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# Clinical and economic burden of drug-susceptible tuberculosis in Indonesia: national trends 2017–19

Deni Iskandar, Auliya A Suwantika, Ivan S Pradipta, Maarten J Postma, Job F M van Boven

## Summary

**Background** The global incidence of tuberculosis is decreasing, yet it remains high in Indonesia. The Indonesian National Tuberculosis Program facilitates mandatory notification, which enables early detection and treatment, minimises complications, prevents transmission, and decreases deaths. This study aimed to assess the characteristics, trends, and economic burden of notified drug-susceptible tuberculosis cases registered in this system from 2017 to 2019.

**Methods** We performed a multiyear cross-sectional study focusing on drug-susceptible tuberculosis notified cases, incidence, geographical tuberculosis case distribution, treatment outcomes, and costs in Indonesia using data from *Sistem Informasi Tuberkulosis* (2017–19). The settings were Indonesian health-care facilities that provide tuberculosis control programmes and services. Eligible patients were those who were diagnosed with drug-susceptible tuberculosis and notified to *Sistem Informasi Tuberkulosis*.

**Findings** Between 2017 and 2019, notified cases increased from 429 219 to 523 614 individuals, corresponding to an increase in incidence from 167 cases per 100 000 to 196 cases per 100 000. In 2019, more than 250 cases per 100 000 inhabitants were notified in Jakarta, North Sulawesi, Gorontalo, and Papua. Treatment success rate increased from 363 098 (84·60%) of 429 219 in 2017 to 452 966 (86·51%) of 523 614 in 2019, with a relatively stable mortality, changing from 3·15% to 3·05%. HIV status was increasingly confirmed, with unknown status decreasing from 66·21% to 43·68%. The costs of visits and monitoring and drug regimens were relatively stable, with total direct medical costs slightly increasing from US$39·40 to $40·40 per case.

**Interpretation** Progress was made on drug-susceptible tuberculosis management in Indonesia. However, further intensified efforts, including case-finding, optimising diagnosis, and cost-effective tuberculosis management are required if Indonesia is to achieve the 2025 WHO End Tuberculosis Strategy target incidence of fewer than 55 cases per 100 000 people. These data are an important starting point for understanding drug-susceptible tuberculosis dynamics in Indonesia and optimising its management.

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## Introduction

Tuberculosis, caused by *Mycobacterium tuberculosis*, is an infectious disease with a substantial global burden.[1] Worldwide, about 9·9 million people were infected by tuberculosis, and 1·3 million people died due to tuberculosis in 2020. WHO's End TB Strategy aims to achieve a 90% reduction in tuberculosis deaths by 2030, an 80% reduction in tuberculosis incidence by 2035, and zero catastrophic costs due to tuberculosis by the end of 2030.[2] Two-thirds of all tuberculosis cases are in eight high-burden countries, including Indonesia.[3] Globally, tuberculosis incidence is decreasing, yet it remains high in Indonesia, despite improved access to health services, funding, surveillance, diagnostics, situation analysis, and policy focus.[1,4]

Estimated tuberculosis incidence in Indonesia was 845 000 in 2020, with 357 199 notified new cases and 13 947 deaths.[3] Gaps in diagnosis and treatment persist: 28% of tuberculosis cases are not diagnosed, and only 34% are successfully treated.[5] In addition, high-quality tuberculosis treatment coverage is limited due to unintegrated referral programmes, inferior treatment regimens, undetected multidrug-resistant and rifampicin-resistant cases, inadequate provision of treatment for patients with both tuberculosis and HIV, and low uptake of preventive treatment.[6] A nationwide survey from 2013 estimated that 660 per 100 000 inhabitants had tuberculosis.[7] In 2016, an inventory study found that half of incident tuberculosis cases were detected and reported to the National Tuberculosis Program (NTP),[8] with incidence about 15% lower than the 2013 survey.[6] Of note, the NTP includes a mandatory notification system for tuberculosis surveillance, contact investigation, outbreak management, and infection control. To be effective, availability of accurate tuberculosis case data over time is essential.[9]

In addition, economic data on tuberculosis is important to inform policy. Previous studies provided cost information in selected populations.[10,11] Nonetheless, up-to-date, nationally representative data and trends in costs of diagnosis, medicines, and treatment based on

## Research in context

**Evidence before this study**

In 2013, a nationwide survey estimated the burden of tuberculosis in Indonesia. Subsequently, in 2016, a study using data from the Indonesian national tuberculosis surveillance systems—*Sistem Informasi Tuberkulosis Terpadu* and electronic Tuberculosis Manager—provided an updated tuberculosis burden estimate. Studies and estimates of the tuberculosis burden in Indonesia were mainly based on these two studies.

