

Estimating tuberculosis burden and reporting in resource-limited countries: a capture-recapture study in Iraq

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SUMMARY

BACKGROUND: The global target for tuberculosis (TB) control set by the Millennium Development Goals is a decrease in TB incidence by 2015. Direct measurement of country-level TB incidence using population-based methods is impractical, emphasising the need for well-performing surveillance systems and, where these are not available, accurate quantification of incidence and under-reporting of TB.

OBJECTIVE: To estimate TB incidence and TB under-reporting in Iraq in 2011.

METHODS: Prospective longitudinal surveillance was established among all eligible public and private non-National TB Programme (NTP) providers in a random sample of eight of the 18 Iraqi governorates from May to July 2011. Record linkage with the NTP and three-

source capture-recapture analysis of data were then conducted using log-linear modelling.

RESULTS: A total of 1985 TB cases were identified after record linkage. The NTP registered 1677 patients (observed completeness 84%). The estimated total number of TB cases was 2460 (95%CI 2381–2553), with identified TB cases representing 81% (95%CI 69–89) after adjusting for sampling design. The estimated ratio of notified to incident cases was 69% (95%CI 58–76).

CONCLUSIONS: We estimate 14 500 TB cases in Iraq in 2011, of which 31% (95%CI 24–42) were unreported. TB surveillance needs to be strengthened to reduce under-reporting.

KEY WORDS: tuberculosis; surveillance; record linkage; capture-recapture analysis; resource-limited

IRAQ HAS ADOPTED the global targets for tuberculosis (TB) control set by the World Health Assembly in 1991, which are to detect 70% of new (i.e., incident) sputum smear-positive cases arising annually and to successfully treat 85% of those detected.¹ The TB control target set by the United Nations Millennium Development Goals is a worldwide reduction in TB incidence by 2015.² Although the ultimate goal of TB surveillance is to measure TB incidence directly based on routine data from the National TB Programme (NTP),² TB incidence is uncertain in many highly endemic or endemic countries, as not all diagnosed cases are notified.^{3,4}

TB surveillance in Iraq was weak for many years following sanctions imposed in 1990. Nonetheless, the DOTS strategy was implemented throughout the country by 2001, and all 18 governorates had a governorate TB centre with a Governorate TB Coordinator (GTC). In subsequent years,^{5,6} district TB Management Units (TBMUs) and a Primary Health Care (PHC)

network were gradually established, facilitating universal access to health care. From the start of the war in Iraq in 2003 there was no contact with the northern governorates until communications were resumed in 2008.

Outside the NTP, private and public provision of health care co-exists in Iraq, with variable referral and notification of TB patients to the NTP.⁷ The DOTS strategy includes public-private mix approaches to improve case notification.⁸ TB notifications in Iraq increased slightly in 2008–2010 (Table 1).⁹ Using updated methodology,^{9,10} the World Health Organization (WHO) published a best estimate of 19 000 incident TB cases in 2008 (incidence rate 64 per 100 000 population), increasing to 20 000 incident TB cases in 2009 and 2010 (incidence rate 64/100 000).⁹ The case detection rate, calculated as notifications of new and relapse TB cases divided by estimated incidence, was estimated at 48% (95% confidence interval [CI] 40–57) in each year.⁹

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Table 1 Number of new notified smear-positive, smear-negative and extra-pulmonary TB cases and relapse TB cases in Iraq, 2008–2010, and the ratio of notified to estimated incident TB cases, previously known as the case-detection rate*

	Year		
	2008	2009	2010
New smear-positive pulmonary	3150	3347	3618
New smear-negative pulmonary	2502	2376	2317
New smear unknown pulmonary	225	290	376
New extra-pulmonary	2718	2904	3009
Relapse	504	468	387
Total	9099	9385	9707
Case detection rate for new and relapse TB cases, % (95%CI)	48 (40–59)	48 (40–59)	48 (40–59)

* Source: Iraq National TB Programme annual reports and WHO report 2011.⁹
 TB = tuberculosis; CI = confidence interval; WHO = World Health Organization.

