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Estimation of subnational tuberculosis burden: generation and application of a new tool in Indonesia

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SUMMARY

SETTING: In many high tuberculosis (TB) burden countries, there is substantial geographical heterogeneity in TB burden. In addition, decisions on TB funding and policy are highly decentralised. Subnational estimates of burden, however, are usually unavailable for planning and target setting.

OBJECTIVE AND DESIGN: We developed a statistical model termed SUBsET to estimate the distribution of the national TB incidence through a weighted score using selected variables, and applied the model to the 514 districts in Indonesia, which have substantial policy and budgetary autonomy in TB. Estimated incidence was compared to reported facility and domicile-based notifications to estimate the case detection rate (CDR). Local stakeholders led model development and dissemination.

RESULTS: The final SUBsET model included district population size, level of urbanisation, socio-economic indicators (living floor space and high school completion), human immunodeficiency virus prevalence and air pollution. We estimated district-level TB incidence to be between 201 and 2,485/100 000/year. The facility-based CDR varied between 0 and 190%, with high variation between neighbouring districts, suggesting strong cross-district health utilisation, which was confirmed by domicile-based CDR estimation. SUBsET results informed district-level TB action plans across Indonesia.

CONCLUSION: The SUBsET model could be used to estimate the subnational burden in high-burden countries and inform TB policymaking at the relevant decentralised administrative level.

KEY WORDS: Target setting; model; decision-making; district-level; incidence

Although tuberculosis (TB) remains the leading cause of death from a single infectious agent, funding to fight the disease remains limited.[1] The burden of TB is widely assumed to be heterogeneously distributed within countries,[2] and policy decision-making, including setting TB care and prevention planning and budgeting, often takes place at the subnational level. To inform decision making at this level, and to tailor TB care and prevention efforts to local epidemiology, subnational estimates of TB burden are key.

While many high TB burden countries have conducted national TB prevalence surveys to obtain a better estimate of their TB burden,[1] these surveys do not provide estimates on relevant subnational administrative levels. Various studies have reported subnational estimations of disease burden,[3–10] though few in TB, but these have often used complex methods that cannot be easily understood by local policy makers.[11–16] Subnational policy makers are thus usually left without estimates to inform their planning. Data on TB notifications are usually available at the subnational level, but provide a poor reflection of disease burden.[2]

Indonesia (2017 population, approximately 260 million people) consists of 34 provinces and 514 districts.[17,18] Since 1999, local (i.e., provincial and district) governments have full autonomy to manage health financing, planning and budgeting.[19] Health care is provided by the public and a large private sector.[20] Although TB notification is mandatory, only 53% of all estimated incident cases were notified to the National TB Programme (NTP) in 2017.[1]

Following a recent inventory study, Indonesia was estimated to have approximately 842 000 incident TB cases a year in 2017.[1] To achieve ambitious targets for ending the TB epidemic by 2030, the Indonesia NTP has encouraged local governments to develop a district action plan (including estimated local burden and health system utilisation) that is linked to the

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Table 1 Variable sources and definitions

Variable	Definition	Range	Data source
Population size	Number of individuals per district	13 763–5 682 911	Projected population of Regency/City 2010–2020, Statistics Indonesia
Level of urbanisation	Proportion of population that lives in urban area	0–100%	National Socio-Economic Survey 2017
Living floor space	Proportion of individuals who live in a house with less than $8m^2$/person	0–92%	National Socio-Economic Survey 2017
Junior high school completion	Proportion of individuals who did not complete junior high school or less	29–76%	National Socio-Economic Survey 2017
HIV	Proportion of individuals with HIV infection	0–23%	National AIDS Programme, 2012
Air pollution	Proportion of individuals with air pollution exposure	5–100%	Meteorological, Climatological, and Geophysical Agency, 2017

HIV = human immunodeficiency virus.

National Strategic Plan but tailored to the local challenges.[21]

Our aim was to develop a tool to estimate district-level incidence and health system use, balancing detail and granularity with simplicity, so both method and result could be effectively disseminated among local government authorities, and adapted by other high-burden countries for use. We describe the development, findings and dissemination of the SUBsET (SUBnational Burden Estimation for TB) tool.

METHODS

Principle of method

To promote acceptability and application of the results by policy makers, we worked from the principle that the model should be as simple as possible, make use of widely available software and involve a limited number of calculation steps while still using available data in an efficient way. TB burden-related data to inform the model were required to be available in 95% of districts.