Prominent and a-priori known publications on tuberculosis burden are the WHO Global Tuberculosis Report and the Global Burden of Disease Study, containing extrapolated and modelled burden estimates for Indonesia at a national level without access to patient-level data. In addition, we searched PubMed for articles published in English on the issue, without publication year limitation and using a combination of the following terms: "tuberculosis" and "Indonesia", plus "disease notification", "mandatory reporting", "notification", "reporting", "detection", or "findings". Of the 235 studies identified, 11 were considered suitable and related to notified drug-susceptible tuberculosis. These studies analysed the burden of tuberculosis regionally, at the province, district, or city level, using primary or secondary data obtained through passive or active case findings, surveys, or operational or implementation research. Only one study estimated the burden nationally, based on the previously mentioned 2013 survey. Another city-level study described the incidence by geographical cluster. The remaining nine studies were province-level studies, mainly based on province-level tuberculosis register data from the National Tuberculosis Program. Thus, no published nationwide up-to-date data on the tuberculosis burden in Indonesia are available.

**Added value of this study**

To our knowledge, this is the first study that describes the status and trend of notified drug-susceptible tuberculosis cases in Indonesia at the national level based on the improved national tuberculosis information system, *Sistem Informasi Tuberkulosis*. A comprehensive trend overview and direct medical cost estimate could be made using detailed unselected patient-level notification data and geographical information. Next to the advantage of being comparable across regions, the data source is of good quality and validity; it can provide detailed identification of key aspects for prioritisation and further research to understand the dynamics of drug-susceptible tuberculosis cases. The data can also be used to establish better estimates and modelling of tuberculosis spread and the effects of interventions. This study showed an increasing trend in new cases over the years, with quarterly variability; potentially related to the operational performance of tuberculosis case management. The distribution of cases highlights the disparities in regional burden. Furthermore, tuberculosis status, resource use, and costs related to treatment could be identified, along with its treatment outcomes.

**Implications of all the available evidence**

With the incidence of tuberculosis steadily increasing in Indonesia, regional burden disparities remain substantial, with specifically high burdens in Jakarta and the eastern part of Indonesia. The increasing number of cases in children indicates a need for further improving case finding among children. The high rate of use of rapid molecular tests for diagnosis supports case findings, although it increases the cost of diagnosis. Furthermore, increased use of microbiological tests is needed for monitoring treatment outcomes. The treatment success rate is increasing, with relatively stable mortality. However, the HIV burden potentially compromises treatment outcomes, requiring better-integrated tuberculosis and HIV services. A relatively high frequency of retreatment indicates problems in drug-susceptible tuberculosis initial treatment; hence, further assessment is needed of the role of patients' status, condition, history, drug regimen, and treatment duration to improve treatment outcomes through optimising interventions and policies. In general, this study emphasises the importance of improving tuberculosis case management through enhanced guidelines and recommendations implementation by public and private health-care facilities, followed by innovative interventions and policies that support treatment monitoring, therapeutic drug monitoring, evaluation, and adherence.

real-world data remain essential, especially in the context of increasing numbers of cases.[12]

The Indonesia national tuberculosis information system, *Sistem Informasi Tuberkulosis* (SITB) captures patient-level data, providing real-world data that can benefit Indonesia's evaluation and policy making process. Compared with previous studies,[7,8] which mainly relied on surveys, models, or trend estimates, these data provide a nationwide and unselected overview of Indonesia's confirmed notified drug-susceptible tuberculosis cases. Notably, real-world patient-level data provides detailed trends in actual cases and care and allows assessment of possible efficacy–effectiveness gaps.[13] This study aimed to assess the characteristics, trends, and economic burden of notified drug-susceptible tuberculosis cases in Indonesia from 2017 to 2019.

## Methods

### Study design and setting

We performed a multi-year cross-sectional study on patient-level national data of notified drug-susceptible tuberculosis cases registered in SITB between Jan 1, 2017 and Dec 31, 2019. Of note, at the time of analysis, the 2017–19 data were the most recent data available within the improved SITB infrastructure. The settings were Indonesian health-care facilities that provide tuberculosis control programmes and services, including community health centres, hospitals, community health centres

specialising in lung health care, and other health-care facilities spread over 34 provinces (appendix p 6). Eligible patients were those who were diagnosed with drug-susceptible tuberculosis and notified to SITB. Ethical clearance was not required since no personal identification information was used.

### Data sources

Unique patient-level drug-susceptible tuberculosis data were extracted from SITB. Tuberculosis case management was based on current guidelines and recorded in specific forms developed by the NTP and notified to SITB. The Directly Observed Treatment, Short-course (DOTS) programme or medical record officer was responsible for the validity of notified data. Indonesian population data were extracted from the National Bureau of Statistics and administrative boundaries data from the Humanitarian Data Exchange (appendix pp 6–7).

