Chapter 15

Epidemiological Burden of Tuberculosis in Developing Countries

Diana M. Castañeda-Hernández and
Alfonso J. Rodriguez-Morales

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/53363

1. Introduction

Tuberculosis (TB) is an infectious disease caused by different species of the genus *Mycobacteria*. Together with human immunodeficiency virus infection (HIV)/Acquired Immunodeficiency Syndrome (AIDS) and malaria, tuberculosis is one of the biggest killers in the Word (Rodríguez-Morales AJ et al 2008, Murcia-Aranguren MI et al 2001). Human disease is usually caused by *Mycobacterium tuberculosis*, also know as the Koch's bacilli (Figure 1), which can affect any organ or tissue in the body, and in some cases due to *M. bovis* (Castañeda-Hernández DM & Rodríguez-Morales AJ 2012a). Although this, pulmonary disease, with their particular hallmarks such as occurrence of cough with expectoration lasting more than 15 days, is the main corporal area affected by this mainly tropical pathogen (Rodríguez-Morales AJ et al 2008; Castañeda-Hernández DM & Rodríguez-Morales AJ 2012). In such cases, previous to a microbiological diagnosis, individuals in such state are so-called respiratory symptomatic.

Besides those symptoms/signs, disease can be manifested with hemoptisis, fever, night sweating, general malaise, thoracic pain, anorexia and weight lost. This disease is still a significant public health problem due to is highly transmissibility, but is highly potentially preventable and treatable condition (Curto et al. 2010, Dim et al. 2011, Orcau et al. 2011, Marais & Schaaf 2010, Glaziou et al. 2009). Even more, in the context of HIV and newer immunosuppressive conditions mycobacterial diseases emerge as public health threat in the World (Vargas et al. 2005).

Tuberculosis is a human threat and still a significant public health problem in the World, but particularly in developing countries. Today, together with the burden of infection due to

Human Immunodeficiency Virus (HIV), this coinfection drives most of the tuberculosis morbidity and mortality in many regions (e.g. Africa) and makes more complicated its control and reduction in many terms. According to the World Health Organization (WHO) Global Tuberculosis Control Report 2011 (the most important and official document regard the epidemiology and other aspects of TB worldwide), in 2010, there were 8.8 million (range, 8.5–9.2 million) incident cases of TB, 1.1 million (range, 0.9–1.2 million) deaths from TB among HIV-negative people and an additional 0.35 million (range, 0.32–0.39 million) deaths from HIV-associated TB (World Health Organization 2011). Important new findings at the global level are: a) the absolute number of TB cases has been falling since 2006 (rather than rising slowly as indicated in previous global reports); b) TB incidence rates have been falling since 2002 (two years earlier than previously suggested); c) Estimates of the number of deaths from TB each year have been revised downwards; d) In 2009 there were almost 10 million children who were orphans as a result of parental deaths caused by TB (World Health Organization 2011).

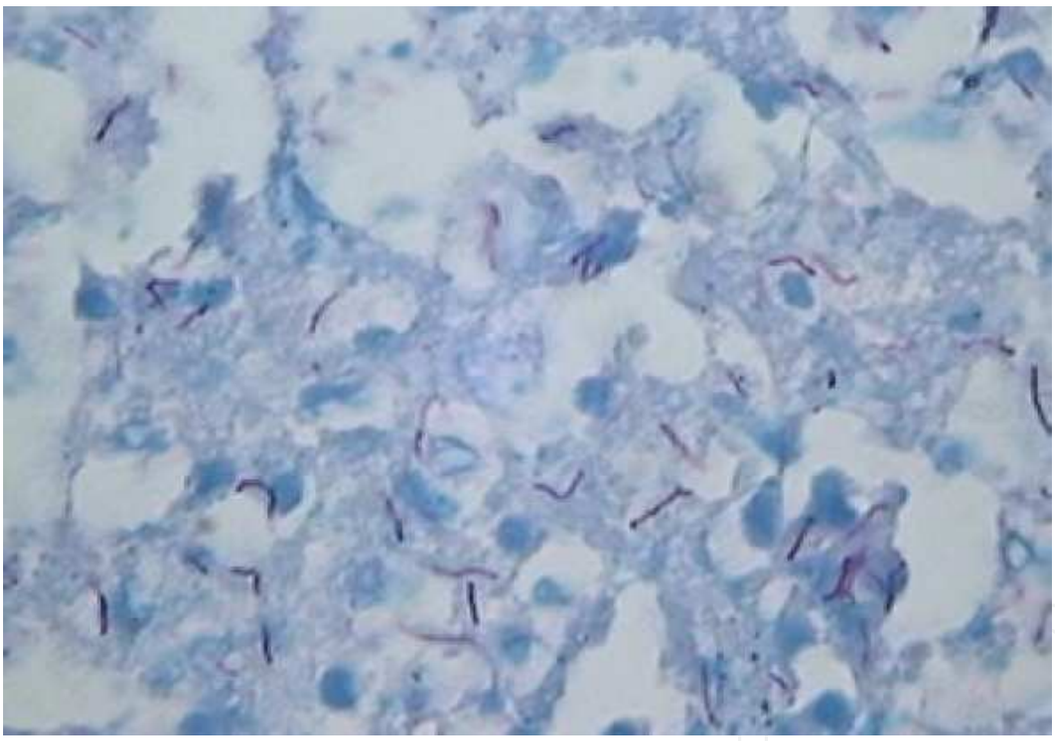

Figure 1. Acid fast-bacilli in a Ziehl-Neelsen stain from a sample of a patient with pulmonary TB (400 X) (Fernández M & Dickson González SM 2007).

Epidemiology of tuberculosis can be influenced by multiple not only clinical factors, but also demographical, geographical and social aspects at local or national levels, as the development of the country (Rodríguez-Morales AJ & Castañeda-Hernández DM 2012), currently measured by indicators such as the Human Development Index (HDI). Finding there, that negative relationships between both morbidity and mortality due to tuberculosis and HDI exist, with better HDI levels lower morbidity and mortality due TB is found (Rodríguez-Mo-

http://dx.doi.org/10.5772/53363

rales AJ & Castañeda-Hernández DM 2012). As has been reported with other diseases with high prevalence in developing countries, burden of diseases such as TB can be an impediment in achieving the Millennium Development Goals (Franco-Paredes et al 2007b). Then strategies to reduce its impact and improving the health of populations, most of the times neglected, should be implemented (Franco-Paredes et al 2007a).

In developing countries another aspect influencing this is the limited research on tuberculosis that usually is made (Castañeda-Hernández DM et al 2012a). For example scientific production on TB in Colombia is low, not just comparing it with developed countries (USA, 4.08 articles/100,000 hab.) but also with others in Latin America with even lower TB incidence such as Chile (19 cases/100,000 hab.) but with a better productivity 2.19 times higher (1.09 articles/100,000 hab.). A higher promotion of research, beginning in undergraduate studies, better interaction between public and private organizations, as well more academic and international cooperation, would allow to decrease those gaps, increase scientific publication and let that the application of that generated knowledge in the same country contribute to improve the TB epidemiology and different aspects of disease (Castañeda-Hernández DM & Rodríguez-Morales AJ 2012a).

Beyond its epidemiology, particularly mostly due to pulmonary disease (Figure 2), other important forms of disease represent also a significant burden in the World. When the infection affects organ other than the lung is called extrapulmonary TB. The most common form of this disease is at the pleura, followed by the lymphatic nodes. Extrapulmonary TB includes various manifestations according to the affected organ. Prognosis and time to develop disease also can vary according to the affected organ (Castañeda-Hernández DM & Rodríguez-Morales AJ 2012a).

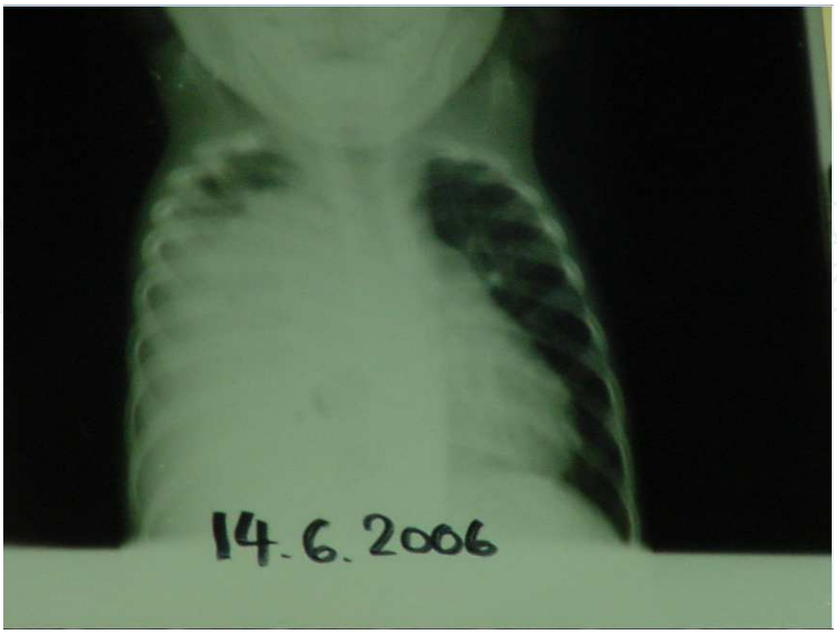

Figure 2. Pulmonary TB in a very young child from Tanzania, Africa (taken by Rodriguez-Morales AJ).

