Improving measurement of tuberculosis care cascades to enhance people-centred care

Lena Faust, Pren Naidoo, Guillermo Caceres-Cardenas, César Ugarte-Gil, Monde Muyoyeta, Andrew D Kerkhoff, Karikalan Nagarajan, Srinath Satyanarayana, Niaina Rakotosamimanana, Simon Grandjean Lapierre, Olusola Adedeji Adejumo, Joseph Kuye, Charity Oga-Omenka, Madhukar Pai, Ramnath Subbaraman

Care cascades represent the proportion of people reaching milestones in care for a disease and are widely used to track progress towards global targets for HIV and other diseases. Despite recent progress in estimating care cascades for tuberculosis (TB) disease, they have not been routinely applied at national and subnational levels, representing a lost opportunity for public health impact. As researchers who have estimated TB care cascades in high-incidence countries (India, Madagascar, Nigeria, Peru, South Africa, and Zambia), we describe the utility of care cascades and identify measurement challenges, including the lack of population-based disease burden data and electronic data capture, the under-reporting of people with TB navigating fragmented and privatised health systems, the heterogeneity of TB tests, and the lack of post-treatment follow-up. We outline an agenda for rectifying these gaps and argue that improving care cascade measurement is crucial to enhancing people-centred care and achieving the End TB goals.

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Department of Epidemiology, Biostatistics and Occupational Health, McGill University, Montréal, QC, Canada (L Faust MSc, Prof M Pai PhD); **McGill International TB Centre, Montréal, QC, Canada** (L Faust, S Grandjean Lapierre MD, Prof M Pai); **Desmond Tutu TB Centre, Department of Paediatrics and Child Health, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa** (P Naidoo PhD); **Instituto de Medicina Tropical Alexander von Humboldt** (G Caceres-Cardenas MD, C Ugarte-Gil PhD) **and School of Medicine** (C Ugarte-Gil), **Universidad Peruana Cayetano Heredia, Lima, Peru; TB Centre, London School of Hygiene & Tropical Medicine, London, UK** (C Ugarte-Gil); **Tuberculosis Department, Center for Infectious Disease Research in Zambia, Lusaka, Zambia** (M Muyoyeta PhD); **Division of HIV, Infectious Diseases and Global Medicine, Zuckerberg San Francisco General Hospital and Trauma Center, University of California San Francisco, San Francisco, CA, USA** (A D Kerkhoff MD); **Department of Social and Behavioural Research, ICMR-National Institute for Research in Tuberculosis, Chennai, Tamil Nadu, India** (K Nagarajan PhD); **Centre for Operational Research, International Union Against Tuberculosis and Lung Disease (The Union), Paris, France** (S Satyanarayana PhD); **South-East Asia Office, International Union Against Tuberculosis and Lung Disease (The Union), New Delhi, India** (S Satyanarayana); **Mycobacteriology Unit, Institut Pasteur de Madagascar, Antananarivo, Madagascar**

Introduction

Care cascades (also known as care continuums) are representations of the proportion of people reaching important milestones in the care pathway for a disease. Gaps between each milestone represent the proportion of people lost at each stage in care, from the number of people with a condition at the population level to those achieving optimal treatment outcomes. For this reason, care cascades are a valuable approach for evaluating the quality of care for a given condition within a health system.[1] The care cascade model has been applied to understand care delivery for several conditions, including hypertension,[2] diabetes,[3] and viral hepatitis B.[4] Notably, in the field of HIV, this model has been used widely since 2017 to assess global progress towards the UNAIDS goals[5] and to monitor the test-and-treat strategy. As such, HIV care cascades have gone beyond merely being a measurement model to serving as a quality improvement[6,7] and advocacy tool with public health impact.[8]

In contrast, despite recent methodological advances in tuberculosis (TB) care cascade estimation,[9] care cascades for TB disease have not been routinely used by national TB programmes (NTPs) to generate actionable data that can improve quality of care. Care cascades for TB disease have been constructed for India,[10] Madagascar,[11] Nigeria,[12] Peru,[13] South Africa,[14] and Zambia,[15] but they have not been routinely included in publicly accessible national TB reports in these countries,[16–18] except in South Africa, which has not published annual TB reports in recent years, but which included an updated (2020) care cascade in its TB Recovery Plan.[19] Care cascades are also not reported in the annual WHO Global TB Reports.[20,21] Identifying and closing gaps in the TB care cascade will be essential to accelerate the current slow global progress in reducing TB incidence.[22] Failure to exploit the full potential of care cascades, therefore, represents a major missed opportunity for the global TB community.

Leveraging this model for public health impact is particularly important given the status of TB as the second leading cause of death from an infectious pathogen worldwide (after COVID-19, as of 2021), with TB having been responsible for about 1·6 million deaths in 2021.[21] Given the disruptive impact of the COVID-19 pandemic on TB programmes globally, which has significantly set back progress on TB elimination,[23,24] care cascades could help to identify which care stages need to be targeted to mitigate these disruptions. The application of care cascade analyses to measure progress towards the End TB goals is also relevant ahead of the 2023 UN high-level meeting on TB. As we are not on track to meet the targets set at the 2018 high-level meeting,[22] routine application of TB care cascades might facilitate transparent tracking of progress towards milestones to which member states have committed.