### Variables

We selected available variables in SITB for a 3-year period (2017–19) and retrieved case distribution information (year, quarter, province, and district), patient characteristics (gender and age), clinical characteristics (anatomical site of tuberculosis, type of tuberculosis diagnosis, and HIV status), treatment (microbiological tests, treatment history, drug source, drug regimens, and start–end dates of treatment), and outcomes (appendix pp 12–14).

### Outcomes

Notified cases refers to the absolute number of drug-susceptible tuberculosis cases reported in SITB per given period (eg, quarter or year), nationally and regionally. Incidence is the number of new and relapse cases in a given period (eg, quarterly) and was calculated as the number of incident cases for a given population unit (per 100 000 inhabitants).[14] Prevalence is the number of cases in each quarter and was calculated as the total number of prevalent cases for a given population unit (per 100 000 inhabitants).[14] Mortality is the number of deaths that occurred per quarter and was calculated as the total number of deaths for a given population.[14] Mortality is presented overall and for HIV-negative cases, following the International Classification of Diseases (ICD-10) revision definition.

Pre-treatment statuses were classified as new cases, retreatment cases (if relapse, failure, or default), transfers-in, or other. Patient pre-treatment status was derived from the treatment history, and is reported as total number and percentage. Patient post-treatment status is the number of patients at the end of treatment with a successful or unsuccessful outcome as derived from the treatment result. Patient post-treatment status is reported as the total number, percentage, and rate.

Treatment success is the proportion of patients with successful outcomes against the total patients with successful and unsuccessful treatment outcomes.

Treatment duration is the interval between the initial treatment date and end date, in months. Patient mortality status is the number of deceased or alive patients identified at the end of treatment, derived from the treatment results. Death, reported as total number and percentage, could be caused by any reason. See the appendix (p 14) for further details.

Patient-level health-care resource use was linked to costs. Costs were assessed from the health-care perspective, involving direct medical costs only. Visit and monitoring costs were calculated by multiplying the visit frequency and capitation fee per visit (appendix p 7). Drug costs were based on the specific tuberculosis drug category used, with unit costs taken from the online national procurement system that provides the drugs for the NTP (appendix p 7). Total costs were estimated by multiplying the drugs required for one course of therapy by the unit cost. Microbiological test costs were estimated by multiplying the microbiological test frequency and the

See **Online** for appendix

For more on the **SITB** see http://sitb.id/sitb/app

| | 2017 | 2018 | 2019 |
|---|---|---|---|
| **Quarter (N=1 426 548)** | | | |
| 1st | 109 205 (25·44%) | 122 156 (25·79%) | 137 245 (26·21%) |
| 2nd | 97 588 (22·74%) | 110 793 (23·39%) | 122 980 (23·49%) |
| 3rd | 114 606 (26·70%) | 123 444 (26·06%) | 135 498 (25·88%) |
| 4th | 107 820 (25·12%) | 117 322 (24·77%) | 127 891 (24·42%) |
| n | 429 219 | 473 715 | 523 614 |
| **Patient characteristics (N=1 424 271)** | | | |
| Age, years | | | |
| Mean (SD) | 39·4 (19·1) | 39·0 (19·3) | 38·6 (19·8) |
| Median (min–max) | 39·0 (1·0–100·0) | 39·0 (1·0–100·0) | 39·0 (1·0–100·0) |
| Age group | | | |
| <15 years | 42 081 (9·82%) | 47 517 (10·05%) | 60 070 (11·50%) |
| ≥15 years | 386 634 (90·18%) | 425 480 (89·95%) | 462 489 (88·50%) |
| Sex | | | |
| Female | 178 707 (41·68%) | 199 219 (42·12%) | 220 615 (42·22%) |
| Male | 250 008 (58·32%) | 273 778 (57·88%) | 301 944 (57·78%) |
| n | 428 715 | 472 997 | 522 559 |
| **Clinical characteristics (N=1 426 548)** | | | |
| Type of tuberculosis | | | |
| Extrapulmonary | 38 530 (8·98%) | 45 735 (9·65%) | 51 682 (9·87%) |
| Pulmonary | 390 689 (91·02%) | 427 980 (90·35%) | 471 932 (90·13%) |
| Diagnosis type | | | |
| Bacteriologically confirmed | 216 075 (50·34%) | 233 550 (49·30%) | 263 037 (50·23%) |
| Clinically diagnosed | 213 143 (49·66%) | 240 165 (50·70%) | 260 577 (49·77%) |
| Missing | 1 (0·00%) | 0 | 0 |
| HIV status | | | |
| Indeterminate | 276 (0·06%) | 69 (0·01%) | 72 (0·01%) |
| Negative | 136 678 (31·84%) | 214 773 (45·34%) | 283 103 (54·08%) |
| Positive | 8098 (1·89%) | 10 553 (2·23%) | 11 691 (2·23%) |
| Unknown | 284 167 (66·21%) | 248 320 (52·42%) | 228 705 (43·68%) |
| Missing | 0 | 0 | 15 (0%) |
| n | 429 219 | 473 715 | 523 614 |