Disease can ranges a spectrum that can begin from a latent infection or reactivation slowly evolving into a focal or whole spread and involvement of multiple organs, which makes it difficult to diagnosis by clinicians and health care workers, who many times could not identify it timely. One of the most severe forms of extrapulmonary TB is the meningitis (TB meningitis), which occurs as a result of hematogenous spread of bacilli into the subarachnoid space. This is known as a complication of primary TB and may occur years later as an endogenous reactivation of a latent tuberculosis or as a result of exogenous reinfection (Glaziou et al. 2009, Hoek et al. 2011, Galimi 2011, Garcia-Rodriguez et al. 2011). Currently in the case of latent TB developing countries usually counts only with the PPD to diagnose this condition. However, recently new alternatives have risen for the diagnosis in these cases, using IFNγ release assays (IGRAs) to diagnose latent TB infection (LTBI). This is actually proposed for public health purposes in developing countries (Castañeda-Hernández DM et al 2012d).

Tuberculosis is a complex disease in terms of the multiple factors that are involved in its occurrence and persistence in the human societies. In first place there are factors associated with the bacillus (viability, transmissibility and virulence), with the host as a biological individual (immune status, genetic susceptibility, duration and intensity of exposure) as well, at the bacillus-host interaction (place of affection, severity of illness) (Castañeda-Hernández DM & Rodríguez-Morales AJ 2012a).

At a second, clinical level, the occurrence of pulmonary tuberculosis undiagnosed or untreated, overcrowding, malnutrition, immunosuppresion from any cause (HIV infection, use of immunosuppressive drugs, diabetes, cancer, chronic renal failure, silicosis, alcoholism and drug addiction), are also important factors (Castañeda-Hernández DM & Rodríguez-Morales AJ 2012a). In developing countries there are also multiple epidemiological contexts where TB can be highly prevalent in comparison with general population, such as in prisons, among homeless persons and indigenous individuals (Castañeda-Hernández DM et al 2012b, Castañeda-Hernández DM & Rodríguez-Morales AJ, 2012b).

At community public health interventional level, protective factors include the BCG (Bacille Calmette Guerin) vaccine, applied in developing countries, which provides protection before exposure and prevent severe infection forms, especially in infants and young children, reaching up to 80% of protection against the development of forms of the disease such as meningeal and miliary TB (Garcia-Rodriguez et al. 2011, Garg 2010, Black et al. 2003, Francis et al. 2002, Arbelaez et al. 2000, Ginsberg 2000).

Additional to those clinical implications, changes in the susceptibility of the etiological agent to the therapy used drugs has imposed more challenges in the management of TB. The magnitude of problem with TB now lies in the fact that one third of the world population is infected by *Mycobacterium tuberculosis*. Even in the 21st century, TB kills more people than any other infective agent. This, then, occurs in part as a result of a progressive decrease in its susceptibility to anti-TB drugs or resistance emergence. Cases of resistant TB, defined by the recommendations of the World Health Organization (WHO) as primary, initial, acquired multidrug resistant (MDR-TB) or extensively drug resistant TB (XDR-TB) are emerging in

different areas of the World (Torres et al. 2011, Solari et al. 2011, Chadha et al. 2011, Arenas-Suarez et al. 2010, Ferro et al. 2011, Martins 2011, Robledo et al 2008).

The development of resistance in TB may result from the administration of mono-therapy or inadequate combinations of anti-TB drugs. A possible role of health care workers in the development of multi drug-resistant TB is very important. Actually, multi drug-resistant TB is a direct consequence of mistakes in prescribing chemotherapy, provision of anti-tuberculosis drugs, surveillance of the patient and decision-making regarding further treatment as well as in a wrong way of administration of anti-TB drugs. The problem of XDR-TB in the world has become very alarming. Only adequate treatment according to directly supervised short regiment for correctly categorized cases of TB can stop the escalation of MDR-TB or XDR-TB, which is actually, in large magnitude, a global threat in the 21st century (Torres et al. 2011, Solari et al. 2011, Chadha et al. 2011, Arenas-Suarez et al. 2010, Ferro et al. 2011, Martins 2011, Robledo et al 2008).

Another important issue in TB is the social component, related to a complex background and multiple interacting factors that internally and externally affect individuals affected by the disease, which still represents a significant stigma in many communities in the World. Given this setting, TB approach is complex and requires not only medical but also psychological and especially sociological approaches in order to improve its management from a collective medicine perspective as well better acceptability by non-affected people surrounding infected individuals at their communities or neighborhoods. In this way, programs approaching taking all these considerations in count will benefit with better strategies that allow good interactions between social actors involve in the complex social matrix in which sometimes TB can be present at societies. Taking advantage from this, regular activities, such as proper diagnosis and treatment would be achieve in a more efficient way (Murray et al. 2011, Santin & Navas 2011, Juniarti & Evans 2011).

One challenge in the current context of TB particularly in developing countries is the access to reliable diagnostic tests (Castañeda-Hernández DM et al 2012d), particularly those than allow to confirm species diagnostics as well to identify those isolates that are not fully susceptible to antimicobacterial first line drugs. However, today many diagnostic tests have been developed, but many of them are only used routinely in developed countries (e.g. IGRAs and molecular biology-based tests) (Castañeda-Hernández DM et al 2012d). Although is clear that DOTS (directly observed treatment strategy, short-course) programmes have contributed in the successful treatment of TB, particularly because this strategy includes six major components that are: (i) pursue high-quality DOTS expansion and enhancement; (ii) address TB/HIV, MDR-TB (multi-drug resistant TB), and the needs of poor and vulnerable populations; (iii) contribute to health-system strengthening based on primary health care; (iv) engage all care providers; (v) empower people with TB, and communities through partnership; and (vi) enable and promote research; it is necessary to increase its coverage and usefulness particularly in those highly TB prevalent countries in the developing World in order to achieve the goals that have been established for 2015 in the Global Plan to Stop TB (2011-2015) of the World Health Organization and the Stop TB Partnership (Castañeda-Hernández DM & Rodriguez-Morales AJ. 2012a). The epidemiological burden of

TB in developing countries can be measured directly from different global and national indicators and estimators, however, those mainly to be addressed should be incidence, prevalence, mortality, MDR-TB incidence, XDR-TB (extensively drug-resistant TB) incidence, case notifications, treatment outcomes and case detection rates. In this chapter, such topics are furtherly revised and prepared in the setting of highest available evidence (evidenced-based public health) and epidemiological data, including a detailed analysis according to some highly endemic countries sources in different developing regions, suggesting also new strategies for control as well providing updated information on epidemiological tools relevant for TB in developing countries. Relevant new epidemiological settings will be also discussed, such as the importance of TB in homeless, indigenous, migrated and prison populations as has been suggested.

2. Tuberculosis in developing countries

Tuberculosis is a disease present, due the raise of HIV coinfection in most countries in the World. Until two to three decades ago, TB was decreasing in importance in the World and was predominantly endemic in developing countries. However after the origin of the AIDS pandemic in June 1981, TB has been increasing again in importance not only in these countries but also in those developed in North America and Europe. Besides this, the multiple problems that countries with a high burden of TB have to face are major in developing countries in Africa, Asia and Latin America, especially when this is also associated to other conditions and diseases, such as HIV, comorbidities, poverty and when living in resource-constrained areas where diagnosis and treatment is not prompt as in other areas.

In order to know the real burden of disease in developing countries is necessary that these make things well in epidemiology and public health regard TB. Recording and reporting of data is a fundamental component of care of patients with tuberculosis (TB) and control of the disease. Data recording and reporting is necessary to monitor trends in the TB epidemic at global, national and subnational levels; to monitor progress in the treatment of individual patients and groups (cohorts) of patients and ensure continuity of care when patients are referred between healthcare facilities; and to plan, raise funds for, implement and evaluate programmatic efforts to control TB, including forecasting the numbers of cases and the associated requirements for staffing, medicines and laboratory supplies; and analysing treatment outcomes (World Health Organization 2012).

Global burden of TB in the World is estimated in 8.8 million (range, 8.5–9.2 million) incident cases of TB (Table 1) for rates ranging 123.7 to 133.9 cases/100,000 pop. (Table 1); however this can be very different among the WHO Regions in the World, being higher in Africa where those estimates can reach 250.9 to 298.7 cases/100,000 pop. (Table 1). Rates of incidence are important because can show the real populational problem of the disease. For example in South East Asia there are more crude number of cases of TB, estimated in 3.5 million (range, 3.2–3.7 million) incident cases, however the incidence rates are quite lower than in Africa, reaching 177.0 to 204.7 cases/100,000 pop. (Table 1) (Figure 4).

http://dx.doi.org/10.5772/53363

		Incidence (cases)			Incidence rates (cases/100,000pop)		
Region	**Population**	**Best**	**Low**	**High**	**Best**	**Low**	**High**
Global burden	6,869,573,000	8,800,000	8,500,000	9,200,000	128.1	123.7	133.9
WHO African Region	836,970,000	2,300,000	2,100,000	2,500,000	274.8	250.9	298.7
WHO South-East Asia Region	1,807,594,000	3,500,000	3,200,000	3,700,000	193.6	177.0	204.7
WHO Eastern Mediterranean Region	596,747,000	650,000	580,000	730,000	108.9	97.2	122.3
WHO Western Pacific Region	1,798,335,000	1,700,000	1,500,000	1,800,000	94.5	83.4	100.1
WHO European Region	896,480,000	420,000	390,000	450,000	46.8	43.5	50.2
WHO Region of the Americas	933,447,000	270,000	250,000	280,000	28.9	26.8	30.0

Table 1. Estimated epidemiological burden of incident TB, according regions by the WHO in 2010 (World Health Organization 2011). Incidence rates were calculated for this chapter.

Regard the prevalence of TB, which for some countries is still difficult to estimate and in many cases even are not reported and/or analyzed. According the WHO, for 2010 the prevalence was estimated in 12.0 million (range, 11.0–14.0 million) prevalent cases of TB (Table 2) for rates ranging 160.1 to 203.8 cases/100,000 pop. (Table 2); however this can be very different among the WHO Regions in the World, being higher in Africa where those estimates can reach 274.8 to 394.3 cases/100,000 pop. (Table 2).

