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Time trends in educational inequalities in cancer mortality in Colombia, 1998-2012: is increasing healthcare insurance coverage in a middle-income country reflected in reducing inequalities in premature cancer mortality?

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STRUCTURED ABSTRACT

Background: Premature cancer mortality in Colombia was documented to decline for all educational levels, although strongest in the higher educated levels.

Methods: In this descriptive study we linked Colombian national mortality data of age groups 20-64 years to census data to obtain age-standardized cancer mortality rates by educational level. Using Poisson regression we modelled premature mortality by educational level estimating rate ratios (RR) and relative index of inequality (RII) and its absolute counterpart, the Slope Index of Inequality (SII).

Results: RR show increased risks of dying among the lower educated compared to the highest educated, this tendency was stronger in women ($RR_{primary}$ 1.35; $RR_{secondary}$ 1.11, both p<0.0001) than in men ($RR_{primary}$ 1.49; $RR_{secondary}$ 1.22, both p<0.0001). In absolute terms (SII) cancer caused a difference of 20.5 per 100.000 male deaths, and 28.5 per 100.000 female deaths between the highest and lowest educated. RII was significantly higher for women than for men and in the younger age categories and initially decreased from 1998-2002 to 2003-2007, but then in the period 2008-2012 they increased significantly back to its previous levels. Among women, no significant increases or declines in cancer mortality over time were observed in recent periods in the lowest educated group, whereas strong recent declines were observed in those with secondary education or higher.

Conclusion: Documented educational inequalities in cancer mortality in Colombia are not only persistent, but increasing, fastest among women, and concentrated in young age categories. This trend was not curbed by the increase in healthcare insurance coverage. These results should urge policy makers to improve equal access to prevention, early detection, diagnostic and treatment facilities.

Strengths and limitations

- Population-based mortality databases with information on educational level provide a unique data source to evaluate educational differences
- Definition of the variable for educational level does not guarantee having terminated the indicated level, there may be variance within the educational groups
- Time period included covers a period of important changes in Colombian society, expected to be reflected in cancer mortality rates
- Multiple imputation improved statistical power and precision of analyses
- The underlying causes of these trends are unknown

Contributorship statement

- Obtaining data: Iván Arroyave, Constanza Pardo
- Study Design: Iván Arroyave, Esther de Vries
- Programming and analysis: Iván Arroyave, Esther de Vries
- Manuscript preparation and revision: Esther de Vries, Iván Arroyave, Constanza Pardo

Introduction

Colombia is a country with very large socioeconomic inequalities, causing, among others, large differences in health-related topics such as life expectancy and incidence, prognosis and mortality of disease [1-3]. In 1993, a major health care reform in Colombia introduced mandatory health insurance coverage (HIC) [4]. Citizens are assigned to two major schemes based on income: (i) the contributory scheme, which covers workers and their families with an income above the cut-off and is financed through payroll and employer's contributions; and (ii) the subsidized scheme, mainly funded via taxes, which subsidizes the poor as identified through a proxy means test [5]. HIC was 23.7% in 1993 just before the reform [6] and rose to 37.7% in 1994, just afterwards [4]. Initially, the coverage slowly improved [4] and a subsequent reform led in 2002 to a noticeable increase of healthcare coverage (reaching around 96% by 2008) by improving efficiency in the use of resources and by reducing its reliance on national budgets [7] (Figure 1). In the poorest income quartile, HIC increased from 6% to over 70% between 1993 and 2009 [5], attributable to the subsidized scheme [8], which shows that the program reached the poorer income groups more aggressively. This increased HIC is expected to contribute to a reduction in health inequalities [4, 5], mainly by improving the situation for the poor: ensuring timely care and bringing patients in closer contact with the health care system [9, 10]. It has been argued, however, that the reform increased the complexity of the system which could potentially lead to delays in certain types of care [11] and reduced spending in prevention and public health [12].

In Colombia, three different periods in the implementation of universal HIC can be discerned (Figure 1): During the period 1998-2002, HIC was relatively low and stable (around 70% during all the period); the second period (2003-2007) covered the years of rapid increase in coverage among the poor (6.9% average annual growth in HIC, 12.2% in subsidized scheme); while during the third period (2008-2012) universal coverage remained stable according to official figures at on average 96.1%. The discrepancy in HIC trends between these three periods offers a natural experiment to examine the impact of HIC on socioeconomic disparities in mortality.

Few studies have examined the impact of different health insurance status on inequalities in mortality and even less is known about inequalities in mortality in middle-income countries, many of whom introduced major health care system reforms during the last decades. As in Colombia the increase of HIC towards universal coverage was deliberately addressed to the poorest population [4, 5], and educational level is a good proxy variable for Socioeconomic Status (SAS) [13], we hypothesize that increased HIC contributed to reducing inequalities in cancer mortality. Cancer mortality is a particularly interesting indicator of the effect of insurance coverage due to the expected increased access to prevention measures, early detection, timely treatment therapies, and high-cost interventions [14-16].

Indeed, previous analyses of time trends of differences in cancer mortality by attained educational level in Colombia (1998-2007) were promising, particularly for gastric and cervical cancer where faster declines in mortality occurred in the lowest educated groups and therefore socioeconomic differences were expected to decrease in the near future [3]. In this paper we evaluate if the seemingly positive trend in cancer mortality by educational level continued, by using a slightly different definition of educational level which allowed us to extend the previous analyses (up to 2007) by 5 extra years, covering 1998-2012.

Methods

Data

Education level criteria

Educational level was categorized in three groups based on the highest educational level accessed (not necessarily graduated) by the deceased: (a) Primary school or less, (b) Secondary school, and (c) Tertiary (post-secondary education). This definition differs from the previously used attained (graduated) educational level variable [1, 3], which was discontinued in the national databases after 2007.

Deaths

National mortality data for cancer deaths (International Classification of Diseases (ICD-10) codes C00-C96, see Appendix-Table 1) for the period 1998-2012 were obtained from the National Administrative Department of Statistics (DANE), which routinely registers information on sex, date and cause of death as well as educational level from death certificates. Although the exact wording for the variable “accessed education” changed in the DANE database since 2008, the new categories were consistent with those of the databases of previous years and could be used. Trends of counts were found to be continuous and regular.

We focused on adult premature mortality (mortality below age 65) because it is known that information on educational level from mortality statistics is unreliable at ages 65 and beyond [17]. Additionally, premature mortality is an indicator of population health believed to be strongly influenced by social, economic and environmental factors [18], and is a common indicator of health system performance [19].

Data on age and sex were available for more than 99% of all deaths, while data on educational level was missing for approximately 16.5% of 190,993 cancer deaths. We used multiple imputation methods [20] implemented in SAS through the IMPUTE procedure to impute educational level for these cases in order to avoid bias due to the potentially higher rates of missing education for lower educated individuals, and to minimize the potential for numerator/denominator bias [17]. In short, this procedure fits a sequence of regression models and draws values from the corresponding predictive distributions. The sequential regression procedure was applied based on a model that included sex, region, urban/rural residence and marital status as covariates. Details of this method are explained elsewhere [20]. The imputation procedure was successful in 90.8% of cases with missing information, resulting in a total of 188,091 (98.5%) cancer deaths for our analyses.

Population

Data on mid-year population counts by age, sex and educational level were obtained from the Colombian Demography Health Surveys (DHS) [21] which contain periodical information on the distribution of education by age, sex and calendar year (1995, 2000, 2005 and 2010). Age 20 was chosen as the lower age limit of this study as almost 100% of individuals accessed their highest educational level by this age.

The resulting proportions of individuals in each educational level were multiplied with the total population numbers per year, age and sex which were obtained from census combined with statistical projections from DANE [22]. These two information sources were combined to estimate the annual population size in each educational group (Appendix-Figure 1). We performed demographic projections to obtain population counts for years in-between every lustrum using the demographic Software PASEX [23]. Additional details on the procedure are available elsewhere [23].

Analysis

All analyses were conducted in each of the five multiple databases generated by the multiple imputation process. Since results were nearly identical for all imputations, we used standard techniques as implemented in the PROC MIANALYZE procedure in SAS to combine estimates from all databases and adjust standard errors to account for uncertainty in the imputation [24]. This procedure reads the parameter estimates and associated covariance matrix for each imputed data set, and then derives valid multivariate inferences for these parameters. This allows for valid statistical inference that appropriately reflects uncertainty due to missing values [24].

All analyses were conducted in SAS® version 9.2.

Age Standardised Mortality Rates (ASMR)

Data on population counts were combined with data on deaths to obtain a complete database of death counts by educational level, sex and five-year age group. We first calculated age-standardized mortality rates by educational level, sex and year using the World Health population of 1997 [25] as standard population, resulting in Age

Standardised Mortality Rates (ASMR) expressed per 100,000 person-years (Figure 2). We also calculated ASMR by sex and year (Figure 2) and by educational level and sex (Table 1).

Annual trends in ASMR by sex and educational level were quantified by calculating the estimated Annual Percentage Change (EAPC) which measures the average rate of change in the mortality rate per year (negative EAPC: decreasing trend, positive EAPC : increasing trend). To test whether an apparent change in mortality trends was statistically significant, we used joinpoint regression, which fits a series of joined straight lines to age-adjusted rates and uses a Monte Carlo Permutation method to identify the best-fitting point (called joinpoint, year in which a significant change in the mortality trend occurred), where the rate of increase or decrease changes significantly [26]. EAPC and joinpoints were determined based on the log-transformed ASMRs and their standard errors. We specified a maximum of 2 joinpoints with at least 4 observation points to either extreme of the data using joinpoint modelling based on the Joinpoint program [27] (Figure 2).

Regression models

We implemented separate Poisson regression models separately by sex with number of deaths as dependent variable and the natural log of person-years as offset variable, incorporating age and educational level as independent variables. We first estimated Rate Ratios (RR) of mortality by educational level, which compared the mortality of all educational groups to the mortality in the tertiary education group. Changes in the rate ratio over time result from changes in both risks and the distribution of educational level [28]. To assess changes in disparities ‘controlling’ for changes in the educational distribution, we estimated the Relative Index of Inequality (RII), regressing mortality on the mid-point of the cumulative distribution of education, thereby taking into account the size of each educational group [28, 29]. Values higher than 1 indicate educational inequalities favouring the higher educated.

