Global Burden of Tuberculosis

Estimated Incidence, Prevalence, and Mortality by Country

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Objective To estimate the risk and prevalence of *Mycobacterium tuberculosis* (MTB) infection and tuberculosis (TB) incidence, prevalence, and mortality, including disease attributable to human immunodeficiency virus (HIV), for 212 countries in 1997.

Participants A panel of 86 TB experts and epidemiologists from more than 40 countries was chosen by the World Health Organization (WHO), with final agreement being reached between country experts and WHO staff.

Evidence Incidence of TB and mortality in each country was determined by (1) case notification to the WHO, (2) annual risk of infection data from tuberculin surveys, and (3) data on prevalence of smear-positive pulmonary disease from prevalence surveys. Estimates derived from relatively poor data were strongly influenced by panel member opinion. Objective estimates were derived from high-quality data collected recently by approved procedures.

Consensus Process Agreement was reached by (1) participants reviewing methods and data and making provisional estimates in closed workshops held at WHO's 6 regional offices, (2) principal authors refining estimates using standard methods and all available data, and (3) country experts reviewing and adjusting these estimates and reaching final agreement with WHO staff.

Conclusions In 1997, new cases of TB totaled an estimated 7.96 million (range, 6.3 million–11.1 million), including 3.52 million (2.8 million–4.9 million) cases (44%) of infectious pulmonary disease (smear-positive), and there were 16.2 million (12.1 million–22.5 million) existing cases of disease. An estimated 1.87 million (1.4 million–2.8 million) people died of TB and the global case fatality rate was 23% but exceeded 50% in some African countries with high HIV rates. Global prevalence of MTB infection was 32% (1.86 billion people). Eighty percent of all incident TB cases were found in 22 countries, with more than half the cases occurring in 5 Southeast Asian countries. Nine of 10 countries with the highest incidence rates per capita were in Africa. Prevalence of MTB/HIV coinfection worldwide was 0.18% and 640 000 incident TB cases (8%) had HIV infection. The global burden of tuberculosis remains enormous, mainly because of poor control in Southeast Asia, sub-Saharan Africa, and eastern Europe, and because of high rates of *M tuberculosis* and HIV coinfection in some African countries.

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THE MOST RECENT PUBLISHED estimates of the global burden of tuberculosis (TB)[1-5] are based on data available up to 1990 and, with 1 exception,[5] give figures for regions of the world rather than individual countries. The magnitude of the tuberculosis problem has changed since 1990, due to changing control practices, spread of human immunodeficiency virus (HIV), and population growth. As an interim measure, the World Health Organization (WHO)[6] published a revised set of estimates for 1996, obtained by scaling earlier World Bank[5] estimates to 1996 population sizes. A more thorough review is needed to take account of nearly a decade of change in TB epidemiology and to accommodate new data.

Our main aim was to estimate risk and prevalence of *Mycobacterium tuberculosis* (MTB) infection and TB incidence, prevalence, and mortality for 1997. The results are the fullest and most up-to-date assessment we can currently make of TB burden by country, by region, and globally. They define the magnitude of the global TB control problem for use in assessing present control efforts and provide a baseline from which to forecast and measure impact of control efforts.

See also Patient Page.

METHODS

Data and Methods of Estimation

For all countries, participants reviewed available data on:

- case notifications (all forms, pulmonary, smear-positive, extrapulmonary) and case detection rate, including evidence for overreporting and underreporting;
- prevalence of infection (via tuberculin surveys), giving estimates of the annual risk of infection (ARI), and annual rate of decline in ARI;

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• prevalence of disease (surveys of smear microscopy and sputum culture studies; x-ray surveys);

• incidence and prevalence of HIV and acquired immunodeficiency syndrome (AIDS) (general population surveys, surveys among special groups such as pregnant women and TB patients);

• numbers of cases untreated; numbers treated under the WHO control strategy (directly observed therapy, short-course [DOTS]) and other programs;

• TB mortality (case fatality rates [CFRs] from vital registration and patient cohort data, DOTS/non-DOTS programs, HIV infected/uninfected);

• duration of illness (DOTS/non-DOTS programs, untreated cases, HIV infected/uninfected);

• proportion of smear-positive cases and ratio of smear-positive incidence to ARI; and

• demography (population size, population fraction >age 15 years, life expectancy from birth).

These data were used to estimate TB incidence (new infections or cases of disease), prevalence (existing cases), and mortality in each country by 3 different methods, based on (1) cases notified to WHO,[6,7] (2) ARI data derived from tuberculin surveys, and (3) data on prevalence of smear-positive pulmonary disease from prevalence surveys. We made estimates for each country using the most reliable of the 3 kinds of data, identified in Appendix 1 (all 4 appendixes are available at http://www.jama.com). We ranked the data by quality, using 3 grades, from low (*) to high (***). *Low* means there were no recent data or the data were not collected using standard epidemiological methods. Estimates derived from relatively poor data were strongly influenced by panel member opinions. More objective estimates were derived from high-quality data collected recently and by approved procedures. For case notifications, reliability was judged by consistency of reports from year to year and from surveillance methods used and coverage within countries. Prevalence surveys of infection and disease, including surveys of HIV, were judged by their design (sample size, choice of study populations, and analytical methods), by whether they appeared to be representative of an entire country, and by survey date. Although the decision regarding best data from a country sometimes required comparison of different kinds of information (eg, case notifications vs prevalence survey), rankings were generally obvious. The following formulas formed the basis of the analysis:

(1) Incidence/10^5 Persons/Year = (Case Notifications/10^5 Persons/Year)/ Estimated Proportion of Cases Detected

(2) Prevalence/10^5 Persons = Incidence/10^5 Persons/Year × Average Duration of Illness, Year

(3) Deaths/10^5 Persons/Year = Incidence/10^5 Persons/Year × CFR

(4) Incidence Sputum Smear-Positive Cases/10^5 Persons/Year = Annual Risk of Infection, % × *S*

S in equation 4 is the empirically derived ratio of smear-positive incidence to percentage ARI. Equations 1 through 4 can be rearranged to estimate incidence, prevalence, and mortality via the 3 methods mentioned herein (notifications [method 1], risk of infection [method 2], or disease prevalence [method 3]).

