EPIDEMIOLOGICAL REVIEW OF TUBERCULOSIS SURVEILLANCE IN NEPAL

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JANUARY 2019





Government of Nepal Ministry of Health and Population Department of Health Services **National Tuberculosis Control Centre** Thimi, Bhaktapur



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SUMMARY

The purpose of the epi review mission to Nepal that took place in January 2019 was to assess the completeness and accuracy of routine tuberculosis (TB) surveillance and vital registration (VR) systems and to investigate the plausible drivers of the TB epidemic in the country.

Objectives

The objectives of epi-review were:

- 1. Describe and assess current national TB surveillance and vital registration systems, with particular attention to their capacity to measure the level of and trends in TB disease burden (incidence and mortality).
- 2. Assess the level of, and trends in, TB disease burden (incidence and mortality) using available surveillance, survey, programmatic and other data.
- Assess whether recent trends in TB disease burden indicators are plausibly related to changes in TB-specific interventions taking into account external factors including economic or demographic trends.
- 4. Evaluate progress since the 2014 epidemiological review and identify actions and resources needed to complete and strengthen new processes and activities

Methods

The checklist and associated user guide from Standards and Benchmarks for Tuberculosis Surveillance and Vital Registration Systems were applied for the assessment. Methods of data collection included: (1) Desk review of available TB control-related policy papers, manuals, guidelines, publications and forms; (2) Interviews and discussions with TB authorities and health care providers at national and district level; (3), Review of TB records, laboratory registers and electronic surveillance systems; (4) Review of electronic databases to assess the level of incompleteness of key variables; (5) Analysis of notification/surveillance data over time and space to identify trends in disease burden and programmatic efforts.

Key Findings

Performance of surveillance and VR system

Despite continuing challenges from limited financial and other resources and the ongoing impacts of the 2015 earthquake, Nepal has made excellent progress in implementing a majority of recommendations from the 2014 epidemiological review, particularly in implementing electronic case-based surveillance, and aligning the case definitions and reporting forms with World Health Organization (WHO) "Definition and reporting framework for tuberculosis, 2013 revision". There was notable improvement in detection and notification of child TB, rifampicin-resistant TB (RR-TB), and TB/HIV co-infection. Of the 13 standards for TB surveillance from the checklist, four were met, five were partially met, and four were not met (Table 1), indicating that there is still room to

improve the TB surveillance system. We can, therefore, assume that notifications substantially underestimate true TB incidence in Nepal, in part because of the population's limited access to health care and the seemingly low sensitivity of commonly employed screening and diagnostic methods. Furthermore, the surveillance system is not currently well designed to assess the loss to follow up during diagnosis and prior to treatment initiation, which will result in further under-reporting.

Table 1 Summary of standards for TB surveillance in Nepal, January 2019

STANDARD		PARTIALLY MET	NOT MET
B1.1 Case definitions consistent with WHO guidelines	\boxtimes		
B1.2 TB surveillance system captures minimum set of variables for reported TB cases	\boxtimes		
B1.3 All scheduled periodic data received and processed at the national level			
B1.4 Data in quarterly reports are accurate, complete, and internally consistent		\boxtimes	
B1.5 Data in national database accurate, complete, consistent, and free of duplicates		\boxtimes	
B1.6 TB surveillance data are externally consistent	\boxtimes		
B1.7 Number of reported TB cases internally consistent		\boxtimes	
B1.8 All diagnosed cases of TB are reported			\boxtimes
B1.9 Population has good access to health care			\boxtimes
B1.10 Vital registration system has high national coverage and quality			\boxtimes
B2.1 Surveillance data provide a direct measure of drug-resistant TB in new cases			
B2.2 Surveillance data provide a direct measure of the prevalence of HIV in TB cases	\boxtimes		
B2.3 Surveillance data for children reported with TB are reliable and accurate			\boxtimes

Strengths

- Presence of a user-friendly web-based electronic database for drug-sensitive TB patients established in a number of districts;
- Good internal consistency of TB surveillance data;
- Use of standard recording and reporting (R&R) forms and case definitions in line with WHO recommendations;
- Extensive data analysis was done at the national level;
- Highly skilled M&E staff at the national level;
- Government commitment and funding for TB surveillance;
- The success of the on-going TB prevalence survey;
- Availability of number high-quality operational research studies on validation of screening and diagnostic algorithms, the yield of screening, and case detection data in various risk groups.

Weaknesses / gaps:

- Interruption to many activities, including TB reporting at district level, due to restructuring and decentralization of health services implemented without sufficient transition planning and support;
- The accuracy of data in quarterly reports is not fully assessed in a representative sample of diagnostic services;
- The database for drug-resistant TB cases is not fully functional at district level;
- Probable under-diagnosis of TB, especially in children, the prison population and males aged 25-44 years;
- Low sensitivity and stability of current screening and diagnostic methods resulting in a low yield of
 presumptive and diagnosed cases during both routine and intensified case finding (ICF) activities;
- Low Gene-Xpert testing coverage, and unknown coverage among priority groups;

- Incomplete or missing notification of TB patients treated in the private sector and inability to quantify the initial loss to follow-up;
- Incomplete availability and use of all R&R forms in all facilities (such as treatment cards, presumptive TB registers, contact tracing registers, preventive TB treatment registers);
- Limited access to healthcare in the general population, as indicated by the child mortality rate and out-of-pocket expenditure on health services;
- TB reporting is not a legal requirement;
- The absence of a functional vital registration system.

Disease burden

Between 2000 and 2010, estimated TB incidence in Nepal was largely stable. From 2010, estimated TB incidence has declined at an average rate of 0.9% a year, due to declining notifications. Between 2010 and 2017, TB notifications declined at an average rate of 2.6% a year, much faster than estimated TB incidence, suggesting a decline in case detection and a growing gap between notifications and true incidence. In 2017 there were an estimated 45,000 estimated incident cases of TB (range: 39,000-50,000) in Nepal, equivalent to a rate of 152 (134-172) cases per 100,000 population, but there were only 31,064 incident TB cases notified (106 notifications per 100,000 population).

From 2012-13 to 2016-17, the notification rate for all forms of TB in Nepal declined by 11%. Over the same period, the rate for bacteriologically confirmed disease declined by 7%, extrapulmonary TB increased by 8%, while the rate for clinically diagnosed pulmonary TB fell by 40%. This large decline in clinically diagnosed TB suggests a change in diagnostic practices or reporting, rather than a true epidemiological reduction in TB burden. This change has coincided with the roll-out of Gene Xpert in Nepal and may be due to inappropriate use of Gene Xpert as a "rule out" test, which is resulting in under-diagnosis of paucibacillary TB.

Notification rates for TB differ somewhat within Nepal by administrative region, and more so by geographic area. Rates are lowest in the mountain areas to the north of the country, and highest in the "terai" (plains) areas in the south, which are more urbanised. Although all provinces reported declining rates from 2012-13 to 2016-17, at the district level trends have been inconsistent. Notification rates are higher in older age groups, consistent with most other countries in the region, and the age structure of the TB patient population is largely consistent from year to year. The proportion of TB cases occurring in children has increased slightly, from 6.2% in 2014-15 to 7.3% in 2016-17, with substantial variation across the provinces (from 4% to 16%). The ratio of male to female TB patients in Nepal is very stable, at 1.8 men per woman.

The estimated TB mortality rate (excluding HIV+TB) in Nepal was estimated to be 20 deaths per 100 000 population (range: 14-27) in 2000 and has been remained approximately stable with up 2014 and increasing since then. In 2017, TB mortality (excluding HIV+TB) in Nepal was estimated to be 23 per 100 000 population (range: 16-30).

TB programming related efforts that could have contributed to a modest decline of the TB epidemic are the introduction and scale-up of rapid diagnostic tests (Gene-Xpert); a microscopy laboratory network and introduction of second-line TB treatment; and high levels of favorable treatment outcomes among drug-sensitive and resistant TB patients. These would have been enhanced by increased TB financing from domestic and donor sources. Additional external factors which could contribute to declines in TB incidence included modest economic growth (increase of GDP per capita); health system strengthening (as evidenced by a decrease in under-five mortality); the decline of under-nutrition; and aggressive HIV-prevention interventions. Aging of the population

and an increase of diabetes prevalence are expected to drive the TB epidemic to upward, however, because these changes are taking place in quite slowly in Nepal their impact on the pattern of TB epidemic is likely to be minimal. A high rate of exposure to indoor solid fuel and persistent challenges in access to affordable healthcare (evidenced by out-of-pocket expenditure) will likely contribute to the persistence of the TB epidemic. The results of the TB prevalence survey will give the highest quality indicator of the true level of TB incidence in Nepal, and the success and level of current case detection.

Despite a 2.2-fold increase in TB funding over the past 6 years, the average expenditure per notified TB case Nepal remains one of the lowest in the world, suggesting that investments to control TB in Nepal is not appropriate to the actual burden of disease.

RECOMMENDATIONS

Recording and reporting

- 1) Develop a plan and devote the necessary resources to maintaining reporting during the federal restructure, for both the paper-based, electronic aggregate, and electronic case-based systems. This could include hiring staff to undertake data entry at the district level, including retrospectively for late 2018 as needed. (Urgent)
- 2) Distribute presumptive TB registers and revise tri-annual report forms to collect data on presumptive TB cases (Urgent)
- 3) Develop a national training plan covering each of the recording and reporting systems and tools, with clear expectations for training and competencies for staff at each level. Begin collecting data on timeliness of staff training (Short term).
- 4) Develop a routine procedure for clinicians to follow up individual patients between facilities and for supervisory staff to cross-check presumptive TB registers, laboratory registers, and treatment registers. Referring facilities should routinely follow-up on results for referred patients, and record data in presumptive and laboratory registers. Registers should be amended to include a free-text field to record the name of both referring and receiving facilities. Supervisory visits should ensure that this activity is being undertaken, and should cross-check the registers and remind clinical staff to fill in any missing data. Registers should also be cross-checked and reconciled at quarterly / biannual data workshops. (Urgent)
- 5) Conduct an inventory study to assess under-reporting from the private sector, from facilities diagnosing and treating children, and between presumptive TB registers, laboratory register and treatment registers (Medium-term)
- 6) Work together with Palika health authorities, district health authorities and private providers to further develop and roll out a system for collecting data from private practitioners which is acceptable to all parties. Develop disaggregated indicators to monitor progress in recording and reporting patients in the private sector (as distinct from NGOs and teaching hospitals), and use these to identify districts where these programs are working well to inform efforts in other districts (Short term).
- 7) Continue to expand contact tracing programs and identify key indicators to evaluate progress. Revise trimester report forms to record more detailed data on contact tracing in all districts: number of identified contacts of all newly diagnosed TB patients, number screened, number symptomatic, number diagnosed, number of children initiated on IPT, number of children completing IPT. Analyse these data to evaluate the progress of programs and to audit the appropriate application of screening algorithms (Short term)
- 8) Continuously evaluate the efficiency of other Active Case Finding programs using data from OPMIS and other sources. Investigate the reasons for low yield in FAST programs and the prison-based screening, and take action to address these (e.g. by revising algorithms to include chest x-ray if appropriate and feasible). Carefully consider the cost-effectiveness of different approaches, e.g. potential cost savings from paying for chest x-ray to save unnecessary Gene Xpert tests (Urgent).

Data Quality Assurance

- 1) Investigate the reasons for increases in reported microscopy and Gene Xpert testing with a concurrent decline in notifications and establish whether these are data quality problems, true changes in case finding effort, laboratory performance, clinical practice, or some combination thereof. (Short term)
- Case-based electronic and aggregate data should be routinely analysed to identify districts or facilities with problematic data, which should be investigated and these facilities should receive more intensive supervision
- a) A staff member should be appointed at the national level to follow up and correct problematic or missing data (Urgent)
- b) Develop targets for data completeness and assess progress at district or Palika level as the electronic systems are rolled out (Short term)
- c) Develop SOPs for data quality checks in electronic and paper systems, including supervisory visits and workshops (Short term)
- Routine cross-checking of registers should be implemented at data quality workshops, with quantitative data collected on referrals and loss to follow-up during screening and diagnosis. (Medium-term)
- 3) The supervisory checklist should be revised. A template is available from the WHO Country Office which can be adapted to the local context. (Short term)

In particular:

- a) Ensure that all standard paper tools are present, filed appropriately, and being properly used and maintained
- b) Include routine cross-checking of different data sources (presumptive, laboratory and treatment registers; treatment cards and treatment registers; treatment registers and aggregate report forms)
- c) Check drug supplies, including supplies of child-friendly dispersible drugs
- d) Include quantitative indicators of data quality, which should be monitored at the national level

Electronic systems

- 1) Develop a plan and devote resources to maintain data entry during the federal restructure, with clear responsibilities for data entry at different administrative levels (e.g. primary responsibility with districts and efforts to provide as many health workers as possible with access to the mobile app to update records for their patients) (Urgent)
- Complete the roll-out of the ETB Manager and MDR-TB case-based electronic systems to all districts, and ensure that the TB Tracker system is being used by all Gene Xpert sites. Ensure as many clinical staff as possible have access to the ETB Manager mobile app and are using it. (Short term)
- 3) Develop brief SOPs for data entry, data quality checking and feedback by district / Palika staff and national staff (Short term)
- 4) Create a function to allow straightforward downloading of complete raw data for analysis (Medium-term)
- 5) Explore possibilities for automated linkage between the three electronic systems and HMIS (e.g. automatic creation of patient records in ETB Manager after a positive result in TB Tracker; aggregated reports to HMIS from ETB Manager) (Long term)

- 6) Develop a probabilistic check for "potential duplicates" based on name, district, age, and case type (not only exact duplicates). Develop an SOP for the management of duplicate records including whose responsibility it is to delete/inactivate these records, and communication between national staff and district / Palika staff (Medium-term)
- 7) A function should be added to the system to allow the creation of a record for a subsequent episode of TB using the same unique identifier, with appropriate data validation checks. (Short term)
- 8) Implement routine confidentiality protections in all case-based systems: suppress names by default, only show in-district or in-catchment patients to staff performing searches with an option to search nationally if needed. Identifying information should be excluded by default from data downloads. (Urgent)
- 9) In 2019-2020, seek detailed feedback from clinicians about the usability of the MDR-TB DHIS2 system and use this to inform improvements to the system. (Medium-term)

Child TB surveillance

- 1) Ensure that all facilities have and are using contact tracing and IPT registers (Short term)
- 2) Develop SOPs for monitoring the expansion of contact tracing and IPT, and evaluate the quality of implementation at the district and national levels (Medium-term);
 - a) Monitor the number and proportion of cases diagnosed in children to evaluate correct application of the screening algorithm (e.g. zero initiation of IPT in symptomatic children without appropriate clinical review);
 - b) Collect data on referrals for diagnosis and monitor loss to follow-up between screening, diagnosis, and treatment initiation;
 - c) Periodically review the quality of diagnosis in children (e.g. using a random sample of cases in ETB Manager and following up with clinicians);
 - d) Monitor completion rates for both IPT and TB therapy;
- 3) Monitor and maintain adequate supplies of child-friendly dispersible drugs (Urgent)

Laboratory surveillance

- 1) Institute a routine quality assurance system for smear microscopy. (Medium term)
- 2) Strengthen data quality checking of laboratory facilities during supervisory visits and develop data quality indicators to be monitored at the national level (e.g. cross-checking of procurement records, supplies, laboratory registers and aggregate records to assess actual and reported numbers of tests). (Medium term)
- 3) Investigate the reasons for large annual changes in the microscopy rate and positivity rate at district level and take action to address these when they are due to procurement or resource challenges; (Urgent)
- 4) Amend triannual report forms to collect data on Gene Xpert testing in priority groups, develop national targets for coverage, and monitor progress towards these; (Short term)

ABBREVIATIONS

AIDS	Acquired Immunodeficiency Syndrome
APC	Annual Percent of Change
ARI	Acute Respiratory Infection
ART	Anti-Retroviral Therapy
BC	Bacteriologically Confirmed
BNMT	Birat Nepal Medical Trust (BNMT Nepal)
CD	Clinically Diagnosed
CDR	Central Region
CNR	Case Notification Rate
CPT	Co-trimoxazole Preventive Treatment
GDP	Gross Domestic Product
GNI	Gross National Income
DALY	Disability Adjusted Life Years
DHS	Demographic Health Survey
DOTS	Directly Observed Treatment Short Course
DST	Drug Sensitivity Testing
EDR	Eastern Region
FAST	Finding, Actively, Separating and Treating
FWDR	Far Western Development Region
GF	Global Fund
HERD	Health Research and Social Development Forum
HIV	Human Immunodeficiency Virus
ICF	Intensified Case Finding
IPD	In-patient Department
IPT	Isoniazid Preventive Treatment
IQR	Interquartile Range
MDR	Multidrug Resistant
MTB	Mycobacteria Tuberculosis
MWDR	Mid-Western Development Region
NGO	Non-Governmental Organization
NNS	Number Needed to Screen
NTP	National Tuberculosis Program
OOP	Out of Pocket

OPD	Out Patient Department
PAF	Population Attributable Fraction
PLHIV	People Living with HIV
P: N	Presumed to Notified
PTB	Pulmonary Tuberculosis
RR	Risk Ratio
RR-TB	Rifampicin Resistant Tuberculosis
SLD	Second-line Drug
ТО	Treatment Outcome
U5M	Under Five Mortality
UN	United Nations
VCT	Voluntary Testing and Counselling
VR	Vital Registration
WDR	West Development Region
WHO	World Health Organization

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INTRODUCTION

Nepal is a landlocked, low-income country between India and China with a population of around 29.3 million, divided into 7 provinces, 77 Districts, and 756 local government units. The terrain varies from plains ("terai"), where more than half of the population reside, to hill and mountain regions, which creates challenges for transport and infrastructure. There is a significant movement of people around the country for work. The country is still recovering from a devastating earthquake in 2015, which caused huge loss of life and extensive damage across the most densely populated central part of the country, including Kathmandu.

Nepal is a moderate TB incidence country, with an estimated TB incidence of 152 cases per 100,000 population in 2016-17 (around 45,000 cases in total). Notifications have declined slightly over the past five years from 35,403 in 2012-13 to 31,766 in 2016-17. Nepal is currently undertaking a TB prevalence survey, expected to be completed in April 2019, which will inform updated burden estimates. The country has begun to implement case-based electronic data collection for Gene Xpert testing, drug-sensitive TB treatment, and MDR-TB treatment. An initial epidemiological review was conducted in late 2014, and this review was requested to assess progress since 2014, analyse and interpret TB data for the past five years, evaluate the new systems for TB data collection in the country, and inform the development of the new national strategic plan.

1.1. Objectives

- 1. Describe and assess current national TB surveillance and vital registration systems, with particular attention to their capacity to measure the level of and trends in TB disease burden (incidence and mortality).
- 2. Assess the level of, and trends in, TB disease burden (incidence, prevalence, and mortality) using available surveillance, survey, programmatic and other data.
- 3. Assess whether recent trends in TB disease burden indicators are plausibly related to changes in TB-specific interventions taking into account external factors including economic or demographic trends.
- 4. Evaluate progress since the 2014 epidemiological review and identify actions and resources needed to complete and strengthen new processes and activities.

1.2. Methods

- 1. Desk review of available TB control-related policy papers, manuals, guidelines, publications and forms
- 2. Interviews and discussions with TB authorities and health care providers at national and district level
- 3. Review of TB records, laboratory registers , and electronic surveillance systems
- 4. Review of electronic databases to assess the level of incompleteness of key variables
- 5. Analysis of notification/surveillance data over time and space to identify trends in disease burden and programmatic efforts.

Most of the TB-related data were provided by the National Tuberculosis Control Centre (NTCC). In addition, other resources were utilized, such as AIDSInfo, WHO Global Health Observatory, International Diabetes Federation, the UN population prospects, and the World Bank to obtain data on TB risk factors and predictors. All data sources are presented in the text and footnotes. Analysis conducted included plotting of annual data followed by visual observation and computation of slopes by linear regression to assess the speed of change of various indicators (where appropriate). District-level data were mapped to identify spatial patterns.

The standard WHO-recommended assessment checklist and associated user guide, from Standards and benchmarks for tuberculosis surveillance and vital registration systems, were applied. The TB surveillance checklist was implemented during a country visit (20 January–02 February 2019).