We evaluated if RRs significantly changed over time and within periods on continuous scales, which was not the case (results not shown). We calculated RII for three 5-year periods (1998-2002, 2003-2007, and 2008-2012) and for three age groups (20-34, 35-49, and 50-64) in order to identify differences in inequalities along age (Figure 2).

To compare the contribution of each cause of death to mortality disparities for non-communicable diseases (classified by their ICD-10 codes, see Appendix-table 1) we calculated the Slope Index of Inequality (SII) (Figure 4). The SII is a measure of absolute disparities that represents the difference in mortality between the population at the top and the bottom of the educational distribution [28]. Further details on the RII and SII are available elsewhere [28].

Results

Table 1 shows counts of cancer deaths and population at ages 20-64 years between 1998 and 2012 in Colombia. After excluding non-imputed cases (1.5%), 106,199 cancer deaths occurred from 1998 to 2012 among women while 81,892 occurred among men, with age-standardized cancer mortality rates (ASMR, per 100,000 person-years) of 58 among women and 49 among men. Men and women with lower levels of education had higher cancer mortality rates than their higher-educated counterparts. In addition, ASMR were larger among women than among men in each educational level.

The risk of dying was significantly and consistently higher among the lower educated. The RRs show clearly and statistically significantly increased risks of dying among the lower educated compared to the highest educated, this tendency was stronger in women ($RR_{primary}$=1.35; $RR_{secondary}$=1.11 both p<0.0001) than in men ($RR_{primary}$=1.49; $RR_{secondary}$=1.22, both p<0.0001).

During the 15 years of observation, the general tendency was for age-standardized cancer mortality rates to decline, with recent stabilizations, reaching an average ASMR in 2012 of 47.3 per 100,000 males and 55.2 per 100,000 females. Average EAPC for males in the periods defined by joinpoint were: 1998-2000: 2.4% (95% CI -2.0; 7.0), 2000-2012: -0.92% (95% CI -1.2; -0.7); for females 1998-2003: 0.7 (95% CI -0.7; 2.1), 2003-2006: -2.8% (95% CI -8.2; 2.9), 2006-2012 -0.6 (95% CI -1.5; 0.3). The general tendency for a declining trend in mortality was not reflected equally by educational level and sex (figure 2). Women had higher mortality rates than men. No significant increases or declines over time were observed in the lowest educated groups, whereas in the middle and high educated groups there was at least one period with significantly declining cancer mortality rates. In these groups, tendencies were for mortality to decrease substantially in the period after 2002/2003, with the exception of the highest educated males who showed recent increases. The strongest declines in cancer mortality over time were observed in the group of women with secondary or tertiary education. The most consistent declines in cancer mortality rates for all educational levels in both sexes were observed in the period 2003-2007, the period with rapid inceases in HIC, particularly among the poor.

RII initially decreased from 1998-2002 to 2003-2007 (reaching significance among women), but then in the period 2008-2012 they increased back to its previous levels (Figure 3, left panel). Trends in the joinpoint for RII are in line with this finding: no significant change was found for educational inequalities among men, whereas there was an initial significant decline (-7.6%) among women up to 2004 followed by a significant increase (+3.8%) in the period 2004-2012 (Appendix-Figure 2). RII also showed that inequalities were significantly higher for the younger age categories compared to older ones and tended to be higher for women (Figure 3, right panel).

Figure 4 shows the contribution to absolute differences in ASMR by education as measured by the SII for non-communicable diseases (appendix-table 1). Cancer was the second largest cause, after cardiovascular disease: explaining 20% of male differences (SII=20.5 deaths per 100,000 population) and 24% of female differences (SII=28.5). Absolute differences in cancer mortality were 39% larger for women than for men (28.5 vs. 20.5), while this difference was only 14% for all non-communicable diseases (SII= 103.2 and 120.3 respectively).

Discussion

We observed strong and persistent educational differences in cancer mortality rates in Colombia. These differences appeared to be diminishing in the period 2002-2007 [3] when healthcare insurance coverage largely grew, especially for the most disadvantaged part of the population. But in recent years, despite the achievement of almost universal HIC, inequalities were widening, particularly among women, with rates in the lowest educational groups being stable or increasing and those in the higher educated groups gradually declining. This means that the lowest educated part of the population is increasingly lagging behind in the progress against cancer, despite the increase in insurance coverage.

Explanation of results

Educational level was found to be previously as a good proxy variable for Socioeconomic Status (SAS) [13]. Lower SES is associated with a higher prevalence of cancer risk factors (such as smoking, alcohol, obesity, occupational risk factors, housing circumstances), and less healthcare utilization (because of lower resources but also lower awareness and poorer access due to longer distances or high impact of family income when taking time off to visit a doctor) [30-32].

Not only absolute cancer mortality rates, but also inequalities in mortality were largely higher for women than for men. In a previous paper we showed this to be almost entirely attributable to cervical cancer mortality, which accounted for 51% of inequalities in total female cancer mortality in 1998-2007 at 25-64 [3]. Several Colombian studies have identified that both characteristics of the health system such as access and delays in diagnosis and treatment, and characteristics of the populations of lower socioeconomic classes contribute to the higher burden of cervical cancer mortality [33, 34]. A previous study showed that lower access to mammography screening for early detection of breast cancer was associated with lower education, affiliation to the subsidized regime or being unaffiliated [35]. In general, financial access to healthcare has been more limited to women [36, 37] which potentially limits access to expensive cancer therapies, particularly for most deprived women.

We also observed clearly increased educational differences in cancer mortality for the youngest age groups, in which mortality from cancer is a relatively rare event. Among males, leukaemias, stomach cancers and Non-Hodgkin lymphomas are important cancer causes of deaths in the age groups 15-39 years (representing 44% of all cancer deaths in this age group); for females these include cervical cancer and leukaemias as well as non-Hodgkin lymphomas (representing 38%) [38]. Previous studies have shown that mortality or survival of these cancer types is very much dependent on socioeconomic status [3, 14, 39]. As these tumours explain an important proportion of cancer deaths in these ages, this probably explains the high RII in the younger age groups as compared to the higher age categories.

Our results clearly illustrate that an almost complete coverage does not necessarily reduce inequalities in health [40, 41]. Particularly, having health insurance may be universal, but depending on income the type of health insurance is different (subsidized, contributory and special or exceptional regimes), with the most wealthy population often buying additional private health assurance to ensure rapid and more broad access [42]. Complete coverage does not automatically guarantee quality of the insurance (translating into early and timely diagnosis and adequate treatment), as seems to be the case: To warrant rights to get access to expensive treatments and medication, as usual in cancer, exceptional legal mechanisms are frequently launched in Colombia: Technical-scientific committees of health assurers, and an action for protection so-called "tutela" [42, 43]. A study shows that those affiliated to the contributory regime are more likely to warrant additional rights more efficiently [43], potentially increasing inequalities between regimes.

In parallel with the increases in HIC, other changes in the Colombian health care system occurred, including increases in investments in care [5, 44]. Of course, our results are consequence of the impact of the entire reform rather than only the increased coverage in health insurance. However, despite the large reforms, inequalities in cancer mortality in Colombia are increasing. This is not unique to Colombia; in several countries, as diverse as Taiwan, Thailand and European countries, inequalities in health increased upon reaching almost universal coverage [45-48].

Strengths and weaknesses

This is one of few studies investigating educational differences in mortality using population-based mortality and population-based educational level. Despite several strengths, some limitations should be considered in our study: We did not correct for misclassification within the cancer groups, but since we studied the group of cancer deaths overall, regardless of the subtype of cancer, most of these errors are cancelled out. In general "cancer" as cause of death is correctly coded [49], and most likely particularly in setting of ages under 65.

Data on mortality were obtained from mortality registries, while data on the population distribution by education were obtained from censuses and demographic projections. This may have led to the so-called numerator/denominator bias, which generally results in an overestimation of disparities [17]. Furthermore, for some years, data on population size were obtained from demographic projections combined with distributions of education from surveys. To assess the impact of this potential bias, we experimented with different education distributions from multiple data sources [50-52], showing that the overall trends in our study were robust to different assumptions on the distribution of education [3].

Potentially, there has been substantial under-registration of deaths in some regions. Previous studies comparing national mortality rates with indirect estimates from census [53, 54] suggest that underregistration is particularly important in the poorest regions, implying that estimates of disparities in mortality by educational level are likely to be an underestimation, because those with lower education are more likely to live in areas with higher underregistration rates. This may also have led to underestimation of the extent to which inequalities have increased, because underregistration decreased over the study period [53, 54]. Our results, therefore, are indicative of potentially larger inequalities in mortality by education, which continue to increase.

Information on education was missing for 16.5% of cancer deaths, potentially leading to an underestimation of disparities, as missing values are usually more common in the least educated [55]. However, we imputed values for educational level for individuals with missing educational information based on a information on age, sex marital status, region and urban/rural residence, thereby limiting the potential impact of this source of bias.

Unanswered questions and future research

Socioeconomic inequalities in mortality of non-communicable diseases have been associated with the unequal distribution of behavioural risk factors, such as smoking, alcohol consumption, an unhealthy diet, sedentary lifestyle higher risk of injuries [2, 56]. This implies underlying inequalities in exposure to risk factors and incidence of these diseases. However, data on the incidence of disease and prevalence distribution of all those behavioural and poverty risk factors by socioeconomic status are largely lacking in Colombia and most developing countries. Studies on the mechanisms underlying the way these risk factors contribute to inequalities in mortality are scarce, even in developed countries. We previously described not only large inequalities in mortality of cancers with a primary infectious aetiology such as gastric cancer [3], but also documented inequalities in survival of gastric cancer measured by both type of health insurance and socioeconomic stratum [14]. These findings indicate that both access and quality of care (health insurance) as other factors related to socioeconomic status independently affect survival for the lower socioeconomic classes negatively. Detailed studies are needed on both types of factors: which barriers exist for timely diagnosis and adequate treatment in situations with universal health coverage and how can they be tackled? And on which other factors related to socioeconomic stratum can interventions be designed? The answers to these questions will be various and, depending on the specific disease, will be quite different in character. It is of high importance that data on socioeconomic indicators are collected in a standard way, so that for example cancer registries can calculate incidence rates by socioeconomic stratum, which, at this moment, is not possible in Colombia [57].