Although the need to improve TB care cascade outcomes is clear, and interventions for doing so have been explored,[25] our focus in this Personal View is specifically on cascade measurement. As a group of researchers who have estimated, or are estimating, care cascades for TB disease across various high-incidence countries,[10–15] and who therefore have a sense of the scope and diversity of challenges in quality, availability, granularity, and timeliness of data in these settings, we built a consensus around the overarching challenges of accurate cascade measurement and the value of care cascades for TB programmes. This process included meetings at which all co-authors shared their experiences of cascade estimation in their setting, reviewed successive drafts of this work, and provided country-specific examples. In the resulting paper, we describe the value of expanding the use of TB care cascades, identify common measurement challenges, and outline an agenda for rectifying these problems. We argue that the construction of care cascades needs to move beyond serving as a theoretical or research exercise that is unlinked to routine care delivery. Rather, enhancing the capacity of TB programmes to measure care cascades routinely and accurately at multiple levels

(N Rakotosamimanana PhD, S Grandjean Lapierre); **Centre de Recherche du Centre Hospitalier de l'Université de Montréal, Montréal, QC, Canada** (S Grandjean Lapierre); **Department of Microbiology, Infectious Diseases and Immunology, Université de Montréal, Montréal, QC, Canada** (S Grandjean Lapierre); **Mainland Hospital Yaba, Lagos, Nigeria** (O A Adejumo MPH); **National Tuberculosis and Leprosy Control Program, Abuja, Nigeria** (J Kuye PhD); **School of Public Health Sciences, University of Waterloo, Waterloo, ON, Canada** (C Oga-Omenka PhD); **Department of Public Health and Community Medicine and Center for Global Public Health, Tufts University School of Medicine, Boston, MA, USA** (R Subbaraman MD); **Division of Geographic Medicine and Infectious Diseases, Tufts Medical Center, Boston, MA, USA** (R Subbaraman)

Correspondence to: Dr Ramnath Subbaraman, Department of Public Health and Community Medicine, Tufts University School of Medicine, Boston, MA 02111, USA
ramnath.subbaraman@tufts.edu

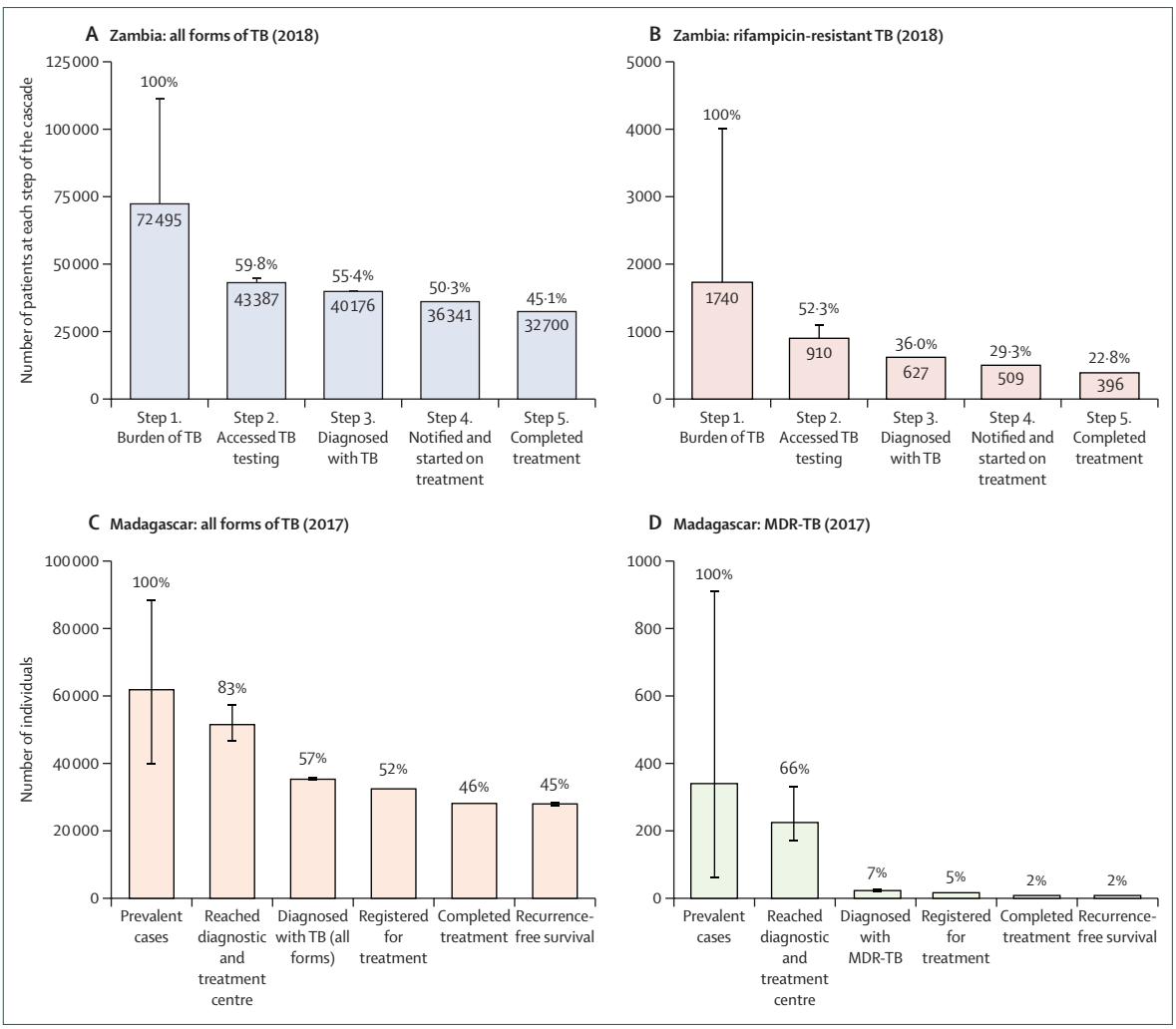

Figure 1: **Examples of TB care cascades from Zambia and Madagascar**
The care cascades for Zambia are reproduced from Lungu et al.[15] The care cascades for Madagascar are reproduced from Knoblauch et al.[11] For Zambia (all forms of TB; A), step 1 shows the WHO TB incidence estimate with 95% CI; step 2 shows missed cases (true test-negative cases based on TB test sensitivity, correcting for those empirically treated) plus cases diagnosed (step 3), with error bars based on the 95% CI for test sensitivity estimates and 95% CI for step 3; step 3 shows the number of people with TB notified and treated (step 4) plus those lost to follow-up before treatment initiation based on the difference between detected cases (from laboratory data) and notified cases, with error bars based on 95% CIs for estimates of pre-treatment loss to follow-up; and step 4 (number started on treatment) and step 5 (number successfully completing treatment) show actual values from notification data. There are no error bars for steps 4 and 5 as they represent the exact national values. For Madagascar (all forms of TB; C), step 1 shows the WHO TB incidence estimate with 95% CI; step 2 shows missed cases (where missed cases are based on local TB test sensitivity) plus cases diagnosed (step 3), with error bars based on 95% CI for test sensitivity estimates and 95% CI for step 3; step 3 shows number of people with TB notified and treated (step 4) plus estimated pre-treatment loss to follow-up based on trimestral TB programme reports and laboratory data, with error bars based on 95% CI for estimates of pre-treatment loss to follow-up; steps 4 (number started on treatment) and 5 (number successfully completing treatment) show actual values from local clinical TB management data (no error bars are presented for steps 4 and 5 as they represent exact national values); and step 6 shows step 5 minus the estimated number of those experiencing relapse based on relapse proportions from the literature, with error bars based on the 95% CI for the estimated proportion of relapse. Percentages are the proportion of people reaching each step, with step 1 (the estimated number of people with TB in the population) being the baseline (100%). More information on how each step was estimated can be found in the original papers.[11,15] MDR=multidrug resistant. TB=tuberculosis.

