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Pulmonary Tuberculosis in Latin America: Patchwork Studies Reveal Inequalities in Its Control – The Cases of Chiapas (Mexico), Chine (Ecuador) and Lima (Peru)

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Additional information is available at the end of the chapter

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1. Introduction

Tuberculosis (TB) has been present in Latin America since pre-historical times. Paleopathological studies have found signs of TB in mummies from many parts of the world. In fact, whenever human mummies have been found, signs of TB have been observed in bones, lungs or skin [1].

Although TB may be considered as nearly as old as humankind, the current epidemiological profile of this disease must not be considered as the natural or expected one, given the large numbers of prevalent and newly occurring cases. The main questions related with the persistence and rise of TB in many regions of Latin America, have to do with social processes and inequalities. In this sense, the different processes usually resulting in TB disease are directly related with social and economic behavior of human communities [1].

TB constitutes one of the most complex situations in the health field. This complexity both makes visible, and raises questions about the existing inequities in the political and socio-cultural structure and in class relations, as it is the result of the health-illness-care process. Among the main elements permitting operationalization of an analysis of this situation, we find social vulnerability and accessibility to a whole spectrum of health services (in geographical, cultural and economic terms), from opportunistic diagnosis to effective treatment (meaning cure).

In this sense, we understand as social vulnerability that set of economic, political, social and cultural conditions which determine that some individuals become infected by the TB bacillus while others do not, depending on the structural conditions which favor or hinder exposure to the disease,¹ as well as those differential aspects by which, among those infected, some get TB disease while others do not, and among those with TB disease some are cured (whether spontaneously or as a result of anti-TB treatment), others remain chronically ill (possibly with multi-drug resistance) while others die (generally those presenting the worst socioeconomic conditions and poorer health in general).

Nevertheless, TB prevention and control programmes are designed as if the disease behaved in a homogeneous way in all countries and regions, based almost solely on biological and medical factors, without taking into account socio-cultural, economic and political factors, such as poverty, malnutrition, health services accessibility and quality, as well as intra and inter-community political conflicts, among others.

This approach impedes acting on the particularities of marginal populations, which are precisely the ones presenting the highest rates of morbidity and mortality of this disease, manifesting various gradients of exposure and susceptibility. This leads governments to act on the basis of global estimates, even when their interpretation of these is limited and partial, because the differential exposures and true extent of TB are unknown.

Furthermore, this way of tackling TB does not reflect the reality of the different regions within a given country, because local or regional variations in rates of morbidity and mortality are disguised. Such variability could easily be quantified by, at the very least, providing the standard deviation corresponding to the global values of these rates for each country. Consequently, areas which should be given priority, paradoxically receive only limited resources for interventions.

In this sense, it is important to point out that TB, like HIV/AIDS, is one of the diseases for which estimations of impact in terms of incidence and prevalence are frequently based only on the registered cases. While it is true that published national and international figures often include estimates of sub-notification, they do not usually include gradients of the magnitude of the disease, or of the intra- or inter-regional under-notification rates, nor the differential rates between different population groups. According to several authors, calculation of the number of cases of TB disease is possible based on the expected evolution of cases of infection [2] or through linear regression modeling involving age-specific prevalence values across a range of differently aged populations [3]. Although this calculation technique for the frequency of TB and HIV status has been considered [4], there are currently no models in which population impact has been measured in terms of social factors.

In summary, in general terms, national and international policies to cope with TB ignore this reality, applying criteria of homogeneity in the calculation of objectives, materials, costs and logistics, among other aspects. While it is well known that marginal groups are the ones presenting the highest TB morbidity and mortality rates, their characterisation is not usually

¹ According to World Health Organization calculations, one third to the human population is infected with TB bacillus

considered in the design of programmes for their prevention and control, so that TB continues to cause high rates of disease, death and ever-rising health costs in these groups, something which represents a violation of their human rights a consequence of governments having been incapable of preventing this situation.

Furthermore, the effectiveness of programs of TB Prevention and Control has been questioned because of their complexity. In this sense, a therapeutic intervention such as the Directly Observed Therapy – Short Course (DOTS) strategy, and socioeconomic and structural factors have been topics of discussion with regard the possible impact of one and the other, due to the decline of TB observed prior the use of antibiotics, as well as the goals met at present by DOTS strategy. In this regard, a correlation has been documented in Latin America between the early diagnosis of smear positive TB cases and improved cure rates [5]. So, one of the main emphasis of strategies to reduce the transmission of *Mycobacterium tuberculosis*, should be the identification of active TB cases, particularly in deprived and highly exposed populations.

The Africa and Latin America Research Groups Network (*Grups de Recerca d'America i Africa Llatines* -GRAAL) has conducted studies in marginal populations which reveal the conditions of patients, as well as the extent of the disease, of multi-drug resistance (MDR) and of mortality in these populations, producing figures which differ widely from the official average values. The main mechanism for tackling these aspects has been through doctoral theses. In this chapter we give examples of research undertaken in three different contexts of high poverty and social exclusion in Mexico, Ecuador and Peru.

2. Patch 1: Chiapas, Mexico

Chiapas is one of the poorest states in Mexico, and has one of the highest rates of indigenous marginalization as well as an acute lack of health care resources. According to official government statistics, Chiapas ranks almost last among all Mexican states in terms of health and socioeconomic indicators [6]. It is precisely in Chiapas where, due to the conditions of social exclusion, poverty, malnutrition and high mortality from infectious contagious diseases, the Zapatista National Liberation Army (EZLN) initiated an armed rising against the Mexican government in 1994, which drew attention, both nationally and internationally, to the precarious living and health conditions of the indigenous and peasant populations, not only in Chiapas, but throughout the entire country.

Several studies have been carried out by our team in areas of high levels of poverty in Chiapas: Our first attempt to analyze the pulmonary tuberculosis (PTB) situation arose out of the discovery that in the only hospital (Comitán General Hospital, Ministry of Health) in the region of the border with Guatemala for patients not covered by insurance (the majority of whom are indigenous),² there was empirical evidence of a high prevalence of PTB cases. In 1994, active case finding of patients with chronic cough (15 days or more) was carried out among all patients aged over 14 years seeking care in the hospital for whatever reason [7]. In this study

² In Chiapas, over 80% of population is not covered by social security [6]

a rate of 21 positive PTB smears per hundred patients was found (95% CI=15.5-26.6), and the main factors associated with PTB were age (35-44 years), occupation (engaged in agricultural) and weight loss. Through a logistic regression model, we found that the subgroup of chronic cough patients aged 35-44 years, agricultural workers and who had lost weight, had the greatest likelihood of being PTB positive (68.7% compared to the overall average of 21% in the studied patients).