Socioeconomic differences were substantially larger for women than for men, in our previous study this difference was almost entirely attributable to inequalities in cervical cancer mortality [3]. In this more recent study we see that the gender inequalities grew despite the virtually universal HIC since 2008. Gender inequalities were larger for cancer than for other non-communicable diseases according SII; more detailed analyses are needed to assess to which extent the growing inequalities are due to an increase in cervical cancer mortality amongst less favoured.

Conclusions

The recent negative curbs in mortality among the lowest educated groups, resulting in increasingly differences between educational groups, are a call for attention by the Colombian health authorities to take measures in both primary prevention, access to early detection and timely and adequate treatment. Underlying causes of the observed differences are multiple, from differences in housing, lifestyle, health-related beliefs, to differences in access to diagnostic facilities and high-quality treatment, which all should be of concern to those in charge [58]. Insurance coverage is clearly not enough to counterbalance the deleterious effects of decreases in spending on primary prevention and other social and economic conditions which determine the growing levels of educational inequalities in cancer.

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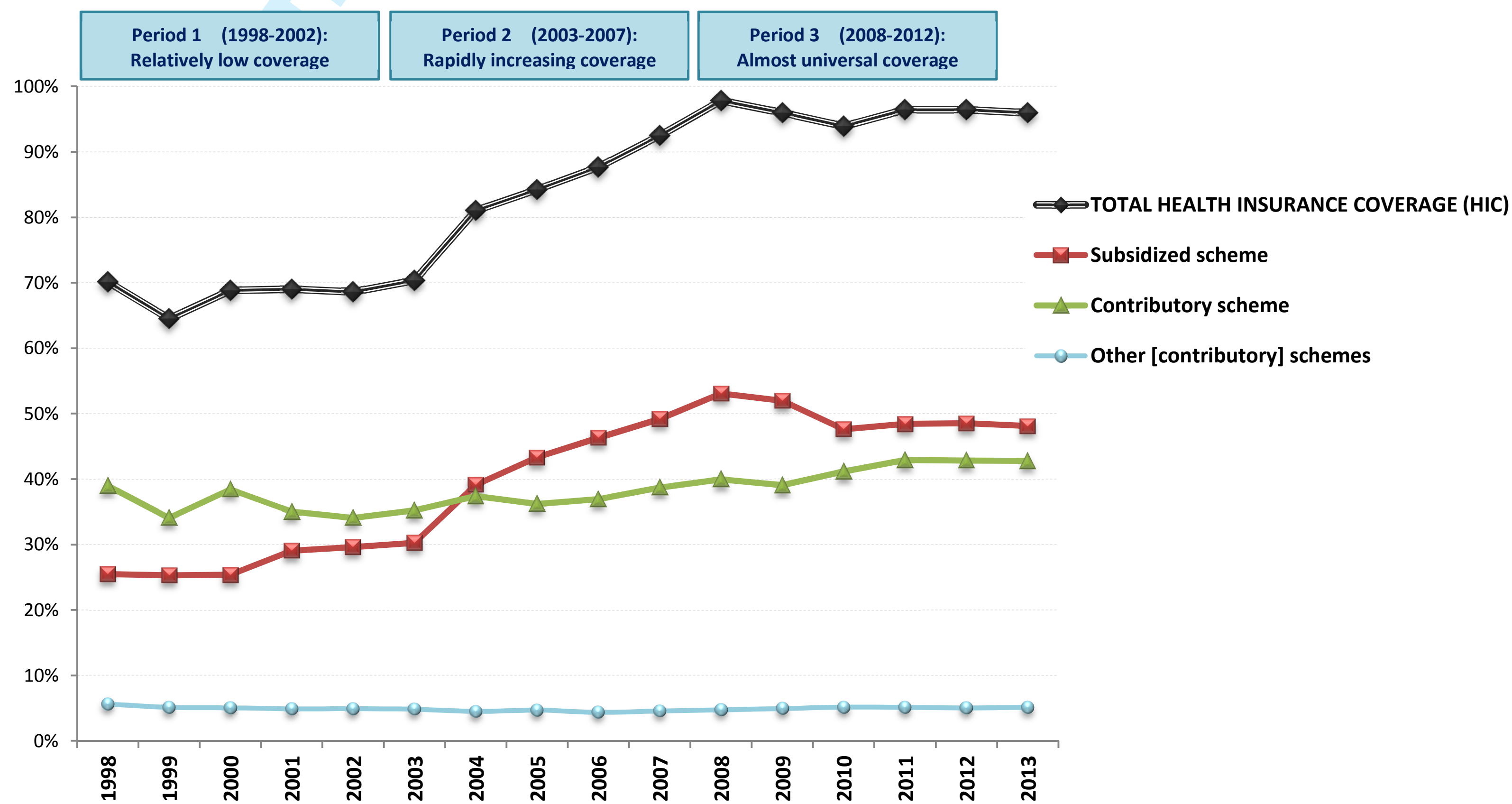
Figures and Tables

Figure 1: Trends in national healthcare insurance coverage (HIC), Colombia, 1998-2012



Other schemes include primarily members of the military and teacher and oil workers syndicate members. Based on Annual reports of the Ministry of Health and Social Protection

Table 1: Descriptives of the study: deaths, population and rates separately by sex and educational level, Colombia, 1998-2012

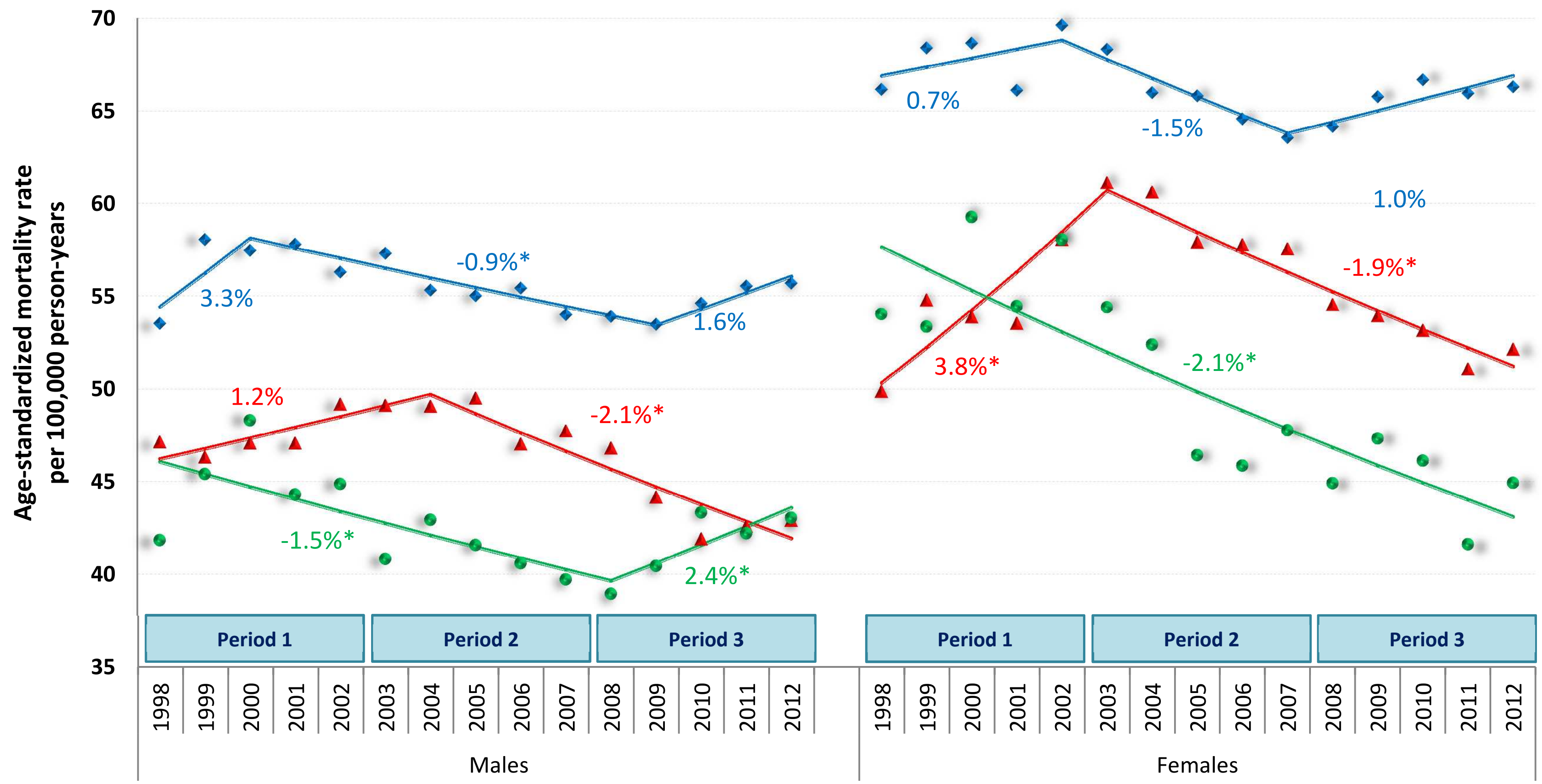
Sex	Educational level [a]	Cancer deaths [b]	Population size	ASMR [c] (95% Confidence Intervals)	
	Primary	50,126	67,815,336	54.0	(53.5, 54.5)
	Secondary	22,273	67,742,806	45.1	(44.4, 45.8)
Men	Tertiary	9,493	30,715,631	41.4	(40.5, 42.3)
	Total	***81,892***	***166,273,773***	***48.9***	***(48.8, 49.1)***
	Primary	65,336	68,637,666	64.7	(64.2, 65.2)
	Secondary	30,414	72,387,214	54.2	(53.5, 54.9)
Women	Tertiary	10,449	35,149,442	47.2	(46.2, 48.3)
	Total	***106,199***	***176,174,322***	***57.8***	***(57.6, 58.0)***