will require improvements in estimation of disease burden, data capture and management, and post-treatment follow-up, which are also essential to achieving high-quality person-centred care.

The value of the TB care cascade model

Although approaches to estimating care cascades vary, based on guidance[9] published in 2019, a general model for TB disease includes the following steps: (1) the estimated TB burden (ie, the number of people with TB in the population, comprising prevalence or incidence), (2) the number who access screening or testing, (3) the number diagnosed with TB, (4) the number who start treatment, (5) the number who complete treatment, and (6) the number who achieve 1-year recurrence-free survival. Examples of TB care cascades from Zambia[15]

and Madagascar[11] are shown in figure 1. In most NTPs, only steps 4 and 5 (ie, treatment initiation and completion) are routinely captured, creating challenges for estimating the remaining steps.

Regarding step 2, it should be noted that this step represents people who truly had TB who accessed testing. It does not represent all people with symptoms who accessed testing based on TB programme data. Step 2, therefore, takes into account people who had bacteriological test-negative TB, which is estimated from subsequent steps based on the known imperfect sensitivity of bacteriological tests (eg, sputum microscopy, Xpert MTB/RIF). Comparison of the number of people with bacteriological test-negative TB in step 2 with the number of people who were diagnosed with test-negative TB in step 3 provides insights into whether TB programmes are empirically diagnosing enough people with test-negative TB, which highlights another value-add of care cascade measurement.

By identifying bottlenecks in TB programmes, care cascade analyses sometimes reveal unexpected findings, which could inform programme priorities. For example, in India (in 2013),[10] Zambia (in 2018),[15] and South Africa (for all forms of TB in 2020),[19] the largest gap comprised people who contracted TB disease but did not reach diagnostic facilities or access a TB test. In contrast, this gap had a smaller contribution to overall losses in Madagascar (in 2017),[11] as well as in South Africa's drug-resistant TB cascade (in 2013;[14] figure 2). In addition, while the treatment stage of care has historically been the focus of TB programmes, these national care cascade studies suggest that, even after people with TB engage with services, more people are lost during the diagnostic workup (in India and Madagascar), or after diagnosis and before treatment initiation (in India and Zambia), than are lost during treatment. Furthermore, where estimates of post-treatment outcomes are available, such as in India, TB recurrence and death appear to be high under programmatic conditions.[10,26] Care cascade analyses show that outcomes are particularly poor for people with multidrug-resistant (MDR) or rifampicin-resistant TB. In all countries studied, the largest gaps occur before the treatment stage,[10–12,14,15] and the least data are available for 1-year recurrence-free survival. Such analyses, therefore, motivate TB programmes to expand their focus beyond the treatment phase alone.[6,27,28] Further, if evaluated serially over time, as was done for MDR-TB in Nigeria,[12] care cascades can help programmes to set and track

	Total losses across all gaps*	Gap 1: pre-evaluation losses†	Gap 2: pre-diagnosis losses‡	Gap 3: pre-treatment loss to follow-up§	Gap 4: on-treatment losses¶	Gap 5: 1-year post-treatment recurrence or death‖
All forms of TB						
India (2013)[10]**						
n	1650763	761973	308121	212068	196074	172527
%	100%	46·2%	18·7%	12·8%	11·9%	10·5%
Madagascar (2017)[11]						
n	33884	10461	16080	2912	4249	182
%	100%	30·9%	47·5%	8·6%	12·5%	0·5%
South Africa (2020)[19]						
n	193278	73738	19139	27091	73310	Not evaluated
%	100%	38·2%	9·9%	14·0%	37·9%	
Zambia (2018)[15]						
n	39795	29108	3211	3835	3641	Not evaluated
%	100%	73·1%	8·1%	9·6%	9·1%	
Drug-resistant TB						
India (2013)[10]**						
n	123587	69000	35938	5764	10477	2408
%	100%	55·8%	29·1%	4·7%	8·5%	1·9%
Madagascar (2017)[11]						
n	333	117	200	6	10	0
%	100%	35·1%	60·1%	1·8%	3·0%	0%
Nigeria (2016)[12]						
n	19037	14800	3509	436	292	Not evaluated
%	100%	77·7%	18·4%	2·3%	1·5%	
South Africa (2013)[14]						
n	19097	3870	2396	6736	6095	Not evaluated
%	100%	20·3%	12·5%	35·3%	31·9%	
Zambia (2018)[15]						
n	1344	830	283	118	113	Not evaluated
%	100%	61·8%	21·1%	8·8%	8·4%	

Proportion of losses

Lowest — 50th percentile — Highest

Figure 2: **Findings from national-level care cascades for TB disease**
Losses at each gap are presented as a proportion of total estimated losses by country. TB=tuberculosis. *Total losses were calculated as cascade step 1 (TB burden estimate) minus the final cascade step estimate (step 5 [completed treatment] or step 6 [recurrence-free survival], as applicable). †Pre-testing losses were calculated as step 1 (TB burden estimate) minus step 2 (accessed testing). ‡Pre-diagnosis losses were calculated as step 2 (accessed testing) minus step 3 (diagnosed). §Pre-treatment loss to follow-up was calculated as step 3 (diagnosed) minus step 4 (started treatment). ¶On-treatment losses were calculated as step 4 (started treatment) minus step 5 (completed treatment). ‖1-year post-treatment recurrence or death was calculated as step 5 (completed treatment) minus step 6 (recurrence-free survival). **For India's care cascade, step 2 and later steps represent public sector estimates only.

