Social determinants and inequalities in tuberculosis incidence in Latin America and the Caribbean

César V. Munayco,1 Oscar J. Mújica,2 Francisco X. León,3 Mirtha del Granado,3 and Marcos A. Espinal4

ABSTRACT

Objective. To identify key social determinants of tuberculosis (TB) incidence among countries in Latin America and the Caribbean (LAC), a geographic area regarded as one of the most socioeconomically unequal in the world.

Methods. An ecological study was conducted at the country level. Data were obtained from several institutional-based sources. Random-effects regression modeling was used to explore the relationship between several social determinants indicators and TB incidence rates in 20 LAC countries in 1995–2012. Standard gap and gradient metrics of social inequality in TB incidence among countries in 2000, 2005, and 2010 were then calculated.

Results. TB incidence rate trends were significantly associated with health expenditure per capita and access to improved sanitation facilities, as well as with life expectancy at birth and TB detection rate, after adjusting for other socioeconomic, demographic, and health services variables. Absolute and relative inequality in TB incidence remained mostly unchanged: countries at the bottom 20% of both health expenditure and sanitation coverage distributions concentrated up to 40% of all TB incident cases, despite a considerable decline in the overall TB incidence mean rate during the period assessed.

Conclusions. Along with the intensity of TB control (reflected by TB detection rate), both access to sanitation (as a proxy of quality of living conditions) and health expenditure per capita (either as an indicator of the level of resources and/or commitment to health care) appear to be key determinants of TB incidence trends in LAC countries. Inequalities in both health expenditure per capita and access to sanitation seem to define profound and persistent inverse gradients in TB incidence among LAC countries.

Key words. Tuberculosis; social determinants of health; social inequality; equity in health; Latin America; Caribbean Region.

Tuberculosis (TB) is still a public health problem in the Region of the Americas, representing the second cause of death by a unique infectious agent (1). The Region accounted for 3.3% of TB incident cases worldwide in 2012 (2). The World Health Organization (WHO) estimated
an incidence rate of 28 cases per 100 000 population in the Americas, ranging from 3.8 per 100 000 in the United States to 222 per 100 000 in Haiti. In the same year, the WHO best-estimate of the TB incidence rate for Latin America and the Caribbean (LAC) was 43 cases per 100 000 population, 11 times higher than the incidence rate for North America (3).

Since 1990, the TB incidence rate in the Americas has declined 2.6% per year on average, and the Region is on track to meet the corresponding Millennium Development Goals (MDG) target (2). This rate of decline, however, has decelerated since 2008 and is considered slow, despite successful implementation of both Directly Observed Treatment Short-course (DOTS) (1996–2005) and Stop TB (2006–present) strategies by national TB programs. In an area dubiously distinguished as one of the most inequitable in the world in goods distribution (4, 5), such deceleration and slow pace of progress toward TB elimination have been attributed to the persistence of prevailing factors linked to poverty, social inequality and exclusion, and rising urbanization. These factors, in turn, generate living conditions and circumstances favorable to TB transmission, regardless of disease control measures put in place (6, 7).

Historically regarded as the social disease par excellence (8, 9), TB plummeted drastically during the 19th century in Europe—a result of social reforms and improved living conditions prompted by the Industrial Revolution and despite the absence of curative chemotherapy (10, 11). Yet, modern TB control strategies have been dominated by the germ theory paradigm. More recently however, in part stirred by the work of the Commission on the Social Determinants of Health (12), and in part by a renewed focus on TB clustering around disadvantaged individuals and communities (13–15), the push has been toward addressing the disease’s more distal determinants. These are the so-called ‘causes-of-the-cause’ that help explain the unjust inequalities (i.e., inequities) in TB burden across the social gradient. Addressing social determinants may be more effective for achieving long-term TB control.

In order to identify potential entry points for intervention, several researchers have recently proposed a number of convergent theoretical frameworks that attempt to integrate a comprehensive model of causal pathways, mediators, and effect modifiers between distal, upstream determinants and proximate, downstream TB risk factors (11, 16–20). In line with these conceptual models—in particular Löffroth’s (18), which highlights the causal role of globalization; migration and urbanization; demographic transition; weak and inequitable economic, social, and environmental policies; low socioeconomic status and poverty; low education; and weak health systems in TB incidence and long-term TB control—the present study conducted an exploratory analysis of potential determinants of TB incidence trends in LAC countries in 1995–2012 and quantified the magnitude of associated inequality. A number of variables from the socioeconomic, demographic, health services, and TB program management domains were studied. The hypothesis was that, unless national TB programs were universally successful in TB control, more distal social and economic determinants would be prominent in driving TB incidence trends and inequality gaps and gradients at the ecological level.