Table 1. Global Values of Parameters Used in Calculating TB Incidence, Prevalence, and Mortality Rates, With Ranges Used for Uncertainty Analysis*

Variable	Value (Range)	Reference Sources
Proportion of HIV-negative incident cases that are smear-positive	0.45 (0.4-0.5)	2
Proportion of HIV-positive incident cases that are smear-positive	0.35 (0.3-0.4)	15, 26, 35-37
Duration of illness in untreated HIV-negative cases, y	2.0 (1.5-2.5)	9, 17
Duration of illness in untreated HIV-positive cases, y	0.5 (0.25-1.0)	10-13
CFR in untreated smear-positive cases	0.7 (0.55-0.75)	2, 16, 17
CFR in untreated smear-negative cases	0.2 (0.1-0.3)	17, 18
CFR in untreated HIV-positive cases	0.9 (0.85-1.0)	Assumed: no data
Ratio of smear-positive incidence/10^5/year to annual risk of infection, %	50 (30-70)	9, 14; This study

*Parameters shown in this table are those having the same values for all countries. Parameters with country-specific values are given in the Appendixes. TB indicates tuberculosis; HIV, human immunodeficiency virus; and CFR, case fatality rate.

Case Notifications, Case Detection, and Incidence

To calculate incidence from case notifications, an independent estimate of the case detection rate is required (equation 1), ie, the proportion of incident cases that is notified to WHO,[1,7] which is often smaller than the proportion of incident cases treated. Tuberculosis cases are mostly underreported, so the case detection rate is generally less than 100%. However, the fraction underreported is sometimes offset by overdiagnosis (especially by x-ray) and by double reporting of individual cases (eg, where patient visits rather than patients are recorded and where referrals are made between notifying treatment centers).

Information is most reliable for smear-positive cases recorded and reported as recommended for DOTS programs.[8] Thus, in this analysis, we first estimated, where possible, the smear-positive incidence rate in DOTS areas. In countries that do not have significant DOTS coverage (<10% of the population[6,7]), we estimated the proportion of treated cases from data on health services coverage, drug availability, and patient condition (eg, advanced disease suggests long delays to seeking treatment and low case detection). The incidence rate for all forms of disease was obtained by dividing by 0.45 (for HIV-uninfected cases; range, 0.4-0.5 for uncertainty analysis; TABLE 1). For HIV-infected cases, we used the divisor 0.35 (range, 0.3-0.4;

Table 1). These are averages across all age groups and accommodate the fact that children with TB rarely produce bacteriologically positive sputum samples. Given the uncertainty associated with crude estimates of incidence, we have not attempted to break down incidence by age or sex, nor have we adjusted the values of the fractions herein for the difference in age distributions of cases between countries.

Prevalence and Duration of Illness

If the incidence is stable through time (with change of <10% per year, as in most high-burden countries), prevalence can be calculated by multiplying incidence by duration of illness (equation 2). Alternatively, crude incidence can be calculated from prevalence/duration, having adjusted the results of adult prevalence surveys for age structure.

Few direct measurements have been made of duration of illness, so judgments were made on the basis of health services quality, including patterns of drug use and availability, and fraction of cases treated in the private sector. The duration of infectious pulmonary disease is easiest to define because it can be equated with the time during which a patient receiving treatment produces visible bacilli in sputum smears, though the delay between the onset of symptoms and diagnosis is often uncertain.

We made separate assessments of the length of illness for patients treated using DOTS, those treated in other programs (non-DOTS), HIV-infected persons, and those receiving no treatment (Table 1 and Appendixes 2 and 3). An untreated individual was assumed to be ill for 2 years (range, 1.5-2.5 years) on average[13] or 0.5 years (range, 0.25-1.0 years) for TB cases with HIV infection.[14-17] Good control programs will reduce average length of illness by minimizing diagnostic delays and ensuring that patients adhere to short-course treatment. Poor programs, in which diagnostic delays are longer and treatment failure is common, can result in an increase in average duration of illness to beyond 2 years. The duration was thus varied from 0.5 to 3.5 years in 6-month steps, according to data for each country. The agreed-on duration of illness was 0.8 years in countries with good DOTS programs (eg, United States and western Europe), and 1.5 years in countries with less effective programs (eg, Laos and Papua New Guinea). The duration of illness in non-DOTS programs is typically more variable and longer on average; the agreed-on range was 1 year (eg, industrialized countries) to 3.5 years (eg, Cambodia and Indonesia, where surveys show relatively high disease prevalence). The weighted average duration was calculated for each country by assessing the proportion of cases in each category, and this weighted average was used in equation 2.