In addition, we noted that in the case of men, patients came to the hospital from near, far and very far distant communities, but in the case of women, the majority of them only came from communities which were near or very near. So we decided to carry out other studies in the hospital's area of influence, with the aim of analyzing factors related with the high PTB prevalence among users of secondary level care, not only in terms of health system aspects, but of demographic and socioeconomic characteristics:

a) In 1997 active case-finding was carried out among all patients aged over 14 years seeking consultation in a random sample of seven primary care centers [8]. We found a PTB positivity rate of 11.1 (95% CI=6.6-17.2) per hundred patients studied. The factors associated with PTB were size and poverty level of the locality of residence. Of the coughers identified, 56% sought care for non-respiratory symptoms.

b) In 1998 active case-finding was carried out among those aged over 14 years who had a cough of 15 days or more of duration, in a convenience sample of 1,894 households in 32 communities chosen at random based on the level of poverty and on travel time to reach the nearest health services (< 1 hour, 1 hour and over). In this study we found a rate of 276.9 per 100,000 persons studied (95%CI: 161-443) and that the only factor associated with PTB was blood in sputum, probably due to the homogenous conditions of extreme poverty among the populations studied [9].

Additionally, we found that the sensitivity of the smear testing was slightly lower than 50% in the primary care centers and in communities, and that the proportion of patients with active PTB that was receiving treatment was only 50% in the primary care centers, and 10.5% in the studied communities [10]. Also, we found high rates of anti-TB treatment defaulting [11], and very high levels of PTB multidrug-resistance (MDR): 4.6% and 29.2% primary and secondary MDR-TB, respectively. In fact, 14% of all studied PTB patients had MDR.

According to the logistic regression model fitted, the main variables associated with MDR were: having received anti-TB treatment previously, cough of three years or more of duration and not being indigenous. This is the only occasion in all our studies, which the condition of being indigenous appeared as a protective factor [12].

In 2000-2001 our team, together with Right to Health Defense Group and Physicians for Human Rights, carried out a population-based study to assess health conditions, and access to health services in the conflict zone initiated in 1994 between the EZLN and the Mexican government [6]. We found that the most affected regions by the armed conflict have fared even worse than the rest of Chiapas State. We performed a household survey in the municipalities most affected by the armed conflict among three types of communities: opposition communities, pro-

government communities, and divided communities, i.e. which contained both opposition and pro-government groups.

This investigation identified serious deficiencies in both detection and treatment of PTB. In the 46 studied communities (n=2,997 households), we detected 29 cases of PTB among the population aged over 14 years. This means a rate of PTB of 85.3 per 100,000 in the general population, and of 161.2 among those aged 15 and older, almost three times the rate reported for the entire state. In this sense, only 13 (45%) cases of the 29 detected, had been identified by health services and were being treated. Of these 13 cases, one had not received any anti-TB treatment and six had defaulted from anti-TB treatment.

We also carried out two evaluations of a cohort of patients aged over 14 years diagnosed with PTB from January 1998 to July 2005, and found poor survival among them. In the first follow-up (performed during 2004-2006), the principal factors associated with PTB mortality were: age (45 years and over, OR=1.3; 95% CI=0.98-1.3), 0-3 years of schooling (OR=3.3; 95% CI=1.1-4.4), not living in the main village of their municipality (OR=1.2; 95% CI=1.0-1.3), living in a rural community (OR=2.7; 95% CI=1.1-6.8), not having been treated in DOTS (OR=1.2; 95% CI=1.0-1.3) and having defaulted from treatment (OR=11.5; 95% CI=5.3-24.8) [13].

In the second follow-up (carried out in 2008-2009), the factors associated with PTB mortality were age (45 years and over) and anti-TB treatment duration of under six months. The median survival time of those patients aged 45 and over who died was 718 days (range 0 to 3,185), while the median survival time in the reference group consisting of patients aged 15-34 years, was 688 days (range 8-1,841). With regard to the duration of anti-TB treatment, the median survival time among patients with incomplete treatment was 261 days (range 0-1,658), whereas among those dying in the reference group (with treatment completed), the median survival time was 1,137 days (range 202-3,185) [14].

The mortality rate in the patients studied was 4.6 per 100 person-years. Of the 78 deaths from PTB documented in this study, 25% occurred during the first six months following diagnosis (in other words, during treatment), 38% by the end of the first year from the date of diagnosis, 53% had died by the end of the second year, and 72% after three years.

The most important features of these studies are shown in Table 1.

3. Patch 2: Chine, Ecuador

During the decade from 1997 to 2006, inequalities of wealth and human development were extremely marked in Ecuador. The indigenous population, such as that residing in the central Andean province of Cotopaxi, has the highest poverty rates, and has many of its basic needs unmet. In Ecuador, up until 2006, the TB Prevention and Control Program was based on passive case finding of patients with respiratory symptoms (health personnel would check whether a patient visiting a health center had a productive cough of more than 15 days of duration). In contrast to what happens in cities, in rural areas the organization and functioning of the program relies on the presence of basic rural health teams; this means that is not

uncommon for health personnel to be absent. This situation, among others, has resulted in TB notification being irregular. Although the average incidence reported is 65/100,000,³ given the important level of under-reporting of TB cases, the true extent of the disease in Ecuador is unknown.

Setting	Frequency	Associated Factors
Chiapas, Mexico (only people 15 years of age and over)	Prevalence of PTB 21% in a hospital-based population with symptoms suggestive of TB	Association with age (35-44 years old), working in agricultural, and weight loss.
	Prevalence of PTB 11.1% among patients, consulting in primary health centers (PHC) with symptoms suggestive of TB	Association with poverty level
	Prevalence of PTB 277 per 100,000 persons studied in household surveys	Presence of blood in sputum; 50% of sensitivity in sputum test performed in PHC setting. High rate of defaulting treatment; and very high MDR-TB rates associated (by Logistic Regression) with previous PTB treatment, cough for more than 3 years and not being indigenous.
	Cohort of patients with PTB	Mortality was associated with poverty and deprivation characteristics and no access to DOTS.