MATERIALS AND METHODS

Study design

This was an ecological, country-level, observational panel data study, from which random-effects regression models were run to determine the relationship between trends in TB incidence and indicators of social determinants across LAC countries; standard gap and gradient metrics of social inequality in TB incidence over time between countries were also measured.

Data analysis

All variables were logarithmically transformed to achieve linearity and stabilize residual variation in the random-effects regression analysis. To determine which independent variables explained TB incidence, a panel data analysis was performed based on a random-effects regression model indexing by country and time. The decision for a random-effect, rather than a fixed-effects regression model, was informed by the Hausman test, which showed that the unique errors were uncorrelated with the regressors. To test the assumptions of this model, diagnostics tests for heteroskedasticity, serial correlation (Lagrange-Multiplier [LM] test), and cross-sectional dependence (Breusch-Pagan LM test of independence) were performed (27).

Selection of variables for inclusion in the model was guided by Löffroth’s theoretical framework, described elsewhere (18). Improvement in the adjusted $r^2$ was used to compare the fit of two models. The statistical significance of the final model was defined by the minimal model containing only variables that were significant at $P < 0.05$ in 2-sided t-tests, those with the highest $r^2$, and compliant with the theoretical framework (28). R language was used to perform all the analyses and data management, and its “plm package” was used specifically to do the random-effects regression model (29, 30).

After identifying the final variables in the model, the analyses explored inequalities in TB incidence between countries by using those variables as equity stratifiers and computing standard metrics of gap and gradient inequality. These were guided by WHO methodology, described in detail elsewhere (31, 32). The inequality analyses were done independently for 2000, 2005, and 2010, to assess changes over time. Unbiased (i.e., population-weighted) TB incidence rates
Unemployment is the proportion of the labor force that is unemployed but available for and seeking work. Definitions of labor force and unemployment differ by country. Definitions of labor force and unemployment differ by country.

**TABLE 1. Variables included in the exploratory study of potential determinants of tuberculosis (TB) incidence in Latin America and the Caribbean (LAC)**