Mortality and CFRs

The annual TB mortality rate was calculated as the product of the annual incidence rate and the CFR (equation 3). The CFR is the proportion of persons with incident cases dying of TB. It includes TB deaths during the 6 to 8 months of short-course treatment and afterward in a proportion of treatment failures, treatment defaulters, and relapses. Like duration of illness, case fatality differs by whether cases are treated in DOTS or non-DOTS programs or not treated, are HIV-infected, and/or have other infectious or noninfectious disease. The CFRs for untreated cases are shown in Table 1.[2,18-22] The CFRs under treatment varied between countries and are shown in Appendix 2.[23-26] The DOTS programs provide relatively accurate data on death in patients evaluated in cohorts[7]; these rates have been adjusted upward to estimate number of deaths in all patients treated via DOTS. Death rates in non-DOTS areas are generally measured less accurately; they are more variable and higher on average than in DOTS areas.[7] The weighted CFR was calculated from the proportions of cases in each category and used in equation 3. Published mortality rates[27] generally underestimate deaths and have been used to put lower bounds on the CFR.

Annual Risk of Infection

The incidence of infectious TB can be calculated from the ARI (equation 4). An increase of 1 percentage point in ARI has been associated with an increase of 49 (95% confidence interval, 39-59) smear-positive cases per 100 000 population.[4,18] The approximate 1:50 ratio has become a rule of thumb in TB epidemiology. However, difficulties using this method arise because the rule was established from only 6 studies of incidence, prevalence, and mortality,[14] the ratio is expected to increase as TB incidence declines due to chemotherapy,[28] it is likely to be affected by rates of HIV, and there are numerous problems in interpreting tuberculin survey results.[29] Since the validity of the 1:50 rule is in question, we checked its usefulness with a mathematical model developed to forecast the impact of TB control.[28] Based on computer simulation results, we chose to use the 1:50 ratio (range, 35-65) where no more than 5% of TB cases had HIV infection.

Prevalence of Infection

Having estimated ARI directly (tuberculin surveys) or indirectly (back-calculated from incidence using equation 4), we calculated the proportion, p, of the population infected with MTB. In the simplest case, where ARI has been constant through time and human survivorship is roughly constant with age, $p \approx (L-[1-e^{-ARI.L}])/(ARI.L)$, where L is life expectancy.[30] This is easily modified for the case where risk of infection has been declining through time. These are approximate calculations of p because (1) estimates of ARI for 1997 are generally imprecise; (2) the rate of ARI decline has rarely been measured accurately and may not have been constant through time; and (3) mortality rate varies with age, more so in developed countries. More sophisticated calculation methods will only be justified by availability of better data.

The best data are for industrialized countries, such as the Netherlands, United States, and Japan, where TB in-

cidence has been in decline (>6% per year) for several decades. For these 3 countries, more refined age-structured models have been used to estimate infection rate.[31-33] We interpolated between the results of these analyses to estimate infection rate in other industrialized countries or regions (western Europe, North America, Australia and New Zealand) and in Caribbean islands, in preference to the method mentioned earlier.

TB AND HIV

The prevalence of MTB infection, *p*, has become especially important in countries with high HIV infection rates because those who are coinfected are at high risk of developing TB.[34] The HIV prevalence in adults and children in 1997 by country has been estimated by the Joint United Nations Programme on HIV/AIDS (UNAIDS) and WHO,[35] and we have used their estimates throughout. A crude estimate of MTB/HIV coinfection prevalence can be obtained from the product of MTB and HIV prevalences in the whole population. The HIV prevalence in all TB cases has been taken from various sources, particularly the US Census Bureau's *HIV/AIDS Surveillance Database, January 1997*.[36]

Parameters having the same values for all countries are given in Table 1. Country-specific values of all other parameters are listed in Appendix 2. These are, for smear-positive and smear-negative patients in DOTS and non-DOTS programs, fractions of patients untreated and treated in different programs, and CFRs. They also include duration of illness, proportion of smear-positive cases notified, ARI, percentage change in ARI per year, and prevalence of smear-positive disease.

With these input data, and using equations 1 through 4, we estimated the values of 11 TB indicators for each country, including incidence (all forms), incidence of smear-positive disease, prevalence (all forms), prevalence of smear-positive disease, prevalence of infection, deaths, CFR, fraction of TB cases infected with HIV, fraction of persons with MTB/HIV coinfection, case detection rate (all forms), and case detection rate (smear-positive disease).

Uncertainty Analysis

Multivariate uncertainty and sensitivity analyses were used to evaluate magnitude and causes of error surrounding estimates of incidence, prevalence, and mortality. For the 22 highest-incidence countries (estimated to have 80% of all new cases), we assigned lower and upper bounds, as well as point estimates, to all parameters (Appendix 4a). To fix these bounds, we used the literature on TB natural history (eg, to assess variation in the fraction of new cases that is smear-positive), confidence limits on point estimates calculated from disease prevalence surveys, and alternative estimates from secondary sources of data (eg, incidence estimated from ARI and notification data). For each country, we assumed triangular distributions for parameter values, with the apex at the most likely value and lower and upper bounds fixing the width of the base. One thousand Monte Carlo simulations were done using Palisade@Risk software (Palisade Corp, Newfield, NY). The 5th and 95th percentiles were used as lower and upper bounds for incidence, prevalence, and deaths.

Software for Estimation

Calculations underpinning the 3 methods of estimation (based on notifications, risk of infection, and prevalence of disease) were arrayed on 3 templates using Microsoft Excel (Microsoft Inc, Redmond, Wash). One template was chosen for each country and calculations carried out with country-specific data. Copies of spreadsheets for all countries are available from the authors.

Consensus

Agreement was reached in 3 steps. First, most of the 86 participants (from more than 40 countries) attended regional workshops. At the workshops, methods were presented, discussed, and agreed on, and preliminary calculations carried out for the major endemic countries within each region. The second round of analyses was done by the principal authors on spreadsheets in standard format using all available data as appropriate. Third, each participant was sent copies of data, assumptions, analyses, and results from round 2 for the relevant countries. These were reviewed and adjusted if new information had become available, and final agreement was reached with WHO staff.