*Table 1:* Notified drug-susceptible tuberculosis population characteristics in Indonesia 2017–19
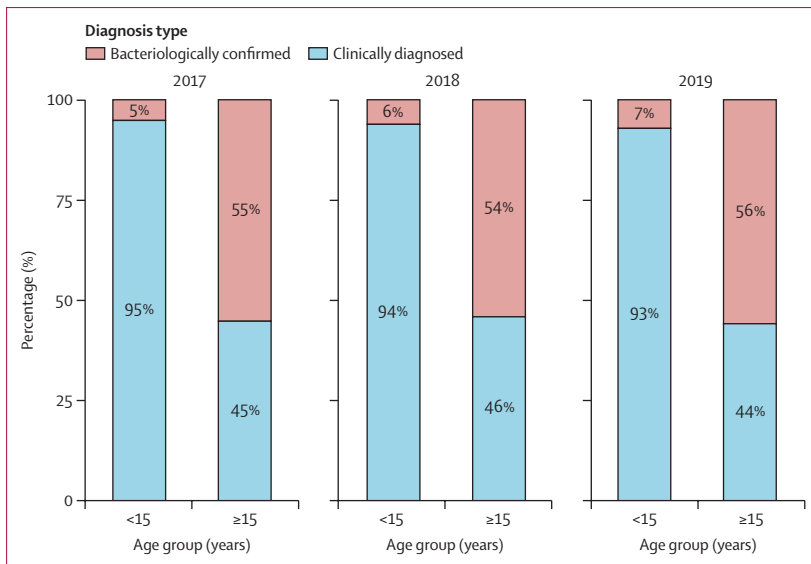
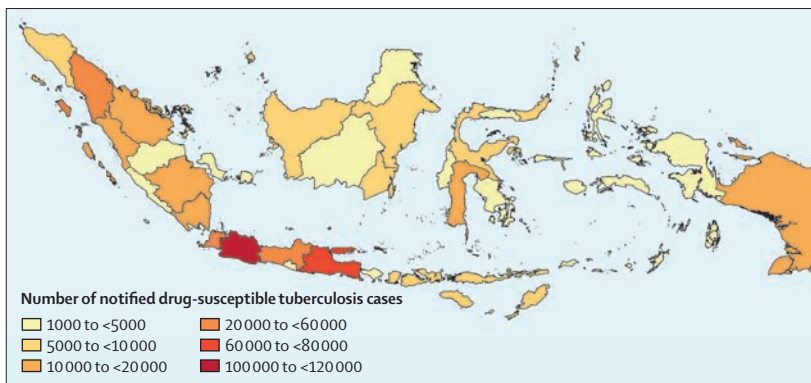Figure 1: Tuberculosis diagnosis type by age group in Indonesia



Figure 2: Distribution of notified drug-susceptible tuberculosis cases in Indonesia (2019)

cost of the test, including pre-treatment and monitoring (in-treatment, post-treatment) tests. Costs were based on figures from a government-owned laboratory in Jakarta (appendix p 7). Costs of visits and monitoring, drugs, and microbiological tests were used to estimate the direct medical costs covered by NTP. Costs were converted into US$ based on average median exchange rates at Bank Indonesia for 2017–19 (appendix p 7). Total costs were sums of visits and monitoring, drugs, and microbiological test costs—ie, costs were calculated from the health-care perspective. Per quarter, total costs were compared with treatment success and mortality rates.

### Statistical analysis

The open-source R statistical software version 4.1.3 was used for descriptive data analysis. Numerical data were presented as means and SDs, and categorical data as numbers and percentages. Analysis was performed using naive analysis with all available data (except for patient

characteristics analysis, which applied a maximum age of 100 years), then for clinical and cost outcomes requiring definite treatment start date and end date, when start date was not later than end date.

The main analysis of the epidemiological outcomes was based on quarterly analysis. For some records, the respective year reflected missing data. In those cases, the year was imputed using other variables in the dataset.

Graphical presentation of incidence, prevalence, mortality, and treatment success was produced using the Locally Estimated Scatterplot Smoothing (LOESS) procedure from the ggplot2 package and based on local polynomial regression. LOESS estimated values around groups of independent variables to fit, predicted nonlinear data, and used a bandwidth based on nearest neighbours of values to visualise uncertainty intervals.[15]

Analyses were performed using the complete dataset or a subset with complete cases. A sensitivity analysis was performed to check the effect of missing data. Differences of more than 5% were considered notable. As the capitation system (including only patient costs) might underestimate actual total costs, a cost estimation using visit costs related to actual administration costs in a community health centre was also performed, using pre-diagnostic visit costs of $4·87 and post-diagnostic visit costs of $2·62.[16]

### Role of the funding source

The funders had no role in the design, analysis, write-up, or decision to submit for publication.