		Prevalence (cases)			Prevalence rates (cases/100,000pop)		
Region	**Population**	**Best**	**Low**	**High**	**Best**	**Low**	**High**
Global burden	6,869,573,000	12,000,000	11,000,000	14,000,000	174.7	160.1	203.8
WHO African Region	836,970,000	2,800,000	2,300,000	3,300,000	334.5	274.8	394.3
WHO European Region	896,480,000	2,500,000	2,200,000	2,800,000	278.9	245.4	312.3
WHO Western Pacific Region	1,798,335,000	5,000,000	3,700,000	6,500,000	278.0	205.7	361.4
WHO Eastern Mediterranean Region	596,747,000	1,000,000	670,000	1,500,000	167.6	112.3	251.4
WHO Region of the Americas	933,447,000	330,000	260,000	410,000	35.4	27.9	43.9
WHO South-East Asia Region	1,807,594,000	560,000	430,000	720,000	31.0	23.8	39.8

Table 2. Estimated epidemiological burden of prevalent TB, according regions by the WHO in 2010 (World Health Organization 2011). Prevalence rates were calculated for this chapter.

Regard the deaths, WHO estimates indicate that around 1.1 million (range, 0.9–1.2 million) deaths from TB among HIV-negative people occurred and an additional 0.35 million (range,

0.32–0.39 million) deaths from HIV-associated TB were also reported (World Health Organization 2011) (Table 3). Higher mortality rates are reported in Africa, ranging 26.3 to 33.5 deaths/100,000 pop. (Table 3), but very close to those reported by South East Asia, ranging 20.5 to 35.4 deaths/100,000 pop. (Table 3).

		Mortality (deaths)			Mortality rates (deaths/100,000pop)		
Region	**Population**	**Best**	**Low**	**High**	**Best**	**Low**	**High**
Global burden	6,869,573,000	1,100,000	920,000	1,200,000	16.0	13.4	17.5
WHO African Region	836,970,000	250,000	220,000	280,000	29.9	26.3	33.5
WHO South-East Asia Region	1,807,594,000	500,000	370,000	640,000	27.7	20.5	35.4
WHO Eastern Mediterranean Region	596,747,000	95,000	74,000	120,000	15.9	12.4	20.1
WHO Western Pacifi c Region	1,798,335,000	130,000	120,000	150,000	7.2	6.7	8.3
WHO European Region	896,480,000	61,000	48,000	75,000	6.8	5.4	8.4
WHO Region of the Americas	933,447,000	20,000	17,000	23,000	2.1	1.8	2.5

Table 3. Estimated epidemiological burden of mortality due to TB, according regions by the WHO in 2010 (World Health Organization 2011) (excluding HIV positive deaths). Mortality rates were calculated for this chapter.

Tuberculosis incidence in HIV-patients is a very relevant indicator worldwide for TB epidemiology and burden (Table 4). Africa presented the highest rates for HIV-Positive Incident TB cases, ranging from 98.0 to 117.1 cases/100,000pop. (Table 4).

		HIV-Positive Incident TB Cases			Rates (Cases/100,000pop)		
Region	**Population**	**Best**	**Low**	**High**	**Best**	**Low**	**High**
Global burden	6,869,573,000	1,100,000	1,000,000	1,200,000	16.0	14.6	17.5
WHO African Region	836,970,000	900,000	820,000	980,000	107.5	98.0	117.1
WHO South-East Asia Region	1,807,594,000	190,000	140,000	230,000	10.5	7.7	12.7
WHO Region of the Americas	933,447,000	35,000	31,000	38,000	3.7	3.3	4.1
WHO European Region	896,480,000	20,000	19,000	22,000	2.2	2.1	2.5
WHO Eastern Mediterranean Region	596,747,000	12,000	9,800	15,000	2.0	1.6	2.5
WHO Western Pacifi c Region	1,798,335,000	35,000	26,000	45,000	1.9	1.4	2.5

Table 4. Estimated epidemiological burden of mortality due to TB, according regions by the WHO in 2010 (World Health Organization 2011) (excluding HIV positive deaths). Mortality rates were calculated for this chapter.

Even more, difference in all these aspect can differ among countries and be higher. For example in Colombia, TB is still a significant public health problem. Figure 3 shows the WHO profile for TB in Colombia for 2010.

http://dx.doi.org/10.5772/53363

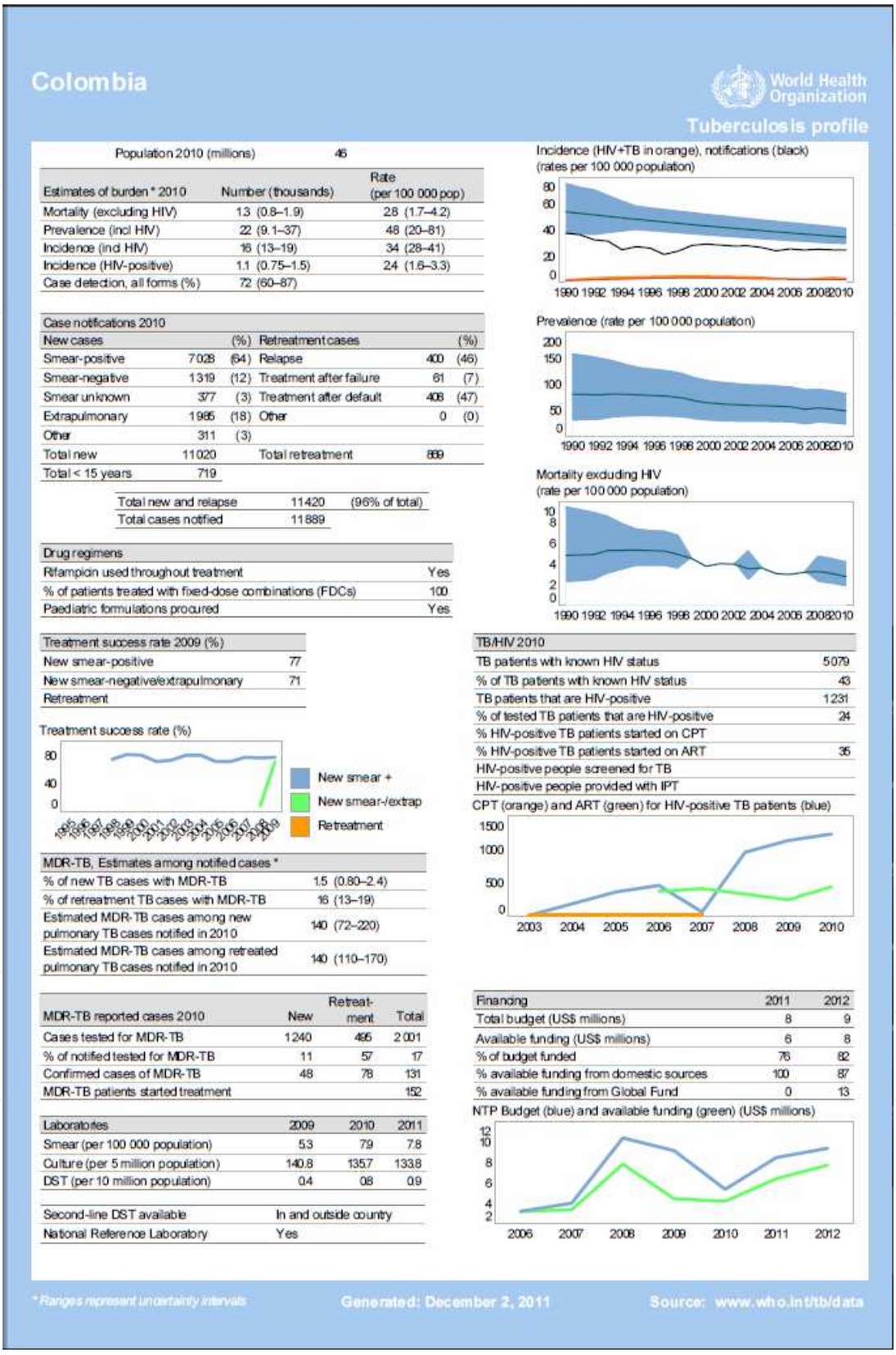

Figure 3. Tuberculosis epidemiological profile for Colombia according to the World Health Organization, 2010.

3. Tuberculosis incidence in high burden developing countries

As has been stated TB is highly endemic in many developing countries, particularly of Africa and Asia highest rates of TB are located. These 22 countries, summarizing 62.9% of the World population (4,321,966,000 pop) concentrated 81.5% of the incident cases of TB in the World (7,169,000 cases), reaching mean incidence rates higher than in the rest of the World, 165.9 cases/100,000pop. (Table 5). However in many of these countries those numbers are higher. India (although considered not official data) in 2010 reported 2,300,000 incident cases (ranging from 2,000,000 to 2,500,000 cases) (Table 5), followed by China with 1,000,000 incident cases (ranging from 910,000 to 1,200,000 cases) (Table 5) and South Africa with 490,000 incident cases (ranging 400,000 to 590,000 cases) (Table 5). Although that, again rates are higher in this last country, South Africa, where for the same year were reported between 797.9 to 1176.9 cases/100,000 pop. (7.9 to 11.8 cases/1,000 pop or 0.8 to 1.2 cases/100 pop) (Table 5). For Asia the country with highest rates is Cambodia (374.9 to 509.3 cases/100,000 pop.) (Table 5). For Latin America the country with highest rates (and the only from that region in this list) is Brazil (35.9 to 51.3 cases/100,000 pop.) (Table 5) (Figure 4).

