and compatible with national databases - Routine (rather than targeted or time-limited) collection of additional data can be expensive and may compromise data quality
Specific surveys	- Increasing capacity to perform surveys for drug-resistant TB - National prevalence surveys are being increasingly performed - WHO guidance is available for performing certain types of surveys[18,40]	- Repeated surveys to better inform longitudinal analyses - Routine surveillance systems that could feed back to national and sub-national authorities - Inclusion of data and reporting systems (e.g., geographic data on drug resistant cases) to inform local policies	- Surveys can be very expensive, politically motivated, and not well integrated into existing routine TB efforts. - In-country capacity to conduct surveys without outside technical assistance is limited. - Infrastructure for surveillance systems is often limited.
Novel data	- Some reference and/or academic laboratories have the capacity to collect and analyse novel forms of data, such as the genetic distance between strains, in order to identify transmission events - WHO has guidance available for some types of novel data[16]	- Creation or adaptation of existing systems to allow for the inputting of novel data - Mechanisms of internal- and external-quality control are not well established - Co-collection of other types of data (e.g., social network data) must be improved to maximize the potential of novel data such as strain genotyping	- IT (e.g., data capturing and storage), laboratory (e.g., infrastructure for culture, DST, and strain genotyping), and human resource capacity challenges need to be overcome in order to generate new types of data - Storage and reporting of some types of novel data (e.g., whole genome sequence data) is not standardized

Element	Current capacity	Potential improvements	Key challenges
Systems for reporting and analyzing 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 centralized) 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 sub-national or local level - Better, automated systems for capturing new data on the ground in clinics (e.g., electronic forms) - Better integration of analytical expertise with other in-country disease control programs - Better systems for data sharing between local TB control programs	- Linkage of disparate IT systems (e.g., for laboratory and patient data) - Lack of human resource capacity to clean data and perform analyses, especially at the sub-national 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 TB incidence (including drug resistance) is heterogeneous at the local level - Mathematical models suggest that local approaches may be more effective and efficient[78]	- Programmatic evaluations and research studies could help to compare the effectiveness of locally targeted strategies against nationally standardized ones. - Cost-effectiveness analyses could evaluate whether the additional cost of local targeting provides sufficient health value to be justified	- Generalizability of data from one epidemic and intervention to another is likely to be difficult. - Infrastructure and incentives (both organizational and financial) for collecting such data are limited, outside of existing academic centers.

Table 2

Possible data items to be collected on individual TB cases, in addition to the WHO minimum set of variables[18]

Purpose	Data type	Items
Drug resistance Surveys	Drug resistance diagnoses	Genotypic (e.g., Xpert MTB/RIF) and phenotypic (e.g., liquid culture) drug susceptibility testing result, 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 levels
Transmission mapping	Strain genotype	MIRU-VNTR, spoligotype, RFLP pattern, WGS
	Geospatial, location, and contact data	Administrative region (e.g. district, city, and suburb), residential address, or GPS co-ordinates of residence. Recent hospital admissions (name of hospital, duration, and reason for treatment) or incarcerations or known TB contacts.
Risk factor analysis	Comorbidities	HIV, diabetes, chronic obstructive pulmonary disease, pneumonia, diabetes testing,
	Occupational exposure	Health care workers, miners
	Substance use	Cigarette pack years, AUDIT alcohol use scores, illicit narcotic usage