Understanding and addressing the tuberculosis case detection gap: national inventory studies to improve estimates of incidence and strengthen surveillance

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Background

Global targets for the reduction in tuberculosis (TB) disease burden were set within the context of the United Nations Millennium Development Goals (MDGs), spanning the period 2000-2015.[1] The targets were that TB incidence should be falling and that TB prevalence and mortality should be reduced by 50% compared with 1990 rates. Building on the MDGs, the recently adopted Sustainable Development Goals (SDGs) include as a target to end the TB epidemic, as measured by TB incidence, by 2030.[2] The World Health Organization's (WHO) post-2015 global TB strategy has corresponding targets of a 90% reduction in deaths and an 80% reduction in the TB incidence rate by 2030.[3] The accurate understanding and measurement of TB incidence, one of the high level indicators consistently used by the global health community since 2000, is pivotal to monitoring progress against targets, and assessing whether investments in TB care and prevention reap benefits.

The level of and trends in TB incidence and prevalence can be directly measured through population cohort studies and prevalence surveys, respectively. There is general agreement that national cohort studies are too expensive and impractical to implement, while many countries do not meet the recommended criteria to conduct a national TB prevalence survey. In settings with state-of-the-art routine surveillance systems where most, if not all of, new TB cases are diagnosed and registered, TB cases notified to the National TB Programme (NTP) of the Ministry of Health provide a good proxy for TB incidence. Most often than not however case detection gaps plague national TB surveillance systems at different stages throughout the patient cascade. Incident TB cases could be missed from national TB surveillance systems: in settings with no universal health coverage and hence no access to diagnosis; due to errors in correctly identifying individuals as having presumptive TB; due to errors in diagnosis of TB; due to TB patients not receiving anti-TB treatment; and due to no notification of TB cases diagnosed or on treatment to the NTP.[4-7] The total case detection gap is the sum of the accessibility, diagnosis, treatment and notification gaps. A customised and more cost-efficient alternative to population cohort studies and prevalence surveys that could inform the extend of such gaps, are TB inventory studies.

TB inventory studies have two broad study objectives, one involving the direct measurement of TB under-reporting and the other, under certain conditions, the estimation of TB incidence through capture-recapture (CR) analysis.[8]

Methods

There are two categories of design for national TB inventory studies: the retrospective design, most often possible in resource-rich settings – which uses existing national, case-based TB surveillance as well as other TB-related databases, such as health insurance, laboratory, hospital admission or pharmacy registers – and the prospective design, most often possible in resource-limited settings, which involves the creation of study registers from a representative national sample of health-care providers who diagnose and/or treat TB, such as private and non-NTP public practitioners.[8] For both designs, linkage of the study registers with the national TB surveillance database is required. This can be done either deterministically, with a unique identifier (e.g. national ID number), or probabilistically with a combination of patient characteristics (e.g. age, sex, postcode). Inventory studies require extensive data management and analytical skills, particularly true when CR analysis is attempted, that may not be available in NTPs. Local research partners and international technical assistance are often needed to support study implementation.

In principle, all countries are eligible for inventory studies. However, they may be most relevant for countries where substantial under-reporting is expected, because reporting of TB is not mandatory or is mandatory but not enforced, or due to a large private or non-NTP public sector with weak or no linkages to the official TB surveillance system. For counties with a strong surveillance system inventory studies could produce clear and quantifiable evidence that TB case notifications are a good proxy for TB incidence.