		Incidence (cases)			Incidence rates (cases/100,000pop)		
Countries	**Population**	**Best**	**Low**	**High**	**Best**	**Low**	**High**
South Africa	50,133,000	490,000	400,000	590,000	977.4	797.9	1176.9
Zimbabwe	12,571,000	80,000	61,000	100,000	636.4	485.2	795.5
Mozambique	23,391,000	130,000	87,000	170,000	555.8	371.9	726.8
Cambodia	14,138,000	62,000	53,000	72,000	438.5	374.9	509.3
Myanmar	47,963,000	180,000	160,000	210,000	375.3	333.6	437.8
DR Congo	65,966,000	220,000	190,000	250,000	333.5	288.0	379.0
Kenya	40,513,000	120,000	120,000	130,000	296.2	296.2	320.9
Philippines	93,261,000	260,000	210,000	310,000	278.8	225.2	332.4
Ethiopia	82,950,000	220,000	20,000	230,000	265.2	24.1	277.3
Pakistan	173,593,000	400,000	330,000	480,000	230.4	190.1	276.5
Bangladesh	148,692,000	330,000	270,000	400,000	221.9	181.6	269.0
Uganda	33,425,000	70,000	56,000	85,000	209.4	167.5	254.3
Vietnam	87,848,000	180,000	130,000	220,000	204.9	148.0	250.4
Afghanistan	31,412,000	59,000	49,000	71,000	187.8	156.0	226.0
India	1,224,614,000	2,300,000	2,000,000	2,500,000	187.8	163.3	204.1
Indonesia	239,871,000	450,000	370,000	540,000	187.6	154.2	225.1
UR Tanzania	44,841,000	79,000	75,000	85,000	176.2	167.3	189.6
Thailand	69,122,000	94,000	78,000	110,000	136.0	112.8	159.1
Nigeria	158,423,000	210,000	99,000	360,000	132.6	62.5	227.2
Russian Federation	142,958,000	150,000	130,000	180,000	104.9	90.9	125.9
China	1,341,335,000	1,000,000	910,000	1,200,000	74.6	67.8	89.5
Brazil	194,946,000	85,000	70,000	100,000	43.6	35.9	51.3
Subtotal	4,321,966,000	7,169,000	5,868,000	8,393,000	165.9	135.8	194.2
% from global burden	62.9	81.5	69.0	91.2	-	-	-
Global burden	6,869,573,000	8,800,000	8,500,000	9,200,000	128.1	123.7	133.9

Table 5. Estimated epidemiological burden of TB incidence in the countries with the considered higher burden of TB, according WHO in 2010 (World Health Organization 2011). Incidence rates were calculated for this chapter.

http://dx.doi.org/10.5772/53363

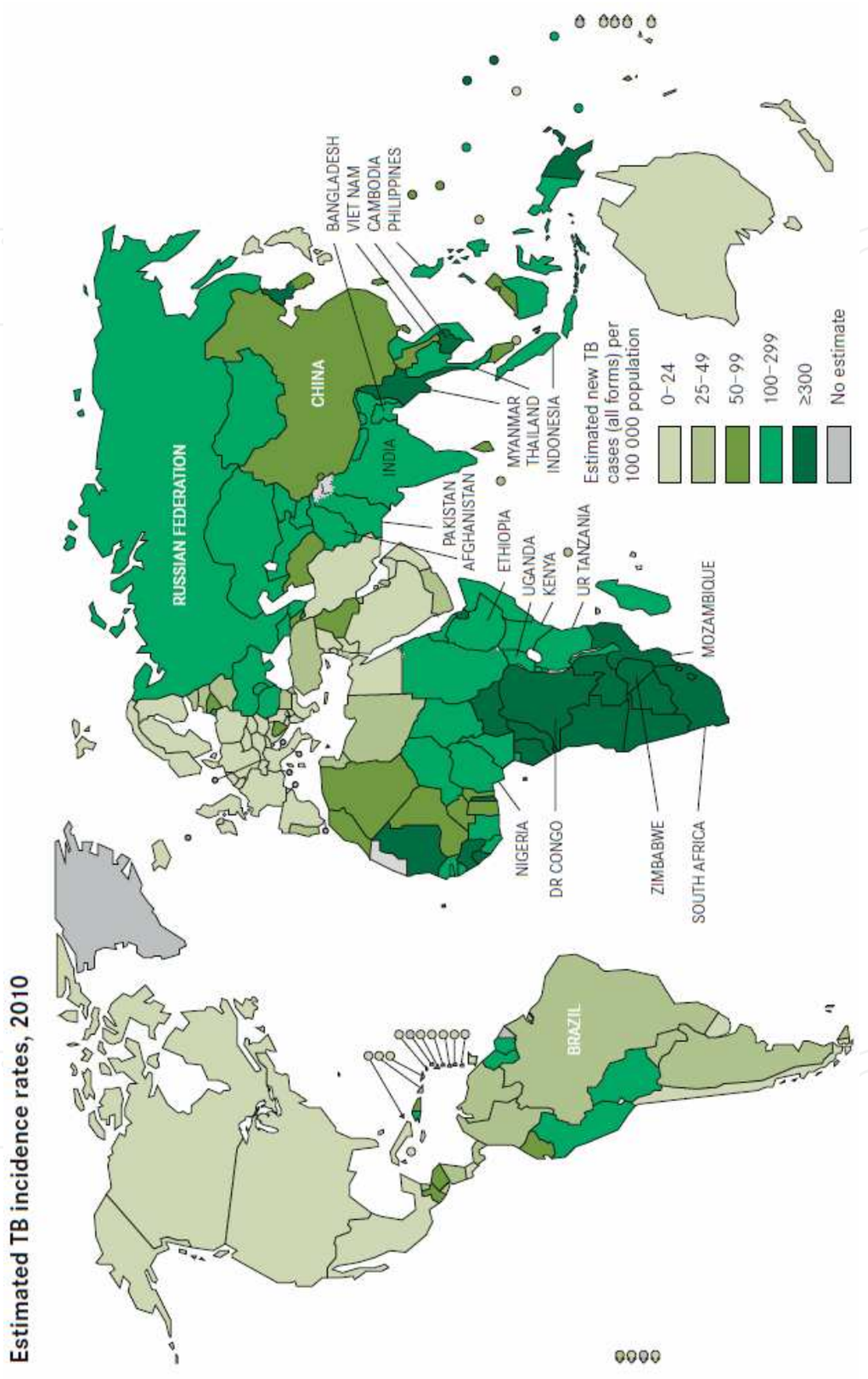

Figure 4. Map of the World with the Tuberculosis incidence rates classified according to the World Health Organization, 2010.

4. Tuberculosis prevalence in high burden developing countries

For prevalence a similar epidemiological situation is seen. These 22 countries, concentrated 83.1% of the prevalent cases of TB in the World (9,972,000 cases), reaching mean prevalence rates higher than in the rest of the World, 230.7 cases/100,000pop. (Table 6). However in many of these countries those numbers are higher. India (although considered not official data) in 2010 reported 3,100,000 prevalent cases (ranging from 2,000,000 to 4,600,000 cases) (Table 6), followed by China with 1,500,000 prevalent cases (ranging from 1,300,000 to 1,700,000 cases) (Table 6) and Indonesia with 690,000 prevalent cases (ranging 300,000 to 1,200,000 cases) (Table 6). Although that, again rates are higher in other countries, such as South Africa, where for the same year were reported between 359.0 to 1256.7 cases/100,000 pop. (3.6 to 12.6 cases/1,000 pop or 0.4 to 1.3 cases/100 pop) (Table 6). For Asia the country with highest prevalence rates is Cambodia (297.1 to 1061.0 cases/100,000 pop.) (Table 6). For Latin America the country with highest rates (and the only from that region in this list) is Brazil (17.4 to 82.1 cases/100,000 pop.) (Table 6).

		Prevalence (cases)			Prevalence rates (cases/100,000pop)		
Countries	**Population**	**Best**	**Low**	**High**	**Best**	**Low**	**High**
South Africa	50,133,000	400,000	180,000	630,000	797.9	359.0	1256.7
Cambodia	14,138,000	93,000	42,000	150,000	657.8	297.1	1061.0
DR Congo	65,966,000	350,000	160,000	560,000	530.6	242.5	848.9
Myanmar	47,963,000	250,000	180,000	310,000	521.2	375.3	646.3
Philippines	93,261,000	470,000	410,000	530,000	504.0	439.6	568.3
Mozambique	23,391,000	110,000	54,000	200,000	470.3	230.9	855.0
Bangladesh	148,692,000	610,000	280,000	1,000,000	410.2	188.3	672.5
Zimbabwe	12,571,000	51,000	23,000	80,000	405.7	183.0	636.4
Ethiopia	82,950,000	330,000	140,000	520,000	397.8	168.8	626.9
Pakistan	173,593,000	630,000	270,000	1,100,000	362.9	155.5	633.7
Afghanistan	31,412,000	110,000	51,000	180,000	350.2	162.4	573.0
Viet Nam	87,848,000	290,000	130,000	510,000	330.1	148.0	580.5
Indonesia	239,871,000	690,000	300,000	1,200,000	287.7	125.1	500.3
Kenya	40,513,000	110,000	49,000	180,000	271.5	120.9	444.3
India	1,224,614,000	3,100,000	2,000,000	4,600,000	253.1	163.3	375.6
Nigeria	158,423,000	320,000	110,000	690,000	202.0	69.4	435.5
Uganda	33,425,000	64,000	32,000	100,000	191.5	95.7	299.2
Thailand	69,122,000	130,000	55,000	210,000	188.1	79.6	303.8
UR Tanzania	44,841,000	82,000	39,000	130,000	182.9	87.0	289.9
Russian Federation	142,958,000	190,000	70,000	330,000	132.9	49.0	230.8
China	1,341,335,000	1,500,000	1,300,000	1,700,000	111.8	96.9	126.7
Brazil	194,946,000	92,000	34,000	160,000	47.2	17.4	82.1
Subtotal	4,321,966,000	9,972,000	5,909,000	15,070,000	230.7	136.7	348.7
% from global burden	62.9	83.1	53.7	107.6	-	-	-
Global burden	6,869,573,000	12,000,000	11,000,000	14,000,000	174.7	160.1	203.8