[a]: *Educational attainment values registered after final imputation. Primary = up to elementary or primary school; secondary = any level of high-school; tertiary = any level of postsecondary education after high school including college and university.*

[b]: *Cancer deaths after imputation.*

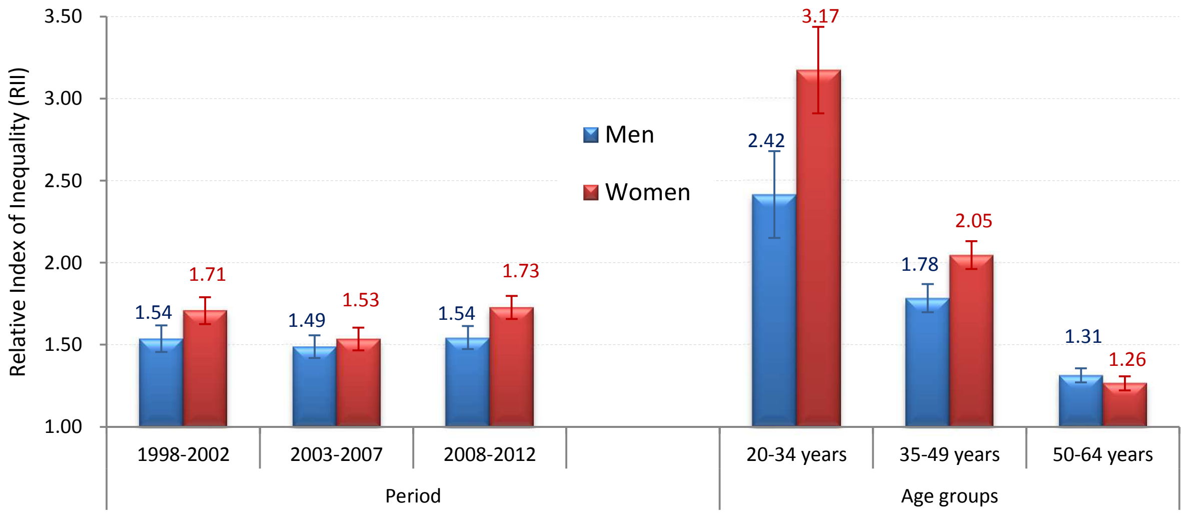
[c]: *ASMR: Age standardized mortality rates per 100,000 population; Estimates (WHO standard population 1997) for educational level combine results from 5 databases generated by multiple imputations, appropriately reflecting uncertainty attributable to missing values.*

Figure 2: Age-standardized cancer mortality trends, including APC based on joinpoint models, by sex and educational level



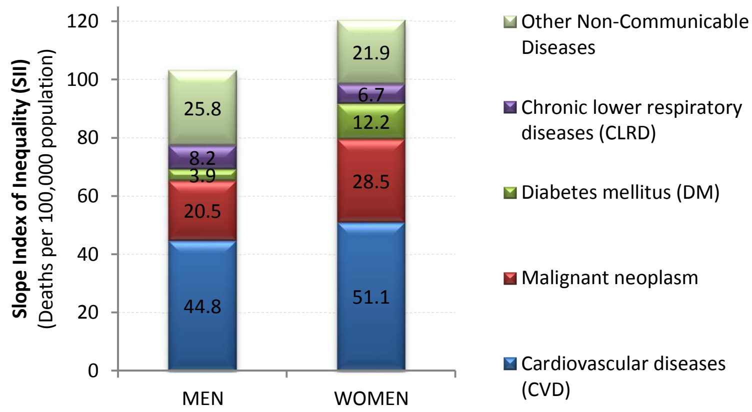
Markers: Observed age-standardized cancer mortality rates. Lines: modelled age-standardized cancer mortality trends. Estimates are results from 5 databases generated by multiple imputations, appropriately reflecting uncertainty attributable to missing values. The points represent ASMR, lines represent the trendlines between joinpoints. Blue, diamonds: maximum primary education; Red, triangles: secondary education; Green, circles: tertiary education. Numbers adjacent to the lines represent estimates annual percent change (EAPC) during the corresponding periods, based on joinpoint modelling; a star indicates statistical significance at α 0.05.

Figure 3: Sex-specific Relative Index of Inequality by period and age group



Estimates from combined results from 5 databases resulting from multiple imputations, appropriately reflecting uncertainty attributable to missing values.

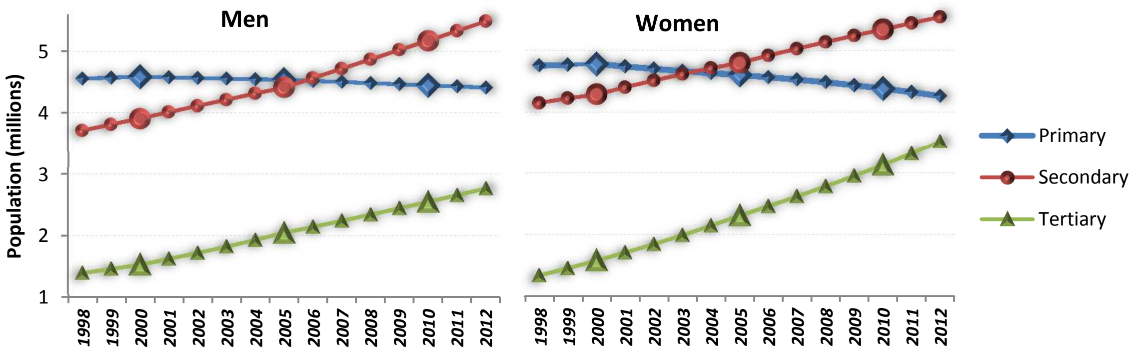
Figure 4. Slope Index of Inequality (SII) for non-communicable diseases



See Appendix-Table 1 for International Classification of Diseases (ICD-10) codes for non-communicable diseases

APPENDIX

Appendix-Figure 1. Educational level trends over time, Colombia, 1998-2012

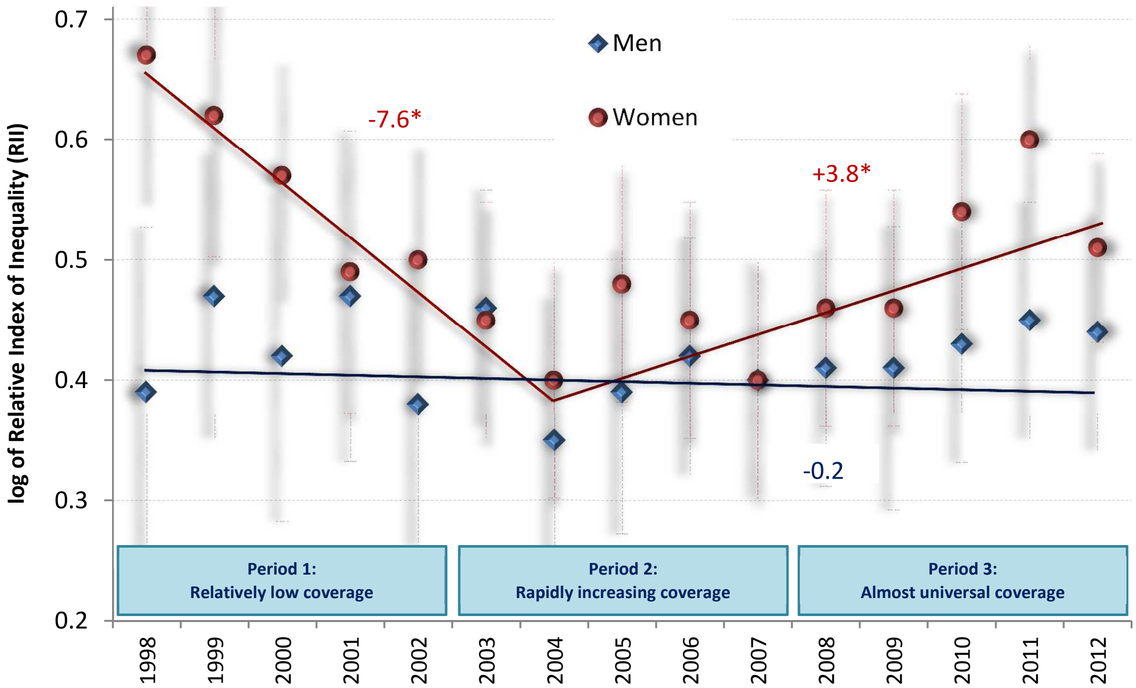


The thicker markers are those from the year with real data available (source: Colombian Demography Health Surveys in 1995, 2000, 2005 and 2010). The points in between were interpolated (see methods)

Appendix-Table 1. **Classification of Causes of death, International Classification of Diseases (ICD-10) codes for non-communicable diseases**

Non-Communicable Diseases		ICD-10 codes
Cardiovascular diseases		I00-I99
Malignant neoplasm		C00-D48
Diabetes mellitus		E10-E14
Chronic lower respiratory diseases (CLRD)		J40-J47
Other Non-Communicable Diseases	Mental and behavioural disorders	F00–F99
	Diseases of the nervous system	G00–G99
	Diseases of the digestive system	K00–K93
	Diseases of the genitourinary system	N00–N99
	Congenital malformations, deformations and chromosomal abnormalities	Q00–Q99

Appendix-Figure 2: **Sex-specific Relative Index of Inequality (RII) trends including APC based on joinpoint models**



Markers: Annual observed cancer mortality RII. Lines: modelled RII trends. Estimates are results from 5 databases generated by multiple imputations, appropriately reflecting uncertainty attributable to missing values.

Time trends in educational inequalities in cancer mortality in Colombia, 1998-2012

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Time trends in educational inequalities in cancer mortality in Colombia, 1998-2012

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Ethics committee approval: This article is based on secondary analysis of data on deaths and population counts in aggregate form made publically available by the National Statistics Office in Colombia. Ethical approval for this study was not required.