### Results

Of the total cases (1426548) retrieved from SITB, 1·12–1·43 million cases were selected depending on the subset and variable being analysed. After missing value deletion, 1227611 cases remained, representing a 14% reduction from the initial data (appendix p 8). Table 1 shows the population characteristics of drug-susceptible tuberculosis cases notified to SITB between 2017 and 2019.

In this predominantly male population with a mean age of 39 years, pulmonary tuberculosis was the dominant form of drug-susceptible tuberculosis (>90% of cases; table 1). The proportion of bacteriologically confirmed and clinically diagnosed cases was similar.

Although direct smear microscopy as a single test was used as a primary diagnostic (appendix p 33), its use decreased from 352735 (82·18%) of 429219 cases in 2017 to 272146 (51·97%) of 523614 cases in 2019. Conversely, the use of rapid molecular test increased from 4636 (1·08%) of 429219 to 113692 (21·71%) of 523614. However, cases without any test also moderately increased, from 59360 (13·83%) of 429219 to 86087 (16·44%) of 523614. Out of the four nationally recommended microbiological tests for treatment monitoring,[6,17] only one to two follow-up tests were usually performed.

The absolute number of HIV-positive cases increased from 8098 (1·89%) of 429219 in 2017 to 11691 (2·23%)

of 523614 in 2019. However, HIV status (positive or negative) was increasingly confirmed with a decrease in unknown status over time (from 66·21% to 43·68%).

Diagnosis type by age group (figure 1) showed that bacteriologically confirmed cases increased slightly from 2017 to 2019 in individuals aged 15 years or older, whereas clinically diagnosed cases decreased. For patients younger than 15 years, more than 90% were clinically diagnosed, compared with less than 50% for patients aged 15 years or older. Age group classification aligned with the WHO Global TB Report 2012.[18]

Notified drug-susceptible tuberculosis cases increased from 429219 to 523614 between 2017 and 2019. In 2019, our most recent year of data, notified cases were heavily concentrated in Java and Sumatra (figure 2). West Java province had the highest number (110473 cases), followed by East Java (64125 cases). North Sumatra had the highest number of cases of the provinces outside Java. As a proportion of the population, the burden was highest in Jakarta, North Sulawesi, Gorontalo, and Papua, with more than 250 cases per 100000 inhabitants (appendix pp 17–19). Bali had the lowest burden, with 50–100 cases per 100000 inhabitants in 2017–19.

Quarterly incidence increased from 43 (SD 16) per 100000 inhabitants in the first quarter of 2017 to 46 (15) per 100000 inhabitants in the fourth quarter of 2019 (appendix p 23). Annually, incidence increased from 167 cases per 100000 inhabitants in 2017 to 196 cases per 100000 inhabitants in 2019, with an approximately 10% annual increase in total incidence (2017–18: 44487 [10·50%] of 423609 and 2018–19: 49458 [9·56%] of 517556).

From early 2017 to 2018, prevalence increased considerably—partly reflecting SITB database filling—from 38 cases per 100000 in the first quarter of 2017 to 116 per 100000 in the first quarter of 2018. From 2018 to the end of 2019, prevalence increased slowly from 123 per 100000 in the second quarter of 2018 to 135 per 100000 in the fourth quarter of 2019 (appendix p 26). From 2017 to 2019, annual prevalence increased from 313 per 100000 to 544 per 100000.

Between 2017 and 2019, the absolute number of deaths increased (appendix p 28), yet corresponded with a relatively stable mortality rate of 3·15% (SD 1·41) in the first quarter of 2017 to 3·05% (SD 1·61) in the fourth quarter of 2019 (figure 3). In HIV-negative cases, the absolute number of deaths increased considerably (appendix p 28), whereas mortality was relatively stable (2·35% [SD 1·58] to 2·60% [SD 1·47]; figure 3).