Table 6. Estimated epidemiological burden of TB prevalence in the countries with the considered higher burden of TB, according WHO in 2010 (World Health Organization 2011). Prevalence rates were calculated for this chapter.

http://dx.doi.org/10.5772/53363

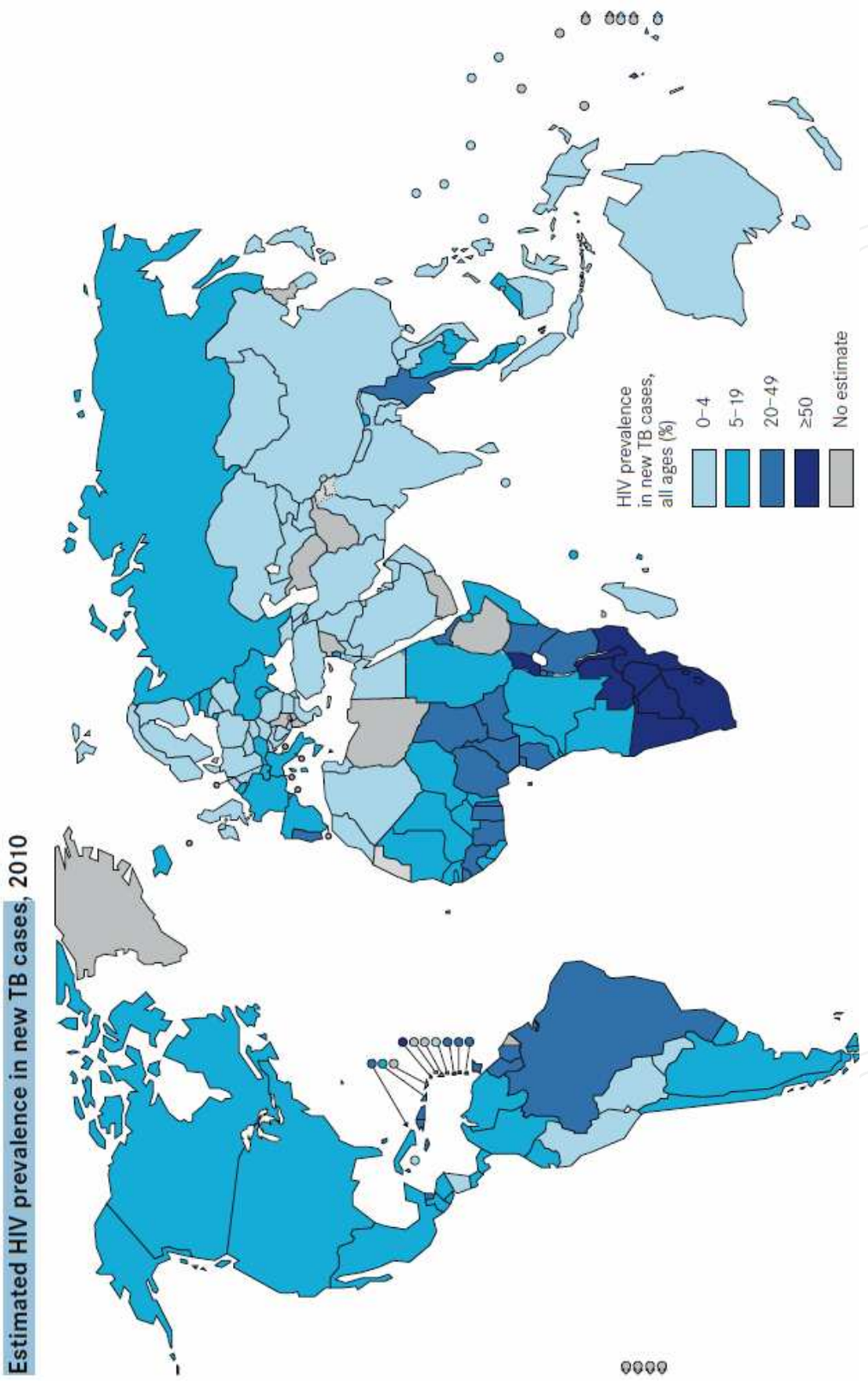

Figure 5. Map of the World with the estimated HIV prevalence in new TB cases classified according to the World Health Organization, 2010.

5. Tuberculosis mortality in high burden developing countries

For mortality a similar epidemiological situation is seen. These 22 countries, concentrated 78.0% of the deaths due to TB in the World (857,800 deaths, ranging 581,900 to 1,229,000 deaths), reaching mean mortality rates higher than in the rest of the World, 19.8 deaths/100,000pop. (Table 7). However in many of these countries those numbers are higher. India (although considered not official data) in 2010 reported 320,000 deaths (ranging from 210,000 to 470,000) (Table 7), followed by Indonesia with 64,000 deaths (ranging from 42,000 to 91,000 deaths) (Table 7) and Bangladesh with 64,000 deaths (ranging 47,000 to 85,000 deaths) (Table 7). Although that, again rates are higher in other countries, such as Cambodia, where for the same year were reported between 43.9 to 84.9 deaths/100,000 pop. (Table 7). For Africa the country with highest mortality rates is DR Congo (40.9 to 68.2 deaths/100,000 pop.) (Table 7). For Latin America the country with highest rates (and the only from that region in this list) is Brazil (1.6 to 4.3 deaths/100,000 pop.) (Table 7).

		Mortality (deaths)			Mortality rates (deaths/100,000pop)		
Countries	**Population**	**Best**	**Low**	**High**	**Best**	**Low**	**High**
Cambodia	14,138,000	8,600	6,200	12,000	60.8	43.9	84.9
DR Congo	65,966,000	36,000	27,000	45,000	54.6	40.9	68.2
South Africa	50,133,000	25,000	16,000	38,000	49.9	31.9	75.8
Mozambique	23,391,000	11,000	7,000	17,000	47.0	29.9	72.7
Bangladesh	148,692,000	64,000	47,000	85,000	43.0	31.6	57.2
Myanmar	47,963,000	20,000	12,000	31,000	41.7	25.0	64.6
Afghanistan	31,412,000	12,000	8,600	16,000	38.2	27.4	50.9
Ethiopia	82,950,000	29,000	23,000	35,000	35.0	27.7	42.2
Pakistan	173,593,000	58,000	39,000	84,000	33.4	22.5	48.4
Philippines	93,261,000	31,000	21,000	43,000	33.2	22.5	46.1
Viet Nam	87,848,000	29,000	19,000	43,000	33.0	21.6	48.9
Zimbabwe	12,571,000	3,400	2,100	5,100	27.0	16.7	40.6
Indonesia	239,871,000	64,000	42,000	91,000	26.7	17.5	37.9
India	1,224,614,000	320,000	210,000	470,000	26.1	17.1	38.4
Nigeria	158,423,000	33,000	11,000	68,000	20.8	6.9	42.9
Russian Federation	142,958,000	26,000	16,000	42,000	18.2	11.2	29.4
Kenya	40,513,000	6,900	4,900	9,400	17.0	12.1	23.2
Thailand	69,122,000	11,000	7,000	16,000	15.9	10.1	23.1
Uganda	33,425,000	5,100	3,300	7,300	15.3	9.9	21.8
UR Tanzania	44,841,000	5,800	4,700	6,900	12.9	10.5	15.4
China	1,341,335,000	54,000	52,000	56,000	4.0	3.9	4.2
Brazil	194,946,000	5,000	3,100	8,300	2.6	1.6	4.3
Subtotal	4,321,966,000	857,800	581,900	1,229,000	19.8	13.5	28.4
% from global burden	62.9	78.0	63.3	102.4	-	-	-
Global burden	6,869,573,000	1,100,000	920,000	1,200,000	16.0	13.4	17.5

Table 7. Estimated epidemiological burden of TB mortality in the countries with the considered higher burden of TB, according WHO in 2010 (World Health Organization 2011). Mortality rates were calculated for this chapter.

http://dx.doi.org/10.5772/53363

6. Tuberculosis-HIV incidence in high burden developing countries

Coinfection in high burden developing countries is one the main problems those countries should face in the public health threat that TB represents. These 20 countries, concentrated 78.1% of the cases of TB-HIV in the World (859,600 cases, ranging 636,200 to 1,128,900 cases), reaching mean TB-HIV rates higher than in the rest of the World, 20.4/100,000pop. (Table 8). However in many of these countries those numbers are higher. Africa in 2010 reported 300,000 cases TB-HIV (ranging 240,000 to 350,000) followed by India (although considered not official data) in 2010 reported 110,000 cases TB-HIV (ranging from 75,000 to 160,000) (Table 8), and Mozambique with 77,000 cases (ranging 53,000 to 110,000) (Table 8). Although that, again rates are higher in other countries. South Africa is the country with highest rates of TB-HIV, 478.7 to 698.1 cases/100,000 pop. (Table 8). For Asia the country with highest TB-HIV rates is Myanmar (43.8 to 118.8 cases/100,000 pop.) (Table 8). For Latin America the country with highest rates (and the only from that region in this list) is Brazil (5.1 to 14.4 cases/100,000 pop.) (Table 8) (Figure 5).