STRUCTURED ABSTRACT

Objectives: To evaluate trends in premature cancer mortality in Colombia by educational level in three periods; 1998-2002 with low healthcare insurance coverage, 2003-2007 with rapidly increasing coverage, and finally 2008-2012 with almost universal coverage (2008-2012).

Setting: Colombian population-based, national secondary mortality data..

Participants: We included all (n=188,091 cancer deaths occurring in age groups 20-64 years between 1998 and 2012, exclusing only cases with low levels of quality of registration (n=2,902, 1.5%).

Primary and secondary outcome measures: In this descriptive study we linked mortality data of ages 20-64 years to census data to obtain age-standardized cancer mortality rates by educational level. Using Poisson regression we modelled premature mortality by educational level estimating rate ratios (RR), relative index of inequality (RII) and the Slope Index of Inequality (SII).

Results: Relative measures showed increased risks of dying among the lower educated compared to the highest educated, this tendency was stronger in women ($RR_{primary}$ 1.49; $RR_{secondary}$ 1.22, both p<0.0001) than in men ($RR_{primary}$ 1.35; $RR_{secondary}$ 1.11, both p<0.0001). In absolute terms (SII) cancer caused a difference per 100,000 deaths between the highest and lowest educated of 20.5 in males and 28.5 in females. RII was significantly higher among women and the younger age categories. RII decreased between the first and second period, afterwards (2008-2012) increased significantly back to their previous levels. Among women, no significant increases or declines in cancer mortality over time were observed in recent periods in the lowest educated group, whereas strong recent declines were observed in those with secondary education or higher.

Conclusions: Educational inequalities in cancer mortality in Colombia are increasing, in absolute and relative terms concentrated in young age categories. This trend was not curbed by increases in healthcare insurance coverage. Policy makers should focus on improve equal access to prevention, early detection, diagnostic and treatment facilities.

Strengths and limitations

- Population-based mortality databases with information on educational level provide a unique data source to evaluate educational differences
- Definition of the variable for educational level does not guarantee having terminated the indicated level, there may be variance within the educational groups
- Time period included covers a period of important changes in Colombian society, expected to be reflected in cancer mortality rates
- Multiple imputation improved statistical power and precision of analyses
- The underlying causes of these trends are unknown

Contributorship statement

Esther de Vries performed the joinpoint analyses, adapted tables and figures and was the main writer of the text. Ivan Arroyave performed the main part of the analyses apart from the joinpoints, discussed with Esther de Vries all initial tables and figures, and commented on the text. Constanza Pardo contributed to content and improvement of the text and figures.

Introduction

Colombia is a country with very large socioeconomic inequalities, causing, among others, large differences in health-related topics such as life expectancy and incidence, prognosis and mortality of disease [1-3]. In 1993, a major health care reform in Colombia introduced mandatory health insurance coverage (HIC) [4]. Citizens are assigned to two major schemes based on income: (i) the contributory scheme, which covers workers and their families with an income above the cut-off and is financed through payroll and employer's contributions; and (ii) the subsidized scheme, mainly funded via taxes, which subsidizes the poor as identified through a proxy means test [5]. HIC was 23.7% in 1993 just before the reform [6] and rose to 37.7% in 1994, just afterwards [4]. Initially, the coverage slowly improved [4] and a subsequent reform led in 2002 to a noticeable increase of healthcare coverage (reaching around 96% by 2008) by improving efficiency in the use of resources and by reducing its reliance on national budgets [7] (Figure 1). In the poorest income quartile, HIC increased from 6% to over 70% between 1993 and 2009 [5], attributable to the subsidized scheme [8], which shows that the program reached the poorer income groups more aggressively. This increased HIC is expected to contribute to a reduction in health inequalities [4 5], mainly by improving the situation for the poor: ensuring timely care and bringing patients in closer contact with the health care system [9 10]. It has been argued, however, that the reform increased the complexity of the system which could potentially lead to delays in certain types of care [11] and reduced spending in prevention and public health [12].

In Colombia, three different periods in the implementation of universal HIC can be discerned (Figure 1): During the period 1998-2002, HIC was relatively low and stable (around 70% during all the period); the second period (2003-2007) covered the years of rapid increase in coverage among the poor (6.9% average annual growth in HIC, 12.2% in subsidized scheme); while during the third period (2008-2012) universal coverage remained stable according to official figures at on average 96.1%. The discrepancy in HIC trends between these three periods offers a natural experiment to examine the impact of HIC on socioeconomic disparities in mortality.

Few studies have examined the impact of different health insurance status on inequalities in mortality and even less is known about inequalities in mortality in middle-income countries, many of whom introduced major health care system reforms during the last decades. As in Colombia the increase of HIC towards universal coverage was deliberately addressed to the poorest population [4 5], and educational level is a good proxy variable for Socioeconomic Status (SAS) [13], we hypothesize that increased HIC contributed to reducing inequalities in cancer mortality. Cancer mortality is a particularly interesting indicator of the effect of insurance coverage due to the expected increased access to prevention measures, early detection, timely treatment therapies, and high-cost interventions [14-16].

Indeed, previous analyses of time trends of differences in cancer mortality by attained educational level in Colombia (1998-2007) were promising, particularly for gastric and cervical cancer where faster declines in mortality occurred in the lowest educated groups and therefore socioeconomic differences were expected to decrease in the near future [3]. In this paper we evaluate if the seemingly positive trend in cancer mortality by educational level continued, by using a slightly different definition of educational level which allowed us to extend the previous analyses (up to 2007) by 5 extra years, covering 1998-2012.

Methods

Data

Education level criteria

Educational level was defined as the highest level in which the individual has been enrolled during his life (i.e. the person accessed but not necessarily graduated this level), and was categorized in three groups based on the highest educational level accessed by the deceased: (a) Primary school or less, (b) Secondary school, and (c) Tertiary (post-secondary education). In previous papers educational level has been used, based on the highest educational level attained (i.e. completed) by the deceased [1 3] but this category is restricted to the period 1998-2007. In our calculations we found both approaches to be similar in terms of the results yielded.

Deaths

National mortality data for cancer deaths (International Classification of Diseases (ICD-10) codes C00-C96, see Appendix-Table 1) for the period 1998-2012 were obtained from the National Administrative Department of Statistics (DANE), which routinely registers information on sex, date and cause of death as well as educational level from death certificates. Although the exact wording for the variable "accessed education" changed in the DANE database since 2008, the new categories were consistent with those of the databases of previous years and could be used. Trends of counts were found to be continuous and regular.

We focused on adult premature mortality (mortality below age 65) because it is known that information on educational level from mortality statistics is unreliable at ages 65 and beyond [17]. Additionally, premature mortality is an indicator of population health believed to be strongly influenced by social, economic and environmental factors [18], and is a common indicator of health system performance [19].

Data on age and sex were available for more than 99% of all deaths, while data on educational level was missing for approximately 16.5% of 190,993 cancer deaths. We used multiple imputation methods [20] implemented in SAS through the IMPUTE procedure to impute educational level for these cases in order to avoid bias due to the potentially higher rates of missing education for lower educated individuals, and to minimize the potential for numerator/denominator bias [17]. In short, this procedure fits a sequence of regression models and draws values from the corresponding predictive distributions. The sequential regression procedure was applied based on a model that included sex, region, urban/rural residence and marital status as covariates. Details of this method are explained elsewhere [20]. The imputation procedure was successful in 90.8% of cases with missing information, resulting in a total of 188,091 (98.5%) cancer deaths for our analyses.

Population

Data on mid-year population counts by age, sex and educational level were obtained from the Colombian Demography Health Surveys (DHS) [21], which contain periodical information on the distribution of education by age, sex and calendar year (1995, 2000, 2005 and 2010). Age 20 was chosen as the lower age limit of this study as almost 100% of individuals accessed their highest educational level by this age.

The resulting proportions of individuals in each educational level were multiplied with the total population numbers per year, age and sex which were obtained from census combined with statistical projections from DANE [22]. These two information sources were combined to estimate the annual population size in each educational group (Appendix-Figure 1). We performed demographic projections to obtain population counts for years in-between every lustrum using the demographic Software PASEX [23]. Additional details on the procedure are available elsewhere [23].

Analysis

All analyses were conducted in each of the five multiple databases generated by the multiple imputation process. Since results were nearly identical for all imputations, we used standard techniques as implemented in the PROC MIANALYZE procedure in SAS to combine estimates from all databases and adjust standard errors to account for uncertainty in the imputation [24]. This procedure reads the parameter estimates and associated covariance matrix for each imputed data set, and then derives valid multivariate inferences for these parameters. This allows for valid statistical inference that appropriately reflects uncertainty due to missing values [24].

All analyses were conducted in SAS® version 9.2.

Age Standardised Mortality Rates (ASMR)

Data on population counts were combined with data on deaths to obtain a complete database of death counts by educational level, sex and five-year age group. We first calculated age-standardized mortality rates by educational level, sex and year using the

World Health population of 1997 [25] as standard population, resulting in Age Standardised Mortality Rates (ASMR) expressed per 100,000 person-years (Figure 2). We also calculated ASMR by sex and year (Figure 2) and by educational level and sex (Table 1).

Annual trends in ASMR by sex and educational level were quantified by calculating the estimated Annual Percentage Change (EAPC) which measures the average rate of change in the mortality rate per year (negative EAPC: decreasing trend, positive EAPC : increasing trend). To test whether an apparent change in mortality trends was statistically significant, we used joinpoint regression, which fits a series of joined straight lines to age-adjusted rates and uses a Monte Carlo Permutation method to identify the best-fitting point (called joinpoint, year in which a significant change in the mortality trend occurred), where the rate of increase or decrease changes significantly [26]. EAPC and joinpoints were determined based on the log-transformed ASMRs and their standard errors. We specified a maximum of 2 joinpoints with at least 4 observation points to either extreme of the data using joinpoint modelling based on the Joinpoint program [27] (Figure 2).