Table 1. Pulmonary Tuberculosis (PTB) and associated factors observed within studies performed by GRAAL members in Mexico.

In Chine, an indigenous community of 653 inhabitants, in the parish of Angamarca, located in Cotopaxi Region, over 90% of its population have their basic needs unmet [15]. It is situated at an altitude of 3,500m above sea level and is two hours walk from the nearest health center, which during the period 2000 to 2004 was practically without staff. One of the co-authors of the present work (Natalia Romero) collaborated with the health team of this parish, during her period of rural medical training several years earlier. Following the diagnosis of one PTB case (the schoolmaster) in 2001, we conducted a study between 2001 and 2003, and found a prevalence rate of PTB-positive cases of 6.7% for the community as a whole [16].

On the basis of this single case, we saw the convenience of studying the total population of the community through a household survey (taking into account the experience obtained in Chiapas, México). The data collected was analyzed using the technique of multiple correspondence analyses, which allowed us to ascertain the risk and exposure factors in the community. All persons with chronic productive cough were asked to provide three sputum

3 World Health Organization. Ecuador: Health profile. Available at: <http://www.who.int/countries/ecu/es/> (accessed 12 August 2012).

specimens. Given the degree of social and geographical exclusion of the community, PTB was diagnosed only by smear test.

Two hundred and two persons were identified with chronic cough (fifteen days or more), 173 of them, productive. Of 92 coughers in which it was possible analyze their sputum, 44 (48%) were PTB positive (representing 6.7% of the whole population and 11.3% of those aged 15 years and over). Among men, the highest prevalence was in the 35–44 age group (20.6%) and among women in the group aged ≥ 45 years (16.7%). Also, 27% of families had between one and four smear positive members. The factors associated with presence of PTB were: previous history of active TB (OR=6.0; 95% CI=2.9-12.3), haemoptysis (OR=3.8; 95% CI=1.5-10.0), and history of participating in seasonal migration (OR=2.44; 95% CI=0.91-6.54) [16].

With the intention of making some contribution to resolving the PTB problem, our team reached an agreement with the inhabitants of the community of Chine, in order to implement the DOTS strategy, while at the same time taking account of aspects of the community’s world view. As consequence of this approach, we obtained a cure rate of 100%, confirmed by three negative smear-tests during the anti-TB treatment and cultures at the end of it (there were no defaults and no deaths) [17].

Although TB prevention and control programs encourage patients to visit health services and follow instructions, if they continue in their tendency to give little attention to socioeconomic, cultural and anthropological aspects, the results will be the same. How can better outcomes be expected if health services persist in acting as they always they do, including opening for restricted hours (from 8 am to 12 pm and from 2 to 6 pm)? In our intervention in Chine, symbolic referents, the religious dimension and rituals, as well as aspects of daily life (working hours, school, community and family calendar, seasonal migration, and traditional medical practices, among others) were taken into account.

The main results obtained in Ecuador, are shown in Table 2.

Chine, Cotopaxi, Ecuador	Prevalence of PTB 6.7% in an entire indigenous community	PTB was associated with prior history of PTB (OR= 6.0; CI 95%: 2.9-12.3), with haemoptysis (OR= 3.8; CI 95%: 1.5-10.0).
		Cure rate of 100% based on community consent for the performing of DOTS strategy

CI: Confidence interval; OR: Odds Ratio

Table 2. Pulmonary Tuberculosis (PTB) and associated factors observed within studies performed by GRAAL members in Ecuador.

4. Patch 3: Lima, Peru

One of the coauthors of the present work (Olivia Horna), as a nurse responsible for coordinating the application of DOTS, realized that the TB Program was relaxing various aspects of

the DOTS application, largely motivated by the economic conditions imposed in the area by the World Bank but also by recommendations from the Pan-American Health Organization itself: cessation of active case finding of coughers of 15 days or more on the grounds that the system was of low efficiency, and a switch to an ambulatory form of DOTS rather than in the patient's home, changes due to a shortage of funds to pay health technicians performing this function.

Given this situation combined with a feeling that the number of patients was rising at a higher rate than that calculated based on national rates, it was decided to perform a study to detect coughers of 15 days or more making use of the structure of the health system itself. The district of Ate-Vitarte was chosen to be targeted, since it consists mainly of lands occupied by migrants from the interior of the country, many forced off their lands due to violence between Peruvian armed forces and guerrilla movements from the interior, in particular Sendero Luminoso.

For this study, as in the cases of Chiapas, Mexico and of China, Ecuador, the health system approved and participated in order to guarantee anti-TB treatment and medical care for possible new cases identified by the study. Thus the same scheme was set up as employed previously in the outpatients department of Comitán hospital, whereby subjects recruited were people approaching the health system facilities in the area for medical care.

We interviewed 150 persons over 14 years of age who had productive chronic cough (fifteen days or more) seeking care in health services (primary care and hospitals). Of these, we obtained sputum samples from 142. The observed PTB prevalence rate was 12% [18], a figure very similar to that obtained in primary care centers in Chiapas (11%) [8]. None of the demographic or socioeconomic indicators analyzed were associated with PTB.

Of the variables studied, those found to be significantly associated with PTB, were: working away from home with respect those working at home (OR=6.99; 95% CI=0.89-54.61), persons commuting by minibuses compared with persons who used individual forms of transportation (OR=4.9; 95% CI=1.06-23.09), and commuting time one hour or more in a minibus (OR=3.35; 95% CI=1.12-10.1) [18].

Given the high prevalence of PTB in peripheral areas of Lima, as is the case of Ate-Vitarte District, and the results mentioned in the previous paragraph, we planned a study to determine whether the use of minibuses was associated with the spread of PTB. Commuting in these minibuses means that people travel in overcrowded situations with closed windows regardless of the weather, making trips of at least 30 minutes duration every day, in the company of TB patients going to a health center to receive DOTS treatment. Furthermore, if there is a strong association between using minibuses and the risk of infection, what would be expected among microbus drivers and fare-collectors that spend more than 8 hours per day in this environment?