No separate ethics approval was obtained as all data were publicly available or anonymised at the time of analysis. Model development, including the selection of variables, was inclusive, with direct input from the NTP, relevant partners and representatives from local academia. Given that programme indicators and milestones for the End TB Strategy were set on incidence rather than prevalence, we chose TB incidence as our outcome.[22]

DATA

Burden estimates

The national level incidence estimate from the 2018 World Health Organization Global TB report was used as the starting point.[1] In 2014, an Indonesian TB prevalence survey found substantial differences in burden between three regions (Sumatera, Java-Bali and Others, i.e., regions other than Sumatera and Java-Bali).[23] We applied the same distribution to the national incidence estimate.

Model variables

Population size for each district was based on estimates from the Central Statistics Agency (Biro Pusat Statistik, Jakarta, Indonesia) that released a 2010–2020 district population projection for each province based on the 2010 National Population Survey.[24]

Additional variables were extracted from the National Socio-Economic Survey, an annual socio-demographic survey which covers the whole nation and is powered for district-level estimates.[25] We identified urbanisation, floor space and education level (see Table 1 for definitions), which were also measured in the prevalence survey. We also included human immunodeficiency virus (HIV) burden,[26,27] and air pollution levels.[28–30]

To inform current health system performance or utilisation, and to check estimated values of the TB burden, the NTP provided both domicile-based (according to patient's address) and health facility-based (according to facility address) notification data for each district.[31]

MODEL

The SUBsET tool combined all available data on the distribution of the national TB burden through a weighted score for each of the 514 districts using the steps outlined below.

Step 1: Regional incidence

Incidence estimate of the abovementioned three regions was calculated by applying the distribution of absolute TB prevalence in the regions among 2017 Indonesia population in the respective regions:

$$I_r^{(case)} = \frac{P_r^{(case)}}{P^{(case)}} \times I^{(case)}$$

Where,
$I_r^{(case)}$ = estimated TB incident cases in region r, $P_r^{(case)}$ = TB prevalent cases (absolute value) in region r, $I^{(case)}$ = national TB incident cases (absolute value), and $P^{(case)}$ = national TB prevalent cases (absolute value).

Step 2: Variable weight

Using multivariable logistic regression, we were able to directly estimate the relative risk (RR) of socio-economic variables by region from the 2014 prevalence survey.[23] Values from the literature were used for HIV prevalence and air pollution.[27–30]

We then calculated a weight for each variable by multiplying the regional RR with the proportion in that district (e.g., proportion living in an urban area):

$$S_d^{(v)} = \left(Pr(v_d) \times RR_r^{(v)}\right) + (1 - Pr(v_d))$$

where,
$S_d^{(v)}$= weight for variable (v) in district d, $Pr(v_d)$ = proportion variable (v) among population in district d, $RR_r^{(v)}$ = TB RR ratio for variable (v) in region r, and $1 - Pr(v_d)$ = 1 – proportion of variable (v) in district d.

Step 3: Calculation of weight score per district

A weight for each district was calculated by multiplying all variable weights with the population size:

$$S_d = N_d \times s_d^{(floor/kapita<8m^2)} \times s_d^{(urban)} \times s_d^{(low\ education)} \times s_d^{(HIV)} \times s_d^{(air\ pollution)}$$

where:
S_d = weight score for district d, N_d = total population in district d, $s_d^{(floor/kapita<8m^2)}$ = weight score for variable living floor space in district d, $s_d^{(urban)}$ = weight score for variable level of urbanisation in district d, $s_d^{(low\ education)}$ = weight score for variable junior high school completion in district d, $s_d^{(HIV)}$ = weight score for variable HIV prevalence in district d, and $s_d^{(air\ pollution)}$ = weight score for variable air pollution prevalence in district d.

Step 4: Distribution of burden

Total weight score per region was calculated by adding the weight score per district in each region. The ratio of district score to the total weight score per region was then calculated. This ratio was multiplied by the regional incidence to estimate incidence at the district level.

$$I_d^{(case)} = \frac{S_d}{S_r} \times I_r^{(case)}$$

where:
$I_d^{(case)}$ = estimated TB incident cases in district d, S_d = weight score in district d, $I_r^{(case)}$ = estimated TB incident cases in region r, and S_r = total weight score in region r.