<table>
<thead>
<tr>
<th>Domain and variables</th>
<th>Definition</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dependent variable</td>
<td>Incidence of tuberculosis is the estimated number of new pulmonary, smear positive, and extrapulmonary tuberculosis cases. Incidence includes patients with HIV.</td>
<td>(21)</td>
</tr>
<tr>
<td>Macroeconomic policy</td>
<td>GDP per capita based on purchasing power parity (PPP). PPP GDP is gross domestic product converted to international dollars using purchasing power parity rates. An international dollar has the same purchasing power over GDP as the U.S. dollar has in the United States. GDP at purchaser’s prices is the sum of gross value added by all resident producers in the economy plus any product taxes and minus any subsidies not included in the value of the products. It is calculated without making deductions for depreciation of fabricated assets or for depletion and degradation of natural resources. Data are in current international dollars.</td>
<td></td>
</tr>
<tr>
<td>Gross Domestic Product (GDP) per capita, PPP (current international $)</td>
<td>GNI per capita based on PPP. PPP GNI is gross national income converted to international dollars using purchasing power parity rates. An international dollar has the same purchasing power over GNI as a U.S. dollar has in the United States. GNI is the sum of value added by all resident producers plus any product taxes (less subsidies) not included in the valuation of output plus net receipts of primary income (compensation of employees and property income) from abroad. Data are in current international dollars.</td>
<td>(22)</td>
</tr>
<tr>
<td>Gross National Income (GNI) per capita, PPP (current international $)</td>
<td>Health expenditure per capita is the sum of public and private health expenditures as a ratio of total population. It covers the provision of health services (preventive and curative), family planning activities, nutrition activities, and emergency aid designated for health, but does not include provision of water and sanitation. Data are in international dollars converted using 2005 PPP rates.</td>
<td>(22)</td>
</tr>
<tr>
<td>Health expenditure per capita, PPP (constant 2005 international $)</td>
<td>Prevalence of HIV refers to the percentage of people 15–49 years of age who are infected with HIV.</td>
<td>(22)</td>
</tr>
<tr>
<td>Public Policy</td>
<td>Life expectancy at birth, total (years)</td>
<td>(22)</td>
</tr>
<tr>
<td>Estimated HIV prevalence</td>
<td>Life expectancy at birth indicates the number of years a newborn infant would live if prevailing patterns of mortality at the time of its birth were to stay the same throughout its life.</td>
<td>(23)</td>
</tr>
<tr>
<td>Estimated incidence rate of AIDS</td>
<td>The detection rate is the number of patients who have been diagnosed with TB compared with estimates by WHO for countries in a given period and is expressed as a percentage. Access to an improved water source refers to the percentage of the population with reasonable access to an adequate amount of water from an improved source, such as a household connection, public standpipe, borehole, protected well or spring, or rainwater collection. Unimproved sources include vendors, tanker trucks, and unprotected wells and springs. Reasonable access is defined as the availability of at least 20 liters/person/day from a source within one kilometer of the dwelling.</td>
<td>(2)</td>
</tr>
<tr>
<td>Life expectancy at birth, total (years)</td>
<td>TB detection rate (%) of estimated tuberculosis cases</td>
<td>(24)</td>
</tr>
<tr>
<td>Access to improved water source (%) of population with access</td>
<td>Access to improved sanitation facilities refers to the percentage of the population with at least adequate access to excreta disposal facilities that can effectively prevent human, animal, and insect contact with excreta. Improved facilities range from simple but protected pit latrines to flush toilets with a sewerage connection. To be effective, facilities must be correctly constructed and properly maintained.</td>
<td>(24)</td>
</tr>
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<td>(24)</td>
</tr>
<tr>
<td>Urban population growth (annual %)</td>
<td>Urban population refers to people living in urban areas as defined by national statistical offices. It is calculated using World Bank population estimates and urban ratios from the United Nations World Urbanization Prospects.</td>
<td>(25)</td>
</tr>
<tr>
<td>Social policy</td>
<td>Unemployment rate (% of the workforce)</td>
<td>(22)</td>
</tr>
<tr>
<td>Unemployment rate (% of the workforce)</td>
<td>Unemployment is the proportion of the labor force that is unemployed but available for and seeking work. Definitions of labor force and unemployment differ by country.</td>
<td>(22)</td>
</tr>
<tr>
<td>Culture and societal values</td>
<td>Incarceration rates refers to the number of people who is incarcerated, expressed as a rate per 100 000 population.</td>
<td>(26)</td>
</tr>
<tr>
<td>Incarceration rate</td>
<td></td>
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</table>

by country-level quartiles of each equity stratifier were computed, followed by computations of the absolute (difference) and relative (ratio) gap between TB incidence rates of the top (the most advantaged) and bottom (the most disadvantaged) quartiles as metrics of gap inequality (i.e., Kuznets-like indexes). Estimates were also made of the slope index of inequality (SII) as the metric of absolute gradient inequality, by regressing country-level TB incidence rate on a relative scale of social position, as defined by the cumulative class interval mid-point of the population ranked by the equity stratifier. This used a weighted least-squares regression model to account for heteroscedasticity of aggregated data, by applying Maddala’s procedure, described elsewhere (33). Finally, the health concentration index (HCl) was computed as the metric of relative gradient inequality, by fitting by non-linear optimization a Lorenz concentration curve equation (i.e., plotting the observed cumulative relative distributions of population ranked by the equity stratifier and TB incident cases, respectively) across the countries studied, and numerically integrating the area under the curve (34).
Because this study did not research human subjects whatsoever, no ethics review was sought or necessary.