Based on these precedents, we decided to carry out a study to assess infection by *Mycobacterium tuberculosis* and working conditions among workers of public transport [19]. In 2008 we performed a cross-sectional study with 104 workers from two public transport minibus companies of the Ate-Vitarte District. These minibus workers were interviewed and a tuber-

culin skin test (TST) administered. An induration greater than or equal to 10 mm was considered positive.

From these 104 workers, TST results were obtained for 73 (70.2%), of whom 56 (77%) were positive. We found that positivity was associated with the time they had worked on minibuses (more than two years, OR=11.04; 95% CI=3.17-38.43), and with working more than 60 hours per week (OR=9.8; 95% CI=2.85-33.72). This exposure gradient, a result of the working hours and time employed in the transport sector, stresses the importance of workers' job conditions.

Furthermore, strict revision of clinical histories of active TB patients in the health centers associated to the health districts of these workers, showed that standardized incidence rates for transport sector workers were 2.7- 4.5 times higher than those in the total working-age male and global populations of the health micro-network studied. The associations between TB and being a transport worker, and between MDR-TB and being a transport worker are both strong (OR 3.06, 95%CI 2.2-4.2 and OR 3.14, 95%CI 1.1-9.1, respectively). These results indicate that the use of informal public transport is a risk factor for TB infection and an occupational risk in countries with characteristics similar to those in Peru [20].

A summary of the main results obtained in Lima, is presented in table 3.

Lima, Peru	Incidence of PTB calculated within general population based on PHC micro-net data	TB associated with transport occupation (OR=3.06; CI 95%: 2.2-4.2) and with MDR-TB (OR= 3.14; CI 95%: 1.1-1.9)
	Prevalence of PTB 12% among commuters in a suburban area of Lima	Use of informal transport system: working away from home (OR= 6,99; CI 95%: 0.89-54.61; PPR = 6.06); commuting in minibuses (OR= 44.9; CI 95%: 1.06-23.09; PPR=4.09) and commuting more than one hour (OR=3.35; CI 95%: 1.12-10.1; PPR= 2.07)
	Prevalence of Mycobacterium Tuberculosis infection through PPD test of 77% among minibus drivers in informal transport	High work-related exposure: more than two years in job (OR= 11.04; CI 95%: 3.17-38.43) and working more than 60 hours per week (OR= 9.8; CI 95%: 2.85-33.72).
CI: Confidence interval; OR: Odds Ratio; PPR: Positive Prevalence Ratio		

Table 3. Pulmonary Tuberculosis (PTB) and associated factors observed within studies performed by GRAAL members in Peru

5. The patchwork: What do these findings mean? Are they useful?

TB, far from being under control, as was believed at the end of the decade of the 1990s, continues to cause many deaths, disability, and health expenditure; indeed, it has been recognized that the situation may be worsening due to an accumulation of structural condi-

tions favoring its appearance and development: increased poverty in important population nuclei (which are the most susceptible to the disease), migratory movements (whether due to economic, work, political or even environmental issues), higher incidence of other immunosuppressive diseases (mainly HIV/AIDS and diabetes), or weakening of health of certain individuals (such as due to malnutrition, and chronic pneumopathies), the increasingly more common appearance of forms of MDR, and the shortage of health resources to cope with TB, mainly in areas of greater socioeconomic exclusion. In this sense, the so-called developed countries have also felt the impacts of the disease, largely due the appearance of HIV/AIDS and to cases among immigrants who, whether legally or illegally, settle in foreign territories seeking to improve on the conditions which caused them to leave their places of origin.⁴ These populations are generally speaking the most socioeconomically disadvantaged groups.

There is no doubt that TB is an outcome indicator of the socioeconomic, cultural and political structure of a population. TB is a historical reflection of the forms of social construction, particularly of the post-industrial revolution era experienced in capitalist countries. TB in this sense feeds, to a greater or lesser degree, depending on circumstances, on the social context in order to reproduce, and this fact finds expression, as documented in the present studies, in various gradients of exposure and susceptibility to the disease, in which the more socioeconomically disadvantaged groups are the ones most affected by the disease, but the ones which, paradoxically, usually receive least attention, whether in terms of prevention, diagnosis, or treatment, and hence cure rates are low.

Two million people die every year from TB, the majority of them in the “under-developed countries”. The Global Plan to Stop TB 2006-2015 aims to treat 50 million people, save 14 million lives, and expand equitable access to quality diagnosis and treatment. According to this Global Plan, by 2010 it was expected “to be using diagnostic test that allow rapid, sensitive and inexpensive detection of active TB... and introduce the first new TB drug in 40 years. It also expects to see a new, safe, effective and affordable vaccine available by 2015” [21]. However, the World Health Organization, Pan-American Health Organization and Governments in general, establishing targets for TB control programs, take as their basis the reports they receive from the countries themselves, with the result that programs elaborated are eminently political, whose objectives and information basis constitute a kind of feedback system which rapidly departs from reality.

TB control programs thus planned are designed as though the social structure of the countries was homogeneous, and this impedes acting in such a way as to take account of the particularities of marginal populations, which are the ones presenting the highest rates of prevalence of this disease. The usual ways of working lead to government planning and actions being based on central estimates and tackling of global objectives. For example, the global medium-term goal for TB control is to halve TB prevalence and death rates by 2015 as compared to 1990 levels, and to achieve a reduction in its incidence, as part of the Millennium Development Goals (number six) [22,23].

⁴ The first report of a rise in cases of HIV/AIDS was published in 1991, affecting New York City, and the status of TB was changed to that of an AIDS-defining disease, although it has been calculated that currently 50% of new TB cases in the European Union occur among immigrants.

This type of planning and programming of objectives apparently does not take account of the particular situations affecting the population, above all those aspects which are notably different from the global mean values. In fact the few population based studies available, some involving Latin American countries, likewise fail to treat marginal populations specially. For example, if it was not for international support, few governments would have sufficient resources to conduct national health surveys, which are usually carried out through household interviews, based on self-perceived morbidity, and which hardly ever include laboratory tests to identify diseased individuals (TB in our case). Generally, the level of disaggregation of surveys of this type goes no further than large geographical regions (north, south, east, etc), tending to disguise inter- and intra-regional heterogeneity, and the data are analyzed based on artificially created convenience categories, not based on observed patterns of disease or deaths.