When TB incidence cannot be determined accurately from notifications, it can be measured directly, using costly, time-consuming and complicated longitudinal cohort studies, which are often not feasible.³ An alternative is periodic indirect estimation of completeness of TB registers, through record-linkage and capture-recapture techniques,^{11,12} as have recently been applied to TB in Egypt and Yemen.^{13,14} The objective of our study was to apply such methods to estimate TB incidence and TB under-reporting in Iraq in 2011.

METHODS

Study population, area and setting

Iraq had a population of 32 326 011 in 2009. Administratively, the country has 18 governorates, which are subdivided into 124 districts. The study was conducted in eight randomly selected governorates with a population of 17 164 779 (53% of the Iraqi population) and covering 60 districts (48%; Table 2).

Health care services consist of public providers, including public, teaching, company, military and prison hospitals and laboratories, and private providers, including private polyclinics, clinics, hospitals and laboratories and non-governmental organisation facilities.

The Iraq NTP has a central unit at the national level, and a GTC and a TB centre with TB diagnostic capability and out-patient clinical and radiological services in each governorate. Bacteriological culture services are available in the major governorates (Baghdad, Basrah, Najaf, Babylon and Ninawa). There are 124 TBMs at district level with district TB coordinators (DTC); 85 of the TBMs have diagnostic capacity. The 39 TBMs without diagnostic capacity refer TB suspects to nearby diagnostic TBMs or the governorate TB centre, but are responsible for patient follow-up. In addition, there are governorate laboratory supervisors and district laboratory technicians. Drug susceptibility testing is only performed at the national TB unit in Baghdad. In-patient facilities are also available only in Baghdad (Ibn Zuhur Hospital).

Directly observed treatment is provided through the TBMU network and 1922 PHC centres at the peripheral level. TBMs submit paper-based quarterly reports and electronic nominal notification data to the GTCs, which send consolidated reports to the national unit. Non-NTP providers are required to refer or notify TB cases to the NTP through uniform referral and notification forms.

Table 2 The eight selected governorates, divided into four strata based on sputum smear-positive tuberculosis notification rates (very high, high, intermediate or low, according to the 75%, 50% and 25% percentiles for the country) and the two governorates (simple) randomly selected per stratum and sampling fraction per stratum

Governorates	Population <i>n</i>	Sputum smear TB notification rates <i>n</i> /100 000
Basrah	2 608 601	24
Duhok	985 402	22
Population in selected governorates	3 594 003	
Population in stratum 1	9 657 794	
Sampling fraction, %	37	
Misan	1 030 306	26
Najaf	1 215 937	26
Population in selected governorates	2 246 243	
Population in stratum 2	4 722 959	
Sampling fraction, %	48	
Baghdad*	7 341 257	33
Sulaymania	1 703 062	32
Population in selected governorates	9 044 319	
Population in stratum 3	10 748 922	
Sampling fraction, %	84	
Diwanyiah	1 124 516	39
Wasit	1 155 698	42
Population in selected governorates	2 280 214	
Population in stratum 4	7 164 751	
Sampling fraction, %	32	
Total population in selected governorates	17 164 779	
Total population of strata	32 326 011	
Average sampling fraction, %	53	

* Baghdad has two sub-governorates: Rasafah (East Baghdad) and Al-Karkh (West Baghdad).

Study design and sampling methods

To obtain a representative sample, stratified cluster random sampling was performed using four strata defined by the sputum smear-positive TB notification rate, according to the 75%, 50% and 25% percentiles for the country. From each stratum, two governorates were selected using simple random sampling, without probability proportional to population size (Table 2). Prospective longitudinal surveillance was established in all non-NTP facilities in the selected governorates for the 3 months from May to July 2011. Non-NTP facilities, which were requested to cooperate by the Federal and Kurdistan Ministry of Health, were mapped out by the NTP in collaboration with the governorate Iraq Medical Association branches. An overview of the number of public and private health care providers in Iraq and the selected governorates and participating providers is shown in Table 3.

Case definition

TB cases were defined as all patients (new and relapse, bacteriologically confirmed and non-confirmed) registered with the NTP, or confirmed as TB cases using NTP criteria when only known to non-NTP providers, between 1 May and 31 July 2011.