Step	Challenges	Solutions

Step 1: estimated TB burden	**Difficulty estimating population-level TB burden**
	• Lack of timely and routine national prevalence surveys to accurately estimate population-level disease burden, especially disaggregated by region and demographic strata
	• Limitations of methods used to derive WHO TB burden estimates
	  • Limited accuracy, especially if based on extrapolation of notifications as notifications do not account for people seeking care via non-NTP pathways and TB deaths before presenting for care
	  • High uncertainty (wide confidence intervals) in these estimates further hinders their utility as the basis of estimation of subsequent cascade steps
	• Spillover cases from previous years pose a challenge as cascade analyses imply following a cohort through milestones in care
	Lack of electronic TB databases and data linkage
	• Triangulation from multiple data sources is challenging (and means that estimated cascades rarely follow the same cohort throughout subsequent steps—ie, each step is not a direct subset of the previous step)
	• Data linkage, such as between vital statistics databases and NTP data, is lacking
	• Processing of paper-based datasets is time-consuming and competes with NTP workers' ability to interpret and act on data
	Lack of timeliness of data capture
	• Data capture is often retrospective and not sufficiently timely to be useful for TB programme management
		• Conduct disaggregated prevalence surveys at periodic intervals
		• Develop operational research and modelling capacity to facilitate subnational burden estimates, building on capacity developed in countries through ongoing initiatives such as the Global Burden of Disease Study[35]
		• Implement post-mortem studies more widely and use the resulting data to inform TB burden estimates (to capture TB deaths before notification)
		• Implement the WHO roadmap on public–private mix,[36] so that disease burden and outcomes in the private sector can be better estimated
		• Invest in digital infrastructure

Step 2: proportion accessing TB testing	**Lack of clarity regarding what this step is attempting to estimate** • Several potential gaps of interest, including those who did not or could not seek care, those who sought care but were not tested, those who were tested but did not receive their results or diagnosis, and those with false-negative test results • Recommendations in some settings for the collection of smears on consecutive days create socioeconomic barriers to access to testing **Data capture, systems, and management** • Many programmes register people with TB at treatment initiation (and some at diagnosis) but not at testing—systems used to capture routine NTP data, therefore, do not align with the data requirements of cascades • People presenting at general health centres (not TB-specific clinics) might not be referred for testing • Data capture at the presumptive TB stage is challenging, especially for those treated empirically and those with paucibacillary disease or extrapulmonary TB—eg, in Zambia, although presumptive TB registers exist at all facilities, their quality is variable, especially compared with the national notification register **Heterogeneity of diagnostic tests for TB** • Varying sensitivity and specificity, particularly in specific populations (eg, GeneXpert MTB/RIF sensitivity is 79% [95% CI 70–86] in people living with HIV and 62% [51–73] in children)[37,38]	• Use standardised questionnaires to help capture symptoms and presumptive cases and whether they sought care but were not diagnosed • Improve data capture at early stages • Conduct more frequent prevalence surveys (to help differentiate between those who were symptomatic but not seeking care *vs* those seeking care but not being tested) • Improve data quality of facility-level presumptive TB registries via NTP-led standardised guidance and training for facilities on data capture • Helpful to have sensitivity estimates for GeneXpert under local NTP conditions and in specific populations • Helpful to know the proportion of people receiving specific tests in local testing algorithms

Step 3: proportion diagnosed with TB	**Limitations of routine programme data quality**
	• Cases that are more likely to have a poor outcome are sometimes not registered due to incentives for programmes to reach certain milestones—for example, regarding treatment success rates
	• Consideration of clinically diagnosed TB as true TB, which could significantly overestimate case detection, particularly in settings where a large proportion of people are clinically diagnosed
	Timing of data capture
	• Pre-treatment loss to follow-up is difficult to measure (requires triangulation with laboratory data) as most NTPs register people at treatment initiation
	• Retrospective data entry from paper records
	Inability to track transfers to other centres before treatment initiation
	• Lack of unique identifiers
	• Illegibility of contact information for people with presumptive TB
	• Lack of electronic data capture systems
	Lack of data linkage
	• For example, lack of linkage of treatment data with laboratory data, or linkage over geographical areas
		• Digitise data capture
		  • Although this would in part facilitate addressing these challenges, the barriers to implementing electronic data systems are significant, as highlighted in step 2)
		• Conduct programme quality monitoring and evaluation
		  • It should be noted that data quality concerns apply to both paper-based and electronic data capture systems, which underlines that other quality improvement efforts are also needed to improve paper-based and electronic records, including, for example, performance feedback[39]
		• Scale up molecular testing

Step 4: proportion initiating TB treatment Step 5: proportion completing treatment	**Under-notification and data quality limitations** • People with TB who are more likely to have a poor outcome might not be registered • Under-notification due to transfers (the use of paper-based systems and lack of unique identifiers to track transfers worsens this) • People diagnosed at non-NTP sites are often not registered **Lack of stratified data** • Although stratified reporting by sex and age group is now required by WHO, stratification by other sociodemographic factors relevant to local contexts is needed for construction of sub-cascades that examine important differences in care-seeking and outcomes across strata	• Recognise the importance of medical colleges and hospitals as reporting units • Conduct data quality assessments and qualitative studies to understand the reasons for under-notification and missed cases and opportunities to enrol people earlier • Examine sub-cascades—eg, multidrug-resistant TB, paediatric TB, and others—to gain a more granular understanding of stratum-specific cascade bottlenecks
Step 6: proportion reaching 1-year recurrence-free survival	**Lack of post-treatment follow-up of people who completed TB treatment for at least 1 year** • Despite a clear rationale for 1-year recurrence-free survival as a measure of durable cure, especially given that most relapses occur within the first year after treatment, this is not captured in routine programme data • In programmes where discharge (at the end of treatment) is the endpoint of follow-up in TB registries, additional follow-up is solely passive • Although 1-year follow-up is included in some NTP guidelines (eg, in India), implementation remains a challenge • Even if 1-year follow-up is done for recurrence and survival, this is unlikely to capture post-TB lung disease	• Establish robust data systems and follow-up capacity, allowing the reliable assessment of the 1-year endpoint • Integrate post-treatment follow-up (and monitoring for post-TB lung disease) into adherence studies

Figure 3: **Challenges, data needs, and potential solutions for estimating each step in the TB care cascade**
NTP=national TB programme. TB=tuberculosis.