In other words, it is usual that global policies emanating from the international agencies and institutions ignore the true situation, applying criteria of homogeneity in the calculation of targets, costs of equipment and supplies and staffing levels, among other aspects. Curiously, despite it being well known that social factors are related with TB, they are not taken into consideration in order to improve the quality of plans to control it.

In order to identify, analyze and ideally contribute alternative solutions to the problem of unmet needs of socioeconomically excluded populations, means working with samples which are not representative of the general population, but rather focused on these sub-populations, biased precisely due to their conditions. In this sense, our team has been employing the patchwork approach, involving studies focusing on marginal or susceptible populations, those with the worst socioeconomic and health conditions. In the case of TB, these circumstances (poverty, social vulnerability, and shortage of health facilities) are well recognized as one of the basic determinants of the presence and spread of the disease, but its characterization usually is not considered by health systems in their solution proposals [24].

For example, in marginalized rural areas, in the best case, active TB case finding is limited in practice, to identifying chronic coughers among users who seek health care. This results in at least three possible situations: a) there may be delays in the TB diagnosis (patients arrive in an advanced stage of the disease);⁵ if the medical consultation is for reasons other than respiratory symptoms, TB may not even be detected;⁶ and, c) that a certain proportion of patients do not use the health services (due to accessibility barriers which may be geographical, economic or cultural)⁷ and hence are not even diagnosed [10].

⁵ Several studies have shown that groups living in conditions of greater socioeconomic marginalization present longer delays in seeking care for health problems [26,27].

⁶ In several studies we found that PTB status is not associated with the reason for visiting health services [10].

⁷ Political conflicts (belonging to a particular organization), religious conflicts (not belonging to the religion predominant in the community), administrative barriers (nearest clinic not the one assigned officially), and conflicts deriving from access to and utilization of natural resources (water, timber, etcetera) can mean that certain individuals are denied access to health services, or they are denied medical care or drugs [6].

In this context, women living in remote and marginalized regions, have a more pronounced lack of access to health services due to gender reasons: there are differences in the process of seeking medical care, and in the quality of the care received between women and men [25].

Furthermore, in Chiapas, Ecuador and Peru, as in many other regions of Latin America, TB cases notified to the information systems of the health sector, and from which incidence rates are estimated, correspond to cases detected in health services by acid-fast bacilli. We have documented that in rural and marginalized areas, its sensitivity is around 50%. This is an important aspect to consider because health system detection of TB cases is based on smear testing, meaning that in marginalized communities many cases are not detected. In consequence, the target of detecting at least 75% of cases is far from being reached, implying the presence of a not unappreciable risk of transmission of TB [9]. Indeed, the detection rate in hospitals studied in Chiapas is below this figure of 75%. The suboptimal case detection rate reflects an inadequate of quality medical care, probably health personnel are often overwhelmed by daily activities, as well as insufficiently trained, motivated, aware, and remunerated [10].

In order to increase detection rates, as it was demonstrated, the health system must take into account the considerable difficulties involved in obtaining and analyzing sputum samples in marginalized areas: cultural barriers (language spoken, world view) and economic barriers, as well as technical problems to be overcome in order to obtain adequate quantity and quality of sputum samples. It is therefore necessary to reduce the cultural and socioeconomic barriers between health care providers and people [10]. Not surprisingly, some results of our investigations show that apart from cultural barriers, there are also structural barriers [11].

In the same way, we have found that a very low proportion of patients eligible for anti-TB treatment effectively receive such treatment, and very high proportions of treatment failures and incomplete follow-up [10].

Two further aspects deserve special attention in the context of the studies conducted in Chiapas, Mexico, as well as in Peru: the problem of MDR, and the high mortality among patients diagnosed of PTB. Both indicators constitute expressions of the complete failure of the health system which, for whatever reason, did not manage to adequately treat these people, who consequently either died of TB, or were left as chronic MDR cases (which would lead to their death also, sooner or later).

In the case of MDR, it is well documented that the vast majority of cases of this type result from inappropriate treatment and follow up by the health system. According to official statistics, worldwide, the rates of MDR recorded in 2009 and 2010 were the highest ever, and trends in MDR rates are unclear in the majority of countries [28]. The observed rates of MDR in Chiapas suggest that in marginalized and excluded regions, it is a serious public health problem of alarming proportions. While the MDR rates calculated for the country as a whole are 1-3% for primary, and 20% for secondary MDR, in our studies these rates were 4.6% and 29%, respectively [12].

Although our results were made known to the health authorities, there are no signs to suggest that the TB situation has improved: the health system continues failing to diagnose cases

appropriately and application of the DOTS strategy is very deficient: even if TB patients are diagnosed, in many cases they begin, but do not complete their anti-TB treatment. In this sense, we must emphasize the following aspects:

- a. It is extremely difficult to perform culture analysis, in order to determine MDR status, in a patient with less than six months of treatment, due to poor quality sputum samples. The main obstacles to obtaining good quality sputum samples are: barriers in communication with indigenous people, distance of the communities from the centers where samples are processed, unsuitable transport conditions of samples (risk of exposure to sunlight or lack refrigeration), among others.
- b. It is very plausible that in indigenous populations, due to their having less contact with health services, there are more undiagnosed TB cases and that, among non-indigenous patients, more TB cases are diagnosed but not necessarily treated adequately [12].
- c. A patient confirmed with MDR condition, is practically impossible to treat, given the high cost of the secondary treatment, and because if the health system is incapable of guaranteeing the follow up of a patient sensitive to the four primary drugs during six months, it is probably even less able to follow up a MDR patient not only in terms of the time required (from 6 months to 1.5 or 2 years) but also in terms of level of patient care, due to the possible secondary effects of the “second line drugs” employed. In this sense, if a program cannot guarantee appropriate follow up and compliance with treatment among TB patients, it should not initiate their treatment, thus condemning them to a situation of no hope of cure, with all that this implies, not only for the patient, but also for his family, who apart from watching their family member suffer, are also exposed to the possibility of their catching the disease.

With regard to mortality due to TB, we have found unacceptably high rates. In addition, a considerable proportion of TB patients die without having received any medical care.⁸ We found that 55% of patients whose death was related to TB, had died within two years of being diagnosed, possibly due to delays in diagnosis, and the poor quality of the follow-up in their anti-TB treatment. Whereas the life expectancy in Chiapas is 72.2 years [29], the average age of deceased patients was 47.4 years, representing an average of at least 24 potential years of life lost [13]. We believe that the accumulation of unfavorable living conditions such as malnutrition, poverty, as well as deficient and/or lack of health services, makes them an especially vulnerable group. According to official statistics, while in 2009 the PTB mortality for the country was 1.7/100,000 inhabitants in Chiapas it was 3.79 with the same denominator [14].