Calculation of district-level case detection rate

To estimate the district-level case detection rate (CDR), the estimated burden in each district was compared to both domicile- and health facility-based reported notifications. Comparing both domicile- and health facility-based notifications within and between surrounding districts allowed assessment of district health system performance and cross-district health utilisation.

Validation of SUBsET results

While model validation with data is desirable,[32] neither the prevalence survey nor the inventory study permitted district-level comparisons. The prevalence survey did not cover complete districts, and the inventory study was powered to provide a national, not district-level estimates. An attempt to use inventory study data at the district level would lead to extremely wide uncertainty intervals around the point estimates, which would therefore be non-informative.

Dissemination and adoption of model

The model was disseminated and discussed at provincial and district levels, followed by a round of revisions during a national-level stakeholder meeting. The final step comprised the addition of two variables to capture strong heterogeneity in HIV prevalence and measured air pollution between districts.

Uncertainty intervals

Uncertainty intervals were calculated by generating 10 000 random draws from the distribution for both the regional incidence estimate, as well as RRs of included variables.[23,27–30]

Sensitivity analysis

To understand the heterogeneity captured by our model, we compared the results of our calculation with an estimate based on regional incidence and population size alone. We also performed a calculation where we removed each individual variable and compared the results with the full model.

The model was set up using Microsoft Excel (MicroSoft, Redmond, WA, USA); multivariate analyses for region specific TB relative risks were conducted in STATA v14 (StataCorp, College Station, TX, USA). We used the spmap ado file in STATA to create the maps which show the distribution of the district TB burden estimates and CDR throughout Indonesia, particularly within provinces, thus allowing us to better understand the connection or relationship between one area and another.

RESULTS

Model

RRs for the model variables used in Step 2 are given in Table 2. The range of values across districts for each risk factor was wide (see Table 2, column 4). When

Table 2 Results from multivariate analysis of 2013-2014 TB Prevalence Survey

Risk factors associated with TB	Region	Relative risk	95% CI
Living in urban area			
	Sumatera	1.72	1.22–2.44
	Java-Bali	1.32	0.93–1.88
	Others	1.30	0.92–1.82
Living in a house less than 8 m^2/person			
	Sumatera	1.50	1.03–2.19
	Java-Bali	1.30	0.83–2.06
	Others	1.15	0.79–1.65
Not completing junior high school			
	Sumatera	1.11	0.78–1.60
	Java-Bali	1.34	0.90–2.00
	Others	1.61	1.10–2.36
HIV prevalence			
	All regions	30	20–45
Air pollution			
	All regions	1.47	1.20–1.80

the RRs were combined with the data for each risk factor, median differences in relative population weight for each district were as follows: Sumatera, 2.52 (range 2.29–2.75), Java-Bali, 1.50 (range 1.37–1.64) and Others, 2.10 (range 1.91–2.29).

District-level tuberculosis incidence

Figure 1 shows the distribution of the TB incidence estimated using SUBsET across the 514 districts in Indonesia. The estimated point values for TB incidence ranged between 201 and 2,485/100 000/year. The estimated TB incidence rates were lowest in the Java-Bali Region (average median 242, range 201–787/100 000) compared to Sumatera (373, range 295–918/100 000) and Others (350, range 280–2,485/100 000). However, as 58% of the total population of Indonesia resides in Java-Bali,[20] this region has the highest absolute number of TB cases.[23]

District-level case detection rate

Figure 2 shows the distribution of the estimated facility-based CDR in all districts. While some districts have very low CDR (0–20%, in dark grey, in dark red in the online colour version), some others have very high CDR (>100%, in light grey, in green in the online colour version), with a range of 0 to 190%. Among 24 (5%) districts with an estimated facility-based CDR of more than 100%, 15 were urban and suburban districts, surrounded by rural districts, which usually have fewer or lower quality TB services (Figure 2, pull outs). Twenty-one districts (4%) had an estimated facility-based CDR of 80–100%.

For domicile-based CDR, nine (2%) districts had an estimated CDR of more than 100%. A further 24 (5%) districts had a domicile-based CDR of 80–100%, and 51 (10%) had a domicile-based CDR below 20%. At the district level, facility and domicile-based CDRs were substantially different. As an example, for the year 2017, Salatiga City, Surakarta and Magelang City had a facility-based CDR of respectively 121%, 129% and 170%, while the domicile-based CDRs were only 32%, 39% and 33% respectively (Figure 2, pull outs).