RESULTS

As expected, data were highly variable in type, quality, and availability. In Appendix 1 (parts a, b, c, d, e, and f), for each country, the types of data obtained and sources are given. In Appendix 2, the input data used for estimates for each country are provided. The estimates were based on case notifications for 141 countries, particularly in Africa, the Americas, and Europe (Appendix 2a); on tuberculin surveys for 24 countries, notably in North Africa and the Middle East (Appendix 2b); and on prevalence surveys for 14 countries, mainly in Southeast Asia and the Western Pacific region (Appendix 2c).

Incidence, prevalence, and deaths for 1997 were calculated as numbers and rates (percentages or per 100 000 persons). TABLE 2 summarizes the results for various parts of the world by WHO region. TABLE 3 presents results for the 22 highest-incidence countries. The results for all countries are shown in Appendixes 3a, 3b, 3c, 3d, 3e, and 3f, and FIGURE 1 and FIGURE 2, including incidence and prevalence of smear-positive disease, prevalence of infection, percentage of cases that were HIV-positive, and rates of MTB/HIV coinfection.

A total of 7.96 million new cases of TB in 1997 were estimated, including 3.52 million (44%) cases of infectious pulmonary disease (smear-positive) (Table 2). In that year, 1.87 million people died of TB. The average CFR was 23% but it exceeded 50% in some African countries with high HIV rates. Point prevalence was 16.2 million cases, of which 7.1 million were smear-positive (the majority of infectious

cases). A total of 1.86 billion people were infected with TB, or 32% of the world population, while 10.7 million people had MTB/HIV coinfection (0.18% of the world population), and 640 000 incident TB cases (8%) were associated with HIV infection. Less than half (42%) of all estimated TB cases and about one third (37%) of smear-positive cases, were reported to WHO.

Uncertainty analysis showed that the top 22 TB countries had 6.36 million new cases, ranging from 5.0 million to 8.9 million (Appendix 4b), ie, these countries might have 21% fewer, or 40% more cases, though we are more confident about results for Brazil (–7% to 21%) and Peru (–6% to 9%). By assuming that errors for estimates for the top 22 countries apply globally (thereby overestimating error), we calculate that the total number of new cases in 1997 was in the range of 6.3 million to 11.1 million cases and global prevalence was between 12.1 million and 22.5 million cases. Mortality could be 23% lower or 47% higher, which places total deaths in the range of 1.4 million to 2.8 million. Thus, highest and lowest estimates are separated by a factor of roughly 2 for incidence, prevalence, and deaths.

Incidence estimated via case notifications (method 1, 12 of 22 high-burden countries) is most sensitive to variation in the case detection rate. Sensitivity analysis showed that death estimates were most influenced by the case detection rate when using method 1 (5 countries, eg, India, Brazil), except where HIV rates were high. Then the HIV infection rate in TB patients was the dominant source of uncertainty (5 countries, eg, South Africa, Ethiopia). Estimates of all indicators (incidence, prevalence, deaths) derived from ARI data (method 2, Afghanistan, Myanmar, Vietnam) depended primarily on *S* and ARI, in that order. Indicators derived from prevalence data (method 3) were most sensitive to the duration of illness under non-DOTS treatment (China, Pakistan, the Philippines, Thailand), or to prevalence itself (Indonesia, Bangladesh).

The 1997 incidence rate per capita was highest in sub-Saharan Africa (259 per 100 000 persons). The Southeast Asian region accounted for the largest number of cases (2.95 million) followed by the Western Pacific region (1.96 million). The European and American regions had the fewest cases, both total and per capita. Africa had by far the highest fraction of persons with MTB/HIV coinfection (1.2%) and the highest fraction of TB cases that were HIV-positive (32%, Table 2). These high rates of HIV partly explain the high CFR in Africa of 34%. Case detection rates were highest in the Americas and Europe, and low in North Africa and the Middle East (WHO's eastern Mediterranean region) and in Southeast Asia. Both of the latter 2 regions reported only 1 out of 4 or 5 estimated smear-positive cases.

The relatively high average incidence rate in Africa south of the Sahara

Table 2. Estimates of TB Burden by WHO Region*

		Rates†										
WHO Region	Population, Thousands	Incidence	SS+ Incidence	Prevalence	SS+ Prevalence	Infection Prevalence, %	TB Death Rate	CFR, %	HIV-Positive Cases, %	TB/HIV	CDR All, %	CDR SS+, %
Africa	611 604	259	108	384	168	35	88	34	32	1194	31	36
The Americas	792 330	52	23	72	32	18	8	16	6	64	60	75
Eastern Mediterranean	475 415	129	58	258	115	29	30	23	3	23	21	19
Europe	870 386	51	23	73	33	15	7	14	2	10	80	57
Southeast Asia	1 458 274	202	91	524	234	44	48	24	2	162	44	28
Western Pacific	1 641 179	120	54	230	96	36	22	18	0	19	43	43
Total	5 849 188	136	60	277	121	32	32	23	8	183	42	37