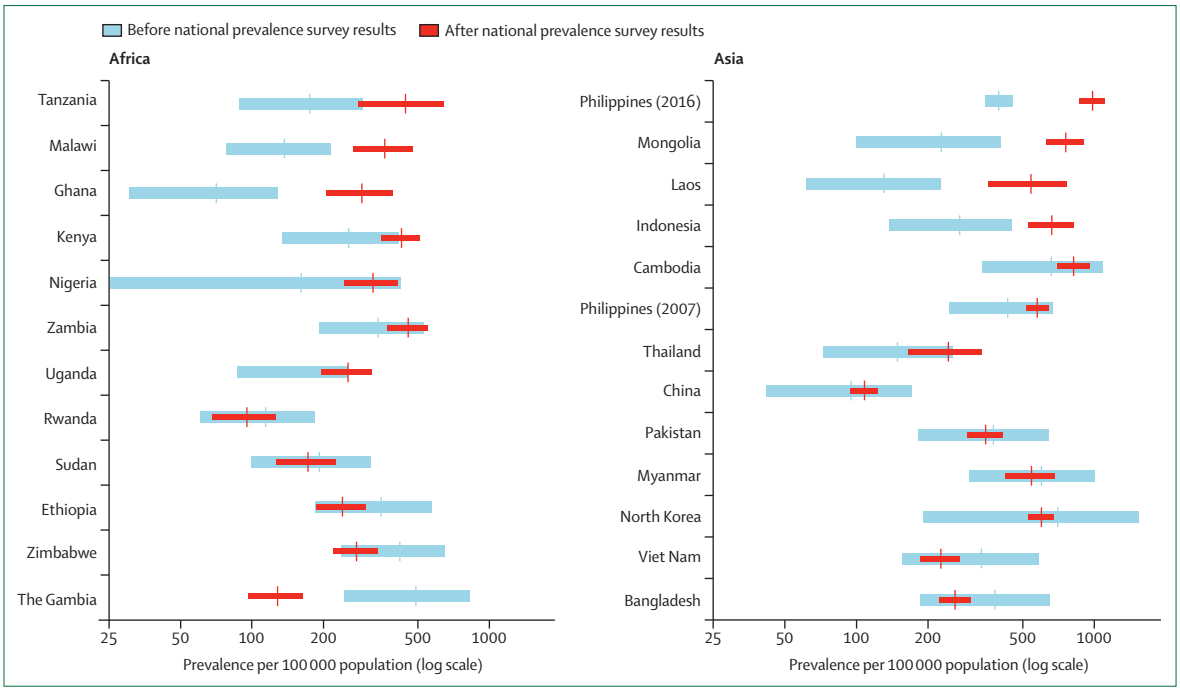

Figure 4: **Estimates of TB prevalence (all ages and all forms of TB) in 24 countries before and after results of national TB prevalence surveys (implemented between 2007 and 2016) became available**

Source: National tuberculosis prevalence surveys 2007–16. Geneva: World Health Organization; 2021, creative commons license CC BY-NC-SA 3.0 IGO.[41] Countries are listed in decreasing order according to before–after difference in estimated prevalence. TB=tuberculosis.

progress towards TB goals and allocate resources based on needs. Apart from guiding quality improvement efforts for programme operations, care cascade estimation can also enhance quality control for programme data, bringing to light data management issues that can then be rectified.

Crucially, as care cascades are descriptive, their estimation will not translate into TB programme improvements unless accompanied by the willingness to take evidence-based action in response to the findings. Encouragingly, recent care cascade analyses have guided some TB programme priorities. Construction of the MDR-TB care cascade in Madagascar facilitated goal setting for MDR-TB surveillance and care delivery, and regional disaggregation of data allowed the targeting of additional MDR-TB centres in priority areas.[11] Care cascade analyses have been used in India to inform the country's national TB strategic plan for 2017–25,[29] to inform differentiated care strategies,[30] and to understand loss to follow-up along the TB care pathway in India's 2007–21 National Health Programme guidelines,[31] leading to the integration of data capture into India's online TB data management system.[32] Furthermore, initiatives are underway in India to implement interventions with private provider support agencies, targeted at specific geographical areas, to translate care cascade findings into TB programme practices.[33] In South Africa, the TB care cascade has contributed to TB programme planning since 2017, having been included in the 2017–22 national strategic plan for HIV, AIDS, TB, and sexually transmitted infections.[34] In general, however, few of the cascades shown in figure 2 have been directly used to inform programme improvement in a manner documented in official reports.

Mapping data gaps across the care cascade

We identify five overarching data gaps that hinder accurate estimation of TB care cascades in high-incidence settings. Descriptions of specific data gaps, and approaches to addressing these challenges to improve the accuracy of care cascades, are shown in the figure 3.

Lack of population-based data on TB burden

As many care cascades begin with an estimate of the TB burden in a country or region as the baseline from which subsequent losses occur, suboptimal data on the burden of TB at the population level is often a major challenge for estimating care cascades. For example, methods used in WHO estimates of TB incidence are heterogeneous[40] and have limitations, especially when extrapolated from a country's case notifications, which might underestimate true TB incidence.