Regression models

We implemented separate Poisson regression models separately by sex with number of deaths as dependent variable and the natural log of person-years as offset variable, incorporating age and educational level as independent variables. We first estimated Rate Ratios (RR) of mortality by educational level, which compared the mortality of all educational groups to the mortality in the tertiary education group. Changes in the rate ratio over time result from changes in both risks and the distribution of educational level [28]. To assess changes in disparities 'controlling' for changes in the educational distribution, we estimated the Relative Index of Inequality (RII), regressing mortality on the mid-point of the cumulative distribution of education, thereby taking into account the size of each educational group [28 29]. Values higher than 1 indicate educational inequalities favouring the higher educated.

We evaluated if RRs significantly changed over time and within periods on continuous scales, which was not the case (results not shown). We calculated RII for three 5-year periods (1998-2002, 2003-2007, and 2008-2012) and for three age groups (20-34, 35-49, and 50-64) in order to identify differences in inequalities along age (Figure 2).

To compare the contribution of each cause of death to mortality disparities for non-communicable diseases (classified by their ICD-10 codes, see Appendix-table 1) we calculated the Slope Index of Inequality (SII) (Figure 4). The SII is a measure of absolute disparities that represents the difference in mortality between the population at the top and the bottom of the educational distribution [28]. Further details on the RII and SII are available elsewhere [28].

Results

Table 1 shows counts of cancer deaths and population at ages 20-64 years between 1998 and 2012 in Colombia. After excluding non-imputed cases (1.5%), 106,199 cancer deaths occurred from 1998 to 2012 among women while 81,892 occurred among men, with age-standardized cancer mortality rates (ASMR, per 100,000 person-years) of 58 among women and 49 among men. Men and women with lower levels of education had higher cancer mortality rates than their higher-educated counterparts. In addition, ASMR were larger among women than among men in each educational level.

The risk of dying was significantly and consistently higher among the lower educated. The RRs show clearly and statistically significantly increased risks of dying among the lower educated compared to the highest educated, this tendency was stronger in women ($RR_{primary}$=1.49; $RR_{secondary}$=1.22, both p<0.0001) than in men ($RR_{primary}$=1.35; $RR_{secondary}$=1.11 both p<0.0001). In order to formally test this higher female risk, we calculated Rate Ratios between sexes by educational levels, using men as reference category. For all educational levels, women had significant larger rate ratios (results not shown). We also found a consistent and slight increase in rate ratios from first, to second, and then to the third period (appendix-table 2) among both men and women and for primary and secondary education compared to higher educated, but the confidence intervals overlap, indicating the differences do not reach statistical significa

During the 15 years of observation, the general tendency was for age-standardized cancer mortality rates to decline, with recent stabilizations, reaching an average ASMR in 2012 of 47.3 per 100,000 males and 55.2 per 100,000 females. Average EAPC for males in the periods defined by joinpoint were: 1998-2000: 2.4% (95% CI -2.0; 7.0), 2000-2012: -0.92% (95% CI -1.2; -0.7); for females 1998-2003: 0.7 (95% CI -0.7; 2.1), 2003-2006: -2.8% (95% CI -8.2; 2.9), 2006-2012 -0.6 (95% CI -1.5; 0.3). The general tendency for a declining trend in mortality was not reflected equally by educational level and sex (figure 2). Women had higher mortality rates than men. No significant increases or declines over time were observed in the lowest educated groups, whereas in the middle and high educated groups there was at least one period with significantly declining cancer mortality rates. In these groups, tendencies were for mortality to decrease substantially in the period after 2002/2003, with the exception of the highest educated males who showed recent increases. The strongest declines in cancer mortality over time were observed in the group of women with secondary or tertiary education. The most consistent declines in cancer mortality rates for all educational levels in both sexes were observed in the period 2003-2007, the period with rapid inceases in HIC, particularly among the poor.

RII initially decreased from 1998-2002 to 2003-2007 (reaching significance among women), but then in the period 2008-2012 they increased back to its previous levels

(Figure 3, left panel). Trends in the joinpoint for RII are in line with this finding: no significant change was found for educational inequalities among men, whereas there was an initial significant decline (-7.6%) among women up to 2004 followed by a significant increase (+3.8%) in the period 2004-2012 (Appendix-Figure 2). RII also showed that inequalities were significantly higher for the younger age categories compared to older ones and tended to be higher for women (Figure 3, right panel).

Figure 4 shows the contribution to absolute differences in ASMR by education as measured by the SII for non-communicable diseases (appendix-table 1). Cancer was the second largest cause, after cardiovascular disease: explaining 20% of male differences (SII=20.5 deaths per 100,000 population) and 24% of female differences (SII=28.5). Absolute differences in cancer mortality were 39% larger for women than for men (28.5 vs. 20.5), while this difference was only 14% for all non-communicable diseases (SII= 103.2 and 120.3 respectively).

Discussion

We observed strong and persistent educational differences in cancer mortality rates in Colombia. These differences appeared to be diminishing in the period 2002-2007 [3] when healthcare insurance coverage largely grew, especially for the most disadvantaged part of the population. But in recent years, despite the achievement of almost universal HIC, inequalities were widening, particularly among women, with rates in the lowest educational groups being stable or increasing and those in the higher educated groups gradually declining. This means that the lowest educated part of the population is increasingly lagging behind in the progress against cancer, despite the increase in insurance coverage.

Explanation of results

Educational level was found to be previously as a good proxy variable for Socioeconomic Status (SES) [13]. Lower SES is associated with a higher prevalence of cancer risk factors (such as smoking, alcohol, obesity, occupational risk factors, housing circumstances), and less healthcare utilization (because of lower resources but also lower awareness and poorer access due to longer distances or high impact of family income when taking time off to visit a doctor) [30-32].

Not only absolute cancer mortality rates, but also inequalities in mortality were largely higher for women than for men. In a previous paper we showed this to be almost entirely attributable to cervical cancer mortality, which accounted for 51% of inequalities in total female cancer mortality in 1998-2007 at 25-64 [3]. The consistently higher RR for women than men are unique to cancer in Colombia; studies evaluating other causes of death consistently show a higher mortality risk for men [1 2], which also coincides with the usually lower life expectancy of men. This illustrates the high burden of certain cancers which are strongly SES related, probably mainly cervical and breast cancer, which, if diagnosed late, have a very poor prognosis even though early detection possibilities are ample. Several Colombian studies have identified that both characteristics of the health system such as access and delays in diagnosis and treatment, and characteristics of the populations of lower socioeconomic classes contribute to the higher burden of cervical cancer mortality [33 34]. A previous study showed that lower access to mammography screening for early detection of breast cancer was associated with lower education, affiliation to the subsidized regime or being unaffiliated [35]. In general, financial access to healthcare has been more limited to women [36 37] which potentially limits access to expensive cancer therapies, particularly for most deprived women.

We also observed clearly increased educational differences in cancer mortality for the youngest age groups, in which mortality from cancer is a relatively rare event. Among males, leukaemias, stomach cancers and Non-Hodgkin lymphomas are important cancer causes of deaths in the age groups 15-39 years (representing 44% of all cancer deaths in this age group); for females these include cervical cancer and leukaemias as well as non-Hodgkin lymphomas (representing 38%) [38]. Previous studies have shown that mortality or survival of these cancer types is very much dependent on socioeconomic status [3 14 39]. As these tumours explain an important proportion of cancer deaths in these ages, this probably explains the high RII in the younger age groups as compared to the higher age categories. Nevertheless we cannot discard that, at least partially, the strong inequalities in younger groups are due to the fact that, when rates are low, relative inequalities tend to show an increasing pattern [40].

In order to test if RII is a good indicator of changes in inequalities [40], we compared trends in relative and absolute measures of inequalities (RII and SII), which were almost identical (results not shown). Mackenbach hypothesized that, in the case of declining mortality rates, RIIs are exaggerating the differences [40], but this was clearly not the case in our study, probably because reductions in premature mortality rates of cancer were relatively smooth, and not very strong and not very divergent between educational levels, with the exception of tertiary educated women. Among women we only found a clear reduction in inequalities during the period 1998-2004, owing to a clearly divergent pattern between educational levels: A rapid significant decrease of ASMRs in the higher socioeconomic group (tertiary educated) and an opposed rapid significant increase of ASMRs among those with secondary education. We have illustrated in previous work that these trends are most likely due to large changes in Cervical cancer mortality [3].

Our results clearly illustrate that an almost complete coverage does not necessarily reduce inequalities in health [41 42]. Particularly, having health insurance may be universal, but depending on income the type of health insurance is different (subsidized, contributory and special or exceptional regimes), with the wealthy population often buying additional private health assurance to ensure rapid and more broad access [43]. The quality of care provided by the insurance (translating into early and timely diagnosis and adequate treatment) is not guaranteed with complete coverage, as seems to be the case: To warrant rights to get access to expensive treatments and medication, as usual in cancer, exceptional legal mechanisms are frequently launched in Colombia: Technical-scientific committees of health assurers, and an action for protection so-called “tutela” [43 44]. A study shows that those affiliated to the contributory regime are more likely to warrant additional rights more efficiently [44], potentially increasing inequalities between regimes. Also, clear differences in gastric cancer survival by type of health insurance affiliation have been documented in a population-based Colombian study, clearly illustrating that, even though in theory there is access to care for all, this does not translate to equal outcomes [45].

In parallel with the increases in HIC, other changes in the Colombian health care system occurred, including increases in investments in care [5 46]. Therefore, our results reflect the impact of the entire reform rather than only the increased coverage in health insurance. However, based on our analyses, it is safe to conclude that all these reforms have not resulted in reducing inequalities in cancer mortality. This is not unique to Colombia; in several countries, as diverse as Taiwan, Thailand and European countries, inequalities in health increased upon reaching almost universal coverage [47-52].

Strengths and weaknesses

This is one of few studies investigating educational differences in mortality using population-based mortality and population-based educational level. Despite several strengths, some limitations should be considered in our study: We did not correct for misclassification within the cancer groups, but since we studied the group of cancer deaths overall, regardless of the subtype of cancer, most of these errors are cancelled out. In general “cancer” as cause of death is correctly coded [53], and most likely particularly in setting of ages under 65.