		HIV-positive incident TB cases			HIV-TB rates (cases/100,000 pop)		
Countries	**Population**	**Best**	**Low**	**High**	**Best**	**Low**	**High**
South Africa	50,133,000	300,000	240,000	350,000	598.4	478.7	698.1
Zimbabwe	12,571,000	60,000	47,000	76,000	477.3	373.9	604.6
Mozambique	23,391,000	77,000	53,000	110,000	329.2	226.6	470.3
Kenya	40,513,000	50,000	45,000	55,000	123.4	111.1	135.8
Uganda	33,425,000	38,000	30,000	46,000	113.7	89.8	137.6
Myanmar	47,963,000	37,000	21,000	57,000	77.1	43.8	118.8
UR Tanzania	44,841,000	30,000	28,000	31,000	66.9	62.4	69.1
Nigeria	158,423,000	51,000	25,000	87,000	32.2	15.8	54.9
Cambodia	14,138,000	4,000	3,400	4,700	28.3	24.0	33.2
DR Congo	65,966,000	18,000	13,000	24,000	27.3	19.7	36.4
Thailand	69,122,000	12,000	13,000	18,000	17.4	18.8	26.0
Brazil	194,946,000	18,000	10,000	28,000	9.2	5.1	14.4
India	1,224,614,000	110,000	75,000	160,000	9.0	6.1	13.1
Viet Nam	87,848,000	7,600	4,600	11,000	8.7	5.2	12.5
Indonesia	239,871,000	18,000	9,900	29,000	7.5	4.1	12.1
Russian Federation	142,958,000	8,100	6,800	9,400	5.7	4.8	6.6
China	1,341,335,000	18,000	10,000	28,000	1.3	0.7	2.1
Philippines	93,261,000	1,000	500	1,800	1.1	0.5	1.9
Pakistan	173,593,000	1,200	700	1,900	0.7	0.4	1.1
Bangladesh	148,692,000	700	300	1,100	0.5	0.2	0.7
Subtotal	4,207,604,000	859,600	636,200	1,128,900	20.4	15.1	26.8
% from global burden	61.2	78.1	63.6	94.1	-	-	-
Global burden	6,869,573,000	1,100,000	1,000,000	1,200,000	16.0	14.6	17.5

Table 8. Estimated epidemiological burden of TB-HIV in the countries with the considered higher burden of TB, according WHO in 2010 (World Health Organization 2011). Rates were calculated for this chapter.

7. Multidrug resistant tuberculosis in high burden developing countries

Multidrug resistant (MDR) tuberculosis is a public health problem (Gotuzzo E 2011, Tamaru et al 2012). Its burden particularly in developing countries is a relevant issue to be addressed. In some countries, proportions as high as 26% of the new TB cases can be MDR-TB (Figure 6).

MDR strains arose over the past 30 years as a variety of antituberculosis drugs were introduced in medicine, and they largely discount the results of chemotherapy for tuberculosis. The most dangerous of them are strains with extensive drug resistance (XDR), which are resistant to four or five different drugs on average. The molecular mechanisms that make a strain resistant are considered. XDR and MDR strains result from successive and usually independent resistance mutations, which arise in various regions of the mycobacterial genome. In addition, the formation of resistant strains is affected by the phenomenon of tolerance and mycobacterial latency in infected tissues (Prozorov AA et al 2012).

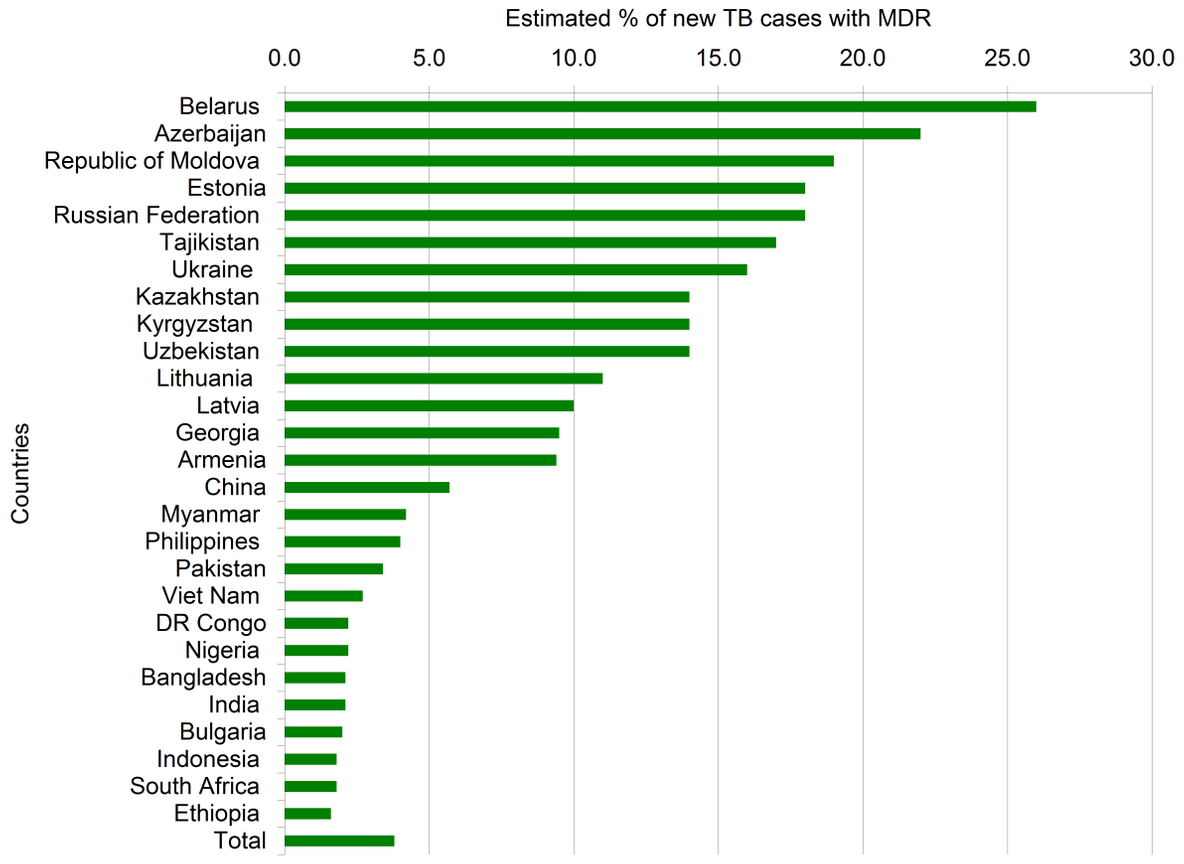

Figure 6. Estimated proportion of TB cases that have MDR-TB.

The increasing emergence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) tuberculosis (TB) in the era of human immunodeficiency virus (HIV) infection presents a major threat to effective control of TB. Drug resistance in *Mycobacterium tuberculo-*

http://dx.doi.org/10.5772/53363

sis arises from spontaneous chromosomal mutations at low frequency. Clinical drug-resistant TB largely occurs as a result of man-made selection during disease treatment of these genetic alterations through erratic drug supply, suboptimal physician prescription and poor patient adherence. Molecular mechanisms of drug resistance have been elucidated for the major first- and second-line drugs rifampicin, isoniazid, pyrazinamide, ethambutol, the aminoglycosides and the fluoroquinolones. The relationship between drug resistance in *M. tuberculosis* strains and their virulence/transmissibility needs to be further investigated. Understanding the mechanisms of drug resistance in *M. tuberculosis* would enable the development of rapid molecular diagnostic tools and furnish possible insights into new drug development for the treatment of TB (Zhang Y & Yew WW, 2009).

8. Tuberculosis in Colombia and in a city of the country: Pereira

In Colombia for 2010 incident cases were 16,000 cases (ranging 13,000 to 19,000 cases) for a rate of 34 cases/100,000 pop (28 to 41 cases/100,000 pop). Prevalence was estimated in 22,000 cases (9,100 to 37,000 cases) for a rate of 48 cases/100,000 pop (ranging 20 to 81 cases/100,000 pop.). Mortality was estimated in 1,300 deaths (ranging 800 to 1,900 deaths) for a mortality rate of 2.8 deaths/100,000 pop. (1.7 to 4.2 deaths/100,000 pop.). All these figures are excluding HIV cases. TB incidence in HIV positive patients is 1,100 cases (ranging 750 to 1,500 cases) for a rate of 2.4 cases/100,000 pop. (ranging from 1.6 to 3.3 cases/100,000 pop.).

As an example of place where the burden of TB is high, Pereira, a city in Colombia can be presented. Pereira is the capital municipality of the Department of Risaralda (Figure 7). It stands in the center of the western region of the country, located in a small valley that descends from a part of the western Andes mountain chain. Its strategic location in the coffee producing area makes the city an urban center in Colombia, as does its proximity to Bogotá, Cali and Medellín.

For 2011, Pereira municipality has an estimated population of 459,690. Official reported records for TB in Risaralda registered a disease incidence for 2010 of 25 cases per 100,000 pop (which is above the national average rate of 24 cases per 100,000 pop). Pereira is divided into 19 urban submunicipalities: Ferrocarril, Olímpica, San Joaquín, Cuba, Del Café, El Oso, Perla del Otún, Consota, El Rocío, El poblado, El Jardín, San Nicolás, Centro, Río Otún, Boston, Universidad, Villavicencio, Oriente and Villasantana. Additionally also has rural townships which include Altagracia, Arabia, Caimalito, Cerritos, La Florida, Puerto Caldas, Combia Alta, Combia Baja, La Bella, Estrella, La Palmilla, Morelia and Tribunas. The municipality of Pereira has a diversified economy: the primary sector accounts for 5.7% of domestic product, the secondary sector shows a relative weight of 26.2%, while the tertiary sector is the most representative with a 68.1%. The GDP of Pereira grew by 3.7% in 2004. For 2010, Pereira reported 301 cases of TB (incidence rate of 65.85 cases per 100,000pop). In Pereira, previously reported interventions have been developed and working intersectorially with the academia in order to increase the impact of activities in TB control (Castañeda-Hernández DM et al. 2012c, Castañeda-Hernández DM & Rodríguez-Morales AJ 2012a).