ASSESSMENT OF TB SURVEILLANCE AND VITAL REGISTRATION SYSTEMS AND THEIR CAPACITY TO MEASURE TB BURDEN

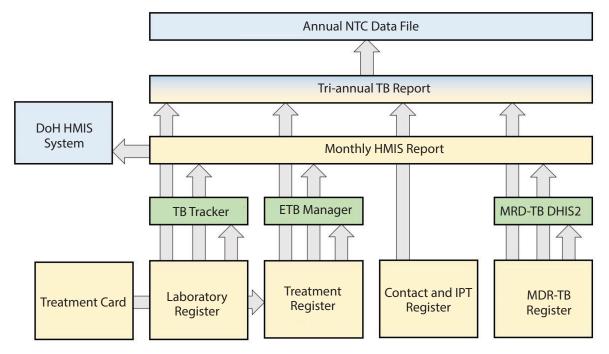
2.1. Description of the TB surveillance system and vital registration system

In Nepal, TB data are collected on paper at the facility level and then on paper and through electronic systems at higher levels. There are three separate electronic systems for Gene Xpert testing, DS-TB treatment registration, and MDR-TB treatment registrations, as well as two national systems for collecting aggregate TB data. Case-based electronic reporting is functioning in some health facilities, particularly referral facilities, and from some district health offices. There is currently no functioning Vital Registration system in Nepal.

The NTC reports data on financial years rather than calendar years. The Nepali calendar year, based on a lunar system, begins in April or May in the Western calendar. The financial year is aligned to the Western calendar, beginning in July and ending in June.

Each health facility is expected to maintain a treatment register and treatment cards for each patient. Facilities with a laboratory on-site are also expected to maintain a laboratory register. Some facilities also have combined contact tracing and IPT registers. Health facilities complete monthly reports for the National Health Information Management System (HMIS) from the TB register (TB reports are only one report among many). These reports are submitted to the district health office.

Figure 1 Flow diagram for TB data in Nepal



(Yellow, paper; Green, case-based electronic; Blue, aggregate electronic)

District health offices maintain a district register, which is completed at monthly visits to each health facility. The district staff then fill out tri-annual reports to the NTC, based on the district register, which includes all indicators specified by the NTC. The district office also submits online tri-annual reports to the aggregated electronic HMIS system, which is maintained by the national Department of Health. This system does not capture all of the relevant indicators for TB, and these reports are not key data sources for the NTC, although they can be accessed.

There are three case-based electronic systems in use: The ETB system for drug-sensitive TB (a bespoke system), the MDR-TB system (based on DHIS2), and the TB Tracker system for laboratory data. Some higher-level facilities have access to the ETB and MDR systems, as do some district health offices, but most lower-level health facilities lack the necessary IT infrastructure (computers and reliable internet connectivity) (Fig 1).

2.2. Capacity of national TB notification and vital registration system to provide a direct measure of TB disease burden

Nepal is currently undertaking its first national TB prevalence survey, which will provide strong evidence on the true burden of TB in the country and the extent to which it is reflected in notification data. However, there are several known challenges for the system and its capacity to reflect the true TB burden, due to possible under-diagnosis, a known lack of reporting from the private sector, recent unexplained declines in TB notifications, and major changes to reporting practices at different administrative levels since the adoption of a new constitution in 2015.

TB notification data have been largely stable in Nepal in recent years, despite the devastating earthquake in 2015. However, there was a moderate decline in notifications between 2012-13 and 2016-17 (-10%, from ~35,400 to ~31,800), largely attributable to a decline in clinically diagnosed TB, the cause of which is not certain. There is some evidence that this may be due to the roll-out of Gene Xpert and misinterpretation of negative results by clinicians, although there is also some ecological evidence to the contrary (see section X), as provinces with higher Gene Xpert testing rates have reported smaller declines in clinically diagnosed TB notifications.

Complete data for 2017-18 were not available as of January 2019, as there has been a significant interruption to reporting from district health offices due to major administrative changes in the country after the adoption of a new constitution in 2015. A drop in notifications may be expected during 2017-18, 2018-19, and possibly 2019-20 while reporting functions are reorganized under the new system. The major online system had reached approximately 60% coverage in 2016-17 prior to the interruption, but only around 1,000 patients have been registered in this system in 2018-19.

Nepal has a large private sector, including pharmacies, individual private practitioners, and private hospitals, all of which can provide TB diagnosis and treatment. Efforts have been made to engage the private sector in recent years and some providers now refer some patients to public services. However, an unknown number of patients continue to access treatment in the private sector, and these patients are not recorded in national data. TB notification is not currently required by law, although advocacy to amend national legislation is underway.

Diagnostic delay and initial loss to follow-up are thought to be challenges in Nepal, with some studies documenting substantial patient and health system delays in accessing care for TB. At present, presumptive TB registers are not widely used, which prevents the quantification of these issues at the national level.

More evidence is needed to quantify the capacity of the TB surveillance system in Nepal to reflect the true burden of TB. Some of this evidence will come from the prevalence survey, however, there are other actions the country can take to both increase case detection and quantify underdetection, which are outlined in the recommendations.

2.3. Strengths of the current systems

Following the Epidemiological Review in 2014, paper tools were updated and case definitions were brought into line with WHO standards. The minimum dataset expected by WHO has been collected each year since 2014-15. During our review, all facilities that we visited were maintaining appropriate TB treatment registers. Data quality was high (although not perfect), and national TB data have good internal consistency for most key variables (with the exception of clinically diagnosed TB).

Nepal has made excellent progress in adopting case-based electronic surveillance since the last review in 2014, and the major system (ETB Manager) appears to be very well designed and user friendly for both national staff and clinicians. In 2016-17, coverage of this system had reached 59% against national aggregated notification data. Further expansion of this system should be supported as a very high priority.

Nepal has also made outstanding progress increasing the coverage of HIV testing among all TB patients, with coverage increasing from only 7% in 2014-15 to 54% in 2016-17.

Gene Xpert roll-out is continuing, with 57 sites established as of 2017-18 and ~12,300 tests performed in 2016-17. A repeat Drug Resistance Survey is planned for 2019-20 to provide updated estimates of the prevalence of MDR-TB among a representative sample of all TB patients.

Age disaggregated data on all forms of TB has been collected since 2014-15, and 7% of new TB notifications pertain to children aged 0-14, within the expected range of 5-15%. Contact tracing programs are expanding and preventive therapy for children under five is being provided in some facilities using dispersible formulations, with a transition from isoniazid to combination therapy expected this year.

2.4. Challenges with the current systems

There are a number of challenges with the current systems related to tracking screening and diagnostic effort, recording treatment outcomes, and maintaining reporting during the federal restructure. Broader challenges remain in Nepal with regard to access to healthcare and vital registration, although many indicators of population health are improving.

Patients are frequently referred between facilities for diagnosis and treatment, with no single facility documenting the entire journey of the patient. Presumptive TB registers are not widely used, rather patients are recorded in out-patient department registers (in hospitals), or not at all (in some primary care facilities). Laboratory testing is recorded by facilities with laboratories on site, which is often a different facility where the patient first presents and is ultimately treated. There is no expectation that facilities routinely follow-up on laboratory results or treatment outcomes after a patient is referred, rather all documentation becomes the responsibility of the receiving facility. Consequently, it is not possible to cross-check registers at the facility level, and the absence of presumptive registers means that it not possible to quantify initial losses to follow up or changes in case-finding effort over time.

Current case finding efforts in most of the settings seem to have low sensitivity. This means that a very small proportion of the screened population is identified as presumptive, and among

the presumptive TB patients, a notable proportion of cases are missed during the diagnostic evaluation. The intensified case finding interventions among close contacts, out-patient department visitors, and prisoners have yielded a very small number of TB cases compared to what might be expected, suggesting that the vast majority of TB cases are not being detected by these programs as currently implemented.

Despite the establishment of a Gene Xpert laboratory network around the country, Xpert machines are still highly under-utilized (there is an average of 34 tests per machine per month). In 2016-17 only 6.6% (11,441/172,588) of presumptive TB patients were tested by Xpert. This level of testing is unlikely to have an impact on TB case-finding at the national level.

Contact tracing and other active case finding activities have been expanding in recent years, including screening in hospital outpatient departments and prisons. Data from these activities are collected in various systems, however, some key data are not currently being collected. As contact tracing expands some facilities are now using contact tracing and IPT registers, however, these are not universally available as yet. Some facilities are consequently recording IPT in the treatment registers. The monthly and triannual report forms do not collect data on numbers of contacts screened or the number of preventive therapy initiations (only the number of people diagnosed through contact tracing), so the expansion of contact tracing programs cannot be well quantified from the national level.

In the registers we saw, treatment outcome was usually not reported on the treatment card, only in the treatment register. In some registers, many patients did not have an outcome recorded in the outcomes column, although it could be seen from their laboratory results that they had been cured. Some facilities did not maintain facility copies of treatment cards at all, only registers and treatment booklets which were retained by the patient, not the facility. This complicates crosschecking and validation of treatment outcome data.

In some facilities using community health volunteers to undertake DOT, the health volunteer maintained a duplicate treatment card for the patient. A consequence of this is that medication adherence, the dates of the continuation phase, and treatment outcomes were not recorded in the health facility treatment cards. There was a separate notebook for community health volunteers to record treatment start and end dates, and this was used to complete the facility register. This complicates cross-checking of treatment outcomes.

In 2015 Nepal adopted a new constitution, and a major reorganization of administration is now taking place in the country. Nepal was previously divided into five regions, and the new system has created seven provinces to replace the regions. Consequently, new provincial governments will take over the services previously delivered by the regional governments. At the same time, many powers and services are now being decentralized from the district to the municipal / sub-district ("Palika") level. This has implications for TB reporting as well as procurement and distribution of drugs and other resources, and it is not yet clear how TB reporting will be undertaken during the transitional period. District budgets have been reduced according to their reduced role, which has led to an interruption to many activities, including TB reporting. At our visit in January 2019, one district office had been able to undertake their reporting duties since the end of the previous June, due to resource constraints.

The ETB Manager, MDR-TB, and TB Tracker online systems are all relatively new and none have been completely rolled out as yet. In 2016-17 the ETB Manager system had achieved 59% coverage, but this has fallen dramatically in 2018-19 due to the interruption to reporting caused by the restructuring.

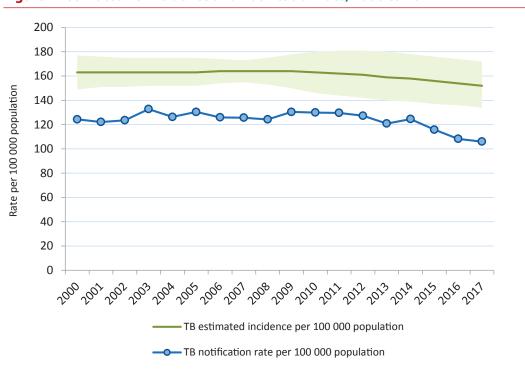
Despite a 2.2-fold increase in TB funding over the past 6 years, the average expenditure per notified TB case Nepal remains one of the lowest in the world, suggesting that investments to control TB in Nepal is not appropriate to the actual burden of disease.

3 ASSESSMENT OF THE LEVEL OF, AND TRENDS IN, TB DISEASE BURDEN USING AVAILABLE SURVEILLANCE, SURVEY, PROGRAMMATIC AND OTHER DATA

This section provides detailed results from an analysis of national and sub-national TB data for Nepal. Long term data were obtained from the WHO global TB surveillance dataset. Other analyses used aggregated national data from 2012-13 to 2016-17, and particularly for 2014-15 to 2016-17 after the 2013 revisions to reporting.

3.1. Analysis of the level and trends in TB incidence

In the absence of certified surveillance system, estimates of TB incidence for Nepal are made using modeling methods, based on notification data (described in the Technical Appendix of the Global TB Report 2018). Based on this method, between 2000 and 2010 TB incidence in Nepal was estimated to be largely stable, because notifications were stable. From 2010 to 2017, TB notifications in Nepal declined an average of 2.6% per year, which informed estimates that TB incidence was likely declining at an average of 0.9% a year. In 2017 there were an estimated 45,000 incident cases of TB in Nepal (range: 39,000-50,000), equivalent to a rate of 152 (134-172) cases per 100,000 population. However only 31,064 cases were notified (106 notifications per 100,000 population, Fig 2). Accordingly, estimated case detection in 2017 was only 70%, lower than the 2010 estimate of 80%. The national TB prevalence survey will provide the highest quality data on the true burden of TB in the country, and the true case detection rate.





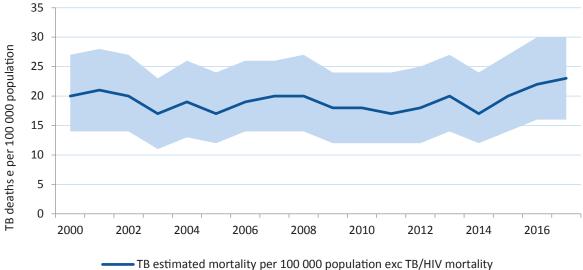
Source: Global TB database

3.2. Analysis of the level of, and trends in TB mortality

As of 2019 there is no functioning vital registration system in Nepal, which prevents direct measurement of TB related mortality. In the absence of such a system, TB mortality is estimated indirectly and is derived from multiplying estimates of TB incidence by estimates of the case fatality rate (Global TB Report 2018, WHO, technical appendix). These estimates are accompanied by a large uncertainty range.

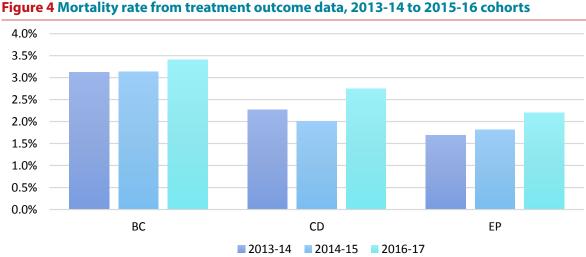
In 2000, TB mortality (excluding HIV+TB) in Nepal was estimated to be 20 deaths per 100 000 population (range: 14-27), with slight fluctuations from year to year, and an increase in recent years consistent with the estimate of a widening case detection gap. In 2017, TB mortality (excluding HIV+TB) in Nepal was estimated to be 23 per 100 000 population (range: 16-30) (Fig 3).

Figure 3 Estimated TB mortality with uncertainty interval, WHO estimates, 2000 to 2017



Data source: Global TB database

Mortality as a reported outcome of TB treatment has been approximately stable from 2014-15 to 2016-17, at 2.5 – 2.9% of all new patients. (Fig 4)



Data source: National Tuberculosis Program

3.3. Analysis and interpretation of the level of and trends in TB case notifications

At the time of writing in February 2019, data for the 2017-18 financial year were not yet complete. This was due to delays in reporting caused by the federal restructuring of Nepal, which has created new administrative regions and reduced the budget available to district health office staff, who had primary responsibility for reporting health data before the restructure. Recording of data at facility level should not be substantially impacted, however reporting by district health staff has been significantly disrupted, affecting both the aggregate and case-based systems. In 2017-18, there were over 16,000 patients registered in the ETB Manager system. In the first 7 months of 2018-19, only 922 patients were reported. Due to the interruption in reporting, data for 2017-18 were not available for our analysis, and we have used data up to 2016-17.

Over the five years from 2012-13 to 2016-17, the notification rate for all forms of TB in Nepal declined from 121 cases per 100,000 population in 2012-13 to 108 cases per 100,000 population in 2016-17 (an -11% decline). Over the same period, the rate for bacteriologically confirmed disease declined -7%, from 62 cases per 100,000 population to 59 cases per 100,000 population. (Fig 5)

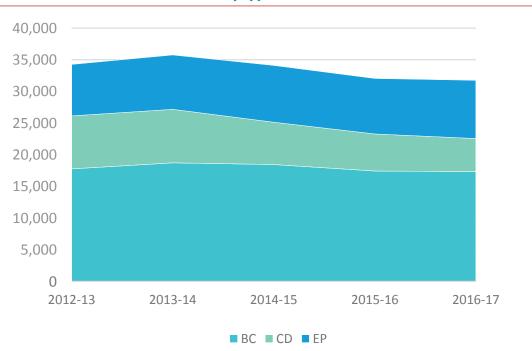


Figure 5 Number of notifications for TB by type, 2012-13 to 2016-17

Data source: National Tuberculosis Program

The notification rate for extrapulmonary TB increased 8% over this period, while the rate for clinically diagnosed pulmonary TB fell -40%. This decline in clinically diagnosed TB was seen in all provinces, with annual rates of decline varying from -2% per year in Province 6 to -15% per year in Province 1. The same trend was seen at the district level, with a majority of districts reporting fewer new clinically diagnosed cases in 2016-17 than in 2014-15. (Fig 6)

These high rates of decline in clinically diagnosed TB suggest a change in diagnostic practices or reporting, rather than a true epidemiological reduction in TB burden. This change has coincided with the roll-out of Gene Xpert in Nepal, and may be due to inappropriate use of Gene Xpert as a "rule out" test, which is resulting in under-diagnosis of paucibacillary TB.

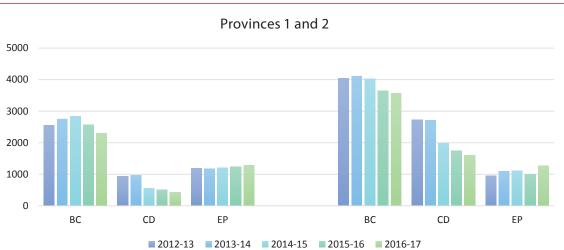
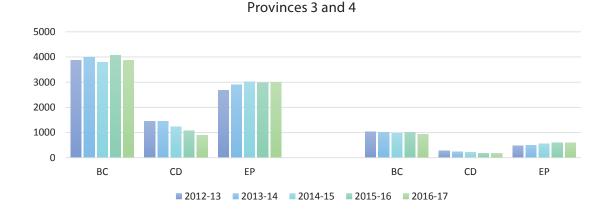
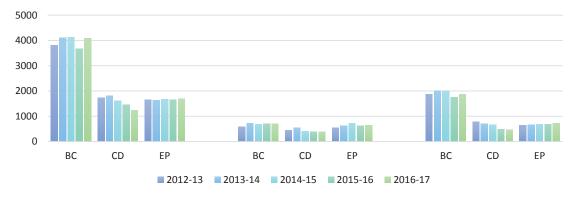


Figure 6 Notifications for each disease type by province, 2012-13 to 2016-17



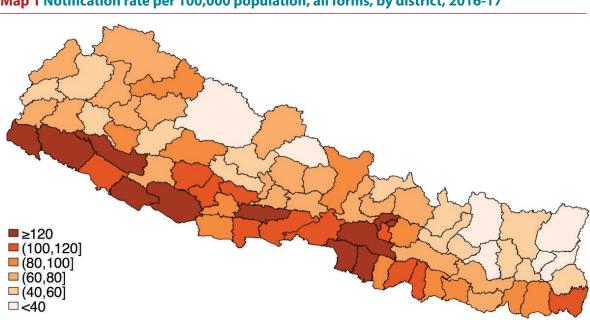
Provinces 5, 6 and 7



Data source: National Tuberculosis Program

3.3.1. Level and trends in TB notifications by administrative region and geographic area

Notification rates for TB differ somewhat within Nepal by administrative region, and more-so by geographic area. Rates are lowest in the mountain areas to the north of the country, and highest in the "terai" (plains) areas in the south, which are more urbanised. Most provinces contain a mixture of geographic terrains. Rates are somewhat lower in the east of the country (Provinces 1 and 2) and somewhat higher in the west, particularly in Province 5. (Fig 7). In each province and most districts, notifications have declined in recent years, due to the decline in clinically diagnosed TB described above (Map 1).