Our findings have provided evidence that in the area studied, patients being aged 45 years and over, not having completed the established six months of treatment, and not having been treated via the DOTS strategy, are all associated with a higher risk of the patient dying from PTB.

⁸ Eighteen percent of patients traced to their homes, in a study carried out in Chiapas, had died. Of the 40 deaths presumed to have been associated with PTB, 33 died without having received medical care [13]

Based on our findings, we can say that people from rural and indigenous communities suffer mistreatment by the health services [30], meaning, among other aspects, deficient application of the DOTS strategy (sometimes due to shortages in the supply of anti-TB drugs [31], or poor follow up), leading to higher mortality and increasing their chances of becoming MDR cases [12,13].

Another fact that reduces the chances of successfully carrying out patient follow up, is migratory movements. Migration in the region is mainly due to economic factors, but can also be for health reasons. Sometimes patients are registered by health services as urban patients when in fact they are not, or they give a false address in order to obtain the first consultation, but subsequently return to their rural communities or find another place to live without notifying the health services.

In addition, health services give little consideration to socio-cultural and anthropological aspects. For example, in indigenous medicine the process of health and illness involves their world view, their personal and community histories, in an atmosphere of trust in which supernatural intervention, transgression of social norms, culpability, or malice on the part of enemies, are all admissible possible causes of the disease [16,32,33]. In this sense, patients may seek care from traditional medicine practitioners, who attend them in accordance with their age-old diagnostic and therapeutic rituals.

On the other hand, the use of public transport is a risk factor of TB not only among users, but also among minibus drivers and fare-collectors, and hence may be considered an occupational disease in these workers, who work in conditions such that not only do they have precarious employment, with all its implications (temporary contract, no social security or medical insurance, among other aspects) but also their job places them in a position of greater vulnerability to TB, since if they don't work, they don't get paid, and hence it is very probable that many of them go to work despite their illness, if they are able to do so, only seeking care when the disease really makes it impossible for them to continue working. In this sense, a worker with active PTB is a source of infection not only for co-workers but also for passengers. In countries where TB is endemic with increased circulation of resistant mycobacteria, the situation could be even worse. In a situation of this kind, the health system should be implementing, at very least, home-based DOTS to avoid exposure as far as possible, as well as implementing specifically designed occupational health programs [19,20,34].⁹

Observation of the particular facts which determine the appearance of TB and its prognosis, shows that the diagnosis and treatment strategies employed by the health services are just that, strategies, rather than ends in themselves, something which, unfortunately, is frequently emphasized. If more clearly focused measures are not taken, TB will not disappear in marginalized areas, despite the fact that trends in the ecological indices suggest that TB is tending to decline in Latin American countries; rather, it will persist as a greater public health problem for years to come.

⁹ In fact, the authors believe that more attention ought to be given to the risk of infection, by any aerielly transmitted disease that utilization of public transport represents, for both passengers and the workers.

In our view, to remain with the idea that TB is decreasing in Latin America, tends to conceal the failure which the rise in MDR patients represents. In any case, countries are alarmed by the rise in MDR because of the cost of treatment and its inefficiency, not necessarily for the health and welfare of TB patients, particularly if they are poor, as our studies suggest.

One discussion point is clear. Objective-oriented programs which attribute to the entire country the same values of incidence and detection rates present a problem known as “trimmed estimation”, meaning that when the established objectives are reached, case finding and detection are relaxed, or the resources to permit continuing with case finding and/or provision of treatment, are cut short.

If, together with these data we take into account cases in areas enjoying lower TB incidence, and if this total was the true number of existing cases, the result would necessarily be a systematic reduction in incidence rates, leading to false optimism, whose historical cost has been a relaxation of efforts to prevent and control TB worldwide during the decade of the 1980s of last century.

Imagine the simple case that we have an incidence rate of X , in a given country. This figure conditions the work plan for the coming year in terms of supplies, staff, anti-TB treatment drugs, etcetera. Later on, 70% of the reporting areas indicate a rate of $0.9X$, another 15% of areas a rate of X , and the remaining 15% provide no data on rates, but their population is taken into account in the denominator. The final rate for this country, based on these hypothetical figures, would be $0.78X$. In other words, not receiving reports from the areas with the worst conditions provokes an apparent reduction in the global rate.

Unfortunately, even without questioning the figures declared, we know that areas which do not report (or report, but at best with high levels of under-notification) are the ones with the poorest conditions, both in terms of the socioeconomic conditions of the population which theoretically must be cared for, and in terms of the lack of resources and other failures in the organization and functioning of the program. Thus, by apparently having fewer cases, the resources dedicated to the TB prevention and control program are also cut back, and this creates a vicious circle which is difficult to break, so that program outcomes may be false, i.e. underestimates of the numbers of cases.

There is therefore a clear need to promote studies specifically aiming to analyze the population groups most vulnerable to TB, and in this way ascertain more precisely their situation, even when they are not representative of what happens in a given country. Continuing to carry out representative population based studies can only yield the probably already known rate for the country as a whole, and the situation of marginal groups will not be reflected in such rate.

In this sense, the patchwork studies contribute very valuable elements which help to make more visible and understandable the situation of population groups which go unnoticed in the global rates utilized in public health. We would encourage potentiating studies which break with the classical schemes, and use methods appropriate for the analysis of samples considered too small by classical approaches, but without renouncing the maximum of scientific rigor, as demonstrated by the doctoral theses developed in projects conducted in the three settings we have dealt with, Chiapas (Mexico), Chine (Cotopaxi,

Ecuador), and Lima (Peru), and whose results have been published in journals of medium and high impact factor.

On the other hand, Ecuador and Peru present changes in their control program strategies: active case finding, incorporation of economic incentives, strategies to reduce stigma among patients, citizens' observatories and integration of TB research in academic circles, among other aspects. It will be fundamental to perform studies which evaluate possible effects of such changes.