Registers and record linkage

Laboratory and TB register forms identical to those used by the NTP were introduced in non-NTP public and private facilities to record demographic, diagnostic, referral and treatment information and NTP verification, as described in detail elsewhere,¹³ with-

out any interventions to change their practice. All non-NTP facilities were visited weekly by the DTC and research assistants to review data collection, check completeness and accuracy of records, ensure filling out of missing information, delete duplicate entries in each of the registers, inspect notifications to the NTP electronic TB register and contact unregistered non-NTP cases and suspects for diagnosis verification (using NTP criteria). To correct for possible misclassification of patients diagnosed before the study period or late referrals or notifications, the NTP register was examined two quarters before and one quarter after the study period, i.e., between November 2010 and October 2011. Confirmed cases were added to the NTP register only after the final distribution of patients over the three linked registers was established at the end of the study period. The forms collected by the DTCs were forwarded through the GTCs to the national level. Deterministic record linkage was performed, using the fixed combination of the first, father's and family name in Arabic script as the principal identifiers.^{13,14} The observed completeness of NTP records was defined as the number of NTP-registered cases divided by the total number of patients observed in at least one register, expressed as a percentage.

Capture-recapture analysis

Capture-recapture methods have been described in detail elsewhere.¹³ Briefly, three-source log-linear capture-recapture analysis was performed using the final distribution data of all TB cases across registers.

Table 3 Overview of the number of public and private health providers in Iraq and the selected governorates (excluding psychiatrists, ophthalmologists, ENT specialists, dermatologists, obstetricians and some neurologists) and the number participating in the record-linkage and capture study

Governorate	Public hospitals		Private hospitals		Private physician clinics		Prison		Private laboratories performing ZN stain
	Total	Participating	Total	Participating	Total	Participating	Total	Participating	
Baghdad	46	40	37	37	2196	1584	26	26	227
Basra	13	12	5	4	631	416	2	2	7
Ninawa	14		2		772				
Misan	6	6	0	0	105	81	1	1	3
Diwaniya	6	6	3	3	168	112	1	1	32
Diala	10		3		191				
Anbar	11		2		261				
Babil	14		3		375				
Karbala	5		2		238				
Kirkuk	7		2		283				
Wasit	8	6	1	1	196	163	2	2	13
Thi Qar	9		2		196				
Muthana	4		0		96				
Salahelden	9		2		207				
Najaf	7	7	3	3	376	376	1	1	7
Erbil	22		10		650				
Duhok	9	8	3	3	162	162	2	2	10
Sulaymania	29	25	13	9	374	301	2	2	15
Total in Iraq	229		93		7477				
In study governorates	124		65		4208		37		
Participating	110		60		3195		37		314

ENT = ear, nose, throat; ZN = Ziehl-Neelsen.

We fitted log-linear models to the $2 \times 2 \times 2$ contingency table of NTP, private and public records of TB in Iraq for a 3-month period in eight governorates. Of the eight possible models (including three possible 2-way interactions), we chose the model presenting the best compromise between lower Akaike information criterion (AIC) values and the biological plausibility of the interactions identified, as described previously,¹⁴ with internal validity analysis.^{15,16} This model was then used to predict the missing cell of the $2 \times 2 \times 2$ data, and hence the proportion of all TB patients referred to NTP in the eight governorates, and adjusted for the sampling design. Analyses were performed using the R statistical package (R Foundation for Statistical Computing, Vienna, Austria).¹⁷ CIs were calculated using the delta method.¹⁸ This estimated proportion was then applied to the annual number of notified TB patients in all governorates in each stratum in 2010, scaled up by the stratum-specific sampling fraction,¹⁴ and summed to obtain an estimate of the total number of TB patients in Iraq in 2011.

The estimated ratios of notified and detected to incident cases were defined as the number of NTP-registered cases and the number of TB cases after record linkage, divided by the estimated number of TB cases through capture-recapture analysis, respectively, expressed as a percentage.

Ethical considerations

Ethical clearance was obtained from the ethics committee of the Iraqi Ministry of Health. Informed consent was obtained from the participating non-NTP providers.