Uncertainty analyses

We used uncertainty analyses to also estimate incidence rate ranges per 100 000/year population at both district and regional levels. The incidence rates per 100 000/year population were as follows: Sumatera Region, 413.4 (95% uncertainty interval [UI] 305.3–530.8); Java-Bali, 268.0 (95% UI 212.3–

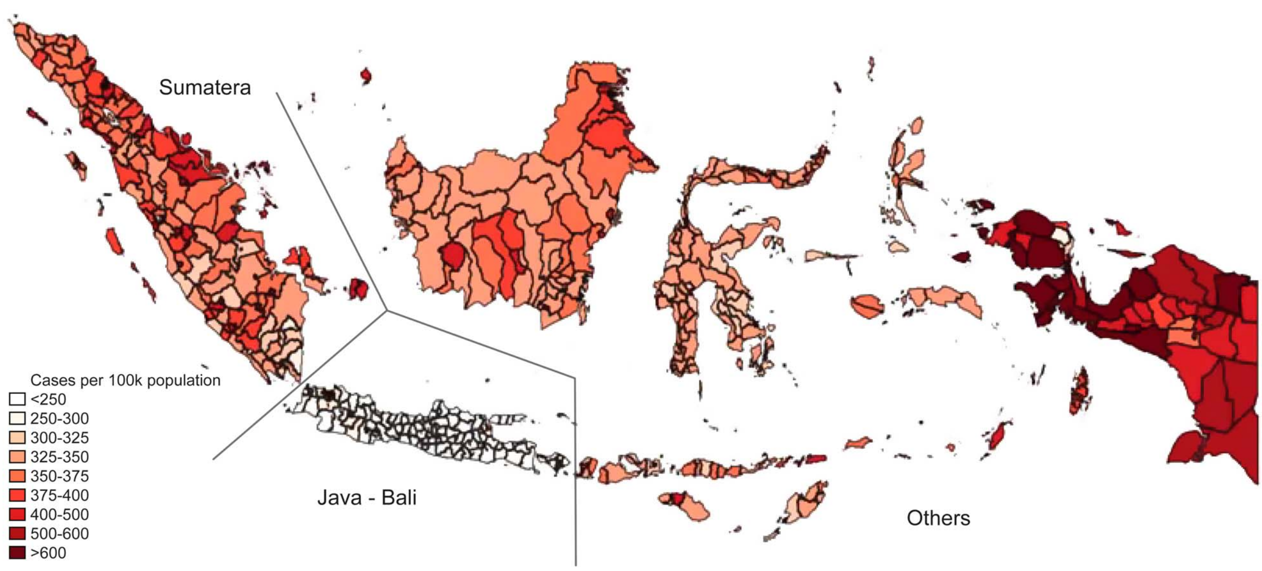

Figure 1 Estimated incidence/100 000/year by district, Indonesia, 2017. Figure shows three regions (indicated by solid lines) and 514 districts with their estimated incidence/100 000 population. TB = tuberculosis.