Data on mortality were obtained from mortality registries, while data on the population distribution by education were obtained from censuses and demographic projections. This may have led to the so-called numerator/denominator bias, which generally results in an overestimation of disparities [17]. Furthermore, for some years, data on population size were obtained from demographic projections combined with distributions of education from surveys. To assess the impact of this potential bias, we experimented with different education distributions from multiple data sources [54-56], showing that the overall trends in our study were robust to different assumptions on the distribution of education [3].

Potentially, there has been substantial under-registration of deaths in some regions. Previous studies comparing national mortality rates with indirect estimates from census [57 58] suggest that underregistration is particularly important in the poorest regions, implying that estimates of disparities in mortality by educational level are likely to be an underestimation, because those with lower education are more likely to live in areas with higher underregistration rates. This may also have led to underestimation of the extent to which inequalities have increased, because underregistration decreased over the study period [57 58]. Our results, therefore, are indicative of potentially larger inequalities in mortality by education, which continue to increase.

Information on education was missing for 16.5% of cancer deaths, potentially leading to an underestimation of disparities, as missing values are usually more common in the least educated [59]. However, we imputed values for educational level for individuals with missing educational information based on a information on age, sex marital status, region and urban/rural residence, thereby limiting the potential impact of this source of bias.

Unanswered questions and future research

Socioeconomic inequalities in mortality of non-communicable diseases have been associated with the unequal distribution of behavioural risk factors, such as smoking, alcohol consumption, an unhealthy diet, sedentary lifestyle higher risk of injuries [2 60]. This implies underlying inequalities in exposure to risk factors and incidence of these diseases. However, data on the incidence of disease and prevalence distribution of all those behavioural and poverty risk factors by socioeconomic status are largely lacking in Colombia and most developing countries. Studies on the mechanisms underlying the way these risk factors contribute to inequalities in mortality are scarce, even in developed countries. We previously described not only large inequalities in mortality of cancers with a primary infectious aetiology such as gastric cancer [3], but also documented inequalities in survival of gastric cancer measured by both type of health insurance and socioeconomic stratum [14]. These findings indicate that both access and quality of care (health insurance) as other factors related to socioeconomic status independently affect survival for the lower socioeconomic classes negatively. Detailed studies are needed on both types of factors: which barriers exist for timely diagnosis and adequate treatment in situations with universal health coverage and how can they be tackled? And on which other factors related to socioeconomic stratum can interventions be designed? The answers to these questions will be various and, depending on the specific disease, will be quite different in character. It is of high importance that data on socioeconomic indicators are collected in a standard way, so that for example cancer registries can calculate incidence rates by socioeconomic stratum, which, at this moment, is not possible in Colombia [61].

Socioeconomic differences were substantially larger for women than for men, in our previous study this difference was almost entirely attributable to inequalities in cervical cancer mortality [3]. In this more recent study we see that the gender inequalities grew despite the virtually universal HIC since 2008. Gender inequalities were larger for cancer than for other non-communicable diseases according SII; more detailed analyses are needed to assess to which extent the growing inequalities are due to an increase in cervical cancer mortality amongst less favoured.

Conclusions

The recent negative curbs in mortality among the lowest educated groups, resulting in increasingly differences between educational groups, are a call for attention by the Colombian health authorities to take measures in both primary prevention, access to early detection and timely and adequate treatment. Underlying causes of the observed differences are multiple, from differences in housing, lifestyle, health-related beliefs, to differences in access to diagnostic facilities and high-quality treatment, which all should be of concern to those in charge [62]. Insurance coverage is clearly not enough to counterbalance the deleterious effects of decreases in spending on primary prevention and other social and economic conditions which determine the growing levels of educational inequalities in cancer.

Acknowledgements

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Figures and Tables

Figure 1: Trends in national healthcare insurance coverage (HIC), Colombia, 1998-2012

Other schemes include primarily members of the military and teacher and oil workers syndicate members. Based on Annual reports of the Ministry of Health and Social Protection

Source: Annual reports of the Ministry of Health and Social Protection to the Congress of the Republic of Colombia

Table 1: **Descriptives of the study: deaths, population and rates separately by sex and educational level, Colombia, 1998-2012**

Sex	Educational level [a]	Cancer deaths [b]	Population size	ASMR [c] (95% Confidence Intervals)	
	Primary	50,126	67,815,336	54.0	(53.5, 54.5)
	Secondary	22,273	67,742,806	45.1	(44.4, 45.8)
Men	Tertiary	9,493	30,715,631	41.4	(40.5, 42.3)
	Total	***81,892***	***166,273,773***	***48.9***	***(48.8, 49.1)***
	Primary	65,336	68,637,666	64.7	(64.2, 65.2)
	Secondary	30,414	72,387,214	54.2	(53.5, 54.9)
Women	Tertiary	10,449	35,149,442	47.2	(46.2, 48.3)
	Total	***106,199***	***176,174,322***	***57.8***	***(57.6, 58.0)***

[a] : Educational attainment values registered after final imputation. Primary = up to elementary or primary school; secondary = any level of high-school; tertiary = any level of postsecondary education after high school including college and university.

[b] : Cancer deaths after imputation.

[c] : ASMR: Age standardized mortality rates per 100,000 population; Estimates (WHO standard population 1997) for educational level combine results from 5 databases generated by multiple imputations, appropriately reflecting uncertainty attributable to missing values.

Figure 2: Age-standardized cancer mortality trends, including APC based on joinpoint models, by sex and educational level

Markers: Observed age-standardized cancer mortality rates. Lines: modelled age-standardized cancer mortality trends. Estimates are results from 5 databases generated by multiple imputations, appropriately reflecting uncertainty attributable to missing values. The points represent ASMR, lines represent the trendlines between joinpoints. Blue, diamonds: maximum primary education; Red, triangles: secondary education; Green, circles: tertiary education. Numbers adjacent to the lines represent estimates annual percent change (EAPC) during the corresponding periods, based on joinpoint modelling; a star indicates statistical significance at α 0.05.

Figure 3: Sex-specific Relative Index of Inequality by period and age group

Estimates from combined results from 5 databases resulting from multiple imputations, appropriately reflecting uncertainty attributable to missing values.

Figure 4. Slope Index of Inequality (SII) for non-communicable diseases

See Appendix-Table 1 for International Classification of Diseases (ICD-10) codes for non-communicable diseases

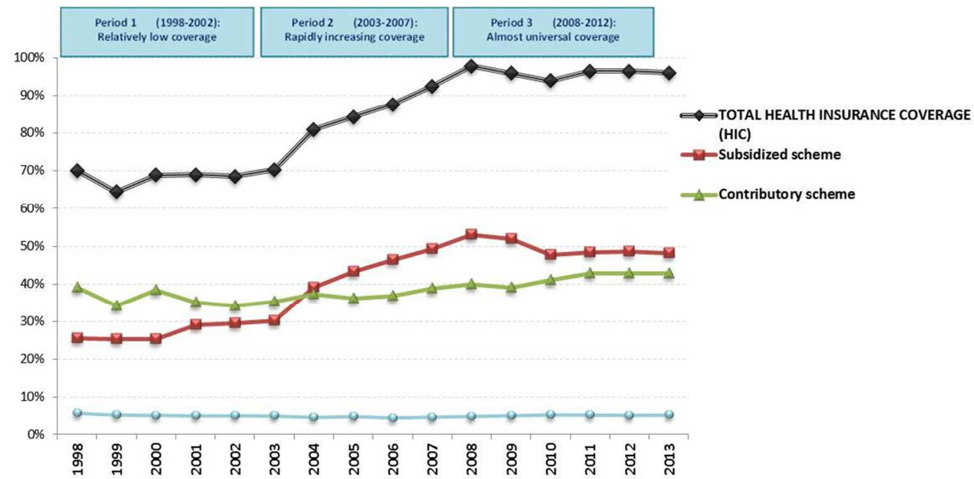

Figure 1: Trends in national healthcare insurance coverage (HIC), Colombia, 1998-2012

Other schemes include primarily members of the military and teacher and oil workers syndicate members.
Based on Annual reports of the Ministry of Health and Social Protection
Source: Annual reports of the Ministry of Health and Social Protection to the Congress of the Republic of Colombia

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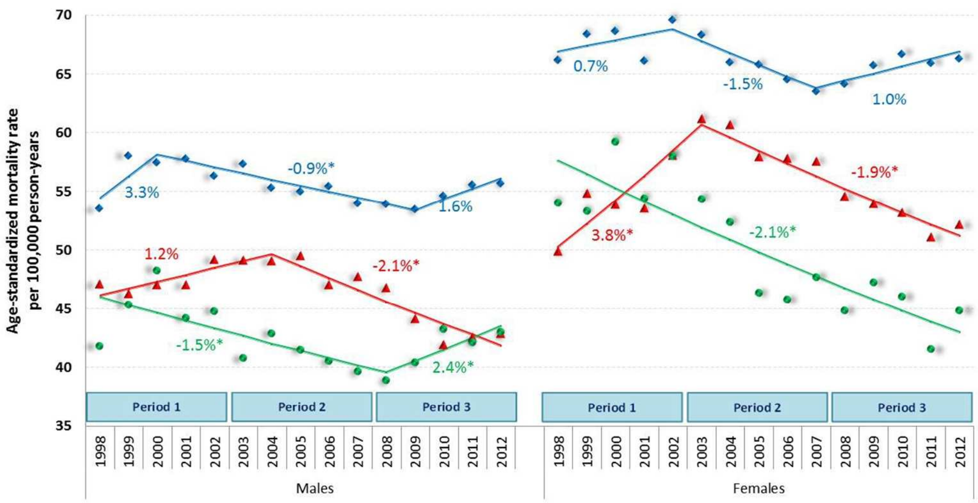

Figure 2: Age-standardized cancer mortality trends, including APC based on joinpoint models, by sex and educational level

Markers: Observed age-standardized cancer mortality rates. Lines: modelled age-standardized cancer mortality trends. Estimates are results from 5 databases generated by multiple imputations, appropriately reflecting uncertainty attributable to missing values. The points represent ASMR, lines represent the trendlines between joinpoints. Blue, diamonds: maximum primary education; Red, triangles: secondary education; Green, circles: tertiary education. Numbers adjacent to the lines represent estimates annual percent change (EAPC) during the corresponding periods, based on joinpoint modelling; a star indicates statistical significance at α 0.05.