RESULTS

Record linkage

Between 1 May and 31 July 2011, 1985 TB cases were identified in the eight study governorates. The Figure shows their distribution across the three registers. The NTP registered 1677 patients (observed completeness 84%). The non-NTP sector diagnosed 993 patients (50%), of whom 649 (65%) were identified by the private non-NTP sector and 378 (38%) by the

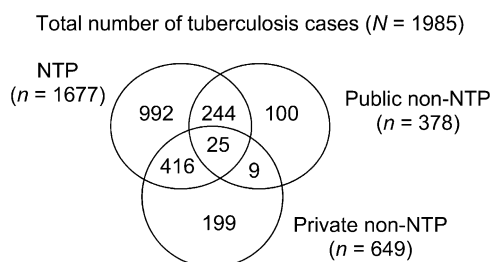


Figure Distribution of observed number of tuberculosis cases (all forms) in eight governorates in Iraq between 1 May and 31 July 2011. NTP = National TB Control Programme.

public non-NTP sector. A total of 685 patients (35%) were known to both the NTP and non-NTP sector, predominantly from private non-NTP providers ($n = 441$). Of the identified cases, 308 (16%) were not notified. The overlap between public and private non-NTP providers was small (5%).

Capture-recapture analysis

No source captured less than 10% of cases, but the overlaps between the public and private non-NTP registers and all three registers were small. The model with the lowest AIC (58.1) contained all main effects and one interaction, i.e., a negative public non-NTP \times private non-NTP interaction (as expected, due to lack of cooperation; Table 4). The selected, marginally different outcome model (AIC 58.7) contained all main effects and two interactions, i.e., a positive NTP \times public non-NTP interaction (although non-significant) and a negative public non-NTP \times private non-NTP interaction, both of which were expected (respectively due to referral of patients suspected or diagnosed through public sources to the NTP and due to lack of cooperation). The total number of TB cases estimated in the eight study governorates using this model was 2460 (95%CI 2381–2553). After adjusting for sampling design, the estimated ratios of notified and detected to incident cases were respectively 69% (95%CI 58–76) and 81% (95%CI 69–89). Internal validity analysis indicated interactions and estimates similar to the selected log-linear model.

An annual number of 14 500 (95%CI 13 200–17 200) TB cases in Iraq in 2011, equivalent to a TB incidence rate of 45/100 000 (95%CI 41–53/100 000), was estimated.

Table 4 The eight possible three-source log-linear capture recapture models with AIC and estimated number of tuberculosis cases in the eight governorates in Iraq between 1 May and 31 July 2011, with 95%CI (not adjusted for sample design)

Model	AIC	n_{est}	95%CI
Independent model	138.5	2508	2438–2590
NTP \times public non-NTP interaction	135.2	2576	2481–2689
NTP \times private non-NTP interaction	139.4	2563	2443–2715
Public non-NTP \times private non-NTP interaction	58.1	2431	2370–2502
NTP \times public non-NTP interaction, NTP \times private non-NTP interactions	115.4	4196	3087–6420
NTP \times public non-NTP, public non-NTP \times private non-NTP interactions	58.7*	2460	2381–2553
NTP \times private non-NTP, public non-NTP \times private non-NTP interactions	59.2	2392	2305–2502
Saturated model	60.6	2502	2224–3208

* Selected model: positive NTP \times public non-NTP interaction (non-significant); negative private non-NTP interaction \times public non-NTP interaction (significant); goodness-of-fit $P = 0.746$. AIC = Akaike Information Criterion; n_{est} = estimated total number of tuberculosis cases; CI = confidence interval; NTP = National TB Control Programme.

DISCUSSION

Our study suggests that there were 14 500 TB cases in Iraq in 2011 (range 13 200–17 200), with 81% (95% CI 69–89) of incident cases detected and 69% (95% CI 58–76) of incident cases notified.

Study limitations

The limitations and assumptions of capture-recapture analysis have been described in detail elsewhere, in general,^{12,19–25} and specifically in the context of TB.¹³

The fixed hierarchic combination of three Arabic names used in our study minimises overmatching due to identical names, is reportedly less prone to pronunciation and spelling errors due to the absence of homonyms in the Arabic language (minimising undermatching due to inconsistent recording), and is routinely applied in data management of NTP surveillance in Iraq. Weekly visits by research assistants also minimised undermatching caused by incomplete registers. Misclassification due to late referrals or notifications was reduced by examining the NTP register up to November 2011. To minimise violation of the closed population assumption, data were collected within a short (3-month) period of time, reducing population mobility but limiting the amount of (overlap) data collected.