		Numbers, Thousands									
		Incidence	Notified Cases, All	SS+ Incidence	Notified Cases, SS+	Prevalence	SS+ Prevalence	Infection Prevalence	TB Death	HIV-Positive Cases	TB/HIV
Africa	611 604	1586	499	662	241	2351	1027	211 318	540	515	7302
The Americas	792 330	411	247	182	137	567	253	142 263	66	25	510
Eastern Mediterranean	475 415	615	127	276	53	1226	547	138 010	141	16	107
Europe	870 386	440	354	197	113	632	284	130 235	64	10	84
Southeast Asia	1 458 274	2948	1311	1321	368	7634	3410	646 385	705	64	2364
Western Pacific	1 641 179	1962	835	882	376	3774	1581	587 670	355	9	307
Total	5 849 188	7962	3372	3521	1287	16 184	7102	1 855 880	1871	640	10 675

*TB indicates tuberculosis; WHO, World Health Organization; incidence, new cases; SS+, sputum smear-positive; prevalence, all forms (new and existing) of cases; infection prevalence, percentage of population infected with *Mycobacterium tuberculosis* (MTB); CFR, case fatality rate among TB cases; TB/HIV, MTB/HIV coinfection; CDR all, all-forms TB case detection rate (all-forms TB case notifications/estimated all-forms incident TB); and CDR SS+, smear-positive case detection rate (SS+ case notifications/estimated SS+ incident TB).
†Data are given as rate per 100 000 persons unless otherwise indicated.

Table 3. Estimates of TB Burden in the 22 Highest-Incidence Countries*

Rank	Country	WHO Region	Population, Thousands	Rates†										
				Incidence	SS+ Incidence	Prevalence	SS+ Prevalence	Infection Prevalence, %	TB Death Rate	CFR, %	HIV-Positive Cases, %	TB/HIV	CDR All, %	CDR SS+, %
1	India	SEAR	960 178	187	84	505	227	44	46	24	3	188	63	34
2	China	WPR	1 243 738	113	51	219	91	36	21	18	0	12	30	30
3	Indonesia	SEAR	204 323	285	128	786	350	49	68	24	1	12	4	7
4	Bangladesh	SEAR	122 013	246	111	508	221	46	55	23	0	8	21	25
5	Pakistan	EMR	143 831	181	81	405	180	40	44	25	1	18	0	0
6	Nigeria	AFR	118 369	214	93	383	166	36	58	27	14	702	7	10
7	Philippines	WPR	70 724	314	141	693	310	47	68	22	0	16	94	83
8	South Africa	AFR	43 336	392	159	604	263	38	166	42	45	2540	62	80
9	Russian Federation	EUR	147 708	106	48	163	73	18	17	16	1	5	78	60
10	Ethiopia	AFR	60 148	260	109	367	161	36	82	31	30	1543	37	24
11	Vietnam	WPR	76 548	189	85	289	102	44	26	14	1	50	59	82
12	Democratic Republic of Congo	AFR	48 040	269	114	397	175	36	81	30	25	706	0	0
13	Brazil	AMR	163 132	75	33	115	51	25	11	15	5	91	68	80
14	Tanzania	AFR	31 507	308	127	396	173	23	99	32	37	1026	48	55
15	Kenya	AFR	28 414	297	122	371	161	36	99	33	40	2013	47	55
16	Thailand	SEAR	59 159	142	63	305	135	43	29	21	10	561	36	36
17	Myanmar	SEAR	46 765	171	77	348	146	41	40	24	5	384	21	27
18	Afghanistan	EMR	22 132	333	150	753	342	34	104	31	5	0	2	2
19	Uganda	AFR	20 791	320	128	451	195	34	146	46	50	1532	42	65
20	Peru	AMR	24 367	265	119	288	129	44	30	11	2	131	65	95
21	Zimbabwe	AFR	11 682	538	207	626	264	36	283	53	65	4603	70	60
22	Cambodia	WPR	10 516	539	241	963	426	64	90	17	3	792	28	50
		Total	3 657 421	174	77	375	164	39	41	24	7	213	41	34

				Numbers, Thousands									
				Incidence	Notified Cases, All	SS+ Incidence	Notified Cases, SS+	Prevalence	SS+ Prevalence	Infection Prevalence	TB Death	HIV-Positive Cases	TB/HIV
1	India	SEAR	960 178	1799	1136	805	274	4854	2182	422 569	437	45	1804
2	China	WPR	1 243 738	1402	419	630	189	2721	1132	445 343	258	5	143
3	Indonesia	SEAR	204 323	583	22	262	19	1606	715	99 920	140	6	25
4	Bangladesh	SEAR	122 013	300	63	135	33	620	270	56 260	68	1	10
5	Pakistan	EMR	143 831	261	0	117	0	583	259	57 110	64	3	25
6	Nigeria	AFR	118 369	253	17	110	11	454	197	42 773	69	35	831
7	Philippines	WPR	70 724	222	208	100	83	490	219	33 523	48	1	11
8	South Africa	AFR	43 336	170	105	69	55	262	114	16 449	72	76	1101
9	Russian Federation	EUR	147 708	156	121	70	42	241	108	26 587	26	1	7
10	Ethiopia	AFR	60 148	156	59	66	16	221	97	21 471	49	47	928
11	Vietnam	WPR	76 548	145	85	65	54	221	78	33 592	20	1	39
12	Democratic Republic of Congo	AFR	48 040	129	0	55	0	191	84	17 140	39	32	339
13	Brazil	AMR	163 132	122	83	54	43	188	83	41 382	19	6	149
14	Tanzania	AFR	31 507	97	46	40	22	125	54	7277	31	36	323
15	Kenya	AFR	28 414	84	40	35	19	106	46	10 156	28	34	572
16	Thailand	SEAR	59 159	84	30	37	13	180	80	25 175	17	8	332
17	Myanmar	SEAR	46 765	80	17	36	10	163	68	19 074	19	4	179
18	Afghanistan	EMR	22 132	74	1	33	1	167	76	7431	23	4	0
19	Uganda	AFR	20 791	66	28	27	17	94	41	7120	30	33	318
20	Peru	AMR	24 367	65	42	29	27	70	32	10 795	7	1	32
21	Zimbabwe	AFR	11 682	63	44	24	15	73	31	4188	33	41	538
22	Cambodia	WPR	10 516	57	16	25	13	101	45	6738	9	2	83
		Total	3 657 421	6367	2583	2824	956	13 728	6011	1 412 074	1506	421	7791