Map 1 Notification rate per 100,000 population, all forms, by district, 2016-17

Data source: National Tuberculosis Program

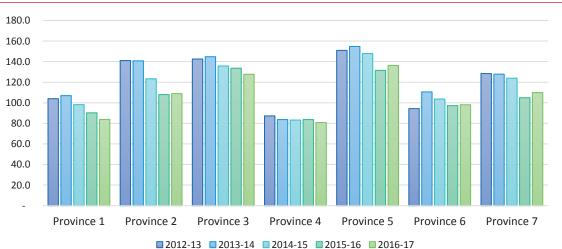


Figure 7 Notification rates for all forms of TB by province, 2012-13 to 2016-17

Data source: National Tuberculosis Program

Although all provinces reported declining rates over the past five years, at the district level trends have been inconsistent, with some districts reporting large reductions in number of patients, and a small number reporting large increases. This is partly due to small numbers of cases in some districts (leading to large fluctuations in relative terms), however the reasons for large fluctuations in districts with high caseloads should be investigated to assess whether this is due to true changes in case finding or to inconsistencies in reporting. (Fig 8, Map 2)

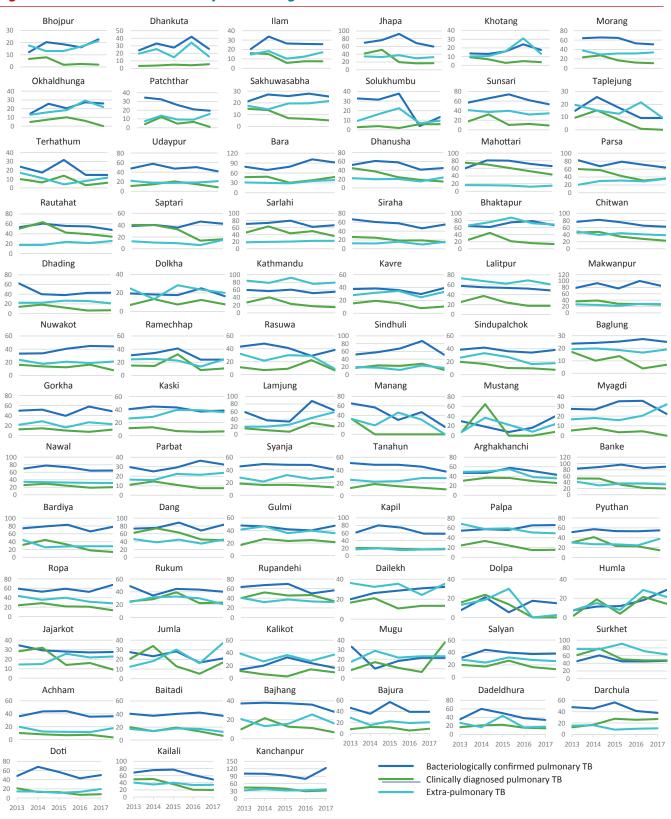
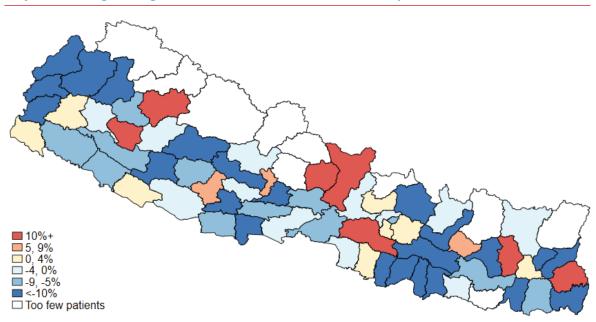


Figure 8 Trend of TB notification by bacteriological confirmation and site of disease at district level

Data source: National Tuberculosis Program



Map 2 Percentage change in number of notifications for all TB by district, 2016-17 vs. 2014-15

Data source: National Tuberculosis Program

3.3.2. Level and Trend of TB notification by Eco terrains

There are three ecozones in Nepal: terrains, hill, and mountain, which have distinct TB risk factors, including population density, poverty, urbanization, ethnic structure, age structure, access to health care, literacy which determines TB burden in the population as well as its detection and trends over the time. In 2017 TB notification rate was highest in terai zones followed by hill then mountain zones with rates of 123, 106, and 63 per 100,000 population in 2016/17, respectively.

The fastest decline was observed in terai zone, were annual average percent of change (APC) over the last five reporting years was -4.9% (from 151 to 123 per 100,000). Trend of decline was consistent across all 20 districts ranging from -1.0% (Dang) up to -8.6% (Dhanusha). In hill and mountain zones the APC was -2.1% and -2.4%, respectively within the same period, however, the trends were not consistent across the districts. In majority of hill districts, TB notification rate remains stable or declined, in four districts increased, while in mountains there was wide variation with inconsistent trends: eight districts showed decline up to -30% annually (Manang), in four districts TB notification increased up to 40% annually in Humla and comparatively stable in the rest of districts (Fig 9). Such large year to year variation at Mountain districts, first of all, is related to small absolute number of TB cases, as well as instability of TB diagnostic service provision.

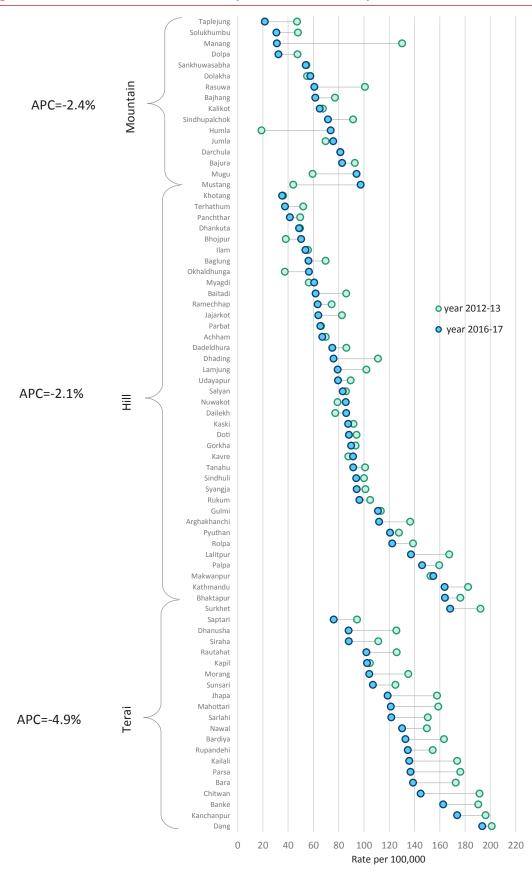


Figure 9 Trend of TB notification rate by districts ordered by ecozones

Data source: National Tuberculosis Program

3.3.3. Trend of TB notification by caxtegory and treatment history

Nepal has only collected treatment history among all TB patients since 2014-15, prior to which treatment history data were only collected for bacteriologically confirmed TB. Category II treatment has remained in use in Nepal until 2018-19, but is expected to be phased out. Thus, category II initiations give the most complete indication of the number of patients with a history of TB treatment over the past five years, which was approximately stable from 2012-13 to 2016-17. It should be noted that owing to the decline in category I treatment initiations, however, that the percentage of all patients initiating category II treatment rose slightly during this period, from 9.3% in 2012-13 to 10.0% in 2016-17. (Fig 10)

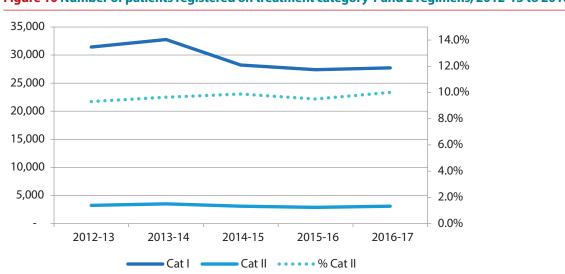


Figure 10 Number of patients registered on treatment category 1 and 2 regimens, 2012-13 to 2016-17

Data source: National Tuberculosis Program

Figure 11 shows the proportion of notified previously treated by province over the recent three years. As it is shown there is no clear trend over time. (Fig 11)

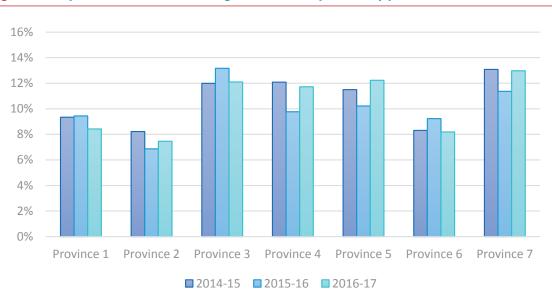
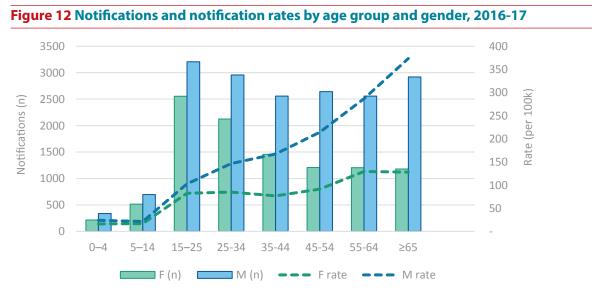


Figure 11 Proportion of retreated among all notified TB patients by province, 2014-15 to 2016-17

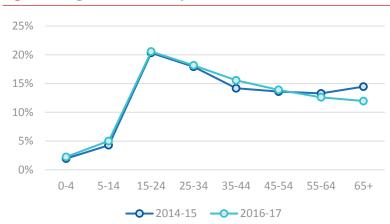
Data source: Nationauberculosis Program

3.3.4. Trends in TB notification by age group

Nepal's population has a young age structure, which is reflected in the age distribution of TB patients, of whom a majority are aged 15 to 44 years. However, per capita, notification rates are higher in older age groups, consistent with most other countries in the region (Fig 12). The age structure of the TB patient population has not changed markedly since 2014-15, when age disaggregated data began to be collected for all new patients. (Fig 13)



Data source: National Tuberculosis Program





Data source: National Tuberculosis Program

3.3.5. Trends in child TB notifications

Nepal has only collected age-disaggregated data on all forms of TB since 2014-15. Since that year, the proportion of all cases occurring in children aged 0-14 years has increased slightly, from 6.2% to 7.3% in 2016-17 (Fig 14). Contact tracing is currently being rolled out across Nepal, with dedicated recording and reporting tools, although these are not yet fully implemented and not all relevant data are currently being collected at the national level. As these activities expand and more data are recorded, the number and proportion of cases diagnosed and reported in children may increase in coming years.

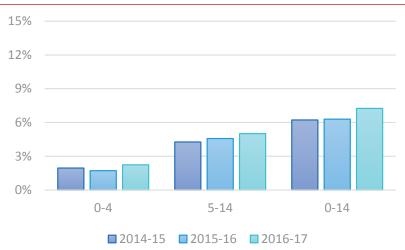


Figure 14 Proportion of all new patients in child age groups, 2014-15 to 2016-17

Data source: National Tuberculosis Program

The proportion of cases in children varies quite markedly across Nepal, which suggests substantial variation in diagnostic practices and in contact tracing activities. At the provincial level, the proportion of cases in children varies from 4% in Province 1 to 16% in Province 6 (Fig 15). At the district level, the variation is even greater, with some districts reporting almost 20% of all new cases as children, while a substantial number report fewer than 5% of all new cases. (Map 3)

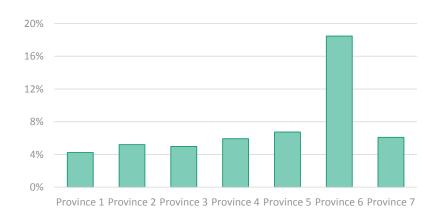
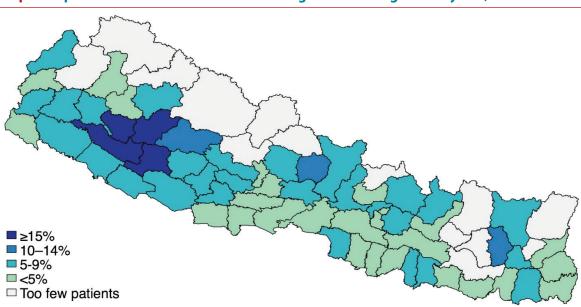


Figure 15 Proportion of all notified cases occurring in children aged 0-14 years, 2016-17

Data source: National Tuberculosis Program



Map 3 Proportion of all notified cases occurring in children aged 0-14 years, 2016-17

Data source: National Tuberculosis Program

Children with TB symptoms are usually referred to district or provincial level hospitals for assessment by pediatricians, who assess whether the child should start TB treatment or IPT. Treatment is then administered by the lower-level health facility who referred the child. Health facility staff noted challenges with dispensing medications to children, because child-friendly dispersible fixed-dose combinations were not available, meaning they have to divide large pills intended for adults. Dispersible INH for IPT was available, however, these pills were also being divided prior to dispersal in order to administer the appropriate dose, which is not best practice (rather the entire pill should be dispersed, and the unneeded liquid then discarded).

3.3.6. Trend in TB notification by sex

The ratio of male to female TB patients in Nepal is very stable, at 1.8 men per woman (Fig 16). The gender ratio is as expected given the generally higher burden of TB among men globally, and the higher prevalence of smoking among men in Nepal compared to women.

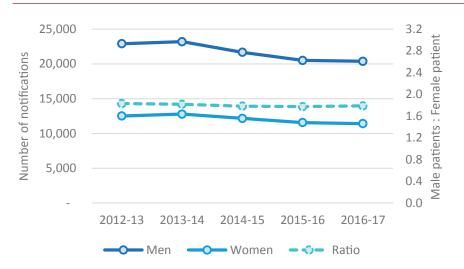
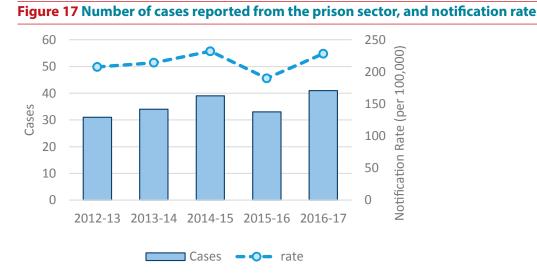


Figure 16 Total TB notifications among men and women, 2012-13 to 2016-17

3.3.7. Trend of TB among people in prison

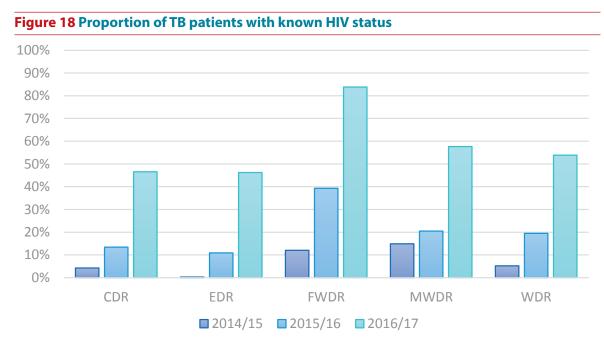
Nepal has collected data on TB diagnosed in prisons since 2012-13, however, the rate is approximately the same as in the general population, suggesting significant under-detection. Efforts should be made to strengthen TB screening and diagnosis in the prison sector. (Fig 17)



Data source: National Tuberculosis Program

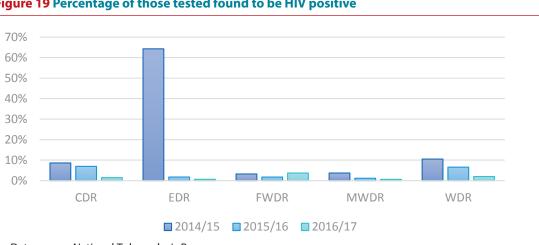
3.3.8. Trend of HIV testing coverage and % HIV among TB

Nepal has substantially expanded HIV testing among people diagnosed with TB over the past several years, with the proportion tested increasing from 6.3% in 2014-15 to 54% in 2016-17. A sentinel survey in 2016 estimated HIV prevalence at 1.1% of all TB patients. Testing increased in all regions, with highest coverage in the Far Western Region (Fig 18).



Data source: National Tuberculosis Program

Consistent with the expansion of testing to patients without known risk factors for HIV, the prevalence among those tested has fallen as testing has increased. In 2016-17, 1.3% of those tested were found to be living with HIV, consistent with the results of the sentinel survey in 2016 (Fig 19).

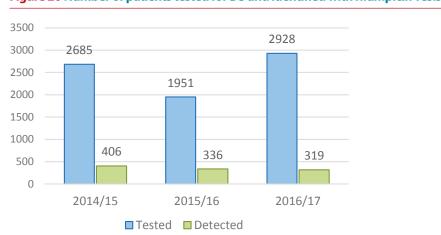




Data source: National Tuberculosis Program

3.3.9. Trend of TB by Rifampicin Resistance

Due to limited access to GeneXpert, the drug-resistance surveillance data are not representative: priority of testing is given to patients that are presumed to have rifampicin resistance, however, data are not collected on coverage in priority groups. The number of PTB patients with rifampicin DST over the last three years varied between 1,951 and 2,928. Total number of cases found with RR declined from 406 in 319 in the same period. (Fig 20)





Data source: National Tuberculosis Program

MDR-TB is treated by provincial hospitals: some patients receive ambulatory care either at their local hospital or at a local health service (for oral regimens), while others reside at MDR-TB hostels during the injectable phase if there is no appropriate facility sufficiently close to their household. Some hostels are operated by NGOs while others are operated by local health authorities, and the availability of psychosocial support programs is variable; some hostels have no psychosocial support services or programs. The hospital overseeing the patient's care maintains an MDR-TB register, while the facility administering the drugs maintains a treatment card.

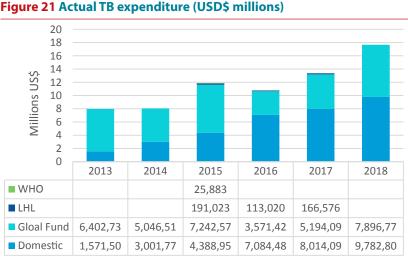
Nepal is in a transitional phase with regard to second-line regimens. A technical working group meeting recently resolved to phase out category II treatment, in line with WHO recommendations. Bedaquiline is currently available in Nepal, and Delaminid is expected to be available from 2021. Some patients are currently on short-course therapy and Nepal plans to phase out injectable drugs.

ASSESSMENT OF EXTERNAL FACTORS AND THEIR LIKELY IMPACT ON TRENDS IN TRUE TB BURDEN AND TB NOTIFICATIONS

4.1. Factors related to TB control programmatic interventions 4.1.1. Government and international donor funding for TB care and control

Funding for and implementation of high-quality TB-specific interventions should result in detection of people with TB and curative treatment; in turn, this should have a direct impact on TB mortality (cutting case fatality rates compared with no treatment or substandard treatment).

TB services in Nepal are financed by two main sources: the Government of Nepal and the Global Fund. Between 2013 and 2018 TB control funding in Nepal increased from 7.97 million to 17.68 million USD, approximately a 2.2-fold increase¹. Total TB funding growth over the recent six years was driven in part by an impressive increase in domestic funding, which constituted only 19.7% of total TB funding in 2013 vs. 55.3% in 2018 (Fig 21). However, despite this increase in TB funding, Nepal still has low funding by global standards relative to the burden of TB in the country. Around the world, the median cost per patient treated in 2017 was USD\$ 1,224 for drug-susceptible TB and USD\$ 7,141 for MDR-TB². By comparison, in 2017 the average expenditure per notified TB patient in Nepal was only USD\$ 421, which is less than one-third of the global average expenditure per-patient (even without accounting for the additional costs of diagnosing and treating RR-TB).







By 2019 the cumulative disbursement of funds by GF to Nepal for TB was about USD\$ 61 million. This was equivalent to approximately 63% of the funding dispersed for HIV (US\$ 97 million). To provide some context for these amounts, the latest estimates (for 2017) of the burden of disease in Nepal in terms of disability-adjusted life years (DALYs) lost due to illness and death are 137 thousand for HIV/AIDS, 169 thousand for TB³, suggesting that appropriate funding for TB should somewhat exceed that for HIV.

Tuberculosis Control Funding Request 2017 and Concept Note 2016 https://www.theglobalfund.org/en/portfolio/country/?loc=N-PL&k=778aa112-0067-4fe9-a0b4-e4bd72ef67de, accessed 03 February, 2019

² Global tuberculosis report 2018. Geneva: World Health Organization; 2018. Licence: CC BY-NC-SA 3.0 IGO.

³ Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2017 (GBD 2017) Results. Seattle, United States: Institute for Health Metrics and Evaluation (IHME), 2018 Available from http://ghdx.healthdata.org/gbd-results-tool.

The observed increase in TB expenditure should have contributed to improving TB control over the past six years. However, the comparatively low TB financing compared to other countries, as well as compared to funding allocated for other diseases within the country, suggests that current levels of investments for TB control is Nepal is still not proportionate to the burden of disease.

4.1.2. Number of health facilities providing TB diagnostic services per 100,000 population

Shortening the duration of disease through detection and treatment of cases will reduce the prevalence of TB in the population, and therefore, transmission. Nepal has a well-functioning TB laboratory network. The first level consists of 604 smear microscopy centres, located across the country (serving about 50 000 population per facility on average). According to NTP annual reports the microscopy laboratories regularly participate in proficiency testing. Between 2009 and 2017 total number of microscopy laboratories increased from 471 to 604. (Fig 22).