Although they are expensive and time-consuming, national prevalence surveys help estimate the extent of missed cases and inform more accurate estimates of TB burden. A WHO analysis of TB prevalence surveys in 24 countries showed that these surveys often result in upward revisions of national prevalence estimates (figure 4).[41] This suggests that care cascades often

underestimate losses, as they might be based on underestimates of prevalence and, therefore, TB incidence, as estimates of incidence are often informed by prevalence estimates. For example, in South Africa, the first national TB prevalence survey, conducted in 2018, found a prevalence of all forms of TB of 737 cases (95% CI 580–890) per 100 000 people,[42] as compared with a lower estimate of 696 cases (390–1088) per 100 000 people reported in the 2015 WHO Global TB Report, which was the last time WHO reported estimates of TB prevalence (as opposed to incidence) for high-incidence countries.[43] Similarly, in India, a national prevalence survey conducted in 2019–21 showed a prevalence of all forms of TB of 312 cases (286–337) per 100 000 people,[44] as compared to the much lower estimate of 195 cases (131–271) per 100 000 people reported in the 2015 WHO Global TB Report.[43] In Peru, funding challenges in the national health system[45] hinder the implementation of national prevalence surveys despite the NTP's strong interest, highlighting funding as a barrier to wider implementation of these surveys.

Even when data from nationally representative TB prevalence surveys are available, apportioning TB burden to achieve accurate subnational-level estimates—to facilitate the construction of locally relevant care cascades—remains challenging. Given sometimes wide disparities in the local burden of TB and important TB risk factors such as HIV or undernutrition, disaggregated data are crucial. Data disaggregation is important not only geographically, but also along demographic and clinical strata, to allow strata-specific cascades to be constructed (eg, for paediatric TB, drug-resistant TB, incarcerated populations). Consequently, bottlenecks along the cascade for specific groups could be more easily identified, and NTPs could target resources to priority groups. Lastly, particularly in the context of public health shocks such as the COVID-19 pandemic, repeated prevalence surveys are needed to produce cascades that can inform programmatic decisions.

Lack of electronic data capture systems

Lack of electronic data capture is a common challenge across many NTPs that affects the estimation of multiple steps of the care cascade. Some NTPs are using systems for data digitisation, including TIER.Net in South Africa,[46] Nikshay in India,[32] and Sistema de Información Gerencial de Tuberculosis (SIGTB) in Peru.[47] Nonetheless, barriers to implementing electronic data capture persist (eg, internet speed and availability), especially in rural health centres. Reliance on paper-based data entry, therefore, continues to delay data collection, increase the risk of data loss, and preclude standardisation of data entry. These factors hinder the timely tracking of people with TB with unique identifiers throughout their care pathway, particularly for people who transfer to other facilities or whose contact information is illegible, incorrect, or missing, which contributes to pre-treatment loss to follow-up.[48,49] As a result, outcomes for these people—including deaths before treatment initiation[48,50]—are unlikely to be captured in the NTP database. In both South Africa and Zambia, the difficulty of tracking transfers has been identified as a major driver of under-notification.[14,15]

In addition to data linkage across facilities, linkage among different databases—such as linkage of NTP data to general laboratory and vital statistics databases—is also important. Electronic data capture would also enable analyses of disaggregated subnational data. Lastly, digitised data systems would facilitate data quality assurance. This is crucial, as recent analyses highlight the variable quality of routine TB programme data,[51] underlining that improvements are needed for these data to serve as a reliable basis for estimating care cascades.

Although constraints in finances and digital infrastructure pose significant challenges to the feasibility of implementing electronic data systems, the COVID-19 pandemic and other public health emergencies have underlined the value—and current shortcomings—of robust national health data systems and governance, while leading to valuable improvements, including data digitisation, in many settings.[52,53] For example, in Uganda, an electronic health logistics data management platform launched during the Ebola epidemic was successfully used for the COVID-19 response, providing timely data for programme planning.[54] Investments in strengthening digital infrastructure as a whole, therefore, have the potential to facilitate the shift to electronic data systems in specific programmes such as NTPs.

Under-reporting of people with TB navigating fragmented and privatised health systems

Under-notification is another barrier to estimating accurate care cascades. Under-notification occurs for several reasons, including the lack of unique identifiers to track people with TB throughout care, but is further complicated by the fragmented health systems people must navigate to access TB care. Unfortunately, a large proportion of people never access TB care in the first place, particularly in rural communities, as noted in a study of tribal populations across 17 states in India.[55] Even when people do seek care, they might not be appropriately referred for testing, as has been noted in standardised patient studies in India,[56] China,[57] Nigeria,[58] and South Africa.[59] Furthermore, in some settings, particularly countries with large migrant populations, it is common for people with TB to seek care and be diagnosed in larger urban centres and then be lost to follow-up during referral back to rural TB centres to start treatment.[48,60,61]

Under-notification can also occur due to non-NTP sites (eg, academic hospitals, private sector providers) not serving as TB reporting units, as is the case in some settings (including in Zambia,[62] Madagascar,

South Africa, and Nigeria[63]), where people diagnosed with TB in hospitals are often not registered in the NTP. Under-notification is a particular concern in countries where the private sector plays a significant role in TB care.[64] In India, for example, although recent initiatives have substantially increased private sector notification, many people with TB in the private sector are still not being notified consistently, despite notification being mandatory.[65]

Even when people with TB are notified from the private sector, treatment and post-treatment outcomes might not be consistently reported for these people, making it challenging to accurately estimate later care cascade stages. Under-reporting of outcomes from the private sector underscores that more work is needed to engage private providers, as suggested by WHO's roadmap for public–private mix, a key recommendation of which is better tracking of the number of people with TB managed in the private sector, along with information on their referrals, notifications, and treatment outcomes.[36] Notably, the Indian TB care cascade[10] accounted for the public sector only. Not accounting for people with TB in the private sector is not a significant limitation in settings such as Zambia, where a small proportion of people with TB seek care in the private sector, and most are accounted for in the national cascade through notification to the NTP. In other settings with large private sectors, however, cascades limited to the public sector cannot fully represent outcomes of TB care delivery.