As the studies have shown, a failure to introduce changes in the structure and functioning of TB prevention and control programs would have as a consequence that this disease will continue to severely affect the most marginalized sectors of society:

In the field of TB prevention, several authors recognize that effective efforts have not yet been fully considered, and that it is necessary to improve this issue, for example through better vaccines and better chemotherapy for preventive treatment [22].

In the field of TB diagnosis, efforts must be made to reinforce active case finding of coughers, as for example, incorporating other diagnostic tests which allow better detection of the disease (from the use of cultures, and conducting molecular tests, to the search for faster diagnostic methods, such as biosensors). Epidemiological surveillance systems rely on smear testing, failing to take into account that in marginalized and rural areas these tests with only around 50% sensitivity, leave large numbers of cases undetected by the health services, or who will only be captured in advanced stages of the disease [12-14]. It is not unusual to find, within a given Latin American country, that while highly developed regions have advanced technologies available for TB diagnosis, in others the only possibility for diagnosis is the smear test. Nor is it unusual in regions of this type to find that smear testing is done badly, both in numerical terms (hardly ever obtaining three samples from a given patient), and in terms of quality (for reasons attributable to the poor quality of samples, such as errors in collection, storage, transport, processing and reading of results) [10,35].

In regard to anti-TB treatment, while the DOTS strategy has achieved a certain level of effectiveness in curing patients and saving lives, the epidemiological impact has so far been less than predicted [22], perhaps among other reasons, because treatment programs do not find patients soon enough to significantly reduce transmission [5]. Thus it is necessary to ensure: a) training, awareness and supervision of health personnel about the importance of avoiding patients defaulting from treatment, as well as guaranteeing the appropriate supply of medication; b) when necessary to adapt the DOTS strategy, both socially and culturally, taking into account the community health agents, community world view, and implementing the scheme in the patient's homes, supporting them and their families economically during their treatment; and c) that patients and their family are accompanied during the six months of treatment, in order to cope with possible secondary effects and to overcome possible barriers (alcoholism, religion, gender issues, seasonal migration, etcetera) which make compliance with anti-TB treatment difficult.

6. Conclusions: Tuberculosis as indicator of structural violence and violations of human rights

One of the main aspects we want to stress in the present work is the fact that analyzing TB through the measurement of global indicators conceals the situation of vulnerability to the disease suffered by socioeconomically disadvantaged population groups. The data obtained in the different studies we have presented show that there is a need for methodological approaches (such as that known as patchwork studies) which allow the measurement and analysis of the distribution of TB among different population groups.

It is well known that TB is one of the infectious diseases which has caused the most deaths among humans [36], above all among the socioeconomically most vulnerable groups [37]. These groups, apart from having higher risks of infection, developing active disease, and dying due to TB, are also the ones facing the greatest barriers (including information barriers) to access health services [38]. In this sense, and given that nowadays the medical resources to cure the disease are available, the fact that even today TB continues to cause deaths may be considered as an indicator of the violation of human rights in excluded and marginalized populations, as well as an indicator of “structural violence”, given that it is precisely the social, economic, cultural and political structures which do not allow certain social groups to achieve their full potential, while other groups do so, due to the unequal distribution of power and available resources, placing some in conditions of social privilege and others in situations of social vulnerability [39].

The social context of TB is strongly related with social justice. The history of TB teaches us that the improvement of social conditions, work conditions and the access to better quality food decreased its mortality in the pre-microbial stage [40].

Taking as a starting point that the appearance, development and distribution of TB is largely influenced by social determinants, and that public health achievements will depend on actions outside the health care sector [41], two forms of interventions are necessary: a) those reducing peoples’ vulnerability, such as poor living and working conditions, and improving nutrition, among other aspects (such as structural and socioeconomic conditions), and b) by seeking alternatives that promote higher levels of prevention, diagnosis and cure of TB.

Two clear examples that help to visualize health related inequalities in respect to TB are firstly, the so-called “10/90 gap”, in reference to the fact that only 10% of worldwide expenditure on health research and development is devoted to the problems primarily affect the poorest 90% of the world’s population, and that 90% of worldwide expenditure is devoted to the problems that affect the richest 10% of the world’s population.

The second example is the comparison between HIV-AIDS and TB. Whereas the first cases of HIV-AIDS were described during the decade of the 1980s of the last century, today it is one of the diseases which have received the most resources for its prevention and treatment, and notable advances have been achieved in these aspects, and in improving survival of patients. At the end of the last century, it was practically a death sentence, and yet today we have a series of drugs which increase both survival and quality of life of these patients.

In contrast, despite the fact that TB has been accompanying humans for thousands of years, and that the etiological agent was first described in 1882, it is the disease which has alone caused the greatest numbers of deaths in the adult population worldwide, and for which the resources currently dedicated are insufficient to lead us to expect, in the foreseeable short or medium term, the appearance of more effective measures for its control. Perhaps this is because it is considered a disease of the poor, and thus there is no incentive to “invest” in it? As some of our colleagues have pointed out: “even if the Global Plan to Stop TB is successfully implemented and results in the expected rate of reduction in incidence of about 6%, the global incidence rate in 2050 would still be of the order of 100 per million of inhabitants, i.e. about 100 times greater than the elimination target” [22].

From the viewpoint of international human rights law, by providing woefully substandard health services to marginalized populations, and failing to assure prevention of disease through appropriate public health measures, governments violate their obligations in human rights [6].

In this sense, high rates of TB constitute a reflection of the fact that certain populations face important obstacles in their exercise of the right to health, and other economic, social and cultural rights, due to the main social determinants of this disease being associated to social exclusion and poverty [31]. The presence of TB constitutes a violation of the right to the highest attainable standard of physical and mental health (“the right to health protection”) which is inextricably related to the right to life and other human rights that allow an individual to live with dignity [6,42].

The International Covenant on Economic, Social and Cultural Rights (ICESCR) in its Article 12, Paragraph 2, sets out the steps states should take in order to fulfill the highest attainable standard of health, and includes “the prevention, treatment and control of epidemic, endemic, occupational and other diseases, as well as the creation of conditions which would assure to all medical service and medical attention in the event of sickness”.

The General Comment issued by the Economic, Social and Cultural Rights Committee [43], establishes that “the underlying determinants of health, such as including adequate sanitation facilities, hospitals, clinics and other health related buildings, trained medical and professional personnel” have to be available in sufficient quantity with the States parties, and specifies that health facilities, goods and services must be available, accessible, acceptable and of adequate quality.