Figure 22 Number and rate (per 100,000 population) of smear microscopy laboratories in Nepal (2009-2017)



Data source: Global TB database

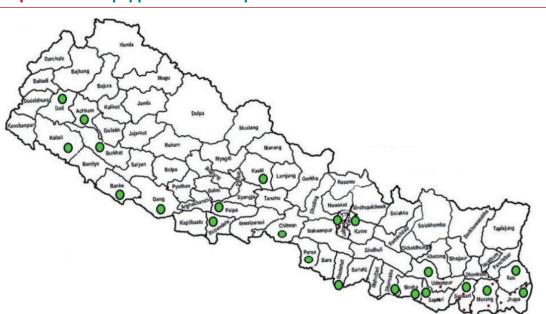
GeneXpert MTB/RIF was introduced in Nepal from 2011 onwards under a TB Reach project, and by the end of 2017 there were 27 laboratories with GeneXpert MTB/RIF machines throughout the country, largely concentrated in urban settings. In 2018, an additional 20 Gene Xpert MTB/ RIF machines were introduced (Fig 23). Two laboratories provide culture-based DST, both in Kathmandu, with a turn-around time of 2-3 months.





Data source: Global TB database

According to the most recent reports, 12,323 Gene Xpert tests were performed in 24 diagnostic centers, ranging from 39 to 3782 per centre. The average number of tests per machine in 2016/17 was only 34 per month, indicating very low utilization of many machines, assuming that the capacity of the GeneXpert IV instrument is 12-16 a day or 3000-4000 tests annually. According to in-depth evaluations, the main barriers for effective implementation of Xpert in Nepal were challenges in the timely supply of cartridges, replacement of damaged modules, maintenance of Xpert machines, stock verification for timely procurement of cartridges, and the lack of laboratory infrastructure for maintaining functional Xpert equipment. In addition, there is cause for concern about inadequate information about Xpert coverage. <u>Map 4</u> shows the districts equipped with Xpert machines.



Map 4 Districts equipped with Gene Xpert machines at the end of 2017

Source: Joshi B et al. https://doi.org/10.1371/journal.pone.0201731.g001

There have been a number of research studies to assess the impact of implementation of Gene Xpert on TB notifications in various population groups and settings in Nepal.^{4,5, 6, 7,8} These studies provided some evidence that the roll-out of Xpert has improved case-finding of TB and identification of RR-TB, and has reduced delays in the start of treatment and time to detection of drug resistant cases. However, in routine programmatic conditions, the use of most of the machines has been low, and therefore access to Xpert testing for presumed cases was very limited. The main method of diagnostic evaluation for presumed TB patients in Nepal remains sputum smear microscopy. In 2016-17, only **6.6%** (11,441/172,588) of presumed TB cases were tested with Xpert, far below the End TB Strategy target of \geq 90%. Such low coverage of Xpert undermines case detection.

⁴ S. Khanal, S. B. (2017). Yield of intensified TB case finding activities. *Public Health Action, I*(2), 147–154. <u>https://doi.org/10.5588/pha.13.0025</u>

⁵ Joshi B, Lestari T, Graham SM, Baral SC, Verma SC, Ghimire G, et al. (2018) The implementation of Xpert MTB/RIF assay for diagnosis of tuberculosis in Nepal: A mixed-methods analysis. PLoS ONE 13(8): e0201731. https://doi.org/10.1371/journal.pone.0201731

⁶ Shrestha, P., Khanal, H., Dahal, P., & Dongol, P. (2018). Programmatic Impact of Implementing GeneXpert MTB/ RIF Assay for the Detection of *Mycobacterium Tuberculosis* in Respiratory Specimens from Pulmonary Tuberculosis Suspected Patients in Resource Limited Laboratory Settings of Eastern Nepal. *The open microbiology journal*, *12*, 9-17. doi:10.2174/1874285801812010009

⁷ Creswell, J., Qin, Z. Z., Gurung, R., Lamichhane, B., Yadav, D. K., Prasai, M. K., ... Sudrungrot, S. (2019). The performance and yield of tuberculosis testing algorithms using microscopy, chest x-ray, and Xpert MTB/RIF. *Journal of Clinical Tuberculosis and Other Mycobacterial Diseases*, 14(November 2018), 1–6. <u>https://doi.org/10.1016/j.jctube.2018.11.002</u>

⁸ Creswell J, Rai B, Wali R, et al. Introducing new tuberculosis diagnostics: the impact of Xpert(*) MTB/RIF testing on case notifications in Nepal. Int J Tuberc Lung Dis 2015;19(May (5)):545–51. <u>https://doi.org/10.5588/ijtld.14.0775.</u>

A recent operational research project described Xpert implementation in 22 districts between 2012 and 2015, and showed that in Nepal under routine conditions the sensitivity of microscopy against Gene Xpert is only 22.4%, indicating that a large majority of TB patients in Nepal who have confirmable disease may be missed by the current diagnostic algorithms, or may only be diagnosed clinically (Khanal et al 2017). The scale of Xpert testing is not currently large enough to have a substantial impact on case notification at the country level. Another issue related to GeneXpert was disproportionate allocation across the country and undefined catchment areas for the machines. This has resulted in unequal Xpert testing coverage and positivity across the regions. Map 4

4.1.3. Number of people investigated for presumptive TB

The TB surveillance system in Nepal does not capture data on number of people investigated for presumptive TB. None of the facilities we visited had presumptive TB registers and there is no field to collect data on these patients in aggregate reporting forms, or in any of the electronic systems. Exceptions are specific intensified case-finding interventions in special populations at risks such as prisoners, TB close contacts, clinic visitors, PLHIV, people living in slums, and the data on routine microscopy services. These activities and data collection is implemented mostly by partner NGOs. More detailed description of these data are provided in the following section.

Data on number of smear microscopy (a proxy for presumptive pulmonary TB patients) in the public sector is available for the most recent 3 years only. Between 2014/15 and 2016/17 reporting years, absolute number of presumptive TB cases increased from approximately 150,000 to 173,000. At the same time the sputum smear positives cases identified increased from 12,452 to 13,170 but decreased in relation to number of tested from 8.3% to 7.6%. At the regional level, the number of presumptive TB cases gradually increased in all five regions over the last 3 years, while the proportion of positives either remained stable (CDR, WDR) or declined (EDR, MWDR, FWDR). (Fig 24)

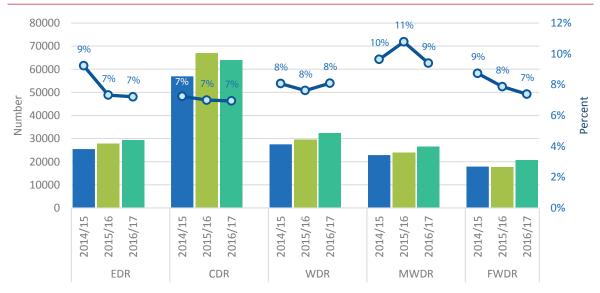
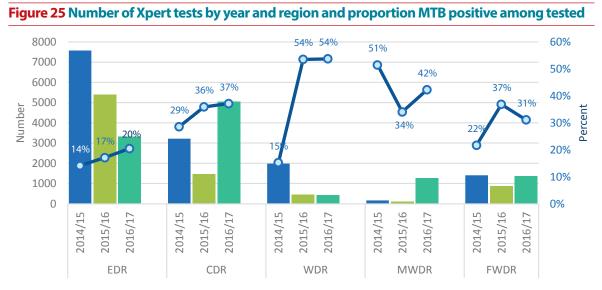


Figure 24 Number of microscopy examinations by year and region and proportions positive among tested

The total number of Xpert tests over the recent 3 years declined from 14,354 to 11,441. Over the same period, the proportion of tests with an "MTB detected" result increased from 18.7% to 32.8%, suggesting that selection criteria for Xpert testing over the time were changed due to restricted access to testing. At the regional level, there was wide variation in number of Xpert tests across

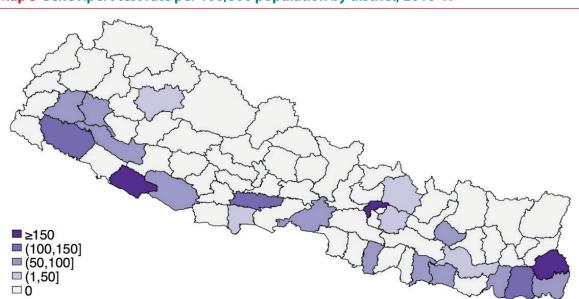
Data source: National Tuberculosis Program

regions, suggesting that distribution of machines around the country may not be optimal, as well as within the same regions over the time, suggesting unstable functionality. Almost in all regions, as the number of tests declined, the proportion of positive tests increased. (Fig 25)



Data source: National Tuberculosis Program

Data on Gene Xpert tests is reported by the laboratory where the test takes place, rather than by the referring facility (a better proxy for where the patient lives). <u>Map 5</u> shows the number of tests performed in each district per 100,000 population, showing the concentration of the machines in the plains areas (however it should be noted that some may be patients travel from other districts to access testing and that in some cases sputum is transported from one facility to another).



Map 5 Gene Xpert test rate per 100,000 population by district, 2016-17

Fig 26 shows the rate of smear microscopy in 2014 versus 2017 by district and region per 1000 population. This measure could serve as an indicator to monitor the access of population to TB diagnostic services, although it is related also to the prevalence of TB in the population. It can be seen that there is no consistency in access to TB diagnostic services over time across the districts: in some districts access to testing increased and in some it decreased. There is also wide variation

between districts in the microscopy rate, ranging from 0.6 per 1000 (Humla and Solukhumbu) up to 18.5 per 1000 in Palpa. It is noteworthy that in 2014/15 seven districts didn't report any TB testing activities (which could be due either to non-functioning laboratories or failure to report data), while in 2017 only two districts reported no microscopy. Overall, the large variation in the microscopy rate indicates instability in access to TB services and the substantial year-to-year variation of the rate within many districts indicates lack of stability of patient identification and reporting. To address these issues, the districts reporting lowest levels of TB diagnostic services, as well as null reporting, and those with large fluctuations should be targeted for identification of possible problems and provided with necessary support.

It would be expected that an increase in the use of microscopy would increase the TB notification rate, however in Nepal over the past three years the increase of microscopy was inversely associated with TB notifications. Possible explanation of this observation might include the following:

- A true decline of TB incidence in the population;
- Instability of TB detection, recording and reporting at facility/district level;
- Change in diagnostic practice (especially for unconfirmed PTB) affected by the introduction of Gene Xpert;
- Increase in proportion of people with TB symptoms tested and treated in the private sector
- A decline in the scope of active case finding activities since 2012-2015 implemented under the TB REACH project

Fig 27 shows the ratio of smear microscopy tests over notified new and relapse cases at district and regional levels. There is a clear pattern of increase of this indicator across most of the districts and all regions, indicating that TB is being less frequently diagnosed among the presumptive patients. The lowest P:N ratio was observed in CDR with 4.1:1 in 2014/15 and 4.8 in 2016/17, while the highest P:N ratio was observed in FWDR with 5.3 in 2014/15 and 6.7 in 2016/17. However, despite this increase P:N ratio remains low in Nepal, suggesting that access to diagnosis is limited and that case finding resources are not adequate to the burden of disease.

Increase in number of presumptive TB cases only partially explains the increasing ratio (which could be due to expanded testing among people with lower risk of TB), as the absolute number of notified TB cases also decreased over this period. Such consistent trend of increase of ratio of presumed to notified cases across districts could indicate a true decline of TB incidence in the population. It should be recognized also that NTP captured data is related to only presumptive TB cases who attended public health facilities and were screened with smear microscopy. There is no information available on the total number of presumptive TB patients, including those who attended private health facilities or who did not receive smear microscopy. Therefore, the trend of presumptive TB cases should be interpreted cautiously, given that this is only part of true presumptive TB population in the country, and which may vary over time. The national TB prevalence survey will provide high-quality data on the true burden of disease in the country and on the true case detection gap, as well as the sensitivity of microscopy in the Nepalese context.

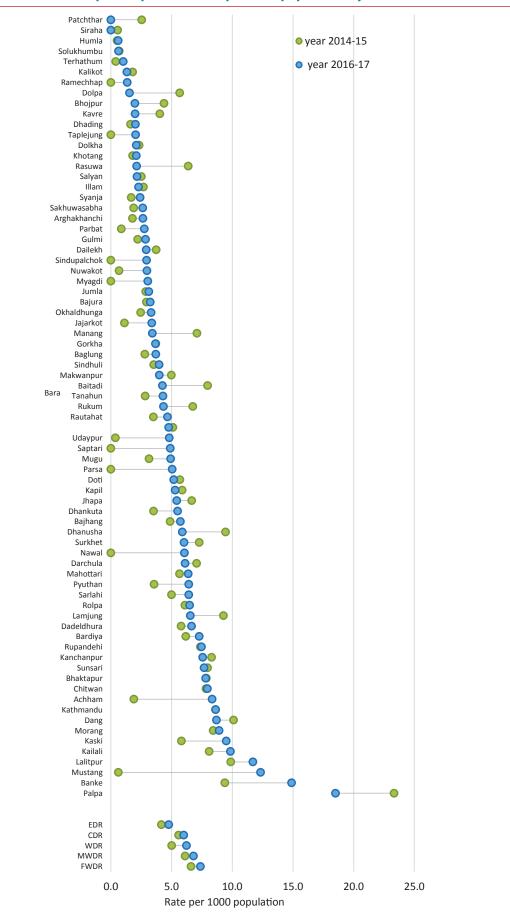
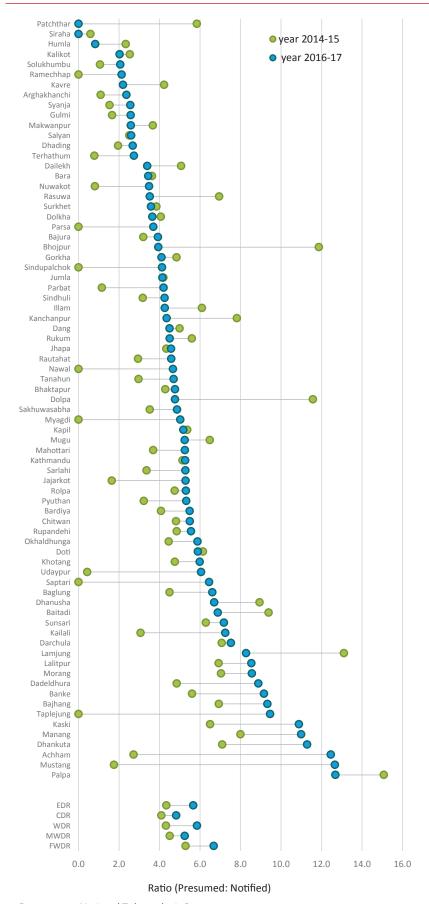


Figure 26 Number of presumptive TB cases per 1000 population by districts in 2014/15 and 2016/17

Data source: National Tuberculosis Program





Data source: National Tuberculosis Program

4.1.4. Performance of active case finding (number of cases screened and detected by each mechanism)

Increased screening in the population should increase case detection, thus reducing TB transmission in population. The WHO recommends intensified case finding (ICF) among selected at-risk groups such as household contacts, people living with the human immunodeficiency virus (PLHIV), people in prisons and other penitentiary institutions, and geographically defined sub-populations with high levels of undetected TB, such as people living in urban slums9.

Under the TB REACH project, the non-governmental organization Health Research and Social Development Forum (HERD, Kathmandu, Nepal), in collaboration with the NTP, has been implementing ICF activities for people living in urban slums, factory workers, prisoners, refugees, monks and nuns, PLHIV, household contacts of TB patients and patients with diabetes¹⁰. The strategies for the ICF included establishment of microscopy camps using mobile vans equipped with microscopy and Gene Xpert, and door-to-door screening for cough >=2 weeks, as well as active identification of close contacts of people with TB (in coordination with DOTS centers), PLHIV (in coordination with VCT/ART centers), screening among people with diabetes, and smear microscopy among presumed TB patients. Those with negative results were supposed to undergo to Xpert testing.

According to routine project data in 22 districts of Nepal between 2013 and 2015, in total 145,679 individuals from different risk groups screened for TB and among them, 28,574 (19.6%) were identified as presumptive cases. Of them, 26,447 (92.5%) underwent sputum microscopy. Of those with microscopy results, only 523 (2.0%) were sputum smear-positive. Of 25,924 individuals with sputum-negative samples, only 9,716 (37%) were tested with Gene Xpert, of whom 716 (7%) tested positive. An additional 2,468 individuals were referred from central hospitals or the private sector for Xpert testing, of whom 404 tested positive, resulting in a total of 1643 positive cases. The yield and number needed to screen under ICF activities among risk groups in 22 districts of Nepal between 2013 and 2015 is provided in the Table 2. (data of additional 404 tested positive at referral facilities is not included)

Target group			Diagnosed with TB		Yield (c/a)	NNS (a/c)	
		n (b)	%	n (c)	%		
Slum dweller	103,027	10,667	10%	523	4.9%	0.5%	197
PLHIV	2,149	1,662	77%	130	7.8%	6.0%	17
Household contacts	14,547	7,619	52%	503	6.6%	3.5%	29
Prisoners	5,490	2,649	48%	21	0.8%	0.4%	261
Factory workers	12,023	3,457	29%	36	1.0%	0.3%	334
Refugees/monasteries	7,424	2,305	31%	24	1.0%	0.3%	309
Diabetics	1,019	215	21%	2	0.9%	0.2%	510
Total	145,679	28,574	20%	1,239	4.3%	0.9%	118

 Table 2 Yield and NNS under ICF activities for TB among risk groups in 22 districts of Nepal, 2013–2015

The yield of screening was highest among (PLHIV) (6.1%), followed by household contacts (3.5%) and urban slum dwellers (0.5%). Among other risk groups, such as prisoners, factory workers, refugees and individuals with diabetes, the yield was less than 0.5%.

10 S. Khanal, S. B. (2017). Yield of intensified TB case finding activities. Public Health Action, I(2), 147–154. https://doi.org/10.5588/pha.13.0025

⁹ World Health Organization. Improving early case detection of active TB through systematic screening. WHO/HTM/TB/2013.04. Geneva, Switzerland: WHO, 2013.

The number needed to screen (NNS) to diagnose an active TB case was 17 for PLHIV, 29 for household contacts and 197 for urban slum dwellers. However, the results are likely to be underestimated, as vast majority of cases were detected by Xpert testing, while Xpert coverage was not optimal: more than half of the presumptive TB patients who were smear-negative did not undergo Xpert testing. There were some differences in the coverage of the Xpert testing, ranging from 21% among prisoners to 68% for PLHIV. Differential coverage of Xpert testing also could affect correct understanding of prevalence of TB in each of risk groups.

Current active cases finding activities include contact tracing, the FAST approach in hospital outpatient departments, regular screening of prisoners and screening of PLHIV under HIV, care which are implemented mainly by partner local and international NGOs. The performance of ICF in 2016/17 among TB close contacts and malnourished children are summarized in Table 3.

Organizations/	Study population	Number	Pres	umed	Tested	Pos	itive	NNS
projects		screened	n	%	n	Ν	%	
BNMT routine contact tracing	TB contacts	24,445				245		100
BNMT	DR family members	517				3		172
BNMT IMPACT TB project	Contact tracing (Chitwan, Dhanusha, Makwanpur, Mahotttary districts)	2,795	2,685	96.1%	2,591	58	2.2%	48
BNMT TB REACH wave 5 project	Contact tracing	5,300	5,239	98.8%	5,688	68	1.2%	78
BNMT Mobile camps	Slum-dwellers	2,373	2,214	93.3%	1,985	14	0.7%	170
BNMT	Children with malnutri- tion/ARI	42,519	2,024	4.8%	1,483	59	4.0%	721

Table 3 ICF performance among PBC TB contacts and children with malnutrition and ARI

As it is shown the number of "presumptive patients" among TB contacts is almost equal to the number of contacts, and as a result, the proportion of positives is low than it would be expected. This indicates that identification of presumptive is highly problematic and sometimes is resource consuming.