Even in countries in which the private sector plays a small role in TB care, public sector under-notification remains significant, as shown in a data quality assessment in Zambia.[61] Difficulties with capturing TB deaths that occur before presenting for care also contribute to under-notification. In Peru, for example, where all people with TB are treated in the public sector[66] (and private sector care-seeking is not considered to be a major factor in under-notification), deaths from TB before registration in the NTP remain difficult to capture, due to limitations in death registry data. Similar challenges have been noted in Zambia, where post-mortem studies offer a strategy for estimating the extent of missed TB cases, with one study reporting incidental autopsy findings of TB in 1·2% of all sudden unexpected deaths in the community.[67] Data from post-mortem studies could, therefore, be incorporated into TB burden estimates.

Furthermore, systematic under-notification of people with TB who are more likely to have poor treatment outcomes jeopardises routine programmatic data quality, particularly in settings where programmes experience pressure to reach milestones. This creates incentives to avoid registering high-risk people with TB,[68,69] which can introduce selection bias in treatment success rates. In Zambia, a nationally representative data quality audit was conducted to determine the number of people with TB who were diagnosed but not notified. This audit found that 33% of people with TB were unnotified (not reported in treatment registers).[62]

Given the various mechanisms by which under-notification occurs, qualitative research could be used to improve our understanding of the reasons for under-notification and to identify opportunities for earlier registration of people with TB. A qualitative study in Peru has shown that imposed programme targets (to carry out a certain number of TB tests per month) incentivised TB testing in individuals not suspected of having TB, delaying detection of actual cases.[70]

Heterogeneity of diagnostic tests for TB

The heterogeneity of diagnostic tests used for diverse forms of TB, and their varying sensitivity and specificity, further complicate estimation of care cascades. Most tests in the TB diagnostic algorithm have suboptimal sensitivity, particularly compared to HIV testing, for example. Given that most HIV tests are highly sensitive and specific, rigorously estimating HIV prevalence using sentinel surveillance or population-based surveys has been possible, in turn facilitating more accurate estimation of HIV care cascades.[71]

Recent studies, including care cascades, have used the known performance characteristics of TB diagnostic tests (sputum smear microscopy, GeneXpert) to estimate the proportion of people with test-negative pulmonary TB who might be missed by TB programmes, with a Guatemalan study estimating that routine use of GeneXpert as a follow-up to smear microscopy would result in a 41% increase in TB notifications through identification of smear-negative cases.[72] However, prospective studies of pathways to care for people with extrapulmonary TB and children with TB are also needed to estimate follow-up throughout completion of the diagnostic workup, thereby facilitating estimation of diagnostic losses in these groups. This will require rigorous local care cascade studies and methodological innovation.

In addition, as countries may use a variety of TB diagnostic modalities (eg, sputum microscopy, molecular tests, chest X-ray), characterising diagnostic test performance under local NTP conditions might enable more accurate care cascade estimation, as would estimates of the proportion of people receiving specific modalities for upfront testing in different settings.

Lastly, counting all clinically diagnosed individuals as true TB cases poses a further challenge for care cascade analyses, as a proportion of these might not have TB (ie, false-positive misdiagnoses). This is particularly challenging in settings where clinical diagnoses make up a large proportion of all diagnoses, which is common in settings where sputum smear microscopy is relied on but is also observed in settings where access to rapid nucleic acid amplification tests (eg, Xpert MTB/RIF) is readily available. For example, in many high TB burden countries, including North Korea, Mozambique,

Panel: **Calls to action to address tuberculosis (TB) care cascade data gaps and effectively use cascade analyses in working towards TB elimination**

Call to Action 1: recognition of the value of care cascades by global agencies and funders, and the creation of an international working group on TB care cascades

So that national TB programmes (NTPs) can be appropriately supported in the routine estimation of TB care cascades, the value of the TB care cascade model—and its potential to improve TB care, if appropriately acted upon—must be recognised by global agencies and funders. First steps towards this include:

- Global bodies convening an international working group to develop recommendations regarding the routine use of care cascades in national TB programmes, including establishing mandatory reporting standards, and the standardisation of methods and approaches used to estimate TB care cascades to facilitate comparability; estimates of all steps (1–6) in the TB care cascade, along with the methods used to derive them, should be reportable to WHO;
- WHO presenting care cascades in annual TB reports, as key indicators of progress towards TB elimination;
- Major funders such as The Global Fund to Fight AIDS, Tuberculosis and Malaria and the US Agency for International Development advocating for TB care cascades as a measure of system performance and allocating resources to global capacity-building in this regard—this will generate capacity, resources, and support for their routine application in NTPs

Call to Action 2: funding and conduct of national TB care cascade studies and TB prevalence surveys

In the short-term, global bodies and funders should support periodic, nationally representative, prospective care cascade studies, as well as TB prevalence surveys (similar to population-based survey initiatives being done for HIV[79])

Call to Action 3: routine application of care cascades to track TB elimination

National TB programmes, with guidance from WHO, should apply care cascades to the regular and transparent tracking of progress towards TB elimination goals, including to:

- Facilitate TB programme monitoring and evaluation (eg, via joint monitoring missions[80] and other evaluations of NTPs);
- Facilitate evidence-based planning for programme improvements;
- Improve visibility of TB management in the private sector (NTPs in countries in which a large proportion of people seek TB care in the private sector will need to step up efforts towards private provider engagement in order to construct meaningful cascades and consequently be able to act on robust findings);
- Hold policy makers accountable to making the investments required to reach TB elimination targets

Call to Action 4: development of capacity for data digitisation and routine care-cascade measurement

In the long term, national TB programmes should work towards developing capacity for routine measurement of the care cascade, including at the local level. This includes developing capacity for:

- High-quality electronic data capture;
- Real-time data entry;
- Wide geographical coverage;
- Data quality assessments

Call to Action 5: integration of post-treatment monitoring into NTP guidelines

Progress should be made towards integrating post-TB care into NTP guidelines, practices, and reporting, including routinely monitoring people for at least 1 year after treatment completion

Myanmar, Papua New Guinea, the Philippines, Tanzania, and Zambia, more than 50% of pulmonary TB notifications are exclusively clinically or radiologically diagnosed, and in several additional high TB burden countries, exclusive clinical or radiological diagnoses exceed 40% of notifications.[21] Case detection rates might, therefore, be overestimated in these settings, limiting the accuracy of care cascades.