In this General Comment, accessibility has four overlapping dimensions [43, paragraph 12 (b)]:

First, the principle of non-discrimination,¹⁰ on the grounds of sex (poorer quality of care among women than men), ethnic group (patients from indigenous communities receive poorer care), color, political filiation (belonging or not to the dominant political party in a region can affect access to care and to medication), religion (care may be denied to community members not belonging to the dominant religion), physical or mental disability, health status, sexual

10 Non-discrimination is a core principle for the full realization of the right to health, as for all human rights [6]

orientation, among others. A violation occurs when there is the intention or effect of nullifying or impairing the equal enjoyment or exercise of the right to health [43, paragraph 18].

Second, physical accessibility, meaning that health facilities, goods and services must be within safe physical reach for all groups, specially the vulnerable or marginalized ones, such as ethnic and indigenous populations.

Third, economic accessibility requires that health facilities, goods and services must be affordable for all, including socially disadvantaged groups. It points out that poorer persons should not be disproportionately burdened with health expenses, and those individuals (e.g. peasants) who through not having access to cash face particular difficulties, need to be considered in governmental policy and practice.

Fourth, the right to seek, receive and impart information and ideas concerning health issues, which includes health information in indigenous languages.

With regard to acceptability, it is understood that “health facilities, goods and services must be respectful of medical ethics and culturally appropriate... [and] requires respect for traditional medicines and practices which have not been shown to be harmful to human health” [43, paragraph 12 (c)].

For adequate quality, it requires that health facilities, goods and services must be scientifically and medically appropriate and of good quality (skilled medical personnel, scientifically approved and unexpired drugs, and hospital equipment, among other aspects) [43, paragraph 12 (d)].

Unfortunately, the findings of our studies indicate that health care is not sufficiently available or accessible (in either quantity or quality) to more disadvantaged social groups, creating mistrust among them of the government health services, something that is reflected in the relatively high percentage of people that do not use these services, even for vaccinations. This situation is more marked when health services are not culturally adapted, when people perceive mistreatment on the basis of their ethnicity or social conditions and health personnel make disparaging remarks about their habits and demeanor [6].

Other indicators of violation of human rights in TB patients are:

- Failure to improve the level of health in a population. The fact that health indicators, in our case indicators of TB do not improve in a population, even though they do not worsen, constitutes a violation of human rights (specifically of the right to “Non-retrogression and Adequate Progress”).
- The presence of inequalities in access to quality and coverage of health services (in the case of TB affecting aspects from prevention to cure).
- The lack of meaningful popular participation, in regard to the making of decisions which involve the design, organization and functioning of health services. It is common to find that local health services nominate a “health promoter”, charged with various activities such as vaccination, routine pediatric checkups, etcetera, but this does not necessarily mean the community has a voice or participates in the definition of its own priorities, decision-making

in regard to planning of activities or elaboration and evaluation of health programs for the community. Veneklasen and colleagues have said [44]: "True rights-based participation requires programs that enable people to be active, informed and critical agents and citizens, rather than objects of charity". In this sense, the International Labor Organization, Convention 169 [45] stresses that health services shall, to the extent possible be, "planned and administered in co-operation with the peoples concerned and take into account their economic, geographical, social and cultural conditions as well as their traditional preventive care healing practices and medicines".

- The lack of accountability in health programs, which in addition are usually not evaluated. In this sense, the fact that a person is not treated appropriately by the health services, which in itself constitutes a violation of his right to health, should also imply a right to compensation by the State, which could take the form of restoration of his health, economic compensation, satisfaction or guarantees that the situation will not be repeated. On the other hand, if it is true that more resources are needed, they must be spent in such a way as to foster self-sufficiency and reduce inequities. Greater health care expenditure does not necessarily reduce inequalities [5].
- This dimension is also related to the enactment and enforcement of laws to provide sanctions for gender based violence or sexual abuse of women patients by health personnel, as well as people affected by mistrust. In addition, a legal framework must be adopted to operationalize the protection of patient human rights in the health services, establishing mechanisms for monitoring their compliance. The figure of a human rights ombudsman is a good example for monitoring, to investigate and sanction perpetrators in cases of abuse or malpractice and medical negligence claims [6].
- The lack of multi-sectorial strategies. Governmental programs should not compete among themselves, but rather be designed *inter alia* to promote health services, improve adequate dwelling conditions, education, work, and adequate nutrition. Until this happens, the plight of marginalized populations will persist. In the last instance, violations of the Economic, Social and Cultural Rights occur "when a state fails to satisfy a minimum core obligation to ensure the satisfaction of, at very least, minimum essential levels of the rights" [46].
- The lack of access to health information. Social participation and monitoring are impossible without access to information. This implies that governments should collect data on a disaggregated basis (by ethnicity, gender, socio-economic status, language, among other aspects) and this information, together with the methodologies used, must be readily available to the public. Of course, it also includes the right of TB patients to see their medical records, to give informed consent in all procedures, and to confidential management of their disease.

The performance of patchwork studies has allowed us to identify, evaluate and measure the situation of marginalized population groups in three different contexts (Chiapas, Mexico; China, Cotopaxi, Ecuador and Lima, Peru). Our findings revealed the poor quality of diagnosis and treatment of TB patients. Our data can be useful not only in the studied regions, but also in other countries with similar socioeconomic inequalities, if they are taken into account by

the health authorities in order to provide all people (especially the more socially vulnerable groups) with: effective prevention programs, a reliable and timely diagnosis, adequate anti-TB treatment and follow-up, clear and appropriate information and counseling about TB (what it is, mechanisms of transmission and possibility of infecting others, etcetera).

In consequence it is necessary change the dysfunctional health system that contributes to the persistence and intensification of exclusion, voicelessness, and inequity, while simultaneously defaulting on its potential and obligation to fulfill human rights and contribute to the building of more equitable, egalitarian and democratic societies. The history of TB teaches us that the improvement of social justice led to increase the global health conditions and thus, it avoids the called “social diseases”, including TB. The academic community has much to say and actively contribute in these aspects. The first step is to do research in order to make visible excluded people. To analyze, sensitize and lead to better socioeconomic conditions is an assignment for all of us.

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