The quarterly proportion of successfully treated cases increased over time, from 84·21% in the first quarter of 2017 to 90·52% in the fourth quarter of 2019 (figure 4). Overall annual increase of successfully treated cases went from 363098 (84·60%) of 429219 in 2017 to 452966 (86·51%) of 523614 in 2019 (appendix p 34). On average, treatment duration was 5·46–5·66 months (appendix p 33).
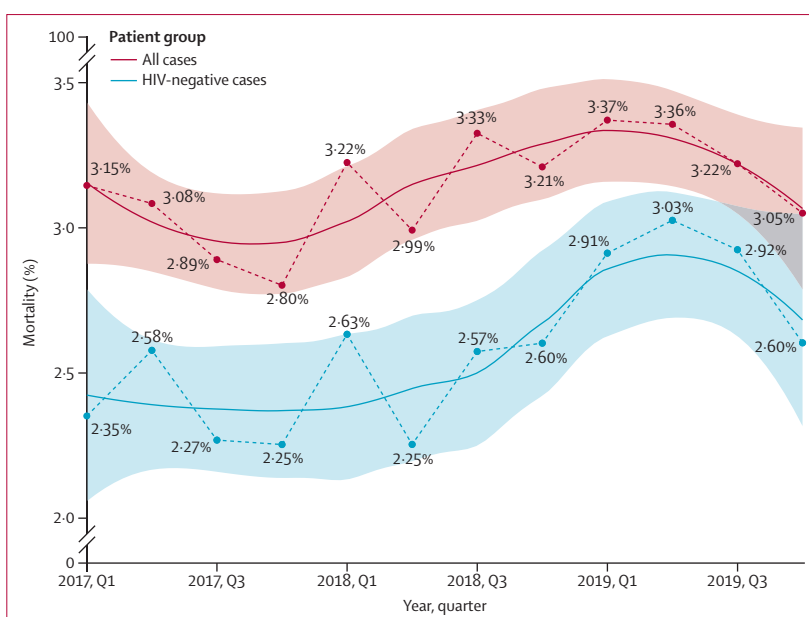


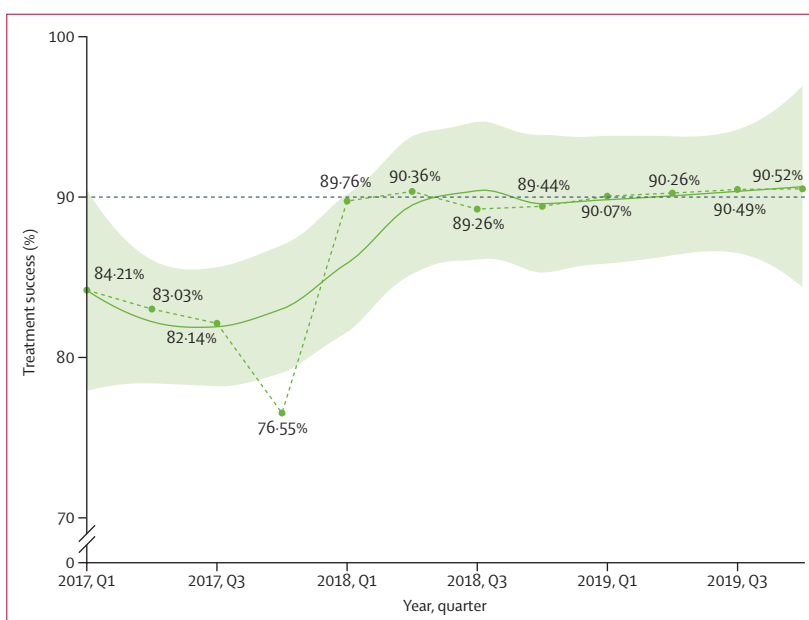*Figure 3:* Mortality of notified drug-susceptible tuberculosis cases in Indonesia from 2017 to 2019



*Figure 4:* Treatment success of notified drug-susceptible tuberculosis cases in Indonesia from 2017 to 2019

Table 2 provides an overview of drug-susceptible tuberculosis related per-patient costs, with total costs provided in the appendix (pp 43–45). Mean total direct medical per patient cost consisting of visits and monitoring, drug regimens, and microbiological tests showed an increasing trend, although within a relatively small margin: $39·40 (SD 9·26) in 2017 to $40·40 (12·2) in 2019—totalling $18734099 annually (appendix pp 43–45). This increased cost was parallel to increasing incidence and prevalence (appendix p 36). The increased cost also tends to be associated with increasing treatment

| | 2017 | 2018 | 2019 |
|---|---|---|---|
| **Visit and monitoring cost** | | | |
| Mean (SD) | 0·56 (0·48) | 0·57 (2·25) | 0·58 (4·91) |
| Median (min–max) | 0·54 (0·08–161·00) | 0·51 (0·10–1090·00) | 1·51 (0·10–2460·00) |
| **Drug regimen cost** | | | |
| Mean (SD) | 34·94 (7·36) | 33·02 (7·11) | 33·05 (7·35) |
| Median (min–max) | 35·06 (20·86–65·63) | 32·94 (19·59–61·66) | 33·13 (19·71–62·02) |
| Missing | 2428·00 (0·64%) | 1102·00 (0·46%) | 3933·00 (0·79%) |
| **Microbiological test cost** | | | |
| Mean (SD) | 4·14 (3·26) | 4·86 (4·71) | 7·04 (5·95) |
| Median (min–max) | 4·48 (0·00–29·90) | 4·21 (0·00–29·50) | 5·65 (0·00–29·70) |
| **Total cost** | | | |
| Mean (SD) | 39·42 (9·26) | 38·30 (10·03) | 40·41 (12·19) |
| Median (min–max) | 40·08 (0·11–196·00) | 37·66 (0·10–1140·00) | 39·28 (0·10–2520·00) |
| n | 380 299·00 | 238 457·00 | 497 190·00 |