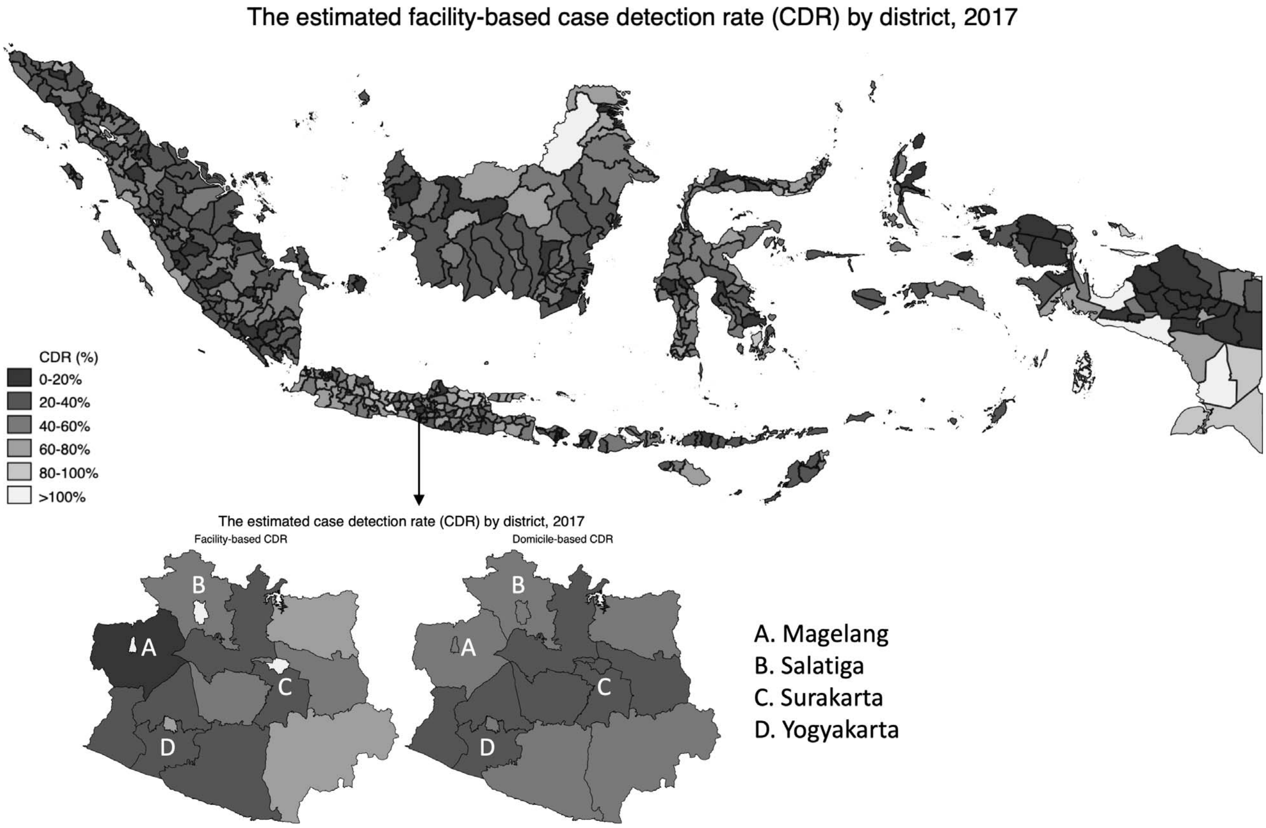

Figure 2 The distribution of the estimated facility-based CDR. National map shows distribution of estimated facility-based CDR across the 514 districts. Pull-out figure shows very high facility-based CDR (more than 100%, in light grey colour/green in online colour version) in central urban districts, and low facility-based CDRs in surrounding districts. Differences in CDR are no longer present when viewed in terms of domicile-based CDR, indicating cross-district health system utilisation. CDR = case detection rate.

321.0); and Others, 380.1 (95% UI 277.8–495.9). District-level UIs are shown in Figure 3.

Sensitivity analyses

Figure 3 shows the additional variation in estimated incidence introduced by the variables in our model by comparing with a model including population size and regional differences in prevalence. We found that 30% of the districts had a higher and 70% had a lower point estimate for TB incidence rates than previous estimates. The newly estimated TB incidence rates were more than 10% different (higher or lower) from the previous TB incidence estimate for 73% of the districts.

Removing a single variable had no relevant impact on the distribution of the estimated burden in the model, which indicates that there is no single model variable that dominates the differentiation between districts. If the dominant influence of population size is taken into account in the burden distribution across districts, a lower or higher RR value in a single variable would lead to a lower or higher UI value.

Model dissemination

The district- and provincial-level TB burden estimates were used to develop District and Provincial Action Plans, and particularly to inform policy decisions on budget, resource allocation and intervention planning. Estimates were also incorporated in the 2016–2020 TB National Strategic Plan, and informed joint AIDS, TB and malaria policy meetings at the national level.[33]

DISCUSSION

The SUBsET tool approach was found to provide an accessible and intuitive model for subnational burden estimation. Our final model included five variables to estimate the distribution of TB incidence from three regional estimates across 514 districts in Indonesia. The model provided substantial differentiation, estimating an incidence ranging between 201 and 2,485/100 000/year. The facility-based CDR varied between 0 and 190%, highlighting low-performing districts and cross-district health utilisation. Dissemination of the SUBsET tool led to rapid uptake and acceptance of results.