RESULTS

Social determinants of TB incidence

In the bivariate random-effects regression analysis, the following variables were significantly associated with reduced TB incidence rates over time: higher gross domestic product (GDP); gross national income (GNI); health expenditure per capita; life expectancy at birth; TB detection rate; access to improved water source; and access to improved sanitation facilities. Variables significantly associated with increased TB incidence rates over time were: incarceration rate and urban population growth. In the multivariate random-effects regression analysis, higher health expenditure per capita (β = −0.24, P < 0.001); access to improved sanitation facilities (β = −0.24, P = 0.0156); life expectancy at birth (β = −3.02, P < 0.001); and TB detection rate (β = −0.25, P < 0.001) were statistically significantly associated with reduced TB incidence rates over time—after adjusting for the other variables (Table 2).

Social inequalities in TB incidence

TB incidence was about 4–5 times greater in the quartile of countries with lowest health expenditure per capita than in the better-off quartile; this excess incidence amounted to 110 cases per 100 000 population in 2000 and around 85 cases per 100 000 in 2010. Similar pattern and trends were observed between extreme quartiles of access to improved sanitation facilities. Figure 1-A and Figure 1-B depict these inequality gaps, showing that the most disadvantaged countries in terms of health expenditure per capita (Haiti, Bolivia, Nicaragua, Guatemala, and Honduras) and access to improved sanitation facilities (Haiti, Bolivia, Guatemala, Trinidad and Tobago, and El Salvador) had the highest average TB incidence rates in the three time points studied. The inequality regression curves (2000, 2005, and 2010) showed an inverse non-linear gradient between TB incidence rate and the social position defined by both health expenditure and access to improved sanitation facilities (Figures 2-A and 2-B, respectively). This means that countries with lower health expenditure per capita and less access to improved sanitation facilities not only had higher TB incidence rates than better-off countries, but that this health inequality was disproportionately concentrated within the most socially disadvantaged countries. A moderate reduction of this absolute inequality was observed between 2000 and 2010; the SII went down from 88.1 excess TB incident cases per 100 000 population to 58.0 in the country gradient defined by health expenditure per capita, and from 85.8 to 63.2 in the country gradient defined by access to improved sanitation facilities. Table 3 also shows smaller inequalities in TB incidence among countries (and smaller changes over time in these inequalities as well) according to gradients of life expectancy. Interestingly, no statistically significant inequalities in TB incidence, nor changes over time among them, were observed by gradients of TB detection rates.

Finally, the health inequality concentration curves showed that the bottom 20% of the most disadvantaged countries, in terms of health expenditure per capita, concentrated up to 40% of burden of TB incidence in LAC; this situation remained unchanged in the period studied. The same social gradient in TB incidence was seen with access to improved sanitation facilities (Figure 3). In fact, the corresponding health concentration indices were around −0.30, showing very little variation between 2000 and 2010.

DISCUSSION

This study showed that in the first decade of the 21st century, LAC countries with lower health expenditure, lower access to improved sanitation facilities, lower life expectancy at birth, and lower TB detection rate have higher TB incidence rates. Despite a limited ability to draw meaningful comparisons given the scarcity of regional studies on this topic at the country level, the findings of this study are...
consistent with those of Dye and colleagues who examined 134 countries globally in 1997–2006 (35). They found a reduction in TB incidence associated with higher GDP per capita, improved water source, improved sanitation, lower mortality rate among those < 5 years of age, and higher new smear+ TB cases detected. More broadly, our findings concur with those of other studies that have established an association between TB morbidity and mortality and the human development index (36, 37), a composite measure of wealth, education, and longevity.

When social determinants of health are not adequately addressed, or just plainly neglected, they cause or reinforce social stratification in the population, leading to unequal distribution, inequality, and social exclusion (4, 12). Inequalities in TB are thus driven by the unequal distribution, ineq

...Among countries: 40% of all new TB cases in LAC were focalized in the lowest quintile of most disadvantaged countries. Moreover, this study provides ecological evidence of the endurance of these social inequalities in TB incidence over time.