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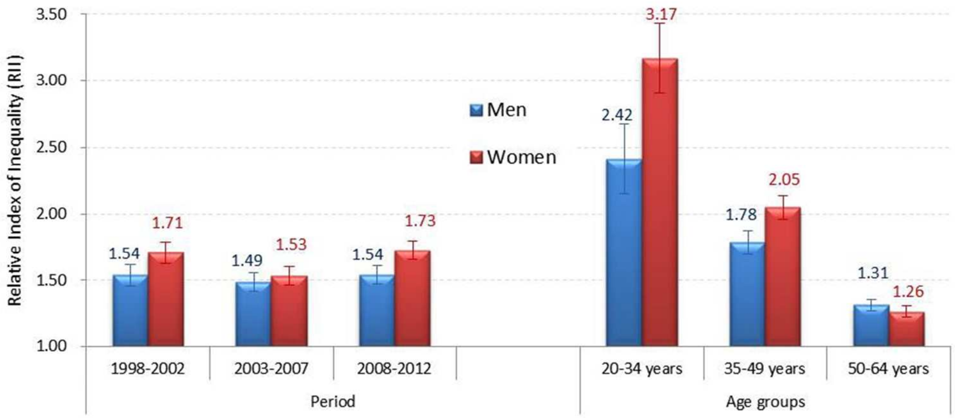

Figure 3: Sex-specific Relative Index of Inequality by period and age group

Estimates from combined results from 5 databases resulting from multiple imputations, appropriately reflecting uncertainty attributable to missing values.

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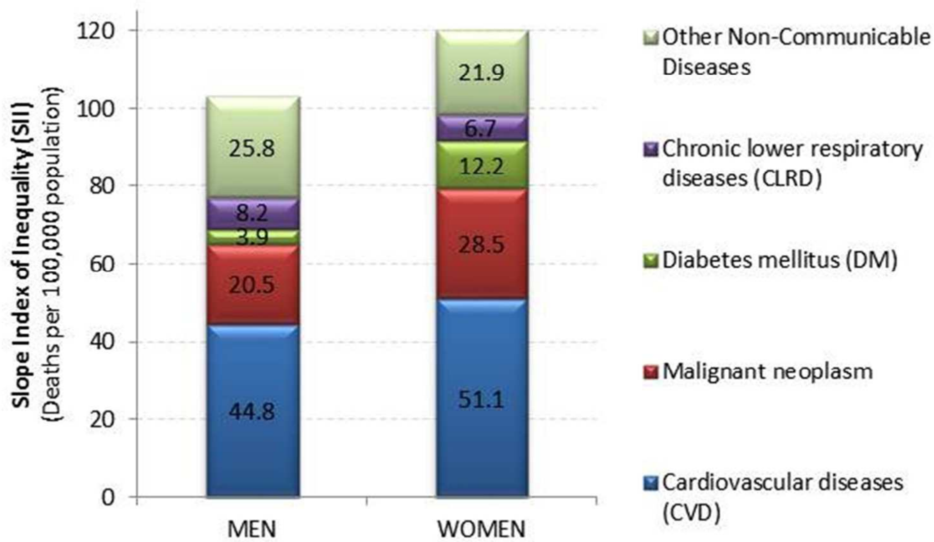


Figure 4: Slope Index of Inequality (SII) for non-communicable diseases

See Appendix-Table 1 for International Classification of Diseases (ICD-10) codes for non-communicable diseases

112x66mm (150 x 150 DPI)

APPENDIX

Appendix-Figure 1. Educational level trends over time, Colombia, 1998-2012

The thicker markers are those from the year with real data available (source: Colombian Demography Health Surveys in 1995, 2000, 2005 and 2010). The points in between were interpolated (see methods)

Appendix-Table 1. **Classification of Causes of death, International Classification of Diseases (ICD-10) codes for non-communicable diseases**

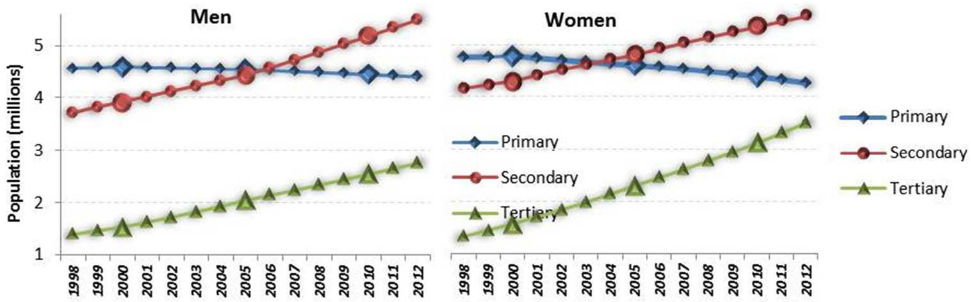
Non-Communicable Diseases		ICD-10 codes
Cardiovascular diseases		I00-I99
Malignant neoplasm		C00-D48
Diabetes mellitus		E10-E14
Chronic lower respiratory diseases (CLRD)		J40-J47
Other Non-Communicable Diseases	Mental and behavioural disorders	F00–F99
	Diseases of the nervous system	G00–G99
	Diseases of the digestive system	K00–K93
	Diseases of the genitourinary system	N00–N99
	Congenital malformations, deformations and chromosomal abnormalities	Q00–Q99

Appendix-Figure 2: Sex-specific Relative Index of Inequality (RII) trends including APC based on joinpoint models

Markers: Annual observed cancer mortality RII. Lines: modelled RII trends. Estimates are results from 5 databases generated by multiple imputations, appropriately reflecting uncertainty attributable to missing values.

Appendix-Table 2. Rate ratio in premature cancer mortality by educational level by 5-years periods and separately for men and women at 20–64 years, Colombia 1998-2012

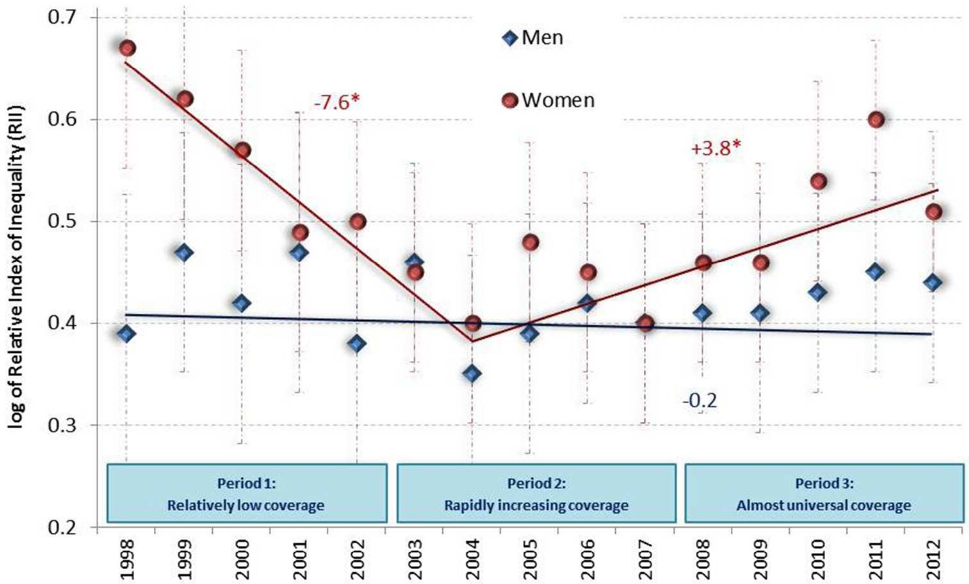
		Period 1 (1998-2002): Relatively low coverage	Period 2 (2003-2007): Rapidly increasing coverage	Period 3 (2008-2012): Almost universal coverage
MEN	Tertiary (Ref)	1.00		
	Secondary	1.08 (0.89 , 1.30)	**1.19 (1.14 , 1.24)**	**1.31 (1.14 , 1.52)**
	Primary	**1.32 (1.11 , 1.56)**	**1.37 (1.31 , 1.43)**	**1.42 (1.23 , 1.63)**
	Year	1.01 (0.98 , 1.04)	0.99 (0.96 , 1.02)	1.02 (1.00 , 1.04)
	Secondary*Year	1.00 (0.96 , 1.03)	1.00 (0.97 , 1.04)	**0.96 (0.94 , 0.99)**
	Primary*Year	1.00 (0.96 , 1.03)	1.00 (0.97 , 1.03)	0.99 (0.96 , 1.02)
WOMEN	Tertiary (Ref)	1.00		
	Secondary	1.10 (0.91 , 1.33)	**1.27 (1.22 , 1.32)**	**1.29 (1.13 , 1.47)**
	Primary	**1.25 (1.04 , 1.51)**	**1.44 (1.39 , 1.50)**	**1.45 (1.28 , 1.65)**
	Year	1.03 (1.00 , 1.07)	0.98 (0.96 , 1.01)	1.00 (0.98 , 1.02)
	Secondary*Year	0.99 (0.96 , 1.03)	1.01 (0.98 , 1.04)	0.99 (0.97 , 1.02)
	Primary*Year	0.97 (0.94 , 1.01)	1.00 (0.97 , 1.02)	1.01 (0.98 , 1.03)



Appendix-Figure 1: Educational level trends over time, Colombia, 1998-2012

The thicker markers are those from the year with real data available (source: Colombian Demography Health Surveys in 1995, 2000, 2005 and 2010). The points in between were interpolated (see methods)

154x51mm (150 x 150 DPI)



Appendix- Figure 2: Sex-specific Relative Index of Inequality (RII) trends including APC based on joinpoint models

Markers: Annual observed cancer mortality RII. Lines: modelled RII trends. Estimates are results from 5 databases generated by multiple imputations, appropriately reflecting uncertainty attributable to missing values.

155x105mm (150 x 150 DPI)