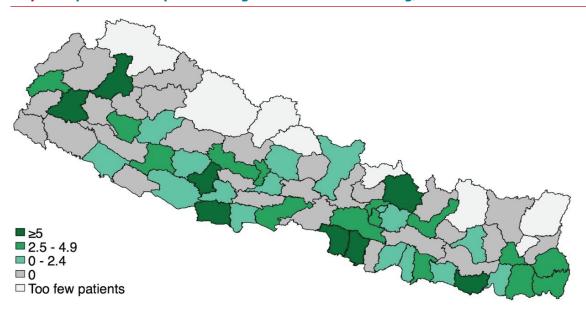
During the most recent 3 years, the total number of TB cases detected by **contact tracing** ranged between 599 to 666, without a clear trend. Given that about 17,000 pulmonary bacteriologically confirmed cases are notified in Nepal annually, average household size in Nepal is 4.99¹¹ and assuming 3.5% TB prevalence among the household contacts¹² we would expect over 2,000 cases to be detected by contact tracing in routine programmatic conditions if contact tracing were conducted well in all districts of Nepal.

Some facilities that we visited were conducting contact tracing among both child and adult contacts, including via household visits by community health volunteers. Contact tracing and preventive therapy registers were present at these facilities and were well filled out. However, monthly reporting forms do not have fields to record the number of people screened through contact tracing, only the number diagnosed. Likewise, reporting forms did not record any data on children initiating preventive therapy, although these data were recorded at some facilities.

¹¹ Nepal Census, 2011

¹² S. Khanal, S. B. (2017). Yield of intensified TB case finding activities. Public Health Action, I(2), 147–154. <u>https://doi.org/10.5588/pha.13.0025</u>

National aggregate data show the status of contact tracing activities in 2016-17, with some districts reporting that more than 5% of all patients were diagnosed through these activities, while in many districts reported 0 diagnoses via contact tracing (Map 6).



Map 6 Proportion of all patients diagnosed via contact tracing, 2016-17

Data source: National Tuberculosis Program

The FAST approach is a type of ICF implemented in outpatient and inpatient general medical settings in Nepal. It includes active surveillance for patients with cough in the waiting or registration area, asking about TB symptoms, fast-tracking them to be screened for other symptoms suggestive for TB, and prompt collection of sputum of those with presumptive TB as per national guidelines. While waiting for laboratory results, patients identified through cough surveillance are educated on respiratory hygiene and moved to a designated, well-ventilated area away from patients to prevent potential transmission of TB. The FAST approach is implemented in clinics with a high number of OPD and IPD patients in high TB burden districts.

During the field visits the epi-review team members observed the FAST implementation in Birat Medical College and Teaching Hospital at Morang district, as well as at Dhulikhel hospital at Kavrepalanchowk district. Despite both clinics have very high flow of patients (up to 1000 visitors per day) the number of presumptive TB cases per day ranged from 1 to 4. Thus, at Birat Medical College and Teaching hospital during the previous month, only 23 presumptive TB patients were identified, and of them, 6 were diagnosed with TB. In the previous month, among 50 presumptive patients, only 4 were diagnosed with TB. There were no records in the presumptive TB register if the identified patients were enrolled into TB treatment, however, the representatives of NGOs (BNMT in Birat and HERD in Dhulikhel) explained that once a patient is identified they contact the relevant DOTS center to inform them about the patients, and they follow-up to ensure that the patient is enrolled into the treatment.

ICF is implemented on regular basis in prisons. In 2016-17 only 41 TB cases were detected in prisons, equivalent to 228 cases per 100,000 population¹³, which is quite close to TB burden in

¹³ Assuming that prison population in Nepal is about 18,000 (source: <u>http://www.prisonstudies.org/</u> <u>country/nepal</u>)

general population (Fig 28). This is an unusually low estimate for prevalence in a prison population compared to other countries: The median estimated annual incidence rate ratio (IRR) for TB in prisons compared to general population-based on most recent meta-analysis¹⁴ is 23.0 (IQR: 11.7–36.1). One of the possible reasons for low case detection in Nepal could be low sensitivity of methods for identification of presumed TB cases.

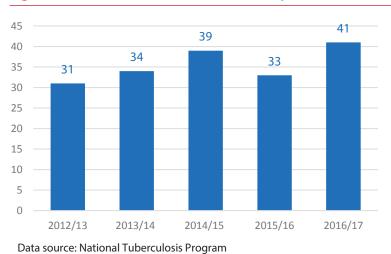


Figure 28 Number of TB cases detected in prisons in the most recent five years, Nepal

Table 4 shows more detailed data on the cascade of ICF from 2 prisons in Nepal. As it is shown NNS is not very different from NNS expected in general population. Accounting that current level of overcrowding (occupation rate=178%) in Nepal prisons¹⁵, the identified number of TB cases suggests possible under-detection and a need to employ another diagnostic algorithm (such as mass chest X-ray) or to improve the implementation of the current approach, due to the very low number of presumptive patients identified in current practice.

Prisons	Screened	Presumptive		Tested*	Positive		NNS	
		n	%		n	%		
Central Jail	2103	527	25.1%	527	8	1.5%	263	
Lalitpur	850	144	16.9%	142	0	0.0%	N/A	
Total	2953	671	22.7%	669	8	1.2%	369	

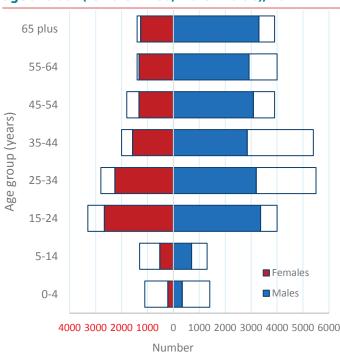
Table 4 Performance of ICF in 2 prisons in Nepal, 2016/17

*in Central jail all presumptive cases were tested by Gene-Xpert, in Lalitpur 134 were tested by microscopy and 38 by Gene-Xpert

Fig 29 shows estimated TB incidence and case notifications disaggregated by age and sex. As it is shown it is estimated the highest proportion of TB cases missed by health systems are children (especially young children) and males aged 25 to 44 years.

¹⁴ Baussano, I., Williams, B. G., Nunn, P., Beggiato, M., Fedeli, U., & Scano, F. (2010). Tuberculosis incidence in prisons: a systematic review. *PLoS medicine*, 7(12), e1000381. doi:10.1371/journal.pmed.1000381

¹⁵ Idem





Data source: Global TB database

4.1.5. Impact of programmatic interventions on trend of TB notification

Currently there are five community-based TB outreach projects in Nepal carried out by NGOs, which are focused on active cases findings among selected high risk groups. Those projects include TB REACH waive 5, IMPACT, BNMT, IOM-Sahara and PDNA with all together cover 39 districts with targeted interventions in addition of NTP routine activities. Of 39 districts in 11 multiple interventions ae implemented. To assess the impact of interventions on TB cases-finding we assessed the trends and annual percent of change in TB notification rate disaggregated by bacteriologically confirmed pulmonary TB, clinically diagnosed pulmonary TB and extrapulmonary TB notification.

Overall APC of PBC notification between 2012/13 and 2016/17 was -1.3%. APC in districts with no specific interventions, one intervention and multiple interventions was -1.9%, -0.7% and -2.1% respectively, indicating no notable difference (Fig 30).

There was clear correlation between the trend in speed of decline of clinically diagnosed TB notification and programmatic interventions: the fastest decline was observed in districts with multiple interventions with APC reaching -17.7%, while in districts with one interventions APC was -12.9% and with no specific intervention -7.2%. (Fig 31)

EPT notification increased in districts with no specific interventions 2.3% annually, while decreased in districts with intervention (APC=-2.0% in districts with one interventions and -1.9% with multiple interventions. (Fig 32)

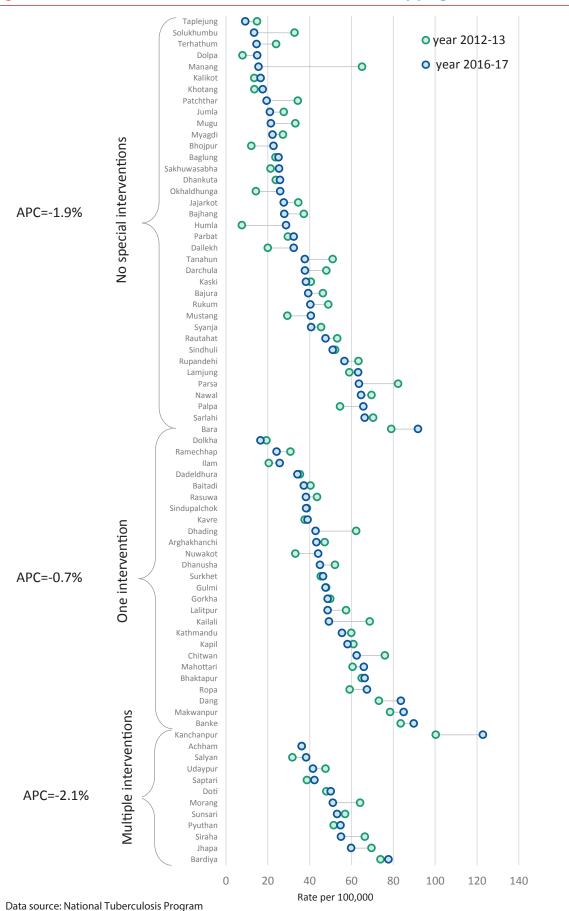


Figure 30 Trend of BC PTB notification rate in districts ordered by programmatic interventions

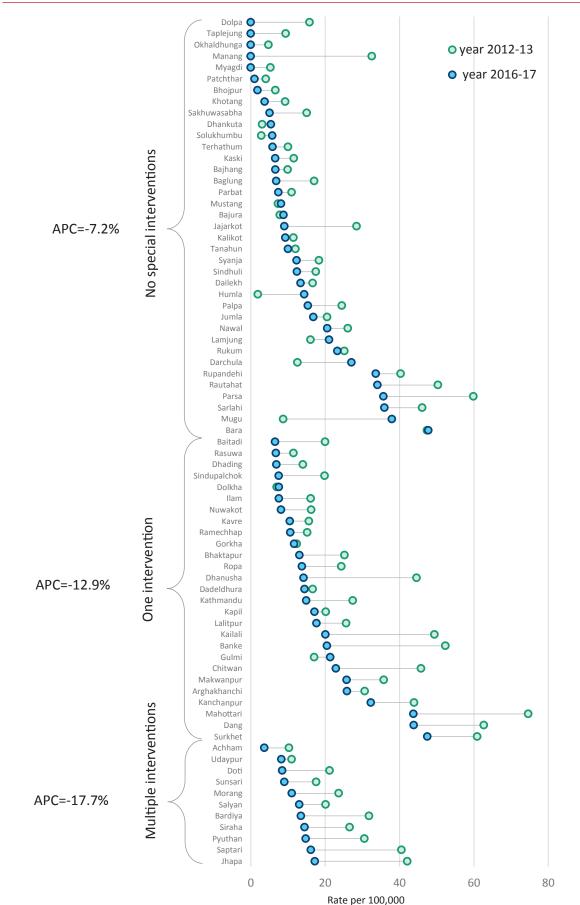


Figure 31 Trend of CD PTB notification rate in districts ordered by programmatic interventions

Data source: National Tuberculosis Program

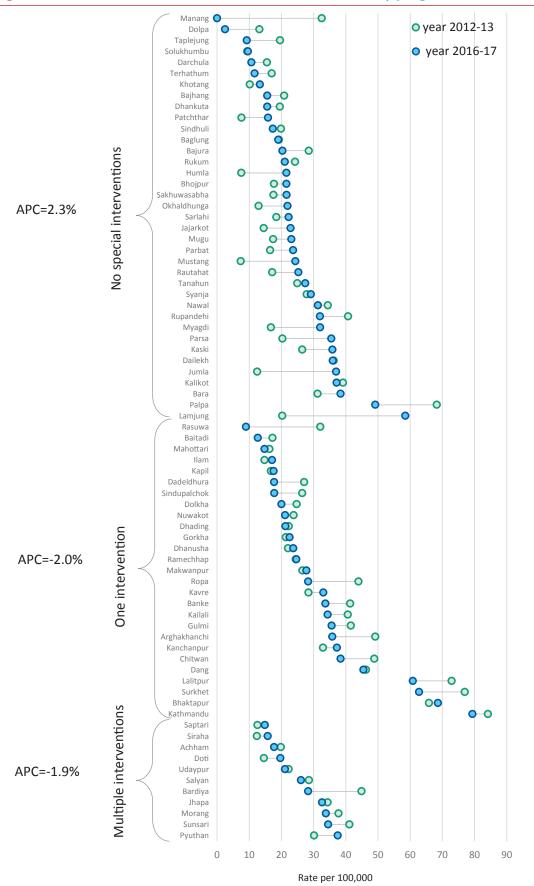


Figure 32 Trend of EPT notification rate in districts ordered by programmatic interventions

Data source: National Tuberculosis Program

4.1.6. Quantitative data on diagnostic delays

We found eight studies evaluating the delay in seeking health care and the initiation of TB treatment in Nepal. Studies conducted before 2010 showed much longer delays compared to the most recent studies. In addition, patients from rural areas had longer delays compared to the urban population. According to the most recent studies the median total delay is a little longer than one month (Table 5)

	Table 5 List of studies of delay of 15 diagnostic and treatment					
Ν	Author	Title	Year	Key Findings		
1	Kc A et al.	Diagnostic and Treatment Delays among the Tuberculosis Patients in the Urban Area of Western Nepal.	2018	diagnostic delay =34 days treatment delay <1 day total delay= 33.5 day		
2	Laohasiriwong W et al.	Health System Delay among the Pulmonary Tuberculosis Patients Presenting in the DOTS Centers of Nepal.	2016	The median total delay= 3 days Unacceptable health system delay=26.74%		
3	Laohasiriwong W et al.	Delay for First Consultation and Its Associated Factors among New Pulmonary Tuberculosis Patients of Central Nepal.	2016	Median total delay=32 days		
4	Mahato RK et al.	Major Delays in the Diagnosis and Management of Tuberculosis Patients in Nepal.	2015	The median patient delay=32 days Health system delay=3 days Total delay =39.5 days		
5	Choudhari M	Factors associated with patient delay in diagnosis of pulmonary tuberculosis in a district.	2012	Overall median patient delay=42 days		
6	Bam TS et al.	Longer delay in accessing treatment among current smokers with new sputum smear-positive tuberculosis in Nepal.	2012	The median total delay 103 days		
7	Rajendra Basnet	Delay in the diagnosis of tuberculosis in Nepal	2009	The median patient delay=50 days health system delay=18 days, and the median total delay=60 days		
8	Yamasaki- Nakagawa M	Gender difference in delays to diagnosis and health care seeking behaviour in a rural area of Nepal.	2001	median total (men) 2.3 months median total (women) 3.3 months		

Table 5 List of studies on delay of TB diagnostic and treatment	Table 5 List of st	udies on delav	of TB diagnostic	and treatment
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During the field visits, we conducted a quick assessment of treatment delay in bacteriologically confirmed PTB cases based on reviews of facility TB registers and/or TB treatment cards. We calculated the difference between date of laboratory confirmation (microscopy or Gene Xpert MTB-Rif) and date of start of treatment. Out of 23 cases assessed in 3 different facilities the median delay was 2.5 days, with range of 0-18 days. Seven out of 23 (30.4%) BC PTB patients had unacceptable (over 8 days) delay. (Fig 33) Because of different formatting of the dates entered into database, it was impossible to evaluate treatment delay from the case-based database.

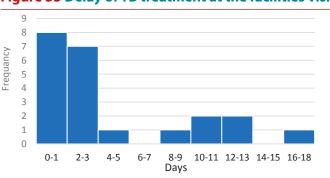
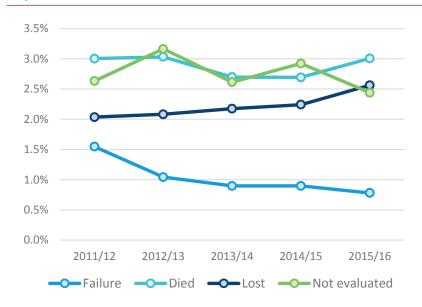


Figure 33 Delay of TB treatment at the facilities visited (n=23)

Data source: Review of R&R forms during site visits

4.1.7. Number of people successfully treated for TB out of all notified

TB treatment is one of the most effective interventions in TB control to reduce the prevalent cases in the population and reduce the transmission of infection. Fig 34 shows the cohort analysis of treatment outcome of new and relapse TB patients at regional level between 2011/12 to 2016/17. Overall, the proportion of patients who died, lost to follow-up or not evaluated were stable over time, while the proportion in whom treatment failed declined between 2011/12 and 2012/13. This could be related to changes in the case definition framework: previously RR/MDR TB cases were classified as having failed first-line treatment when moved onto second-line TB treatment, while according to 2013 WHO reporting framework RR/MDR cases are to be removed from the DS-TB treatment cohort if they are enrolled into second-line treatment.



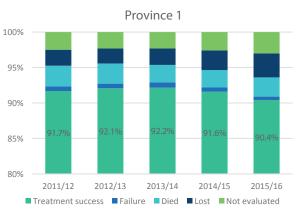


Data source: Global TB database

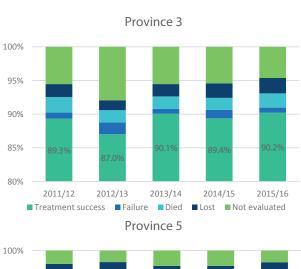
The treatment success rate for new and relapse TB patients over review period at national level has been consistently above 90%. At the regional level, only the Eastern Development Region has reported a gradual decline of the treatment success rate from 91.6% in 2011/12 to 87.3% in 2015/16. The reason for the decline is an increase in the proportion of patients being lost to follow-up, and in deaths (Fig 35).

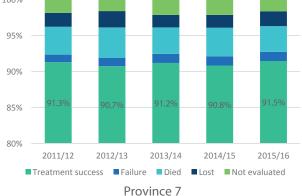
The high level of treatment success is likely to contribute to reducing disease transmission and could be regarded as one of key factors to drive the TB epidemic downwards. However, the treatment success rate is likely to be over-estimated in the national data, as there is no routine recording of initial loss to follow-up. A recent study conducted in the eastern 16 districts of Nepal identified 20% pre-treatment loss to follow-up, which was higher than other findings from Asia¹⁶.

¹⁶ Creswell, J., Rai, B., Wali, R., Sudrungrot, S., Adhikari, L. M., Pant, R., ... Uranw, D. (2015). Introducing new TB diagnositics - the impact of Xpert MTB RIF testing on case notifications in Nepal.pdf, *19*(January), 545–551.



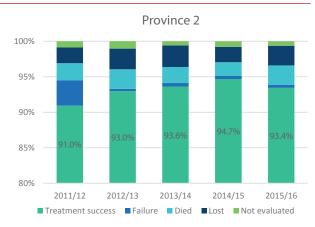




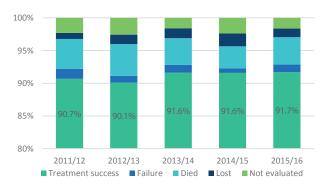


100% 95% 90% 85% 91.6% 90.8% 90.2% 88.7% 87.3% 87.3% 2011/12 2012/13 2013/14 2014/15 2015/16 Treatment success Failure Died Lost Not evaluated

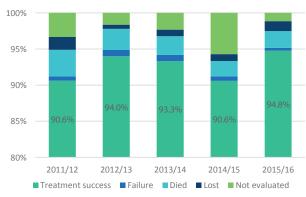
Data source: National TuberculosisProgram



Province 4



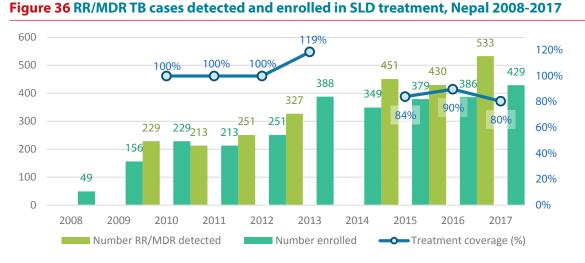
Province 6



4.1.8. MDR-TB treatment coverage and treatment outcomes among MDR-TB patients

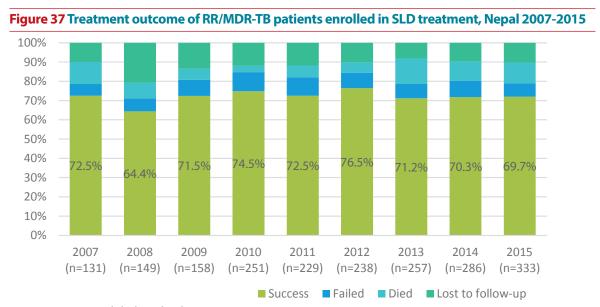
It is estimated that annually about 1,500 incident cases of RR/MDR are occurring in Nepal (range: 840-2,400). If all notified PTB patients had access to DST, it is estimated that health system could detect about **900** RR/MDR cases annually among notified TB cases (range: 590-1,200). However, during the most recent reporting year, only **429** (319 according to NTP provided datasheet) were detected in Nepal, which suggests a case detection rate of approximately **48%** (or 35% according to the NTP data).