*These countries are ranked by number of cases and are positioned in a list of the 22 highest-incidence countries on the basis of numbers of new cases. TB indicates tuberculosis; WHO, World Health Organization; incidence, new cases; SS+, sputum smear-positive; prevalence, all forms (new and existing) of cases; infection prevalence, percentage of population infected with *Mycobacterium tuberculosis* (MTB); CFR, case fatality rate among TB cases; TB/HIV, MTB/HIV coinfection; CDR all, all-forms TB case detection rate (all-forms TB case notifications/estimated all-forms incident TB); CDR SS+, smear-positive case detection rate (SS+ case notifications/estimated ss+ incident TB); SEAR, Southeast Asian region; WPR, Western Pacific region; EMR, Eastern Mediterranean region; AFR, African region; EUR, European region; and AMR, American region.
†Data are given as rate per 100 000 persons unless otherwise indicated.

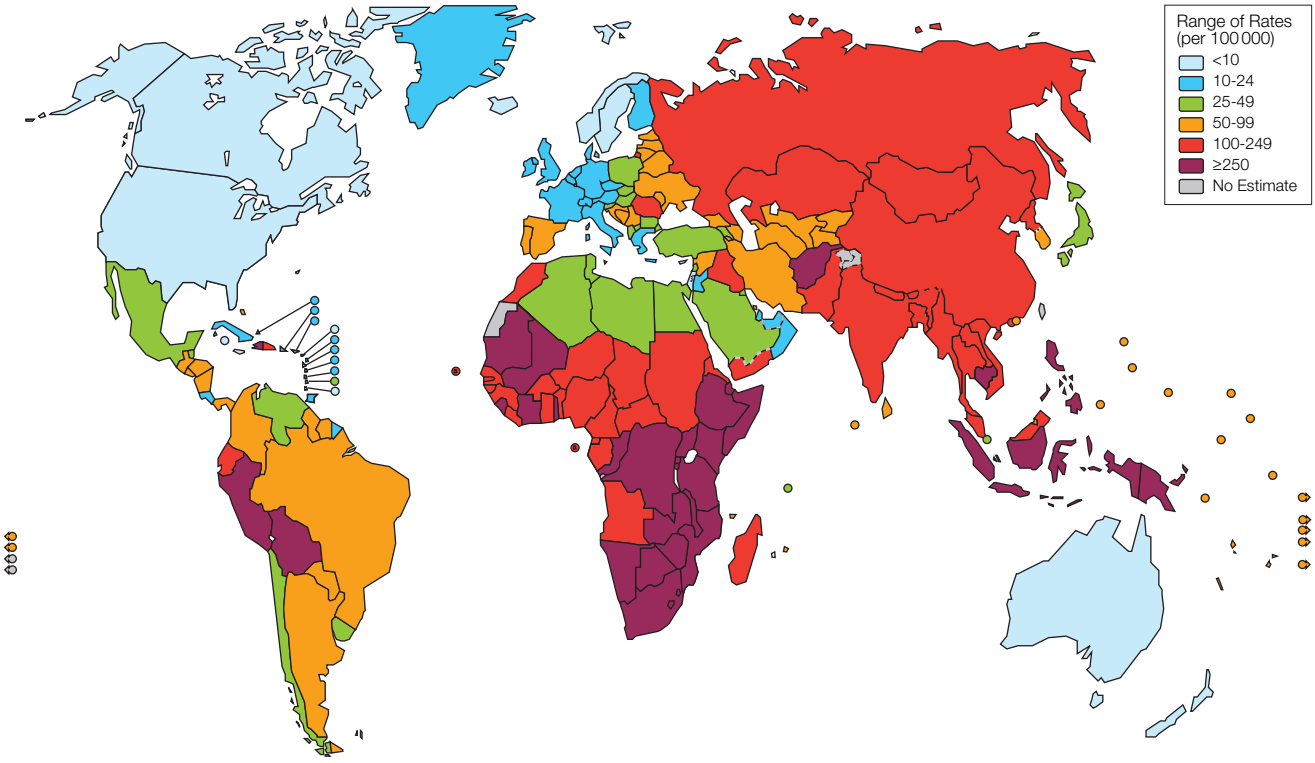
(Table 2) is influenced by very high rates in some southern African countries. Of the 10 countries with the highest incidence rates per capita, 9 were in Africa (Cambodia is the exception). They include Botswana, Namibia, South Africa, Zambia, and Zimbabwe, and all have incidence rates of about 400 per 100 000 persons or more. These high rates were associated with high MTB/HIV coinfection rates (more than 2.5% in the general population). East African and coastal West African countries had intermediate incidence rates in the range of 250 to 300 per 100 000 persons, while lower rates (up to about 250 per 100 000 persons) are found inland in West and Central Africa (Burkina Faso, Cameroon, Central African Republic, Chad, Niger).