Possible violation of the homogeneity assumption has been described in detail for a similar study elsewhere.¹³ Bias occurs when factors driving heterogeneity are correlated, for example when the same factor drives heterogeneity in all registers.²⁶ Some possible, but moderate,²⁶ bias as a result of heterogeneity cannot be ruled out.

Violation of the independency assumption can be partially examined and controlled when more than two registers are linked by incorporating possible pair-wise interdependencies in the log-linear models as interactions.^{12,24,27,28} Interaction terms can control direct dependence (i.e., being detected by a source changes the probability of being detected by another), and indirect dependence as well (which is due to violation of the homogeneity assumption). In this study, the selected model included two pair-wise interactions (negative public non-NTP \times private non-NTP and positive NTP \times public non-NTP), in line with prior expectations and observations after record linkage.

Lack of cooperation created a strong negative dependence between both non-NTP registers and, through referral or notification (71%), a positive dependence (although not significant in the model) existed between the public non-NTP and NTP registers. It is unknown if the non-NTP providers would have referred or notified as many cases to the NTP without being motivated by the weekly visits of the research staff, but these visits ensured good quality of the non-NTP records and could stimulate future engagement of the non-NTP providers in referral and

notification. Low overlap between the two non-NTP registers possibly resulted in less precise estimates with wider CIs.²⁹ The pair-wise capture-recapture analyses showed internal consistency of the interactions and estimates of the selected log-linear model, with a dominant negative interaction between public non-NTP \times private non-NTP, some positive interaction between the public non-NTP and the NTP and absence of interaction between the private non-NTP and the NTP. The estimate of 2460 TB cases was similar to the public non-NTP \times private non-NTP and NTP \times private non-NTP estimates.

Violation of the accurate diagnosis assumption, i.e., no false-positive cases remaining in the registers, was minimised through exclusion of cases either captured outside the study period or not having TB by examination of the NTP register 6 months before the study period and confirmation using NTP criteria of cases known only to non-NTP providers. The burden of TB disease in Iraq could be underestimated when false-negative diagnoses are made in symptomatic cases.

Although not strictly an assumption, the prospective longitudinal surveillance used in this study challenged initial perceptions that capture-recapture methods were cheap and quick when existing registers are used.

Capture-recapture estimates do not include TB cases with a zero probability of being registered, such as asymptomatic cases in the absence of active case finding, or individuals with no access to health care.

Study strengths

A major strength of our study was that almost half of the health care providers in Iraq were sampled, representing 53% of the population. The involvement of the private and public non-NTP sectors also improved the current and likely future completeness of routine TB surveillance notification, and the timely estimation of the ratio of notified to incident cases for Iraq in 2011 allowed very timely presentation of results to the GTCs of the selected governorates in November 2011. The study also reinforced earlier experience that these methods are feasible in countries with a similar organisation of health care and TB services.

Capture-recapture analysis in resource-limited conditions

The applications, limitations and recommendations of capture-recapture analysis in resource-limited settings have been discussed extensively in a separate paper.³⁰ In this study, the estimated ratio of notified to incident cases of the NTP surveillance for all TB cases in Iraq is higher than the latest WHO estimates. This could indicate that the WHO estimates were not accurate or that this study, despite instructions and training, influenced the notification behaviour of the physicians in the public and private sectors in a

positive way. However, sub-analyses of the NTP data in Iraq for 2011 showed that there was no increase in the number of notified TB cases in the selected governorates compared to the months before and after the study period. The Iraq NTP should enhance the observed positive interaction with the public and private non-NTP sector to further improve the ratio of notified to incident TB cases.