Second-line TB treatment was introduced in Nepal since 2008 and has expanded. Up to 2013, the total number of enrolled patients reported in national data exceeded the number of confirmed cases from laboratory data. During the most recent 3 reporting years there was a gap between the number notified and the number enrolled into SLD treatment, ranging from 10-20%. (Fig 36) High rates of enrollment into SLD treatment should reduce transmission of MDR-TB, however, because of low DST coverage among pulmonary TB patients, over half estimated RR/MDR TB cases among notified remain undiagnosed.



Data source: Global TB database

The treatment success rate of RR/MDR-TB patients enrolled in second-line treatment since 2007 has ranged between 64 to 77%. In most recent years it declined slightly to 70%, which is nonetheless very high compared to the global average of 50%. (Fig <u>37</u>).



Data source: Global TB database

It should be noted that the number of patients enrolled in RR/MDR treatment does not match the cohort size of treatment outcome reported for the given year. Consequently, there is a risk that reported indicators of treatment success rate might be biased. (Fig 38)



Figure 38 Comparison of RR-TB enrolled and Treatment outcome reported, Nepal 2007-2015

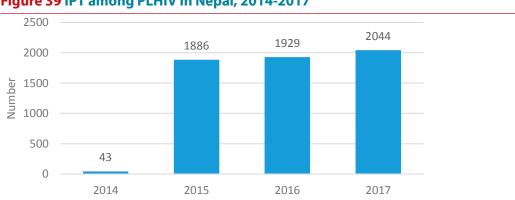
Data source: Global TB database

4.1.9. TB preventive treatment among children and people living with HIV

There will be an impact on TB incidence if transmission can be reduced sufficiently and/or if preventive treatment of people with latent TB infection is effectively implemented on a large scale. TB preventive treatment is a key component of the End TB Strategy, and TB preventive treatment coverage among those eligible is one of the top 10 indicators to monitor progress.

WHO recommends offering preventive TB treatment to household contacts of adults with pulmonary TB, with priority given to children under 5 years of age. According to WHO estimates, in 2017 there would have been 6,900 (range: 6,300-7,500) children under five years eligible for preventive TB treatment in Nepal. Starting from 2017, the NTC has been implementing IPT among children under 5 years old in 38 high burden districts of Nepal where contact tracing is being done. The total number of children enrolled in IPT was 82 in 2016/17. This constitutes only 1.1% of all children eligible for preventive TB treatment, and as such, there is a need for increased investment and support to massively expand contact tracing and IPT in Nepal.

For PLHIV in Nepal, preventive therapy services are being provided through ART Centers. IPT initiations among HIV patients in Nepal increased from 43 patients in 2014 to 2044 patients in 2017. (Fig 39) Despite this increase, the coverage TB preventive treatment among PLHIV remains far below of WHO recommended level of 90%.



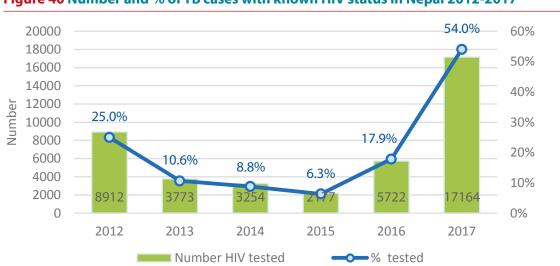


Data source: Global TB database

4.1.10.HIV testing, ART and CPT coverage of TB patients, and treatment outcomes among PLHIV

To ensure effective integrated TB and HIV service delivery, WHO recommends provision of HIV testing to all TB patients, providing ART and CPT to TB patients living with HIV, TB screening on regular basis among people living with HIV, and offering IPT to people living with HIV who do not have active TB.

Over the recent years, there was notable improvement in HIV testing coverage among TB patients in Nepal, which increased from 10.6% in 2013 to 54% in 2017. (Fig 40)





Despite increased HIV testing coverage over the recent 3 years, the absolute number of HIV/TB co-infected patients identified did not increase (Fig 41). This is explained by the fact the at early stages the HIV testing was implemented among the high-risk group population and in locations known with high level of HIV prevalence, and as testing has expanded, people lower risk are receiving testing, reducing the proportion positive among those tested.

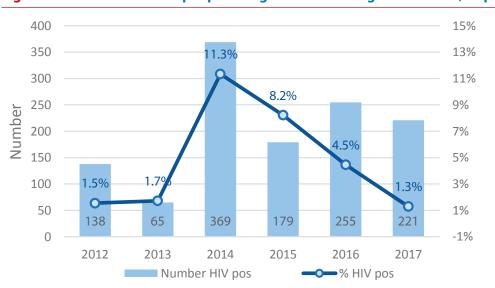
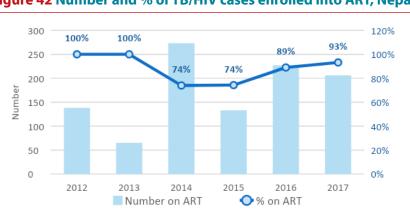


Figure 41 Number and % of people living with HIV among those tested, Nepal 2012-2017

Data source: Global TB database

Data source: Global TB database

Reported ART coverage among identified TB/HIV patients was consistently high, ranging between 74 and 100%. (Fig 42)

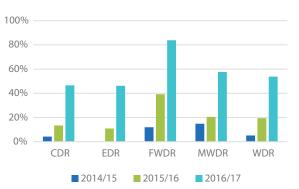




Data source: Global TB database

HIV testing coverage improved in all districts over the recent 3 years. By 2017 the highest level of coverage is recorded in FWDR. ART coverage also improved in all districts except EDC. CPT coverage moderately improved, but in general is low ranging between 20 to 53% across the regions (no data in MWDR). (Fig 43)

Figure 43 HIV/TB collaborative activities at regional level



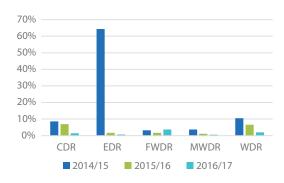
Percent of TB cases with known HIV status

TB/HIV cases enrolled into ART

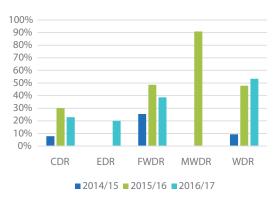


Data source: National Tuberculosis Program

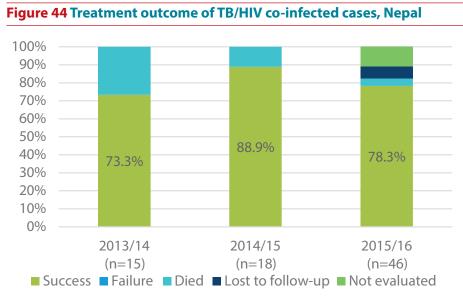
% of TB cases with positive HIV test results



TB/HIV cases enrolled into CPT

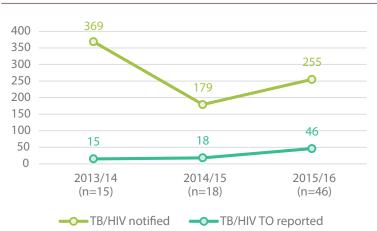


Reported treatment success of TB/HIV co-infected patients is within the range of 73 to 89% during the recent 3 years. (Fig 44)



Data source: National Tuberculosis Program

It should be noted that the notified number of HIV/TB cases and size of reported treatment cohorts differ substantially (Fig 45), therefore treatment success rates among all people treated for HIV-associated TB might be much lower than what is reported.





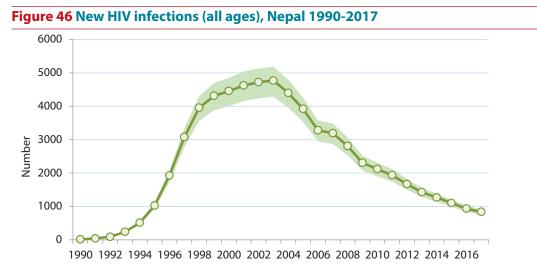
Data source: National Tuberculosis Program

Because of the low prevalence of HIV in both the general population and among people with TB, the impact of TB/HIV collaborative activities on the overall TB epidemic in Nepal will be limited. However, the increase of HIV testing coverage, high rate of ART enrollment have likely contributed preventing deaths, increasing treatment success rates, and reduction of transmission of infection among people living with HIV.

4.2. Broader external factors not specifically related to TB-specific funding

4.2.1. Prevalence of HIV among the general population, and ART coverage

HIV is the most potent risk factor for TB within the individual. HIV prevalence in Nepal peaked in 2003. Due to aggressive programmatic interventions rapidly increasing trend of HIV incidence was reversed and since then it is declining (Fig 46). Since 2010, new HIV infections have declined by 61%.



data source: http://aidsinfo.unaids.org/

In 2017 the estimated number of people living with HIV in Nepal was 31,000 (range: 27,000-36,000). HIV epidemic remains concentrated, with an estimated prevalence of 0.2% among the population (all ages). Fig 47 shows time changes in estimated number of PLHIV in Nepal in recent decade.

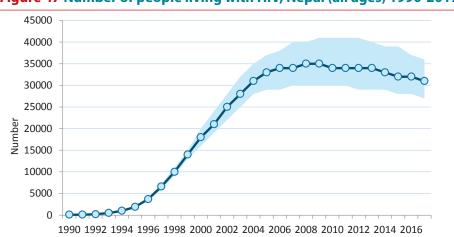


Figure 47 Number of people living with HIV, Nepal (all ages) 1990-2017

There is strong evidence that timely initiated anti-retroviral treatment (ART) and preventive Isoniazid therapy may reduce the risk of progression from infection to disease. Access to antiretroviral therapy in Nepal gradually increased from 17% in 2010 to 49% 2017 (Fig 48).

data source: http://aidsinfo.unaids.org/



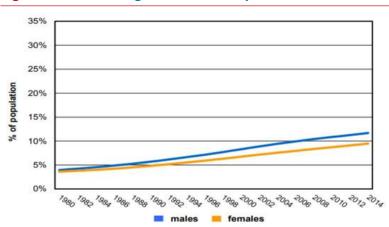


data source: http://aidsinfo.unaids.org/

Improvement in ART coverage would reduce the AIDS-related deaths, improve HIV survival, however, because HIV prevalence in the population is small, the overall impact of ART, CPT coverage on the TB epidemic in Nepal will be very limited.

4.2.2. Prevalence of diabetes

Historically, diabetes was considered a disease of developed countries. However, the recent estimates suggest that over the past decade, diabetes prevalence has risen faster in low- and middle-income countries than in high-income countries.¹⁷ According to International Diabetes Federation¹⁸ estimates in 2017, there were 657 thousand patients with diabetes mellitus aged 20-79 years, equivalent to 3.96% (range: 2.74%-7.98%). About 81% of people with diabetes were estimated to be undiagnosed. According to WHO estimates, the age-standardized prevalence of diabetes in Nepal almost doubled between 1980 and 2014, reaching 9.1% (Fig 49). Diabetes triples a person's risk of developing TB. Given a large proportion of diabetes patients are not diagnosed in Nepal and their diabetes remains unmanaged, the risk of the increasing diabetes prevalence might be one factor moderating the decline of TB burden in Nepal.





Data source: WHO, Diabetes country profile https://www.who.int/diabetes/country-profiles/npl_en.pdf?ua=1

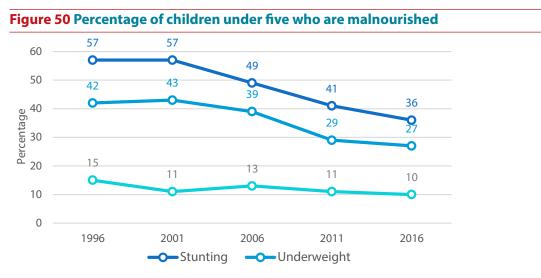
¹⁷ World Health Organization, Global Report on Diabetes, 2016

¹⁸ IDF Diabetes Atlas- 8th Edition

¹⁹ Diabetes Country Profile, World Health Organization <u>https://www.who.int/diabetes/country-profiles/npl_en.pdf?ua=1</u>

4.2.3. Malnutrition

According to the Nepal Demographic Health Survey conducted in 2016, overall, 36% of children under age 5 are stunted, with 12% being severely stunted (too short for their age); 10% are wasted, with 2% severely wasted (too thin for their height); and 27% are underweight, with 5% severely underweight (too thin for their age)²⁰. The prevalence of stunting and underweight among children under age 5 have markedly decreased, from 57% to 36%, and from 42% to 27%, respectively, in the last 20 years (1996-2016). This indicates stunting in children declined by 14% between 2001 and 2006, declined by an additional 16% between 2006 and 2011, and dropped by 12% between 2011 and 2016. A similar downward trend is observed for underweight children. However, in the same time period, changes in wasting were minimal (Fig 50). Given that malnutrition almost triples the risk of TB, assuming that nutrition among adults improved at similar rates, such impressive declines in malnutrition most probably was one of drivers of observed decline of TB over the recent decades.



Data source: Nepal DHS 2016

4.2.4. *Tobacco use*

According to the DHS Nepal conducted in 2017 men are more likely than women to use tobacco. **Twenty-seven** percent of men use any type of tobacco, compared with 6% of women. Among those who smoke various tobacco products, cigarettes are most common (27% of men and 6% of women) While almost 73% of men are nonsmokers, 17% smoke on a daily basis and 11% smoke occasionally. Use of cigarettes has decreased slightly during the past 5 years, from 9% to 6% among women and from 30% to 27% among men.

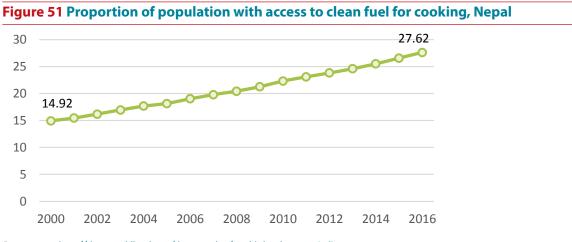
4.2.5. Exposure to indoor air pollution

Exposure to smoke inside the home, either from cooking with solid fuels or smoking tobacco, has potentially harmful health effects. Relative risk of indoor air pollution on TB is 1.5 (95% CI: 1.0-1.5). According to DHS Nepal 2016, cooking takes place inside the home in slightly more than two-thirds (68%) of households, while 26% of households have a separate building for cooking.

About two-thirds of households (**66%**) use solid fuel for cooking, and this practice is more common in rural households (88%) than urban households (52%). Wood is the most common type of solid fuel used for cooking, and it is used more often in rural (77%) than urban (48%) areas. Use of clean fuel (electricity and liquefied petroleum gas/natural gas/ biogas) is more common in urban areas than in rural areas (48% and 12%, respectively).

²⁰ Demographic Health Survey, Nepal 2017 https://dhsprogram.com/what-we-do/survey/survey-display-472.cfm

There is daily exposure to tobacco smoke in 31% of households (34% in rural areas and 30% in urban areas). According to the World Bank the proportion of population with access to clean fuel for cooking Increased from 14.9 in 2000 to 27.6% in 2016. (Fig 51). Vast majority of population in Nepal still is exposed to indoor air pollution and this observed improvement can have only modest effect on TB epidemic.



Data source: http://data.worldbank.org/data-catalog/world-development-indicators

The relative contributions of key risk factors of tuberculosis are presented in the table below, which could be considered in prioritizing TB control interventions. Population Attributable Fraction (PAF) of each of risk factors was calculated using formula:

 $PAF = \frac{Prevalence * (PR-1)}{Prevalence * (RR-1)+1}$

The PAF is a statistic used to estimate the proportion of cases that would be prevented if the risk factor were eliminated from the population. The highest PAFs for TB in Nepal are associated with indoor exposure of solid fuel, undernutrition, smoking, diabetes and HIV in that order (<u>Table 6</u>).

Table 6 Prevalence and Population Attributable Fractions (PAF) of selected TB risk factors, Nepal				
Risk factor (risk group)	Prevalence of Risk factor in Nepal (%)	RR ²¹	PAF in the population age group (%)	PAF in total population (%)
HIV (15-49y)	0.222	26.7	4.9	2.6
Undernutrition	9.5 ²³	3.2	17.3	17.3
Diabetes (20-79y)	3.96 ²⁴	3.1	7.7	4.4
Smoking (>15)	16.5 ²⁵	2.0	14.2	8.1
Indoor use of solid fuel for cooking	66.0 ²⁶	1.4	20.9	20.9

4.2.6. Changes in prison population size

Increases in the prison population can drive a TB epidemic upward if people are at much higher risk of TB in prison than in the community. In Nepal, the incarceration rate is not high by global

26 Idem

²¹ Lönnroth K, Castro KG, Chakaya JM, Chauhan LS, Floyd K, Glaziou P, et al. Tuberculosis control and elimination 2010-50: cure, care, and social development. Lancet. 2010;375(9728):1814–29.

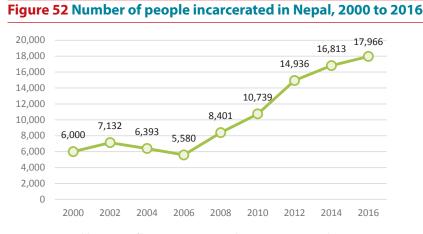
²² Data source: http://www.unaids.org/en/regionscountries/countries/nepal/ accessed on January 30, 2019

²³ Food security Report http://www.fao.org/3/I9553EN/i9553en.pdf

²⁴ International diabetes federation http://www.diabetesatlas.org/across-the-globe.html, accessed on January 30, 2019

²⁵ Demographic Health Survey, Nepal 2017 https://dhsprogram.com/what-we-do/survey/survey-display-472.cfm

standards: there were 60 prisoners per 100,000 population in 2017 (world range: from 655 in the US to 10 in Guinea Bissau)²⁷. However, in recent years the rate of incarceration has steadily increased (Fig 52), and there is cause for concern about over-crowding, as prison occupancy was **178% in June 2017.**



Data source: World Prison Brief http://www.prisonstudies.org/country/nepal

The annual number of notified TB cases from prison s in the recent 5 years ranged from 31 to 41 (rate from 208 to 228 per 100,000). Because of the small prison population in Nepal and small number of TB cases reported in prisons overall impact of increase in prison population is negligible. However, more in-depth examinations are needed using more sensitive diagnostic methods, as total number of notified TB cases from prisons looks implausibly low, especially from mass screening activities.

4.2.7. GDP per capita

Economic growth has an important effect on many TB determinants including over-crowding, education, nutrition, health care-seeking behaviour. Consequently, economic growth can reduce both transmission of infection and the risk of progression to disease, as well as improving access to diagnosis and treatment. The following plot shows time changes in GDP per capita in Nepal from 2000 (Fig 53). Between 2000 and 2017 the GDP per capita in Nepal increase about 4 times. However, in most recent years the growth was stagnated and with GDP per capita, Nepal remains low by international standards, which likely contributes to maintaining the TB epidemic.