Not surprisingly, the Americas were the most epidemiologically diverse of the 6 regions (Appendix 3). Incidence rates in major countries varied from less than 10 (Canada, the United States) to more than 250 per 100 000 persons (Bolivia, Haiti, Peru), and the prevalence of MTB/HIV coinfection varied from almost 0% to more than 1% in Haiti. The greatest numbers of cases were in Brazil and Peru, the 2 South American countries that are represented in the top 22 (Table 3).

More than 60% of the new cases in North Africa and the Middle East were in 3 countries: Pakistan (42%), Afghanistan (12%), and Sudan (9%). Afghanistan reported only 2% of the estimated total number of cases, and Pakistan did not report any cases in 1997. The high incidence rate in Djibouti (668 per 100 000 persons) is due to many TB cases coming from neighboring countries solely for TB treatment. We have included these nonnationals in our estimate because they are also included in the case notifications reported to WHO. Compared with the rest of the region, a relatively high proportion of cases (15%) had HIV infection in Djibouti and Sudan.

Europe remains divided between west and east in terms of TB rates. Incidence rates in western Europe were below 25 per 100 000 persons in 1997, except for Spain (61 per 100 000) and Portugal (55 per 100 000). In eastern Europe, rates were more than 30 per 100 000, except in the Czech Republic (20 per 100 000), and more than 70 per 100 000 in Romania, the Russian Federation, and the 5 republics of central Asia. Independently estimated incidence and CFRs were only weakly correlated across Europe. The explanation is that, in low incidence countries of western Europe, a high proportion of cases occur in elderly people who die of other causes while undergoing TB treatment. Eastern Euro-

Figure 1. Estimated Per Capita Incidence Rates of Tuberculosis (All Forms) by Country in 1997



No estimates are available for disputed territories Taiwan, Kashmir, and Western Sahara. Estimates for French Guyana and Guadeloupe are included with France, following their system of case notification. Circled arrows represent islands off the map. Left, top to bottom: Cook Islands, French Polynesia, Pitcairn Island, Niue. Right, Tokelau, Samoa, American Samoa, Wallis and Futuna, Tonga. Printed with permission from the World Health Organization.

pean countries have a higher incidence, but mortality is markedly reduced by drug therapy, though patients receiving inadequate regimens may remain chronically ill.

Southeast Asia contained 3 of the 4 highest-burden countries: India (1.8 million new cases in 1997), Indonesia (583 000 cases), and Bangladesh (300 000 cases). Thailand and Myanmar also ranked among the top 22 (Table 3). The smear-positive case detection rate was low in all these countries, especially Indonesia (7%). While MTB/HIV coinfection rates were highest in Africa, more people were coinfected in India (1.8 million in 1997) than in other countries.

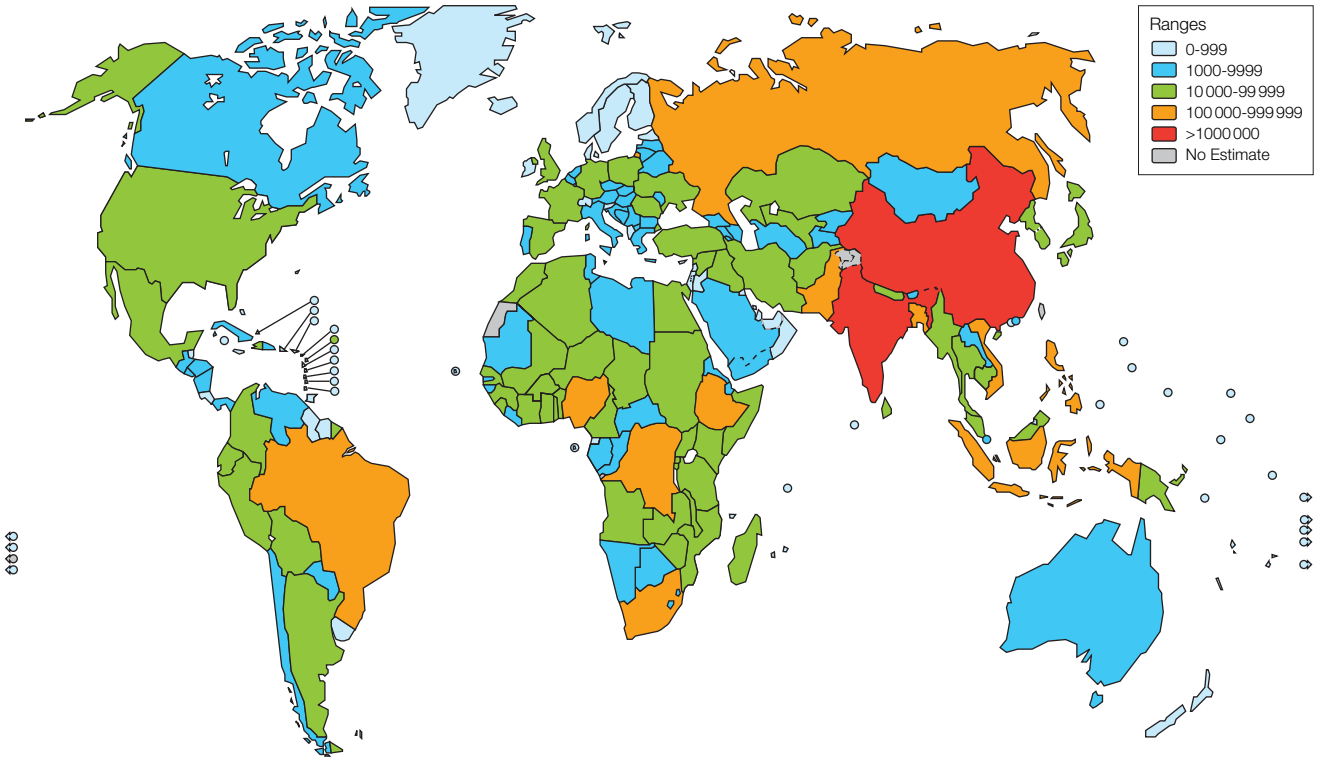
The Western Pacific region is dominated by China, which in 1997 supported three quarters (76%) of the region's population and a similar fraction of TB cases (1.40 million [72%]). Next in importance were the Philippines (219 000 cases) and Vietnam (145 000 cases) followed by Cambodia, Korea, Japan, and Malaysia. Less than 1% of all TB cases and deaths in the region were associated with HIV. Cambodia, where 3% of cases are linked to HIV, departed most markedly from the regional average.