*Table 2*: Per patient costs (US$) of drug-susceptible tuberculosis treatment in Indonesia (N=1 115 946)

success rates (appendix p 47). Details regarding visits and monitoring, drugs, and test costs are provided in the appendix (pp 43–48).

In sensitivity analyses, no notable differences were identified in mortality, treatment success rate, and costs. Other outcomes were unchanged or slightly improved, although there was a decrease in total cost (appendix pp 48–53). Using the alternative visit cost estimation, total direct medical per patient cost increased approximately 1·5 times, from $39·37 to $58·33 (appendix pp 43–45, 55–56).

## Discussion

Between 2017 and 2019, the annual number of notified cases of drug-susceptible tuberculosis in Indonesia gradually increased. Java province had the highest absolute number of notified cases, yet Jakarta, Papua, and North Sulawesi had the highest incidence per 100 000 inhabitants. Treatment success rates improved; however, there was little effect on overall mortality owing to population growth. Rapid molecular test uptake for diagnosis increased considerably, but less than half of the recommended number of microbiological tests for treatment monitoring were performed. Documented HIV status improved, and the costs of drug-susceptible tuberculosis treatment remained stable.

Drug-susceptible tuberculosis incidence in this study was based on notification data from NTP, a good proxy for estimating (confirmed) incidence.[19] The geographical distribution of cases showed no significant difference with previous studies, surveys, or reports in terms of trend and proportion;[6–8] the difference was in the number of cases, which increased over time. As the population of Indonesia is heavily concentrated in the Java islands, the absolute number of tuberculosis cases has always been higher there than in other areas.[20] However, underserved smaller districts located in remote areas, such as Papua and West Papua, are not

fully covered by the national DOTS program.[21] As a result, the relative tuberculosis burden in these less densely populated and remote eastern parts of Indonesia is high, and treatment coverage is low. Geographical factors affect the availability and distribution of health-care services, resulting in utilisation disparity across provinces and districts. With Jakarta having a better health-care infrastructure, its tuberculosis burden by population is high, probably related to its densely populated setting.

Incidence estimates for Indonesia were also made in the WHO Global Tuberculosis Report[3] and the Global Burden of Disease (GBD) Study.[22] In 2020, the WHO Global Tuberculosis Report estimated the incidence of all types of tuberculosis at 301 cases per 100 000 inhabitants.[3] Our analysis found a lower incidence (196 per 100 000) because it only accounted for notified drug-susceptible tuberculosis cases. This difference highlights the potential missing tuberculosis cases that need further case-finding. Still, both figures are above the 2025 End Tuberculosis Target for the Indonesian drug-susceptible tuberculosis notification rate, which is 55 cases per 100 000 inhabitants.[2] The GBD estimated mortality at 4%[22] was similar to the calculated mortality in our study of 3–4%, but for HIV-negative people our study found a lower rate (2–3%). Differences were expected because WHO and GBD estimates were based on aggregated country-level data[19] or modelling,[1] whereas we used patient-level data of actually registered cases. A study in Indonesia estimated that the incidence of tuberculosis was 201–2485 per 100 000 per year,[23] which is still higher than our result and not comparable because we only included drug-susceptible tuberculosis cases.

The HIV status of tuberculosis patients is crucial for patient management and treatment.[24] This study found a notable improvement in HIV status information in 2019 (56%) compared with 2017 (34%).[6] In Indonesia, several activities have been done to improve this—for example, increasing diagnostic capacity, training tuberculosis programme officers to conduct HIV tests, providing integrated tuberculosis and HIV services, and providing information, counselling, or education on tuberculosis and HIV to patients, based on the National Strategy of Tuberculosis Control and current guidelines on tuberculosis management.[17] However, it will be challenging to reach the national target of 90% HIV status availability by 2024.[25] The increasing number of HIV-positive people in this study reflects previous global trends,[4] which might contribute to higher risk of drug resistance,[26] compromising treatment outcomes. A higher male-to-female tuberculosis patient ratio is an early indicator of a higher HIV burden in men. However, this ratio should be interpreted cautiously because it could obscure the prioritisation of providing care to female and male patients with tuberculosis and HIV, since more deaths and incident cases occurred among women than among men in people who are HIV-positive.