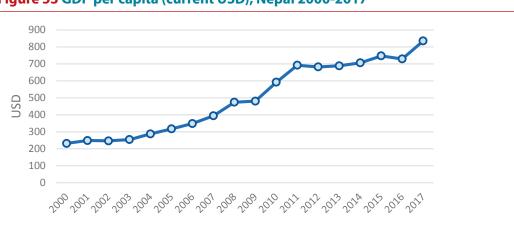


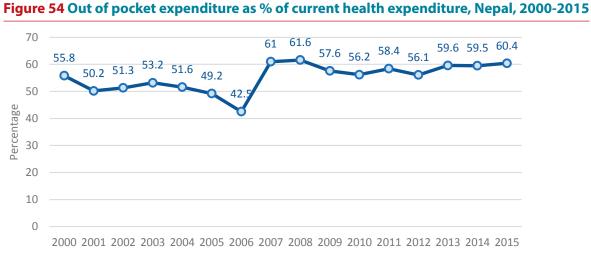
Figure 53 GDP per capita (current USD), Nepal 2000-2017

Data source: World Bank

²⁷ World Prison Brief, Institute for Criminal Policy Research, http://www.prisonstudies.org/country/nepal

4.2.8. Coverage of financial protection for health care costs

Health care financing in Nepal predominantly is financed by out-of-pocket (OOP) payments: as of 2015 60.4% of total health expenditure was covered by OOP. From 2000 to 2007 OOP declined from 55.8% to 42.5%, but in 2008 again it sharply increased and has been largely stable since then (Fig 54). OOP health expenditure in Nepal is much higher than the \leq 25% benchmark set by WHO. It is known that OOP payments by their nature are highly regressive, as poorer households are forced to pay a greater proportion of their income for health services than richer households. This suggests that access to quality health care is not affordable for many vulnerable people at highest risk of TB, and thus limited access to care is likely to drive the TB epidemic upward.



Data source: World Bank

4.2.9. Demographic changes

TB is strongly associated with age and sex, being more common in the population aged 25–55 years and in males. Therefore, demographic changes caused by natural movements or migration can drive the TB epidemic in a country upwards or downwards, depending on changes in proportions of different age groups. Fig. 55 shows the age pyramids for Nepal in 1997, 2007 and 2017, Each pyramid represents the distribution of the population by age and sex. Observation of pyramid shapes indicates gradual changes in the structure of the population. The pyramid for 2017 is narrower at the bottom due to decline in fertility in recent years and larger at the top half, indicating an increase in life expectancy.

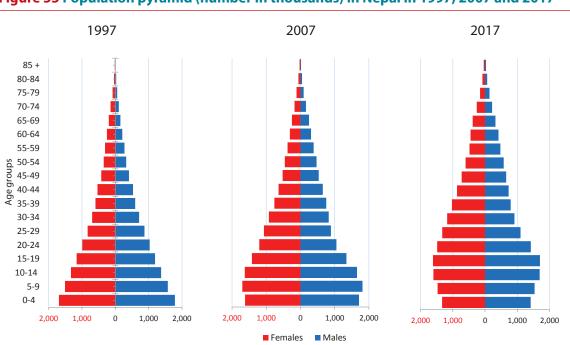


Figure 55 Population pyramid (number in thousands) in Nepal in 1997, 2007 and 2017

Consequently, the relative proportion of children (aged <15 years) in Nepal has decreased from 41.0% in 2000 to 32.6% in 2015, while the proportion of the elderly population (aged >64 years) over this period increased from 3.8% to 5.5% (Fig 56). Decline of proportion of children and increasing proportion of adults could drive the TB epidemic upward as TB is less common in children. However, as these changes are taking place quite slowly in Nepal, therefore the impact of demographic changes on the pattern of TB epidemic is likely to be minimal.

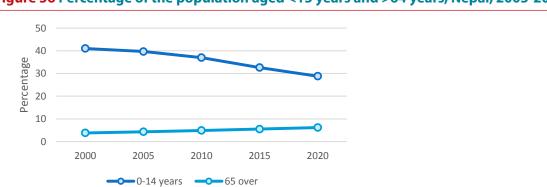


Figure 56 Percentage of the population aged <15 years and >64 years, Nepal, 2005-2020

4.2.10. Under-5 mortality rate (as an indicator of the overall performance of the health-care system)

It is assumed that improvement in the general population's health is associated with a decreased TB burden. Under-five mortality (U5M) is commonly used as a proxy indicator of overall population health and therefore for access to health services. The figure below represents the estimated trend in under-five mortality in Nepal since 1990. Between 2010 and 2017 estimated under-five mortality steadily declined, with an average annual decline of 4.9%. (Fig 57) This suggests that population health and access to healthcare has improved in Nepal over this period, which could contribute to reductions in the burden of TB.

Data source: World Population prospectshttps://population.un.org

Data source: World Population prospects <u>https://population.un.org</u>

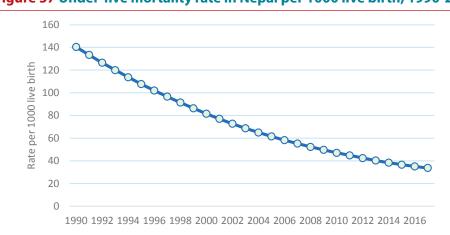


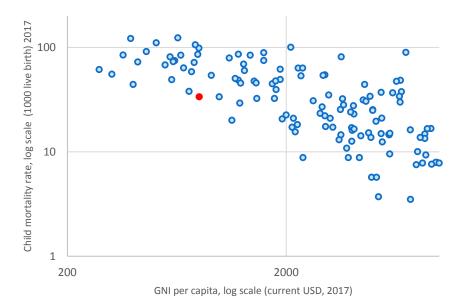
Figure 57 Under-five mortality rate in Nepal per 1000 live birth, 1990-2017

data source: <u>https://data.worldbank.org/indicator/SH.DYN.MORT?locations=NP</u>

Compared to other countries with the similar income U5MR in Nepal was lower in 2017 than it would be expected from the size of the economy expressed in GNI per capita, suggesting comparatively better performance of health system (as measured through the U5MR indicator) (Fig 58).

Figure 58 Scatterplot of under-5 mortality rate against GDP per capita (2017).

Each blue dot represents a country pair of data points. Nepal is shown in red



STANDARDS AND RENCHMARKS ASSESSMENT	

5.1. PART A: Characteristics of the TB surveillance system

Before completing the checklist, it is important to characterise the national TB surveillance system. Please provide answers to the following questions.

COUNTRY NAME: Nepal

DATE OF ASSESSMENT: January 2019

	KEY ACTION(S) REQUIRED TO ADDRESS THE GAPS	All possible steps should be taken to support uninterrupted TB reporting during the federal restructure, both through the HMIS system as well as to the electronic case-based systems, including hiring extra staff if needed. The NTC should aim to complete the rollout of the ETB Manager system to the district level and to ensure all health workers administering TB treatment have access to the ETB Manager mobile app. Aggregate reporting forms should be modified to collect data additional indicators for contact tracing, IPT, and the use of Gene Xpert in priority groups (see detailed recommendations). It should be ensured that all Gene Xpert Sites have access to the TB Tracker system, including the required IT infrastructure. The NTC should assess the feasibility of using the TB Tracker system to record microscopy data as well as Gene Xpert data.
	Description details	Data at clinics are recorded on paper (tools: treatment cards, DS-TB treatment registers, contact tracing and IPT registers, MDR-TB registers, laboratory registers, community DOT logbooks). Monthly paper reports are sent from the health facilities to the Department of Health on multiple conditions, including dedicated two-page reports for TB, as part of the National Health Information Management System ("HMIS" [sic]). Some facilities (e.g. some provincial and district hospitals) also have access to online case-based systems: ETB Manager (DS-TB), and a DHIS2 system for MDR-TB. These systems are being rolled out to district level, but this roll-out was not complete as of January 2019. Due to the federal restructuring of Nepal, there has been a major interruption to reporting from July 2018 onwards, with fewer than 1,000 patients reported in the 2018-19 financial year, compared to over 17,000 the previous year. There is a mobile phone app for the ETB Manager system through which lower-level health workers can update records created by district or referral-facility staff. Gene Xpert sites have access to an online case-based laboratory register, TB Tracker. There is no electronic data collection for contact tracing and IPT, except for a field in the triannual report which records the number of patients diagnosed with TB via contact tracing and IPT, eccorded at facility level but is not included in trimester reports.
-	OUTCOMES (Best practices are in bold)	 Data are recorded electronically on a national internet- based system Data are recorded electronically on a state/provincial/ regional internet- based system Data are recorded electronically on a local system Data are not recorded on paper
	QUESTIONS	A1. How are data recorded for individual TB cases at the service delivery level (e.g. in TB diagnostic units, health centres, clinics)? (<i>Tick all that apply</i>)

QUESTIONS C	OUTCOMES (Best practices are in bold)	Description details	KEY ACTION(S) REQUIRED TO ADDRESS THE GAPS
 A2. Do all service del □ Yes, completely ⊠ Mostly □ Partially □ No, not at all Some facilities were to 	 A2. Do all service delivery points systematically use standardised TB data co Yes, completely Mostly Partially No, not at all Some facilities were using obsolete treatment cards for patients in 2016-17. 	 A2. Do all service delivery points systematically use standardised TB data collection forms and tools? Yes, completely Mostly Partially No, not at all Some facilities were using obsolete treatment cards for patients in 2016-17. 	District staff should review all paper tools at supervisory visits and ensure that all health facilities have sufficient supplies of the current versions and that these are being used, maintained, and filed appropriately.
A3. Which TB cases are included in the national TB surveillance data? (<i>Tick all</i> <i>that apply</i>)	 All TB cases from all parts of the country some TB cases are excluded Some part(s) of the country are excluded Some case types are excluded Some care providers, e.g. non-NTP providers, prisons, private practitioners, are excluded. Others: 	All public services report to the NTC, as well as some private sector providers. Nepal's system is a treatment register rather than a true surveillance system. Most facilities we visited did not have presumptive TB registers, rather presumptive patients were recorded in the out-patient department registers (or not at all). Patients who are diagnosed with bacteriologically confirmed disease are included in the laboratory register at their diagnosing facility, but they are expected to be recorded in the treatment register at the facility in which they initiate treatment. There is no routine follow-up of referrals between presenting facilities, diagnostic sites (e.g. district hospitals) and treatment sites (e.g. local health sub-centres). Patients who do not initiate treatment are not recorded in registers and it is therefore not possible to assess loss to follow up prior to treatment initiation. The NTP has been working to engage the private sector in reporting, however there are some private hospitals, and a large number of private practitioners and pharmacies that do not currently report to the NTP.	Presumptive registers should be provided to all facilities and aggregate reporting forms should be amended to record the number of presumptive TB cases seen and referred for diagnosis. SOPs should be developed for routine follow-up of referred patients by the referring facility (e.g. subcentre to district hospital for diagnosis, and district hospital to sub-centre for treatment). Registers should be amended as needed to collect information on referrals, including free text fields for facility names. During supervisory visits, the completeness of follow-ups should be evaluated by cross-checking registers and ensuring that data are complete (e.g. that laboratory outcomes are recorded in presumptive TB registers, and that treatment start date and facility are recorded for positive cases in laboratory registers). The NTC should work together with district and Palika staff, as well as with private providers, to develop a system for data collection from the private sector which is acceptable to all parties.

QUESTIONS	OUTCOMES (Best practices are in bold)	Description details	KEY ACTION(S) REQUIRED TO ADDRESS THE GAPS
A4. What types of TB data are available at the national level? (Tick all that apply)	 Patient-level data that allow multiple episodes of TB in the same person to be identified are available Case level data are available for all of the country Case level data are available for parts of the country Aggregated data are available, i.e. summaries for groups of cases 	Aggregated data are available for the region and district levels. The ETB system roll-out is not complete. In 2015-16, coverage of the system had reached 60% of all patients in aggregate reports. The federal restructure has caused a major interruption to reporting, however, and fewer than 1,000 patients have been reported to the system between July 2018 and January 2019. Downloading line listing data for this system is cumbersome, as it requires NTP staff to download Excel spreadsheets for each of 75 districts - no "master file" download option is available. The system can however generate reports for NTC staff, including on data quality problems. The eTB system uses a unique patient identifier assigned by the Tacker system. If this patient subsequently presents to TB services, staff can search for the ID using the patient's identifying information and could identify the previous treatment episode. However, staff cannot add a recurrent episode of TB using the same patient identifier, rather a new record with a new ID would be created.	All possible steps should be taken to support uninterrupted TB reporting during the federal restructure, both through the HMIS system as well as to the three case-based systems. The NTC should aim to complete the rollout of the ETB Manager system to the district level and to ensure <i>all</i> health workers administering TB treatment have access to the ETB Manager mobile app. The ETB, TB Tracker and MDR systems should all be modified to allow downloading of "master files" of raw data to CSV format (excluding patient names, dates of birth, and residential addresses). A function should be added to the system to allow creation of a record for a subsequent episode of TB using the same unique identifier, with appropriate data validation checks.
A5. What is the expected frequency of data transmission from the first sub-national administrative level to the national level? (<i>Tick all that apply</i>)	 Real-time More often than monthly Monthly Quarterly Less often than quarterly 	Aggregated reports are sent from district to national level every four months (triannually). Monthly reports are also sent from health facilities to district health offices as part of the national HMIS system. District staff facilities visit monthly to complete the district register, from which they compile tri-annual electronic reports in Excel which they send to the NTC, as well as tri-annual electronic HMIS reports. The NTC report contains additional TB indicators which are not collected in HMIS reports. Some Gene Xpert sites enter patient data into the TB Tracker system in real-time, as this system can print laboratory reports which are given to the patient in their results management appointments. Some higher-level health facilities enter data into the ETB Manager and MDR-TB systems in real-time.	Timely reporting to both case-based and aggregate systems during the federal restructure should be supported with additional resources as required, including retrospective reporting for 2018 as needed. Efforts should be made to complete the rollout of the electronic systems, with the expectation that data are entered in real-time. Timeliness of reporting should be monitored by staff at the national level by comparing dates of record creation with dates of treatment initiation.

QUESTIONS	OUTCOMES (Best practices are in bold)	Description details	KEY ACTION(S) REQUIRED TO ADDRESS THE GAPS
A6. At what levels of the system are TB data systematically verified for accuracy, timeliness and completeness? (Tick all that apply)	 A From the service unit upwards From the 1st administrative level upwards Conly at the national level Not at any level 	At present, district staff are expected to visit clinics monthly and provide verbal and written feedback on the quality of data in the treatment cards and registers. In many facilities we visited, there was no written feedback in the registers. Provincial staff provide biannual feedback to sub-districts at data quality workshops. National staff provide biannual feedback to provincial staff at data quality workshops. This system is currently changing because Nepal has undergone a major administrative restructuring. Some federal powers have been devolved to newly created Provinces, and many functions of Districts have been decentralised to Sub-districts. This has created some confusion and interruptions to reporting and auditing while staff are reassigned and budgets are redistributed. In one district, no data collection or reporting had been undertaken between July 2018 and January 2019 due to budget reductions. The ETB Manager system contains a number of automated validation checks, which are visible through a "notifications" tab.	The NTC should carefully analyse data for the 2017-18, 2018-19 and 2019-2020 years to assess the impact of the federal restructure on reporting and data quality as reporting responsibilities are decentralised. All efforts should be made to maximise the quality of data during this period, including retrospective data entry and reporting for 2018-19 as needed. Written feedback should be provided to clinical staff at every supervisory visit. Provincial staff, and the quality of written feedback. Routine cross-checking of registers should be implemented at data quality workshops, with quality to health facilities by district staff, and the quality of written feedback. Bound the quality of source and data quality workshops, with quality workshops, with quantitative data collected on loss to follow-up during screening and diagnosis. Data validation checks in all three of the case-based systems should be reviewed to ensure that all critical data elements are being validated.
A7. What types of quality assurance procedures are systematically undertaken for TB data? (Tick all that apply)	 Quality controls are in place for the electronic surveillance system (automated checks at data entry and batch checking, plus SOPs) Data are reviewed during supervisory monitoring visits to service units and subnational levels (How often?) Data are reviewed during meetings with TB staff (How often?) Other (specify:) 	There are monthly supervisory visits by sub-district staff to health facilities. There is a twice-yearly workshop at the district level to assess data quality and provide feedback to health facility staff. There is a twice-yearly workshop at provincial level to assess data quality and provide feedback to sub-district staff. There is a twice-yearly workshop at national level to assess data quality and provide feedback to provincial staff. There is a twice-yearly workshop at national level to assess data quality and provide feedback to provincial staff. There is a twice-yearly workshop at national level to assess data quality and provide feedback to provincial staff. There is a twice-yearly workshop at national level to assess data quality and provide feedback to provincial staff.	As above.

QUESTIONS	OUTCOMES (Best practices are in bold)	Description details	KEY ACTION(S) REQUIRED TO ADDRESS THE GAPS
A8. Is feedback on TB data quality systematically provided to all lower reporting levels?	 Yes, completely Mostly Partially No, not at all 	Health facility staff receive feedback from district staff. District staff receive feedback from provincial staff, and those using the eTB system can also view automated notifications regarding data quality issues. Feedback is supposed to be written on the front page of the register, where there is a dedicated table. However this was not used in all registers which we saw.	Provincial staff should conduct audits to assess the actual frequency of feedback visits to health facilities by district staff, and the quality of written feedback.
A9. When are national TB case data for a given calendar year considered ready for national analyses and reporting?	 Before April the following calendar year Before May the following calendar year following calendar year following calendar year On or after beginning of June the following 	Nepal uses financial rather than calendar years for reporting, with data from July-June usually available for analysis in August. However, during our visit in January 2019, data for the 2016-17 financial year were available, but not for the 2017-18 calendar year, due to the federal restructure. There was evidence of major interruptions to reporting for the 2018-19 financial year as well.	Resources should be dedicated to maintaining timely reporting during the federal restructure.
A10. Are there national guidelines for recording and reporting of TB data e.g. documentation or instructions? (Tick all that apply)	 Yes. They are posted on the internet. Yes. They are available in a manual or other reference document, e.g. training materials No 	There are no dedicated reporting guidelines for the paper systems, however staff receive training in the HMIS system through the Department of Health. The treatment registers contain instructions as to how they should be filled out, with definitions. There is a manual for the ETB Manager system in Nepali which is available in hard copy and PDF.	Manuals should be developed for the TB Tracker and MDR-TB systems and distributed to all staff using these systems.

QUESTIONS	OUTCOMES (Best practices are in bold)	Description details	KEY ACTION(S) REQUIRED TO ADDRESS THE GAPS
A11 . Does the national TB programme have a training plan which includes staff involved in data collection and reporting at all levels of the reporting process?	No No	There is no national training plan for the paper-based or electronic systems.	The NTC should develop a training plan with appropriate documents and SOPs for training of staff at all levels, in all systems.
A12. How often do TB programme staff receive training specifically on TB surveillance (i.e. recoding and reporting)? (<i>Tick</i> <i>all that apply</i>)	 Training is routinely received at national and sub-national levels (How often?) Training is received on an ad hoc basis Staff receive training when they are hired No routine training is received 	New staff attend workshops for the national HMIS system, although sometimes a long time after they are placed in their posts – some staff who we spoke with were not formally trained until are trained in a timely fashion.	The NTC should develop a training schedule for the roll-out of the electronic systems, and ensure that staff are trained in a timely fashion.

QUESTIONS	OUTCOMES (Best practices are in bold)	Description details	KEY ACTION(S) REQUIRED TO ADDRESS THE GAPS
A13. How many staff work on TB surveillance at the national level? (Tick all that apply)	 Epidemiologist, full- time () Epidemiologist, part- time () Statistician/ data manager, part-time. Statistician, part-time Data manager, full-time Data manager, part- time () Data quality officers, full-time. Data quality officers, part-time M&E Coordinator M&E Specialist 	Several staff work on M&E at the national level. There are serious skill shortages within the health system, and few epidemiologists and statisticians are employed or available.	
A14. Is a national TB surveillance report routinely produced and disseminated on an annual basis?	⊠ Yes □ No	During our visit we were provided with a copy of the 2016-17 annual report (in English). The 2017-18 report has been delayed due to interruptions to reporting caused by the federal restructure.	Additional resources should be dedicated to timely reporting during the federal restructure.
A15. Are there written goals of the surveillance system?	⊠ Yes □ No	The goals of the surveillance system are described in the national TB manual.	No gaps to address.
A16. Policies and procedures are in place to protect the confidentiality of all surveillance data e.g. records, registers.	 Yes, completely Mostly (names only appear on TB registers/ treatment cards/lab registers at facility level) Partially No, not at all 	In the case-based systems, by default, patient identifying information is available to staff at all levels regarding all patients. For example, when staff search for a patient in the TB Tracker system using their name, the results page includes all patients nationally with the same name. As well as violating patient confidentiality, this complicates searches as many irrelevant results are returned.	By default, patient identifying information (names, dates of birth, addresses) should be suppressed. When facility staff search for patient records, results should be restricted by default to the catchment area for their facility (e.g. sub-district or district for health sub-centre staff, district or neighbouring districts for laboratory staff).