In terms of ecological evidence on the social determination of TB incidence, our study exposed some interesting and even debatable issues. Despite the well-known correlation between health and GDP/GNI per capita (11–13, 16–19), these two highly collinear proxies of income and wealth were not retained in our final model. Instead, health expenditure per capita showed a better association with TB incidence rate over time. In spite of a likewise high collinearity between health expenditure and GDP/GNI, this may suggest that, over the period observed, the absolute level of economic resources in LAC countries may not have been as relevant for TB incidence as the specific commitment to health care, as conveyed by the level of health expenditure per capita. Indeed, a distinctive feature of our analysis was the exploitation of a panel data regression approach, which provides superior estimates in describing change over time (27, 28). In this regard, a desirable improvement to our model would have been the inclusion of precise economic expenses incurred by TB control programs in each country, had such data been available. On a more
upstream, distal level, access to improved sanitation facilities and improved water sources are essential development indicators (16): it is just in those environments lacking access to these services where TB clusters and propagates. Our final model suggests that only the former remains a significant environmental determinant of TB incidence in LAC countries over the period assessed. This is consistent with the 2012 WHO/UNICEF Joint Monitoring Program assessment on progress towards the MDG 7 on access to water and sanitation, declaring that LAC had already attained target 7-C for access to safe drinking water (24).

The reported non-association between HIV/AIDS and TB incidence at the aggregated level may be explained by the fact that in LAC, most countries have concentrated HIV epidemics that have a milder effect on TB incidence. The high coverage of highly active antiretroviral therapy (HAART; roughly 70%) in LAC has also contributed to this observation (2, 39). With regard to unemployment, incarceration, and urban growth—shown

TABLE 3. Summary metrics of country-level inequalities in tuberculosis (TB) incidence according to social stratifier and year assessed, Latin America and the Caribbean, 2000, 2005, and 2010

<table>
<thead>
<tr>
<th>Metric</th>
<th>2000</th>
<th>2005</th>
<th>2010</th>
</tr>
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<tbody>
<tr>
<td><strong>Health expenditure per capita</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absolute Kuznets index</td>
<td>110.2a</td>
<td>115.9a</td>
<td>84.2a</td>
</tr>
<tr>
<td>Relative Kuznets index</td>
<td>4.1a</td>
<td>5.8a</td>
<td>4.4a</td>
</tr>
<tr>
<td>Social gradient</td>
<td>−88.1a</td>
<td>−79.4a</td>
<td>−58.0a</td>
</tr>
<tr>
<td><strong>Access to improved sanitation facilities</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Slope index of inequality</td>
<td>−0.30a</td>
<td>−0.32a</td>
<td>−0.29a</td>
</tr>
<tr>
<td>Health concentration index</td>
<td>−0.31a</td>
<td>−0.32a</td>
<td>−0.29a</td>
</tr>
</tbody>
</table>

**Life expectancy at birth**

<table>
<thead>
<tr>
<th>2000</th>
<th>2005</th>
<th>2010</th>
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<tbody>
<tr>
<td>116.8a</td>
<td>107.8a</td>
<td>92.5a</td>
</tr>
<tr>
<td>4.8a</td>
<td>5.8a</td>
<td>5.3a</td>
</tr>
<tr>
<td>−71.8a</td>
<td>−65.5a</td>
<td>−60.6a</td>
</tr>
<tr>
<td>−0.22a</td>
<td>−0.23a</td>
<td>−0.25a</td>
</tr>
<tr>
<td>0.02a</td>
<td>−0.11a</td>
<td>−0.07b</td>
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</table>

**TB detection rate**

<table>
<thead>
<tr>
<th>2000</th>
<th>2005</th>
<th>2010</th>
</tr>
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<tbody>
<tr>
<td>72.9a</td>
<td>61.7a</td>
<td>52.9a</td>
</tr>
<tr>
<td>2.5a</td>
<td>2.3a</td>
<td>2.0a</td>
</tr>
<tr>
<td>−8.8a</td>
<td>−21.2a</td>
<td>−19.4a</td>
</tr>
<tr>
<td>0.02a</td>
<td>−0.11a</td>
<td>−0.07b</td>
</tr>
</tbody>
</table>

**Note:**

- s Uncertainty range statistically different from null value (i.e., 0 in the absolute scale and 1 in the relative scale) at level P < 0.001.
- P value ≥ 0.05.
elsewhere to be associated with TB incidence (11, 13, 15, 19, 20)—the fact that they were excluded from our final model despite their significance in the unadjusted one, may reflect the inability of the current level of aggregation to detect relevant contextual effects, or else differing definitions across countries.