At the district level, the SUBsET model facilitated comparisons between facility-based and domicile-based CDRs, which highlighted previously unrecognised cross-district health system utilisation. This encouraged these districts to improve their own

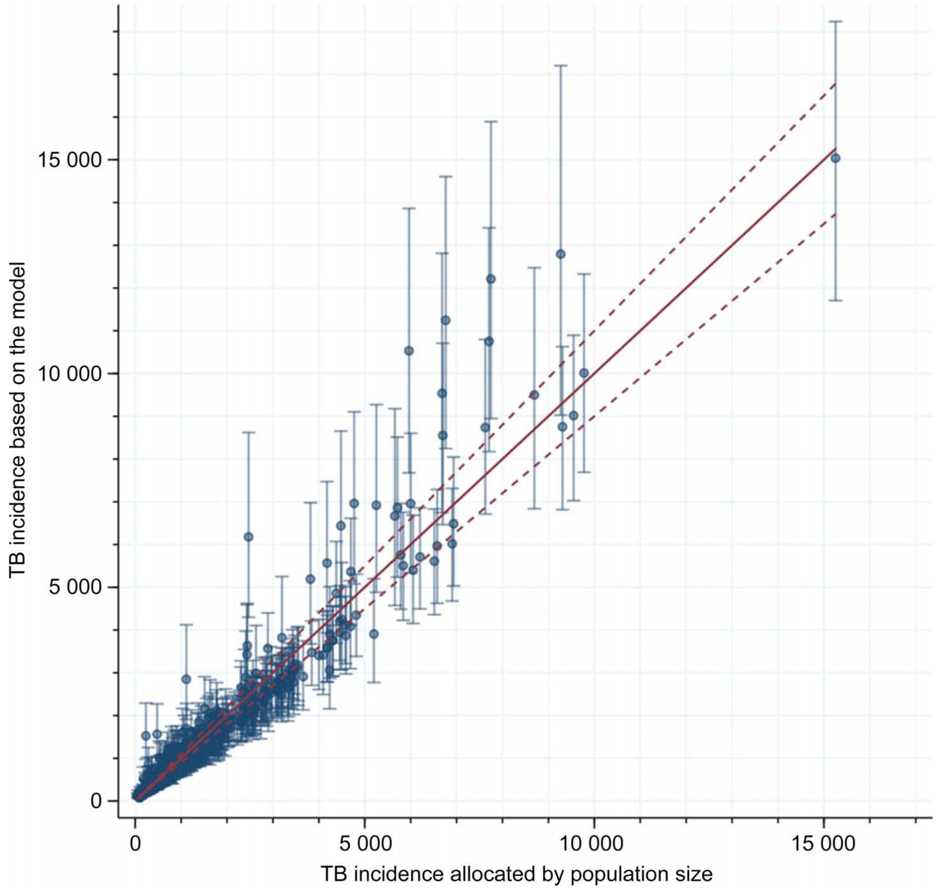

Figure 3 Heterogeneity captured by model variables. Figure shows change in estimated absolute incidence with 95% uncertainty interval from a model with population size and regional differences in prevalence only (*x*-axis), and a model from SUBsET (*y*-axis). Markers above/lower diagonal solid line indicate districts with a higher/lower estimate based on the full model compared to the simple model. TB = tuberculosis.

health care and case detection system, as well as improve collaboration with neighbouring districts.

Limitations

Our work had several limitations. Both the regional distribution of incidence and associations between TB burden and socio-economic variables were based on the 2014 national TB prevalence survey, and not on directly measured incidence. While these associations may be slightly different if directly calculated based on incidence, we believe that they are a reasonable approximation, and the limited bias is outweighed by the ability to directly calculate RRs for a specific population and time period. For HIV, these associations correspond to the RR (range) of developing TB in HIV-positive persons in high and low HIV prevalence areas; likewise, the association between air pollution and the risk of developing TB corresponds with results found in various studies from low- and middle-income settings.[27–30]

Second, we acknowledge the likelihood of residual or uncaptured variations in TB incidence beyond that captured by the model, for example, due to differential levels of malnutrition or in additional subcategories within the variables included, but data on these variables were not available for inclusion in the model.

Third, we recognise the inability to validate our results due to the unavailability of data. This prevents the assessment of consistency between the results of our model and other evidence and/or the true burden at district level; however, with future availability of data, the model can be continuously updated and results validated.

Advantages

Within these limitations, we achieved our main aim, which was to keep the SUBsET tool simple and intuitive; this enabled its rapid dissemination and eventually, further adaptation by each country. Results were acceptable to the autonomous District Health Office as publicly available data were used. While it is theoretically possible that a more complicated (and effective 'black box' model[11,13]) approach would have been equally successful as our intuitive and open approach, input from Indonesian stakeholders at the start, and local feedback throughout the process, suggests that our approach was correct.