QUESTIONS	OUTCOMES (Best practices are in bold)	Description details	KEY ACTION(S) REQUIRED TO ADDRESS THE GAPS
A17. Is there a long term financial plan and budget in place to support TB surveillance activities?	Xes No	National Strategic Plan (NSP) for Tuberculosis Prevention, Care and Control 2016-2021 provides a summary of NSP cost by activity disaggregated by years and activity area, including operational research, M&E and Program management and supervision. According to this document between 2016-2021 3.98% (\$4,188,678) of total NSP budget is allocated for M&E. The budget available per-patient in Nepal is low by international standards.	Further funding is needed to support TB activities in general, and M&E in particular.
A18. When was the last time the TB surveillance system was evaluated?	 Within the past 5 years Within the past 5-10 years Never (in a systematic and standardised way, but as part of programme reviews) 	An epi review was carried out in late 2014, including standards and benchmark assessment.	No gaps to address. A repeat epi review should be planned for early 2022.

5.2. PART B

5.2.1. Part B (section 1): Checklist for TB surveillance and vital registration systems

Indicate 'Met', 'Partially met', "Not met" or 'Not applicable' in the results column. Describe the key results and any action recommended to improve the For each standard, please assess whether the system is able to satisfy the associated benchmark(s), using the methods recommended in the user guide. quality of the system in the last two columns.

STANDARD	BENCHMARK(S)	RESULTS	RESULTS (DESCRIPTION) INCLUDING KEY ACTION(S) REQUIRED TO ADDRESS THE GAPS	ESTIMATED BUDGET REQUIREMENTS TO AD- DRESS KEY ACTION(S)
TB SURVEILLANCE SYSTEM DATA QUALITY	EM DATA QUALITY			
B1.1 Case definitions are consistent with	All three benchmarks should be satisfied to meet this standard:	MetPartially met	Since 2014-15, data have been collected on treatment history across each major site of disease.	N/A
WHO guidelines	 Laboratory-confirmed cases⁷ are distinguished from clinically diagnosed cases 	□ Not met	No gaps to address.	
	 New cases are distinguished from previously treated cases 			
	 Pulmonary cases are distinguished from extra- pulmonary cases 			
B1.2 TB surveillance system is designed to capture a minimum	Data are routinely collected for at least each of the following variables:	MetPartially met	Data have been collected for all key variables since 2014-15.	N/A
set of variables for reported TB cases	Age or age group	Not met	No gaps to address.	
	• Sex			
	 Year of registration 			
	Bacteriological results			
	 History of previous treatment 			
	Anatomical site of disease			
	 For case-based systems, a patient identifier 			

STANDARD	BENCHMARK(S)	RESULTS	RESULTS (DESCRIPTION) INCLUDING KEY ACTION(S) REQUIRED TO ADDRESS THE GAPS	ESTIMATED BUDGET REQUIREMENTS TO AD- DRESS KEY ACTION(S)
B1.3 All scheduled periodic data submissions have been received and processed at the national level	 For paper-based systems: 100% of expected reports from each TB basic management unit have been received and data aggregated at national level For national patient-based or case-based electronic systems that import data files from sub- national (e.g. provincial or regional) electronic systems: 100% of expected data files have been imported 	 Met Partially met Not met Not applicable 	As of January 2019 some triannual reports for the 2017-18 financial year remained outstanding, due to the federal restructure. In the ETB system, there were 16,592 patients registered in 2017-18. As of February 1 st , 2019, there were only 922 patients registered for the 2018-19 financial year, reflecting the impact of the federal restructures on data reporting. Additional resources should be dedicated to maintaining TB reporting from the district level during the federal restructure, including reporting to the case-based systems. The NTC estimates the resources required at USD 600,000.	USD 600,000 to meet human resources and IT requirements to maintain reporting from district health offices during the transition period.
B1.4 Data in quarterly reports (or equivalent) are accurate, complete, and internally consistent (<i>For paper-</i> <i>based systems only</i>)	 All benchmarks should be satisfied to meet this standard: Sub-totals of the number of TB cases by age group, sex, and case type equals the total number of reported TB cases in ≥95% of quarterly reports (or equivalent) from BMUs. The number of TB cases in ≥95% of quarterly reports (or equivalent) from BMUs. The number of TB cases in ≥95% of quarterly reports (or equivalent) matches the number of cases recorded in BMU TB registers and source documents (patient treatment cards and laboratory register) Data for a minimum set of variables are available for ≥95% of the total number of reported TB cases in quarterly reports. 	 Met Partially met Not met Not applicable 	In some facilities, we visited there were minor discrepancies between treatment cards, treatment registers, and monthly reports. However, in other facilities, staff could not locate treatment cards or monthly reports for data validation. In most facilities outcomes were recorded only in registers and not in treatment cards, preventing coss-validation of outcomes. There was usually good (but not perfect) concordance between registers and aggregate paper reports. During supervisory visits, district staff should ensure that health facility staff have all paper tools needed and that these are filed appropriately, in order to allow data validation.	NA

STANDARD	BENCHMARK(S)	RESULTS	RESULTS (DESCRIPTION) INCLUDING KEY ACTION(S) REQUIRED TO ADDRESS THE GAPS	ESTIMATED BUDGET REQUIREMENTS TO AD- DRESS KEY ACTION(S)
B1.5 Data in national database are accurate, complete, internally consistent, and free of duplicates (<i>For electronic case-based or patient-based or patient-based</i> systems only)	 All benchmarks should be met to reach this standard: Data validation checks are in place at national level to identify and correct invalid, inconsistent, and missing data in the minimum set (B1.2) For each variable in the minimum set (standard B1.2), > 90% of case records are complete, valid and internally consistent for the year being assessed <1% of case records in the minimum being assessed are unresolved potential duplicates. 	 Met Partially met Not met Not applicable 	 Data validation checks are in place in the ETB system, including checks to identify missing data. In 2016-17, 59% of all records were missing some baseline registration data, but not for the minimum variables. Age or age group: Mandatory field Sex: Mandatory field Sex: Mandatory field Year of registration: Automatically generated Bacteriological results: Mandatory field (BC, CD, EP) History of previous treatment: Mandatory field (BC, CD, EP) Anatomical site of disease: mandatory field (BC, CD, EP) Patient identifier: Automatically generated Patient identify duplicates, but it flags only exact duplicates which were entered on the same date. The ETB system should be modified to identify <i>potential</i> duplicates based on name, age, case type and district. Technical support should be requested to review and strengthen data collection and data quality assurance in the case-based systems, particularly the MDR-TB system. 	IT / M&E consultant to provide technical assistance for the case-based systems: USD\$30,000
B1.6 TB surveillance data are externally consistent	 Among new TB cases, the percentage of children is between 5-15% in low- and middle-income and <10% in high-income countries 	 Met Not met 	In 2016-17, 7.3% of all new patients were aged 0-14 years. There was however substantial variation at the provincial and district levels, with several districts in the west of Nepal recording 15-20% of all new notifications in children. The proportion of child patients should be monitored by NTC staff, and in districts where this proportion is lower than 5%, the accessibility of diagnostic and treatment services for children should be investigated. In districts where more than 15% of notifications come from children, this should also be investigated, the quality of TB diagnosis in children should be audited to assess possible over-diagnosis (for example, via inappropriate interpretation of symptoms through new contact tracing programs).	N/A

STANDARD	BENCHMARK(S)	RESULTS	RESULTS (DESCRIPTION) INCLUDING KEY ACTION(S) REQUIRED TO ADDRESS THE GAPS	ESTIMATED BUDGET REQUIREMENTS TO AD- DRESS KEY ACTION(S)
B1.7 Number of reported TB cases is internally consistent	If vital registration data are available, then the following benchmark should be satisfied for this standard to be met: 1. Year-to-year change in the national number of reported TB cases is consistent with year- to-year change in national TB mortality (HIV-negative, from national vital registration) i.e. trajectories with the same direction. If vital registration data are not available, then the following benchmarks should be satisfied for this standard to be met: 2. Ratio of notified pulmonary to extra-pulmonary TB cases 3. Ratio of male to female TB cases 4. Proportion of childhood TB out of all TB cases 5. Year-to-year change in the case notification rate for new smear-positive TB and if data are available, 7. Ratio of the number of people with presumptive TB to total notifications of TB cases	□ Met ■ Not met	At the national level, key indicators have been broadly consistent from 2012-13 to 2016-17, without dramatic changes from year to year. Most changes have been in the expected direction, for example, an increase in the proportion of notifications from children coinciding with the implementation of contact tracing. The exception to this is clinically diagnosed TB, which has declined an average of 15% per year since 2014-15, from ~8,500 notifications in 2014-15 to ~5,200 in 2016-17. This is thought to be due to the roll-out of Gene Xpert, with doctors misinterpreting a negative Xpert result to mean that the patient does not have TB. This has led to a -15% decline in the notification rate for all forms of TB in Nepal, from 134 cases per 100,000 population in 2012-13 to 114 cases per 100,000 in 2016-17, despite an expansion in contact tracing and other active case finding activities, a higher number of people investigated with smear microscopy, and the roll-out of Gene Xpert, which should all have acted to increase notifications. The NTC should investigate the reasons for the decline in CD-TB, particularly in districts which have reported substantial declines since 2014-15. Data on presumptive TB should be routinely recorded and reported.	MA
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STANDARD	BENCHMARK(S)	RESULTS	RESULTS (DESCRIPTION) INCLUDING KEY ACTION(S) REQUIRED TO ADDRESS THE GAPS	ESTIMATED BUDGET REQUIREMENTS TO AD- DRESS KEY ACTION(S)
B1.8 All diagnosed cases of TB are reported	 Both benchmarks should be satisfied to meet this standard: TB reporting is a legal requirement >90% of TB cases are reported to national health authorities, as determined by a national-level investigation (e.g. inventory study) conducted in last 10 years 	 Met Partially met Not met 	TB reporting is not a legal requirement. A Public Health Act was recently passed, however, TB was not included in the list of notifiable conditions. National staff are advocating for TB to be included on the list in an amendment to the Act. No inventory study has been conducted. An inventory study evaluating the number of patients diagnosed and treated in the private sector should be conducted, with a concurrent evaluation of the completeness of reporting for child TB.	Cost of an inventory study assessing both the private sector and childhood TB: USD\$300,000
B1.9 Population has good access to health care	 Both benchmarks should be satisfied to meet this standard: Under-5 mortality rate (probability of dying by age 5 per 1000 live births) is <10 <25% total health expenditure is out-of-pocket 	 Met Partially met Not met 	In 2015-16, the most recent year for which data are available, the child mortality rate in Nepal was 35 deaths per 1,000 live births. Over half of all health expenditure was out of pocket (55%). There is a need for further investments in improving the accessibility and affordability of healthcare in Nepal.	Beyond the scope of this review.
B1.10 Vital registration system has high national coverage and quality	 Both benchmarks should be satisfied to meet this standard: Cause of death documented in ≥90% of total deaths recorded in a) national vital registration system OR b) sample vital registration system <10% of deaths have ICD codes for ill-defined causes (defined as ICD-9 780-799 and ICD-10 R00-R99) 	 Met Partially met Not met 	Nepal does not have a functional vital registration system, despite efforts to establish such a system since the 1970s. Investments should be made to improve vital registration in Nepal, especially registration of both fact and cause of death.	Beyond the scope of this review.

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Indicate 'Met', 'Partially met', "Not met" or 'Not applicable' in the results column. Describe the key results and any action recommended to improve the For each standard, please assess whether the system is able to satisfy the associated benchmark(s), using the methods recommended in the user guide. quality of the system in the last two columns.

STANDARD	BENCHMARK(S)	RESULTS	RESULTS (DESCRIPTION) INCLUDING KEY ACTION(S) REQUIRED TO ADDRESS THE GAPS	ESTIMATED BUDGET REQUIREMENTS TO ADDRESS KEY ACTION(S)
SURVEILLANCE OF DRUG RESISTANT TB	JRUG RESISTANT TB			
B2.1 Surveillance data provide a direct measure of drug-resistant TB in new cases	One of the two benchmarks should be satisfied to meet this standard: • Rifampicin susceptibility status (positive/negative) documented for ≥75% of new pulmonary TB cases • Rifampicin susceptibility status (positive/negative) documented for a nationally representative drug resistance survey of new pulmonary TB cases	 Met Partially met Not met 	A Drug Resistance Survey was carried out in 2011-12, finding a prevalence of MDR of 2.2% among new cases and 15% among re-treatment cases. A repeat survey is planned for 2019-20. Gene Xpert has been introduced in Nepal and there were ~12,300 Gene Xpert tests reported in 2016-17. There were ~3,000 patients initiated on re-treatment regimens that year, however data collection practices do not allow an assessment of the proportion of retreatment patients who received a Gene Xpert test. The ETB system records Gene Xpert results but there is no option to generate reports regarding either testing or results. Gene Xpert reporting options should be added to the ETB Manager system's "statistics" tab. In the short term, Nepal should aim to provide Gene Xpert tests to all retreatment patients, and evaluate progress towards this target via the ETB system. In the long term, Nepal should aim to transition to using Gene Xpert as the first line test for all TB suspects.	Cost of cartridges to provide Gene Xpert for 75% of suspected pulmonary TB patients (who currently receive sputum smear microscopy): USD\$1.76 million
B2.2 Surveillance data provide a direct measure of the prevalence of HIV infection in TB cases	 One of the two benchmarks should be satisfied to meet this standard: HIV status (Positive/Negative) documented for ≥80% of all notified TB cases HIV status is available from a representative sample from all TB cases notified in settings with a low-level epidemic state⁸ where it is not feasible to implement routine surveillance. 	 Met Partially met Not met 	Nepal has substantially expanded the provision of HIV testing to TB patients, with the proportion of patients receiving a test increasing from 7% in 2014-15 to 54% in 2016-17. In 2016-17. 1.3% of those tested were found to be living with HIV. There was a sentinel survey of HIV prevalence in 2016, also finding a prevalence of 1.1%. Nepal has made excellent progress increasing the coverage of HIV testing for TB patients, and these efforts should be continued in order to reach the target of ≥80%.	N/A – HIV testing for TB patients is funded via HIV activities, not by the NTC.

STANDARD	BENCHMARK(S)	RESULTS	RESULTS (DESCRIPTION) INCLUDING KEY ACTION(S) REQUIRED TO ADDRESS THE GAPS	ESTIMATED BUDGET REQUIREMENTS TO ADDRESS KEY ACTION(S)
B2.3 Surveillance data for children reported with TB (defined as ages 0-14 years) are reliable and accurate AND all diagnosed childhood TB cases are reported	Both of the benchmarks should be satisfied to meet this standard: • Ratio of age groups 0-4 to 5-14 years is in the range 1.5-3.0 • ≥90% of childhood TB cases are reported to national health authorities, as determined by a national-level investigation (e.g. inventory study) conducted in last 10 years	□ Met □ Partially met ⊠ Not met	In 2016-17, the ratio of 0-4 year olds to 5-14 year olds among new TB patients was 0.5:1, suggesting under diagnosis of young children. Children are usually referred to hospital-based paediatric services for diagnosis, and then referred back to their local health facility for treatment. As contact tracing efforts are expanded, the NTC should regularly review child TB data to assess whether case detection among young children is increasing as expected. District staff should review the basis on which children are initiated on IPT vs. TB treatment, for example ensuring that all symptomatic children under 5 identified through contact tracing were treated for TB. No inventory study on childhood TB has been conducted. An inventory study should be conducted to ensure that all children diagnosed in specialist paediatric services are started on TB treatment and recorded appropriately in health facility treatment registers.	Cost of an inventory study assessing both the private sector and childhood TB: USD\$300,000

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- 2. Mr Ratna Bhattarai, Senior M&E Officer
- 3. Mr Gokul Mishra, Liverpool School of Tropical Medicine (LSTM)- TB IMPACT Project, Liaison Officer
- 4. Mr Badri Nath Gyawali
- 5. Nilaramba Adhikari
- 6. Dr. Suvesh Shrestha
- 7. Lok Raj Joshi, Data Management Coordinator
- 8. Ms Basundhara Sharma
- 9. Kathryn Snow
- 10. Arax Hovhannesyan

LIST OF PEOPLE MET

- 1. Dhan Kumari Rai, AHW/DOTS Focal Person, Saghurigadhi HP, Dhankuta
- 2. Chudamani Ghimire, AHW, Saghurigadhi HP, Dhankuta
- 3. Mina Magar, ANM, Saghurigadhi HP, Dhankuta
- 4. Krishna Bahadur Mijar, Sr. PHA, Health Office, Dhankuta
- 5. Pramod Dahal, TB focal person, Health Office, Dhankuta
- 6. Suja Amatya, Sr. AHW/CB-DOTS focal person, Health Office, Dhankuta
- 7. Satya Raj Shakya, Senior Auxiliary Health Worker, Lumbini Provincial Hospital
- 8. Maya Thepa, Nurse, Lumbini Provincial Hospital
- 9. Sanumayn Thapa, Office Assistant, Lumbini Provincial Hospital
- 10. Laboratory Officer, Lumbini Provinicial Hospital
- 11. Urmila Shahi, Health Assistant, Parroha Health Post
- 12. Bindu Wagle, Sr. ANM/DOTS provider, BPKIHS
- 13. Shalahudin Ansari, DOTS focal person, BPKIHS
- 14. Dr. Raj K. Rauniyar, Vice-Chancellor, BPKIHS
- 15. Dr. Khem Raj sharma, Assist. Professor, BPKIHS
- 16. Dr. Narayan Raj Bhattarai, Associate Professor, BPKIHS
- 17. Ram Naresh Thakur /DTLO-Morang
- 18. Muluk Chandra Rajbansi/DTLO-Morang
- 19. Gyanendra Shrestha, Program Manager/BNMT
- 20. Honey Gurung, Intern-BNMT
- 21. Alina, BNMT
- 22. Poonam Bista, Program Coordinator/BNMT
- 23. Dr. Gyanendra Karki, Chairman, Birat Medical College and Teaching Hospital
- 24. Dr. Sangit Shah, Hospital Director, Birat Medical College and Teaching Hospital
- 25. Dr. Danish Karki, Vice-Director, Birat Medical College and Teaching Hospital
- 26. Sudip Rathor, Hospital Administrator, Birat Medical College and Teaching Hospital
- 27. Dr Pushpa Raj Gyawali, Medical Superintendent, Palpa
- 28. Mr Bishwo Neupane, TB and Leprosy Officer, Palpa
- 29. Mr Chandra Tara Bashyal, Health Assistant, Palpa District Hospital
- 30. Ghanashyam Koirala, Programme Coordinator, NATA Morang

- 31. Lokendra Kumar Malla, Member, NATA Morang
- 32. Dr. Asmitananda Thakur, Consultant Physician/Pulmologist, NATA Morang
- 33. Bhim Thapa, NATA Morang
- 34. Sarita Bhattarai, Staff Nurse, NATA Morang
- 35. Sati Ram Biswas, Lab. Assistant, NATA Morang
- 36. Ashok Kumar Yadav, X-Ray Focal Person, NATA Morang
- 37. Dhurba Raj Thapa, X-Ray Focal Person, NATA Morang
- 38. Mr Netra Prasad Ghimire, Senior Assistant Health Worker, Madanpokhara Health Post
- 39. Ms Ganga Subedi, Community Health Volunteer, Madanpokhara Health Post
- 40. Mr Lok Raj Joshi, Data Management Co-ordinator: TB, Save the Children
- 41. Mr Diwas Achaya, Program Co-ordinator: TB, Save The Children
- 42. Ms Sanumayn Thapa, Office Assistant, Lumbini Provincial Hospital
- 43. Laboratory Officer, Lumbini Provinicial Hospital
- 44. Ms Urmila Shahi, Health Assistant, Parroha Health Post
- 45. Mr Chandra Tara Bashyal, Health Assistant, Palpa District Hospital
- 46. Mr Netra Prasad Ghimire, Senior Assistant Health Worker, Madanpokhara Health Post
- 47. Ms Ganga Subedi, Community Health Volunteer, Madanpokhara Health Post
- 48. Dr. Dirgha Singh Bam
- 49. Dr Ashish Shrestha, WHO Consultant, NTC
- 50. Dr Lungten Z. Wagchuk, Team Lead, Communicable Disease, World Health Organization
- 51. Dr Jos Vandelaer, Representative, World Health Organization
- i. i.e. by smear, culture or WHO-endorsed molecular test (e.g. Xpert MTB/RIF).
- ii Low-level epidemic state: HIV prevalence has not consistently exceeded 5% in any defined subpopulation.



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