COMMENT

This country-by-country analysis has yielded a relatively high number of incident TB cases globally (7.96 million) compared with previous estimates for 1990.[1-5] In carrying out this study, we have had to work with the considerable uncertainties that surround estimates for many countries. These uncertainties explain some of the differences between present results and previous ones. However, our new estimate of worldwide incidence probably reflects real and marked increases in human population size and HIV infection rates, and changes in control practices occurring since 1990.

The highest incidence of HIV infection is in Africa; Kenya and Zimbabwe now rank among the top 22 TB-endemic countries, and South Africa, Ethiopia, and Tanzania have moved further up the list.[6] Tuberculosis control has improved substantially in some countries but deteriorated in others. Breakdown of control in some countries has led to obvious increases in reported cases (eg, the Russian Federation), but improvements elsewhere have not yet caused convincing declines in incidence (eg, Peru, Morocco).[6,7] If global TB incidence is increasing, the rise appears roughly consistent with the forecast of 8.4 million new cases in the year 2000[28]; the higher prediction of 10.2 million cases[1] now seems less likely.

Figure 2. Estimated Numbers of Tuberculosis Cases (All Forms) by Country in 1997



No estimates are available for disputed territories Taiwan, Kashmir, and Western Sahara. Estimates for French Guyana and Guadeloupe are included with France, following their system of case notification. Circled arrows represent islands off the map. Left, top to bottom: Cook Islands, French Polynesia, Pitcairn Island, Niue. Right, Tokelau, Samoa, American Samoa, Wallis and Futuna, Tonga. Printed with permission from the World Health Organization.

While incidence is high, our estimate of the TB death rate in 1997 (32 per 100 000) is lower than some previous estimates. This reflects the growing conviction among TB experts that CFRs have previously been overestimated. Inferior drug treatment may not definitively cure patients or significantly reduce transmission, but it will often prevent death. We have also assumed lower CFRs for smear-negative disease (average, 20%) than some previous authors.[2] If there has been any real reduction in case fatality globally or in the major endemic countries since 1990, this analysis is not sensitive enough to detect it.

The proportion of TB cases with HIV infection has certainly been rising during the 1990s. Our global 1997 estimate of 8% is 2 to 10 times greater than the 1990 estimates.[1,3] However, it appears not to have increased as fast as in previous forecasts of 8.4% for 1995 and 13.8% for 2000.[1] The burden of HIV per capita is outstandingly high in sub-Saharan Africa (32% of TB cases infected), though there is great variation among African countries (0%-75%). However, the largest number of coinfected individuals resides in India.

We would like to be able to call the results presented here "best estimates" in a formal statistical sense. However, given the poor quality of much of the underlying data, they are better thought of as plausible estimates. They represent a consensus among many TB experts around the world but will certainly be subject to improvement when better data are available. The uncertainty surrounding incidence and mortality estimates is large: uncertainty analysis for the 22 highest-burden countries suggests that global incidence and prevalence could be 21% lower or 40% higher. There could be 23% fewer or 47% more deaths. The difference between lower and upper estimates is a factor of about 2. Percentage errors on estimates from low-burden countries will be lower, but these smaller errors attached to lower incidence estimates will have little impact on uncertainty on a global scale.

There are various ways to improve data quality, and each has its merits. Special surveys of the prevalence of disease or infection can provide accurate estimates of the TB burden in selected countries. For example, a recent disease prevalence survey in the Philippines[37] has greatly improved understanding of the scale of the TB problem there. But good prevalence surveys of both infection and disease are scarce, and resources are not available to survey the entire world. On top of this, surveys of MTB infection prevalence have become harder to interpret in the presence of HIV. The rule of thumb that smear-positive incidence increases by 50 per 100 000 persons per year for every 1% increase in ARI[18] does not hold in areas where HIV infection rates are high and where TB incidence is in rapid decline.[28]

The only way to improve data quality globally is to increase case notification reliability, ie, by improving TB surveillance. In this analysis, incidence estimates for most countries (141 of 179 countries and island groups) were obtained by dividing case notification rate by estimated case detection rate (equation 1). In general, this method is less accurate where the case detection rate is low, and the case detection is thought to be less than 50% (all forms or smear-positive cases) for about half of the top 22 countries (Table 3). The case detection rates for many countries are probably lower than estimated here because notifications include cases reported more than once. Moreover, certain forms of TB are difficult to diagnose, especially smear-negative disease, even when facilities are ideal. But the error for the case detection rate could be reduced for many countries, perhaps to within 10%. Reaching this goal would bring significant benefits because good TB surveillance often encourages good TB control, and routinely collected data would give a more accurate picture of the global impact of control efforts.

Web Site Posting: The appendixes referred to in this article are available at http://www.jama.com.

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It is not the answer that enlightens, but the question.
—Eugène Ionesco (1912-1994)