The SUBsET model filled an urgent need within the Indonesia NTP to help inform with- and between-districts discussions. Furthermore, as adding variables or new districts to the model is relatively easy, SUBsET could be used as a template for other countries to consider in support of subnational advocacy, where data are available.

CONCLUSIONS

The transparent modelling approach applied in SUBsET enabled understanding, ownership and acceptance among the sub-national decision makers in Indonesia. Our approach shows how local data can be utilised to estimate subnational TB burdens, thus providing a template for adaptation in other high-burden countries to inform TB policy at the relevant, decentralised administrative level.

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RÉSUMÉ

CONTEXTE : Dans de nombreux pays durement frappés par la tuberculose (TB), il existe néanmoins une hétérogénéité géographique substantielle en matière de poids de la TB. De plus, les décisions relatives au financement et aux politiques en matière de TB sont très décentralisées. Des estimations sous nationales du poids de la TB sont cependant généralement indisponibles pour la planification et le choix des objectifs.

OBJECTIF et SCHÉMA : Nous avons développé SUBsET afin de distribuer l'incidence nationale de la TB à travers un score pondéré basé sur des variables sélectionnées, et appliqué aux 514 districts d'Indonésie, qui ont une politique substantielle et une autonomie budgétaire en matière de TB. L'incidence estimée a été comparée aux notifications envoyées par les structures de santé et les visites à domicile afin d'estimer le taux de détection des cas (CDR). Les partenaires locaux ont conduit l'élaboration du modèle et sa diffusion.

RÉSULTATS : Le modèle final de SUBsET a inclus la taille de la population du district, le taux d'urbanisation, des indicateurs socio-économiques (surface habitable et scolarité secondaire), la prévalence du VIH et la pollution de l'air. Nous avons estimé l'incidence de la TB au niveau du district entre 201 et 2485/100 000/an. Le CDR en structures de santé a varié de 0 à 190% avec une grande variation entre districts voisins, suggérant une importante utilisation des services de santé inter districts, qui a été confirmée par l'estimation du CDR à domicile. Les résultats de SUBsET ont informé les plans d'action TB au niveau du district dans toute l'Indonésie.

CONCLUSION : Appliquer SUBsET afin d'estimer le poids sous national de la TB peut être important pour les pays durement touchés et informer les décisions politiques en matière de TB au niveau administratif décentralisé.

RESUMEN

MARCO DE REFERENCIA: En muchos países con una carga de morbilidad por tuberculosis (TB) alta se observa una heterogeneidad notable de su distribución geográfica. Además, las decisiones que conciernen el financiamiento y las políticas en materia de TB son en gran parte descentralizadas. Con frecuencia se desconocen las estimaciones subnacionales de la carga de morbilidad en el momento de la planificación y la definición de las metas.

OBJETIVO Y MÉTODO: Se desarrolló el modelo SUBsET con el fin de distribuir la incidencia nacional de TB mediante una puntuación ponderada a partir de variables escogidas y se aplicó a los 514 distritos de Indonesia, que cuentan con una autonomía política y presupuestaria notable para la TB. Se comparó la incidencia estimada con las notificaciones comunicadas según la dirección de los establecimientos de atención o la dirección de los hogares, con el fin de estimar la tasa de detección de casos (CDR). Diversos interesados directos locales dirigieron el desarrollo del modelo y su difusión.

RESULTADOS: El modelo SUBsET final incluyó el tamaño de la población del distrito, el grado de urbanización, indicadores socioeconómicos (la superficie del espacio habitable y la culminación del bachillerato), la prevalencia de infección por el virus de la inmunodeficiencia humana y la contaminación ambiental. La estimación de la incidencia distrital de TB osciló entre 201 y 2485/100 000 habitantes/año. La CDR según la dirección de los establecimientos osciló entre 0 y 190% con una gran variabilidad en los distritos circundantes, lo cual indica una intensa utilización cruzada de los servicios de salud en los distritos, que se confirmó con la estimación de la CDR según la dirección de los hogares. Los resultados del modelo SUBsET fundamentaron los planes de acción en materia de TB en toda Indonesia.

CONCLUSIÓN: La aplicación del modelo SUBsET para estimar la carga subnacional por TB sería muy útil en los países con carga de morbilidad alta y puede fundamentar la formulación de políticas al nivel administrativo descentralizado pertinente.