Results

There has been considerable momentum during the last ten years in the implementation of national inventory studies to measure TB under-reporting, and in many cases in combination with capture-recapture analysis, in countries including the Netherlands[9], the UK[10], French Guiana[11], Egypt[12],

Yemen [13], Iraq[14], Pakistan[15] and Kenya[16]. Hypothesis-generating investigations to assess the level of TB case detection gaps were also completed in India[17] (cross-sectional survey of households), Indonesia[18] and Viet Nam[19] (nested within a national prevalence surveys among adults). The level of TB under-reporting found was context-dependent ranging around 15% in European countries, 20% in Africa, 30% in the Eastern Mediterranean region, and 50% in countries in Asia with a large private sector. These data have all informed national estimates of TB disease burden.[20]

Results from inventory studies provide the platform and evidence to make programmatic changes to better address TB. Studies in Pakistan and Vietnam, settings with rapid growth of the private sector and the availability of TB drugs in private pharmacies, identified the need to strengthen TB surveillance in both countries and to scale up public-public and public-private mix (PPM) interventions to address high levels of under-reporting from that sector. In both countries, study results informed the national strategic plans and guided investment in concept notes submitted to the Global Fund. Inventory studies have also provided evidence to NTP programs on where to target their efforts to strengthen surveillance. For example, results from a study in Kenya found differences in the level of under-reporting by region.[16] Under-reporting was also more likely in patients who were older, had scanty smear results, and were diagnosed at large or private facilities. Results were used by the NTP to inform the development of systems to improve linkages between laboratories and TB facilities and to track diagnosed patients who do not return for treatment in areas with the highest levels of under-reporting. In countries such as the UK, capture recapture studies have informed specific modifications to the surveillance system to decrease under-reporting. For example, laboratory reports are automatically flagged to local teams to encourage the clinical reporting of cases supported by an automated record linkage programme in the surveillance system.

Discussion

The role of TB inventory studies is critical in quantifying how much of a gap in under-reporting of TB there is in a country and where that gap is in terms of the type of health care providers who diagnose

the disease. Next to that, these studies produce national level data that improve the estimates of the level of and trends in disease burden and make monitoring of progress towards international targets for TB a more robust and methodologically sound exercise. The contribution of national inventory studies is particularly important for childhood TB where they are currently the only option to provide direct measurements that improve our understanding of burden due to TB and this way contribute to better scale up response.

Furthermore, the results and lessons learnt from inventory studies provide invaluable insight for national TB programmes with respect to health care seeking behaviour of TB patients and reporting practices of health care providers that diagnose TB. Inventory studies may support the establishment or expansion of PPM recording and reporting by building links with sectors that are not normally under the purview of the NTP, such as paediatric specialists or private laboratories; they showcase the benefits of case-based electronic TB surveillance solutions; they provide a better understanding of existing diagnostic and case management practices in the non-NTP sector; they promote the institutionalisation of components of inventory study type investigations as part of annual quality checks of the TB surveillance system; lastly where the prospective design is implemented the studies provide detailed mapping of health-care providers in the sampled areas and a clear understanding of the different types of facilities that diagnose and treat TB in the country.

Promising recent interest from agencies such as the European Centre for Disease Prevention and Control and UNITAID has resulted in the planning of much needed national TB inventory studies in countries in Asia and Europe. In general, inventory and capture-recapture studies are less costly than other population-based sampling methods relevant to TB. Reasonable budget estimates for these surveys are around USD 200,000 – 400,000 for prospective and USD 50,000 – 100,000 for retrospective designs.[8]

Limitations to these studies include: failure to establish linkage of records that appear in a non-sampled area or that were recorded outside the timeframe of the study resulting in misclassification of

reported (or not reported) TB cases; change in recording and reporting practices of health care providers during study implementation; errors with record linkage; unmet conditions necessary for the successful implementation of capture-recapture analysis most importantly the independence of case source registers. [21] Lastly, in resource-limited settings where the retrospective design is not possible and a large percentage of the population lacks access to basic health care, inventory studies may not be useful in that only a small percentage of TB cases can be identified as a proportion of the much larger pool of missing cases which are not detected by the health system at all.

Conclusion

Strengthening national TB surveillance systems and the data they produce is the only credible way to ensure the robust and routine monitoring of progress towards international targets for TB. Inventory studies are an important tool, one of the few available to us today, to achieving that goal for TB surveillance. As countries begin working towards the new TB incidence targets set within the SDGs and WHO post-2015 global TB strategies, increased commitment from NTPs and funding agencies to conducting and funding TB inventory studies is urgently required.

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