CONCLUSIONS

Record-linkage studies and capture-recapture techniques can be used to estimate the completeness of TB notifications in resource-limited countries, facilitating strengthened TB surveillance and enhanced collaboration among all providers of TB diagnosis and care. Similar studies are warranted in many other countries, once standardised guidance, at the advanced stages of development and due to be published by the WHO in 2013, is available. All countries should strengthen their routine surveillance systems in the context of the Stop TB Strategy.^{10,30}

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R É S U M É

CONTEXTE : La cible mondiale pour la lutte antituberculeuse (TB) précisée au sein des Objectifs de Développement du Millénaire est une chute de l'incidence de la TB d'ici 2015. La mesure directe de l'incidence de la TB au niveau d'un pays au moyen de méthodes basées sur la population n'est pas pratique, ce qui fait ressortir la nécessité de systèmes très performants de surveillance, et, lorsqu'ils ne sont pas encore disponibles, celle d'une quantification précise de l'incidence de la TB et de sa sous-déclaration.

OBJECTIF : Estimer l'incidence de la TB et celle de la sous-déclaration de la TB en Iraq en 2011.

MÉTHODES : On a mis en route un système de surveillance prospective longitudinale chez tous les pourvoyeurs de soins éligibles du secteur public et du secteur privé en dehors du Programme National contre la Tuberculose (PNT) dans un échantillon randomisé de huit

des 18 Gouvernorats Irakiens entre mai et juillet 2011. On a recoupé les enregistrements avec le PNT et on a mené une analyse capture-recapture des trois sources de données au moyen d'une modélisation log-linéaire.

RÉSULTATS : Après recoupement des enregistrements, on a identifié au total 1985 cas de TB. Le PNT a enregistré 1677 patients (achèvement observé 84%). Le nombre total estimé de cas de TB a été de 2460 (IC95% 2381–2553) et les cas de TB identifiés ont représenté 81% (IC95% 69–89) après ajustement pour le schéma d'échantillonnage. Le ratio estimé des cas déclarés sur les cas incidents a été de 69% (IC95% 58–76).

CONCLUSIONS : Nous estimons le nombre de cas de TB en Iraq en 2011 à 14 500, dont 31% (IC95% 24–42) n'avaient pas été déclarés. La surveillance de la TB doit être renforcée afin de réduire les niveaux de sous-déclaration.

R E S U M E N

MARCO DE REFERENCIA: La meta mundial del control de la tuberculosis (TB) establecida en los Objetivos de Desarrollo del Milenio consiste en una disminución de la incidencia de TB en el 2015. La medición de la incidencia de TB a escala nacional, mediante técnicas basadas en la población, es poco práctica, lo cual pone en evidencia la necesidad de contar con sistemas de vigilancia de gran rendimiento o, en su defecto, mecanismos de cuantificación precisa de la incidencia y la subnotificación de los casos de TB.

OBJETIVO: Se buscó calcular la incidencia de TB y la subnotificación de casos en Iraq en el 2011.

MÉTODOS: Se puso en marcha una vigilancia longitudinal prospectiva entre mayo y julio del 2011 en la cual participaron todos los profesionales sanitarios del sector público y el sector privado que cumplían con las condiciones de inclusión y que no formaban parte del Programa Nacional contra la Tuberculosis (PNT); se practicó un muestreo aleatorio en ocho de las 18 prefecturas

iraquíes. Se reconciliaron los registros obtenidos con los registros del PNT y luego se realizaron tres análisis de captura y recaptura de las fuentes de datos, mediante la aplicación un modelo semilogarítmico.

RESULTADOS: Después de la reconciliación de los registros se detectaron 1985 casos de TB. En el PNT se registraron 1677 pacientes (compleción del tratamiento observada 84%). El cálculo del número total de casos de TB fue 2460 (IC95% 2381–2553), con lo cual los casos detectados correspondieron al 81% de todos los casos (IC95% 69–89) tras corrección según el tipo de muestreo. El cálculo de la proporción de casos notificados con respecto a los casos nuevos fue 69% (IC95% 58–76).

CONCLUSIÓN: Se calculó que ocurrieron 14 500 casos de TB en Iraq en el 2011, de los cuales no se notificó un 31% (IC95% 24–42). Es necesario fortalecer la vigilancia de la TB a fin de disminuir la subnotificación de casos.