Lack of routine post-treatment follow-up

There is growing awareness of the importance of post-TB lung disease[73] and the need to assess long-term outcomes for people treated for TB. Most TB recurrence (91%) occurs in the first year following treatment,[74] especially in low HIV prevalence settings,[75] providing a strong rationale for following people with TB for at least 1 year after treatment completion. Given high TB recurrence rates under programmatic conditions in many settings,[26,76,77] routine post-treatment follow-up would not only estimate durable cure, providing a highly motivating outcome metric for TB programmes, but it would also serve as an efficient form of active case finding, facilitating increased and early identification of TB recurrence, and continuity of care. This is particularly important given that previously treated people with TB have substantially poorer treatment outcomes than people with new TB.[78] However, despite its clear utility, 1-year recurrence-free survival is not measured routinely in most TB programmes, with episodes of recurrence detected only if the person presents to the health system again. Routine post-treatment follow-up would also be opportune for the continued engagement of people in the health system to provide care for post-TB lung disease and other comorbidities, such as HIV and diabetes.[73] The current lack of post-treatment follow-up is, therefore, a major missed opportunity for TB programmes to improve care. Consequently, the proportion of people achieving 1-year recurrence-free survival without post-TB lung disease should be seen as the final endpoint of the care cascade and should be reportable to WHO, along with estimates for previous care cascade steps.

Conclusion and calls to action

To rectify data gaps in TB care cascades, NTP data systems and reporting practices must be improved, including through digitisation of data capture, data linkage, and addressing under-notification. If applied routinely for the purpose of identifying bottlenecks in TB programmes, care cascades could serve as valuable quality improvement tools to point towards the most needed interventions. Once robust care cascade analyses are available, acting upon them to improve TB outcomes at a population level will be even more crucial.

To fully tap into the potential of care cascade analyses as a strategy for accelerating TB elimination, we present five calls to action (panel). First, we call on global agencies and funders to recognise the value of TB care cascades,

so that investments can be made to support NTPs in the routine estimation of national and sub-national care cascades to inform programme monitoring and improvement. A diverse international working group should be convened to develop recommendations regarding the routine use of care cascades by NTPs, including establishment of mandatory reporting standards, as well as standardisation of methods for estimating cascade steps, to allow comparability across settings and time. Eventually, estimates for key steps in the TB care cascade should be reportable to WHO, along with a description of the methods used to derive these estimates.

Second, we recommend that global bodies and funders support periodic, nationally representative, prospective care cascade studies, which can be paired with community TB prevalence surveys. Such studies are being successfully implemented for HIV, where population-based surveys are identifying where to target resources to make progress most effectively. For example, the Population-based HIV Impact Assessment (launched in 2014) conducts nationally representative surveys in 14 countries to determine HIV prevalence and estimates of the care cascade to the endpoint of viral load suppression.[79] While these surveys found high viral load suppression in individuals who were aware of their HIV status, the most difficult gap to close has been the high proportion of individuals—particularly men and young people—who are still unaware of their status. This has highlighted that HIV awareness programmes should prioritise these groups.[71] The surveys have also been used to identify gaps in care, such as treatment coverage gaps among children,[81] and long-term outcomes such as HIV-free survival among children born to mothers with HIV.[82] For TB, accurate country-level care cascades could be similarly estimated through nationally representative sampling of TB facilities, followed by prospective follow-up. If paired with population-based TB prevalence surveys, this could facilitate periodic rigorous estimates of the entire care cascade to inform a country's TB response.

Third, with the necessary support from global agencies, we call for the care cascade model to be applied to the regular and transparent tracking of progress towards the TB elimination goals to which countries have committed. This includes using care cascades to facilitate TB programme monitoring and evaluation (including private sector TB care, in countries with large private health sectors), to provide an accurate foundation for evidence-based programmatic improvements, and to hold policy makers accountable for making the investments required to reach TB elimination targets. To this end, we hope WHO will include national TB care cascades in the annual Global TB reports.

Fourth, as a long-term yet critical call to action, NTPs should work towards developing capacity (eg, high-quality electronic data capture systems with real-time data entry and wide geographical coverage) for routine measurement of the care cascade, including at the local level. Given that outcomes are heterogeneous within countries, local data will most directly drive improved outcomes for people with TB by identifying local bottlenecks and allowing precise resource allocation. It should be noted, however, that processes for establishing robust digital data capture will differ by setting, depending on the extent of infrastructure already available. In some settings, overall investment in general digital infrastructure will be required before specific TB-related systems can be adopted, and the implementation of electronic data systems should be accompanied by appropriate data governance policies.[83] Data digitisation is an overarching and critical challenge that, if addressed, would significantly improve data availability and quality for the estimation of care cascades.

Our final call to action asks that progress be made towards integrating post-TB care into NTP guidelines and practices, including routinely monitoring people for at least 1 year after treatment completion. Beyond active follow-up for recurrence and survival, there must be additional efforts to monitor and provide care for post-TB lung disease and morbidity[84] and to include measures of post-TB lung disease as part of the final outcome of the care cascade. This will advance multiple goals, including improving care for people with TB, serving as a form of active case-finding (through increased and earlier identification of recurrence), and providing a measure of durable cure, which is a better indicator of TB programme performance.

Together, these calls to action offer a way forward for effectively using care cascades as tools for identifying gaps in TB care and facilitating evidence-based improvements to TB programmes globally.

Contributors

RS and LF conceived the study; were responsible for data curation, analysis, and visualisation; and wrote the first draft of the manuscript. RS and MP supervised the study. All authors reviewed and edited the manuscript and were responsible for the final decision to submit for publication. LF and RS accessed and verified all of the data reported in the study.

Declaration of interests

MP serves on the Scientific Advisory Committee of the Foundation of Innovative New Diagnostics (FIND), a non-profit global alliance for diagnostics. MP is also an adviser to the Bill & Melinda Gates Foundation. He has no financial or industry conflicts. CU-G has received research support from the International Development Research Centre (Canada) and the Canadian Institutes of Health Research, the National Institutes of Health, FIND, and Abbott for projects unrelated to this work. CU-G has also received honoraria from Molbio for presentations unrelated to this work. All other authors declare no competing interests.

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