Limitations

This study had some limitations, mostly inherent to its ecological design: since country-level aggregated data were used in the analyses, these results cannot be inferred at the individual level, and we cannot claim causal relationships between TB incidence and the socioeconomic independent variables explored. Another study limitation was shaped by data unavailability and data paucity, i.e., other variables could not be included that have been shown to be related with TB: e.g., human development, gender, alcohol consumption, drug abuse, diabetes prevalence, and nutritional status.

Moreover, the panel design carries the caveat of any observational study, and therefore, endogeneity and omitted variable bias cannot be ruled out. Despite these limitations, these study findings are useful for informing health decision-makers on the need to improve public policies that include reducing the social inequity gaps and gradients in TB incidence at the collective level.

Conclusions

Currently, countries affected by this public health problem have the challenge of promptly stopping TB transmission in the community by applying interventions aimed at tackling comorbidities and social determinants of health, building upon the current strategy of diagnosis and curative treatment (11). In LAC, more resources need to be designated to improving and strengthening access to health services, and at the same time, to improving the conditions in which people are born, grow, live, work, and age—such as better housing, jobs and wages, nutrition, water and sanitation, transportation, and the like. To the same extent to which TB has been regarded a social disease (8, 9), we contend that TB prevention and control should also be viewed as a paradigmatic example of why health matters for economic growth: a TB-free workforce adds to the human capital of a nation, and a healthier society, in turn, results in growth (40, 41).

These results support the call to go beyond what we are doing now to control TB and aim at the elimination of unfair social inequities in TB transmission. Without undermining ongoing efforts on the more proximal determinants—especially those affecting quality access to care—TB control and prevention efforts should address TB root causes, i.e., its social determinants. Despite scant evidence on cost-effective interventions to address the social determinants of TB, we believe that sound social policies sensitive to health equity—such as preferentially targeting the most vulnerable and...
disadvantaged (42), coupled with more interdisciplinary action and scaled-up innovation, can positively impact TB control in Latin America and the Caribbean, and elsewhere.

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Conflicts of interest. None.

Disclaimer. Authors hold sole responsibility for the views expressed in the manuscript, which may not necessarily reflect the opinion or policy of the RPSP/PJPH and/or PAHO.

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RESUMEN

Determinantes sociales y desigualdades en la incidencia de tuberculosis en América Latina y el Caribe

Objetivo. Establecer los determinantes sociales clave de la incidencia de tuberculosis (TB) en los países de América Latina y el Caribe (ALC), una zona geográfica considerada como una de las más afectadas por las desigualdades socioeconómicas en el mundo.

Métodos. Se llevó a cabo un estudio ecológico a nivel de país. Los datos se obtuvieron de diversas fuentes institucionales. Mediante un modelo de regresión de efectos aleatorios se exploró la relación entre varios indicadores de determinantes sociales y las tasas de incidencia de TB en 20 países de ALC durante el periodo de 1995 al 2012. A continuación, se calcularon los valores ordinarios de la brecha y el gradiente de desigualdad social en la incidencia de TB entre países en el 2000, el 2005 y el 2010.

Resultados. Las tendencias en la tasa de incidencia de TB se asociaban significativamente con el gasto per cápita en salud y el acceso a mejores instalaciones de saneamiento, así como con la esperanza de vida al nacer y la tasa de detección de la TB, tras ajustar para otras variables socioeconómicas, demográficas y de servicios de salud. La desigualdad absoluta y relativa en la incidencia de TB se mantuvo prácticamente inalterada: los países que se distribuían en el 20% inferior del gasto en salud y la cobertura de saneamiento aglutinaban hasta un 40% de todos los casos nuevos de TB, a pesar de una considerable disminución de la tasa general media de incidencia de TB durante el periodo evaluado.

Conclusiones. Junto con la intensidad de las actividades de control de la TB (reflejada por la tasa de detección de la TB), tanto el acceso al saneamiento (reflejo de la calidad de las condiciones de vida) como el gasto per cápita en salud (ya sea como indicador del nivel de recursos o del compromiso con la atención de salud) parecen ser determinantes clave de las tendencias en la incidencia de TB en los países de ALC. Las desigualdades tanto en el gasto per cápita en salud como en el acceso al saneamiento parecen definir los gradientes inversos profundos y persistentes en la incidencia de TB entre los países de ALC.

Palabras clave: Tuberculosis; determinantes sociales de salud; inequidad social; equidad en salud; América Latina; Región del Caribe.