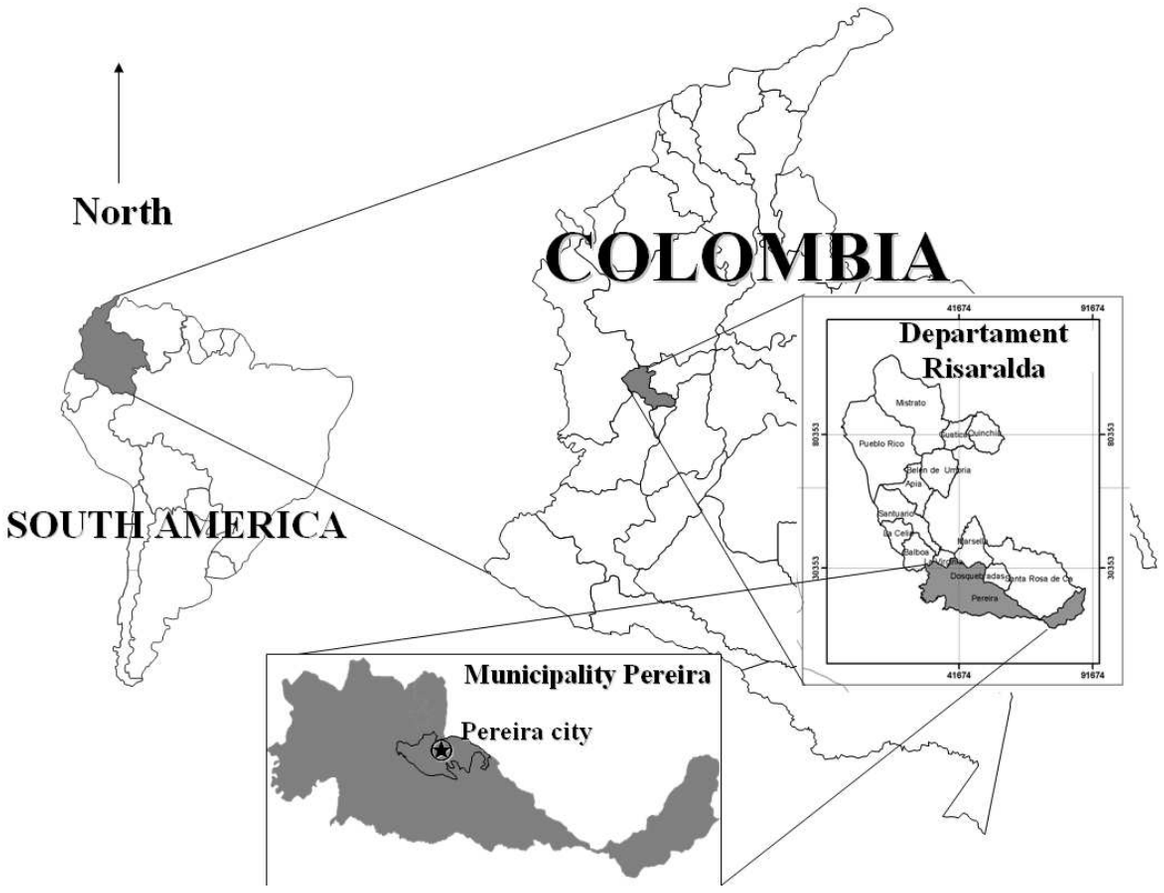

Figure 7. Relative location of Pereira, Risaralda, Colombia, South America.

In the country, the strategic plan "*Colombia Libre de Tuberculosis para la Expansión y Fortalecimiento de la Estrategia Alto a la TB, 2010-2015*" (Colombia Free of TB for the Expansion and Enhancement of the Strategy Stop TB, 2010-2015), define as goal the achievement of notifications of new positive baciloscopy cases in more than 70% and a curation rate of at least 85%. In this context the routine surveillance allow to follow management and measurement of the impact of the realized actions by the control programs at municipal, departmental and national level, in order to generate interventions that contribute to achievement of the established goals to stop the advance of TB in the country.

In Pereira, control of TB among homeless have found that between 2007 and 2010, 74 homeless persons with TB were evaluated, from a total of 1,470 registered homeless persons (from the Social Development Secretary of Pereira) (cumulated incidence=50.3 cases/1,000pop., range 5.44 to 22.44; year 2010=16.32). Outcome condition was in 43.2% treatment self-withdrawal (range 36.4%-55.6%), therapeutical failure, 4.1%(0.0-9.1%), deaths, 2.7%(0.0%-8.3%), cured, 39.2%(33.3%-42.4%) and finished treatments, 10.8%(4.2%-25.0%). Comparing the 2010 TB incidence among homeless persons with that of the general population (0.6585/1,000pop.) that is 76.45 times higher in that risk population. In the same way, case fatality rate in 2010 was 2.5 times higher than in the general population (3.3%). These results have important implications in public health as well in the management and

evolution of TB in these individuals, persistence of infection, drug-resistance and potential transmission to those that can be around these populations (Castañeda-Hernández DM & Rodríguez-Morales AJ, 2012b).

Also, as part of the integrative control of TB in special populations, surveillance have included control in a prison. Evaluating TB among prisoners between 2010 and 2012, seven prisoners with TB (AFB+), from a total of 1,508 registered prisoners at the penitentiary were diagnosed (cumulated incidence=4.64 cases/1,000pop., 2.99 in 2010 and 2.13 in 2011). Mean age was 40.5 y-old (100% males), all were pulmonary disease. All of them received voluntary counseling and testing for HIV, one of them was HIV+. Three of them are under anti-TB treatment, 2 were transferred, 1 finished treatments and 1 was a therapeutical failure. Comparing the 2011 TB incidence among prisoners with that of the general population (0.67/1,000pop.) that was 3.19 times higher in that risk population. In 2010 in Pereira was 0.66/1,000pop., then being 4.55 times higher in prisoners (Castañeda-Hernández DM et al 2012b). These results have important implications in public health as well in the management and evolution of TB in these individuals, persistence of infection, drug-resistance and potential transmission to those that can be around these prisoners. This is in agreement with recent data indicating that TB incidence rates among prisoners can be as higher as approximately 5 to 50 times higher them than in general population. In Brazil this has been reported as high as 61.8 times higher for latent TB and 36.08 for active TB. Prisoners are at risk rapidly progress to a latent TB or have an active TB posterior a recent infection or reactivation due to latent coexisting pathologies, particularly HIV infection, IV drug use and poor nutritional status. It has been shown that workers in such facilities as well the community, are at risk. For these reasons strategies oriented to bring an integral, social, epidemiological, clinical, diagnostic and therapeutic management, are proposed and for the Americas, the Pan-American Health Organization (PAHO) guideline for the TB control in population in prisons should be followed (OPS 2008).

9. Conclusions

Tuberculosis control in the XXI century requires new approaches and interventions, particularly those based in education and prevention with a community-based orientation to continuously progress in the achieved reduction of burden of disease in the region of the Americas, including in countries such as Colombia. Different approach programs such the development of social networks for control program, as has been developed in Pereira, Colombia (Castañeda-Hernández DM & Rodríguez-Morales AJ 2012a), should performed in other highly endemic places. As the WHO recommends to pursue the ACMS (advocacy, communication and social mobilization), strategies as the social network allow to enhance particularly the communication and social mobilization components. Unfortunately at many national plans of TB control, how translate the ACMS in specific actions is not well defined in most occasions.

As has been previously stated, in the establishment of a social network for TB, previous diagnosis, including geo-referenced characterization, it is necessary to select the areas where

the nodes will be established, taking also in consideration the suitability as the willingness of the potential participants of the network in each area and node. Finally, with the mining of the activities described, but also beginning with the idea of raise the awareness about the disease, taking in consideration a high level of diversity on the activities, as has been stated in order to warrant the continuous interest and participation of the network members on it.

In the future, in order to enhance the function and structure of the whole social network, further meetings between the nodes are expected. As now, only nodes interact internally, but the idea for the future activities in this setting is increase the links internally, but also between the main nodes in order to potentially increase the participation in the whole network.

Activities such as the development of social network of TB in Pereira will enhance the prevention, education and surveillance in the community, allowing a better integrated approach to the TB control in these scenarios and increasing the health profile in the community decreasing the lost opportunities for diagnosis and treatment of TB cases, finally leading to an improvement of the TB prevention and control.

Integrating additionally control in populations were TB is highly prevalent such as in prisons and homeless persons (Figure 8) (Castañeda-Hernández DM et al 2012b, Castañeda-Hernández DM & Rodríguez-Morales AJ, 2012b), an integrative control of disease can be achieved and finally control and reduce the burden of disease in a developing country.

Figure 8. Homeless persons in the center of Pereira, Colombia (taken by Rodriguez-Morales AJ).

Author details

Diana M. Castañeda-Hernández[1] and Alfonso J. Rodriguez-Morales[2,3]

1 Tuberculosis Control Program, Health and Social Security Secretary, Pereira and Fundación Universitaria del Área Andina, Pereira; Committee on Tuberculosis, Asociación Colombiana de Infectología (ACIN), Bogotá, Colombia

2 Department of Community Medicine, Faculty of Health Sciences, Universidad Tecnológica de Pereira, Pereira; Office of Scientific, Research, Cooperativa de Entidades de Salud de Risaralda (COODESURIS), Pereira; Postgraduate in Epidemiology, Fundación Universitaria del Área Andina, Pereira, Colombia

3 Instituto José Witremundo Torrealba, Universidad de Los Andes, Trujillo, Venezuela

References

[1] Arbelaez MP, Nelson KE, Munoz A. 2000. BCG vaccine effectiveness in preventing tuberculosis and its interaction with human immunodeficiency virus infection. Int. J Epidemiol. 29(6):1085-91.