With high unknown HIV status, the mortality disaggregated by HIV status still needs to be better understood.

To confirm the tuberculosis diagnosis, we identified an increased use of rapid molecular tests. Rapid molecular tests are superior to smear microscopy and comparable with culture tests, although they have a shorter turnaround time.[27] Rapid molecular tests are also recommended by WHO. The introduction of rapid molecular tests in Cape Town, South Africa, caused an increase in the number of bacteriologically confirmed tuberculosis cases and a decrease in the total notification rate,[28] although this is yet to be seen in Indonesia. Due to the high number of underdiagnosed cases,[5,29] the total notification rate is still increasing[30] and has not yet reached the point where there is a marginal decline in new notified cases, which should happen when most new cases can be identified, diagnosed, and notified.[12]

The treatment success rate slightly increased over 2017–19 and even surpassed the global trend;[3] however, mortality was relatively stable. As we identified several retreatment cases in this study, retreatment cases might be one of the causes.[31] Retreatment cases and patients who do not show a sputum conversion in the second month should receive extra attention because these are associated with poor treatment outcomes.[32]

Outpatient direct medical costs totalled $40 for one course of therapy over 6 months and were comparable with a previous estimate of $48,[5] and another study that divided costs into pre-treatment costs ($33) and post-diagnosis costs ($12),[16] with an average total of $44. However, this cost is somewhat lower than another study that reported tuberculosis costs of approximately $129, focusing on multiple low-income countries, not Indonesia specifically.[33] However, estimating costs using a fraction of the capitation fee for visits might underestimate its actual cost, especially in private facilities, and indeed our sensitivity analysis using a broader costing perspective resulted in higher costs. Our direct medical cost estimations are relevant for governmental budget planning to support the national strategy of tuberculosis care and prevention[34] and can also be used as an input to modelling and cost-effectiveness analyses.

To reduce the tuberculosis burden across different regions in Indonesia, the government is advised to expand the availability and coverage of health-care services (including advanced testing facilities) by strengthening the primary public sector, accompanied by conditional financial incentives (eg, financial reward for every suspected tuberculosis finding by the primary care facilities), and establishing better public–private partnerships. Expanding collaboration with the potential private sector in tuberculosis case detection is essential to reduce the number of missing cases in Indonesia.[35] In addition, further analysis of the relationship of patients, treatment, and clinical characteristics with treatment outcomes should be explored. First, HIV could complicate treatment outcomes, and with around half of the patients' HIV status still being unknown, its burden is yet to be fully understood, and increased efforts to detect HIV status are needed. Second, investment in more rapid case-finding and preventive treatment initiation,[36] easier patient pathways,[37] treatment monitoring (eg, by therapeutic drug monitoring),[38] and (digital) adherence support[39] is recommended to achieve better treatment outcomes and lower mortality. Of note, at the time of the COVID-19 pandemic in 2020, there were changes in government funding; quality of care and treatment; case detection and rapid diagnostic services; and activities in monitoring, evaluation, and surveillance of tuberculosis.[40] However, to what degree these changes affected drug-susceptible tuberculosis is yet to be elaborated. Further study based on SITB data from 2020 onwards is necessary to compensate for possible decreased progress in tuberculosis care.

One of the key strengths of this study is the use of comprehensive national tuberculosis data, providing a result that is generalisable to the national level. In addition, our direct medical cost estimation, which is based on actual notified cases, could serve as an input parameter to update any cost modelling or estimation. Yet, with the high number of under-reported cases in Indonesia, generalising to all tuberculosis cases should be carefully done, as this study was limited to drug-susceptible tuberculosis cases only. A further limitation is that we could not confirm whether tuberculosis was the cause of death, as per ICD-code, and the cost analysis was limited to direct medical costs only. On the clinical outcomes, we described successful and unsuccessful clinical outcomes as a general overview of treatment performance, not yet describing a complete and detailed analysis based on the WHO outcomes classification. Missing data were still notable, but no significant trends were observed in a sensitivity analysis. Finally, data were from before the COVID-19 pandemic; hence, we did not consider the effect of COVID-19 on tuberculosis.

Progress was made on drug-susceptible tuberculosis management in Indonesia between 2017 and 2019. However, further intensified efforts in case-finding, diagnostics, and tuberculosis treatment optimisation are required if Indonesia is to achieve the 2025 WHO End Tuberculosis Strategy target incidence of fewer than 55 cases per 100 000 people. Current national tuberculosis data are an important starting point to understand drug-susceptible tuberculosis dynamics in Indonesia and optimising its management. However, this approach is also relevant to any other countries or health systems, as having a well structured database of tuberculosis cases will facilitate better case management.

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