[2] Arenas-Suárez NE, García-Gutiérrez AM, Coronado-Ríos SM, Beltrán-Bocanegra CA, Acosta-Botero SM, Gómez-Marín JE, Quintero-Álvarez L. 2010. Prevalence of childhood tuberculosis in Armenia, Colombia. Rev Salud Publica (Bogota) 12(6):1000-9.

[3] Black GF, Weir RE, Chaguluka SD, Warndorff D, Crampin AC et al. 2003. Gamma interferon responses induced by a panel of recombinant and purified mycobacterial antigens in healthy, non-mycobacterium bovis BCG-vaccinated Malawian young adults. Clin. Diagn. Lab Immunol. 10(4):602-11.

[4] Castañeda-Hernández DM, Bolívar-Mejía A, Rodríguez-Morales AJ. 2012a. Scientific research in tuberculosis: bibliometric assesment of the colombian contributions to the literature. Infectio 16(S1):33.

[5] Castañeda-Hernández DM, Martínez-Ramírez JE, Rodríguez-Morales AJ. 2012b. Tuberculosis en una prisión de risaralda: epidemiología e implicaciones para el programa de control. Infectio 16(S1):66.

[6] Castañeda-Hernández DM, Mondragón-Cardona A, Canapo Betancourth CF, Tobón-García D, Alzate-Carvajal V, Jiménez Canizales CE, Rodríguez-Morales AJ. 2012c. Impacto de una Actividad Formativa en los Conocimientos, Actitudes y Percepciones (CAP) sobre Tuberculosis (TB) de Estudiantes de Medicina de una Universidad de Risaralda, Colombia. Gaceta Médica de Caracas 120(1):40-47.

[7] Castañeda-Hernández DM, Rodríguez-Morales AJ. 2012a. Social Networking in Tuberculosis: Experience in Colombia. In: Rodriguez-Morales AJ. (Editor). Current Top-

ics in Tropical Medicine. ISBN 978-953-51-0274-8. InTech, Croatia, March. Chapter 5: 67-80.

[8] Castañeda-Hernández DM, Rodríguez-Morales AJ. 2012b. Epidemiología de la tuberculosis en habitantes de calle, municipio Pereira, Risaralda, 2007-2010 y propuesta de un proyecto para mejorar su abordaje y evolución. Infectio 16(S1):33-34.

[9] Castañeda-Hernández DM, Rodríguez-Morales AJ, Sepulveda-Arias JC. 2012d. Importancia del uso de pruebas de medición de la liberación de interferon-gamma en la vigilancia epidemiológica de la tuberculosis. Rev Med Chile 140(1):128-129.

[10] Chadha SS, Sharath BN, Reddy K, Jaju J, Vishnu PH, Rao S, Parmar M, Satyanarayana S, Sachdeva KS, Wilson N, Harries AD. 2011. Operational challenges in diagnosing multi-drug resistant TB and initiating treatment in Andhra Pradesh, India. PLoS One 6(11):e26659.

[11] Curto M, Scatena LM, de Paula Andrade RL, Palha PF, de Assis EG et al. 2010. Tuberculosis control: patient perception regarding orientation for the community and community participation. Rev. Lat. Am. Enfermagem. 18(5):983-9.

[12] Dim CC, Dim NR, Morkve O. 2011. Tuberculosis: a review of current concepts and control programme in Nigeria. Niger. J Med 20(2):200-6.

[13] Fernández M & Dickson González SM. 2007. Coloraciones especiales e impregnaciones argénticas. Rev Soc Med Quir Hosp Emerg Perez de Leon 38(1):8-10.

[14] Ferro BE, Nieto LM, Rozo JC, Forero L, van Soolingen D. 2011. Multidrug-resistant Mycobacterium tuberculosis, Southwestern Colombia. Emerg Infect Dis 17(7): 1259-62.

[15] Francis J, Reed A, Yohannes F, Dodard M, Fournier AM. 2002. Screening for tuberculosis among orphans in a developing country. Am. J Prev. Med 22(2):117-9.

[16] Franco-Paredes C, Jones D, Rodriguez-Morales AJ, Santos-Preciado JI. 2007a. Commentary: improving the health of neglected populations in Latin America. BMC Public Health 7:11.

[17] Franco-Paredes C, Von A, Hidron A, Rodriguez-Morales AJ, Tellez I et al. 2007b. Chagas disease: an impediment in achieving the Millennium Development Goals in Latin America. BMC Int. Health Hum. Rights 7:7.

[18] Galimi R. 2011. Extrapulmonary tuberculosis: tuberculous meningitis new developments. Eur. Rev Med Pharmacol. Sci 15(4):365-86.

[19] Garcia-Rodriguez JF, Alvarez-Diaz H, Lorenzo-Garcia MV, Marino-Callejo A, Fernandez-Rial A, Sesma-Sanchez P. 2011. Extrapulmonary tuberculosis: epidemiology and risk factors. Enferm. Infecc. Microbiol. Clin. 29(7):502-9.

[20] Garg RK. 2010. Tuberculous meningitis. Acta Neurol. Scand. 122(2):75-90.

[21] Ginsberg AM. 2000. A proposed national strategy for tuberculosis vaccine development. Clin. Infect Dis. 30 Suppl 3:S233-S242.

[22] Glaziou P, Floyd K, Raviglione M. 2009. Global burden and epidemiology of tuberculosis. Clin. Chest Med 30(4):621-36, vii.

[23] Gotuzzo E. 2011. Xpert MTB/RIF for diagnosis of pulmonary tuberculosis. Lancet Infect Dis 11(11):802-3.

[24] Hoek KG, Van RA, van Helden PD, Warren RM, Victor TC. 2011. Detecting drug-resistant tuberculosis: the importance of rapid testing. Mol. Diagn. Ther. 15(4):189-94.

[25] Marais BJ, Schaaf HS. 2010. Childhood tuberculosis: an emerging and previously neglected problem. Infect Dis. Clin. North Am. 24(3):727-49.

[26] Murcia-Aranguren MI, Gómez-Marin JE, Alvarado FS, Bustillo JG, de Mendivelson E, Gómez B, León CI, Triana WA, Vargas EA, Rodríguez E. 2001. Frequency of tuberculous and non-tuberculous mycobacteria in HIV infected patients from Bogota, Colombia. BMC Infect Dis 1:21.

[27] Organización Panamericana de la Salud. 2008. "Guía para el control de la tuberculosis en poblaciones privadas de libertad de América Latina y el Caribe". Washington, D.C.: OPS.

[28] Orcau A, Cayla JA, Martinez JA. 2011. Present epidemiology of tuberculosis. Prevention and control programs. Enferm. Infecc. Microbiol. Clin. 29 Suppl 1:2-7.

[29] Prozorov AA, Zaĭchikova MV, Danilenko VN. 2012. *Mycobacterium tuberculosis* mutants with multidrug resistance: history of origin, genetic and molecular mechanisms of resistance, and emerging challenges. Genetika 48(1):5-20.

[30] Robledo J, Mejia GI, Paniagua L, Martin A, Guzmán A. 2008. Rapid detection of rifampicin and isoniazid resistance in Mycobacterium tuberculosis by the direct thin-layer agar method. Int J Tuberc Lung Dis 12(12):1482-4.

[31] Rodríguez-Morales AJ, Lorizio W, Vargas J, Fernández L, Durán B, Husband G, Rondón A, Vargas K, Barbella RA, Dickson SM. 2008. Malaria, Tuberculosis, VIH/SIDA e Influenza Aviar: ¿Asesinos de la Humanidad? Rev Soc Med Quir Hosp Emerg Perez de Leon 39(1):52-76.

[32] Rodríguez-Morales AJ, Castañeda-Hernández DM. 2012. Relationships Between Morbidity and Mortality from Tuberculosis and the Human Development Index (HDI) in Venezuela, 1998-2008. Int J Infect Dis 16(9):e704-e705.

[33] Solari L, Gutiérrez A, Suárez C, Jave O, Castillo E, Yale G, Ascencios L, Quispe N, Valencia E, Suárez V. 2011. Cost analysis of rapid methods for diagnosis of multidrug resistant tuberculosis in different epidemiologic groups in Perú. Rev Peru Med Exp Salud Publica 28(3):426-31.

[34] Tamaru A, Nakajima C, Wada T, Wang Y, Inoue M, Kawahara R, Maekura R, Ozeki Y, Ogura H, Kobayashi K, Suzuki Y, Matsumoto S. 2012. Dominant Incidence of Mul-

tidrug and Extensively Drug-Resistant Specific *Mycobacterium tuberculosis* Clones in Osaka Prefecture, Japan. PLoS One 7(8):e42505.

[35] Torres J, Sardón V, Soto MG, Anicama R, Arroyo-Hernández H, Munayco CV. 2011. Cluster of multidrug-resistant tuberculosis cases in a school of the district of Ica, Peru. Rev Peru Med Exp Salud Publica 28(3):497-502.

[36] Vargas J, Gamboa C, Negrin D, Correa M, Sandoval C et al. 2005. Disseminated Mycobacterium mucogenicum infection in a patient with idiopathic CD4+ T lymphocytopenia manifesting as fever of unknown origin. Clin. Infect Dis. 41(5):759-60.

[37] World Health Organization. 2011. 2011 Global Tuberculosis Control, Geneva: WHO.

[38] World Health Organization. 2012. Electronic recording and reporting for tuberculosis care and control, Geneva: WHO.

[39] Zhang Y, Yew WW. 2009. Mechanisms of drug resistance in *Mycobacterium tuberculosis*. Int J Tuberc Lung Dis 13(11):1320-30.