

EPIDEMIOLOGY

Temporal Trends of Asthma Mortality Rates in Brazil from 1980 to 2010

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Objective. Mortality from asthma has varied among countries during the last several decades. This study aimed to identify temporal trends of asthma mortality in Brazil from 1980 to 2010. **Method.** We analyzed 6840 deaths of patients aged 5–34 years that occurred in Brazil with the underlying cause of asthma. We applied a log-linear model using Poisson regression to verify peaks and trends. We also calculated the point estimation and 95% confidence interval (CI 95%) of the annual percent change (APC) of the mortality rates, and the average annual percent change (AAPC) for 2001–2010. **Results.** A decline was observed from 1980 to 1992 [APC = -3.4 (-5.0 to -1.8)], followed by a nonsignificant rise until 1996 [APC = 6.8 (-1.4 to 15.6)], and a new downward trend from 1997 to 2010 [APC = -2.7 (-3.9 to -1.6)]. The APCs varied according to age strata: 5–14 years from 1980 to 2010 [-0.3 (-1.1 to 0.5)]; 15–24 years from 1980 to 1991 [-2.1 (-5.0 to 0.9)], from 1992 to 1996 [6.8 (-6.7 to 22.2)], and from 1997 to 2010 [-3.9 (-5.7 to -2.0)]; 24–25 years from 1980 to 1992 [-2.5 (-4.6 to -0.3)], from 1993 to 1995 [12.0 (-21.1 to 59.1)], and from 1996–2010 [-1.7 (-3.0 to -0.4)]. AAPC from 2001 to 2010 was -1.7 (-3.0 to -0.4); the decline for this period was significant for patients over 15 years old, women, and those living in the Southeast region. **Conclusion.** Asthma mortality rates in Brazil have been declining since the late 1990s.

Keywords bronchial diseases, case fatality, epidemiology, joint point regression

INTRODUCTION

Asthma is a highly prevalent disease, afflicting 300 million worldwide and causing 250 thousand deaths annually. The case-fatality rate of asthma is low, and there is a consensus that deaths from asthma are avoidable (1). In the late 1970s, a peak of asthma-related deaths in New Zealand and the United Kingdom among people aged 5–34 years triggered concern about the levels of asthma mortality rates (2, 3). This peak was determined to be associated with the prescription and use of short-acting beta 2-agonist inhalers—specifically, fenoterol—as summarized in a seminal meta-analysis of four case-control studies addressing fatal asthma in New Zealand and Canada (4). Rises of asthma mortality rates were also identified in Japan for patients aged 5–34 years old in 1980, with another peak in 1993–94, followed by a slight decline associated with use of beta 2-agonist inhalers (5). In the United States—where fenoterol use was not authorized, only the use of other short-acting beta 2-agonists—the asthma mortality rates increased from 1977 to 1988, followed by flat rates until 1998, and since then have shown a downward trend (6). In five European countries, asthma death rates declined from 1994 to 2004, except for a short period of increase in Italy (7). Nowadays, the debate about short-acting beta 2-agonists has been resolved (8), and there is strong evidence of the benefits of using inhaled corticosteroids plus late-acting beta 2-agonists for helping patients avoid hospitalizations and reducing fatal cases of asthma (9).

For international comparison, it is important to stress that all of the above-mentioned studies were of countries

with a well-established health statistics office and regular medical care, including access to asthma medicines. It is a different challenge to explain the tendencies of asthma mortality in Brazil, a large country with some regions (such as the Amazon river basin) where deaths were largely underreported until the 2000s, which has experienced a rapid improvement of medical care access and public health policies since the late 1980s (10). The first evaluation of temporal changes in asthma mortality in Brazil was performed in the largest state—Sao Paulo—from 1970 to 1992 (with two different International Classification of Diseases, ICD-8 and ICD-9) using a broad definition (bronchitis plus asthma). This study does not identify any peak in asthma deaths; the data only indicate a slight decline in the rates (11). Another study investigated asthma mortality in the southern state of Rio Grande do Sul, and reported an increase of asthma death rates between 1970 and 1992, only for people aged 5–19 years old (12). Later, the same authors published a reappraisal of these data along with new data, from 1981 to 2003 in Rio Grande do Sul, which showed a decline of death rates since the late 1990s (13).

The quality of the mortality information system in Brazil has been improving since the early 2000s, with better coverage and significant reduction of the proportion of underlying causes of death coded as “ill-defined.” The aim of this study is to verify the annual percent change of asthma death rates and the point of inflection of the mortality curve from 1980 to 2010 in Brazil for people aged 5–34 years.

METHODS

Data Collection

All data included in the analysis are from the Brazilian National Health System for Health Statistics

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(<http://www.dataus.gov.br>) that centralizes all information about mortality, morbidity, health indices, demographic, and socioeconomic data in the country. We used this information extracting data about asthma death according to age-strata, gender, and region of the country. Mortality data in Brazil come from the municipalities to the federal level, and all deaths are classified by a selected team of nosologists at the Ministry of Health. In 1996, Brazil began to adopt the 10th Revision of the International Classification of Diseases (ICD-10), which considers an “asthma case” as all underlying causes of death or main causes of hospitalization classified as ICD-10: J-45-J-46 (1996–2010). As the ICD-10 incorporated the previous definition of asthma according to ICD-9: 493 (1980–95) as a case of asthma, it was possible to include the ICD-9 definition of asthma permitting the analysis since 1980. For many diseases there was a change in the classification from ICD-9 to ICD-10. However, this does not occur in the case of asthma permitting to analyze the period of the ICD-9 and the ICD-10 together.

In contrast to countries with a long-term official health statistic with a good quality, in Brazil, the mortality statistics changed from a fair to a good mortality system in all five regions—North, Northeast, Center-West, Southeast, and South—only during the most recent decades due to an action to improve the quality of death certification coordinated by the Ministry of Health on state and municipalities. Until the 2000s, only South and Southeast regions had a mortality system with complete coverage of all fatal events and low rate of ill-defined deaths. This quality improvement for the whole country is reason to assume some caution for international comparisons of the Brazilian mortality data.

As there was a possibility of misclassification of the death notification of asthma even when it was filled up by an expert physician, we ran three types of temporal trend analysis. The first type including only cases classified as asthma. The second adding for all cases classified as asthma and the cases classified as bronchitis (adding the codes ICD-9: 466, 490–492, 494, 496 and ICD-10: J-20-21, J-40-44, and J47); and a third type including all respiratory diseases. The objective of this approach was to verify if a shift of diagnosis occurred between asthma and bronchitis and, further between asthma–bronchitis and other respiratory diseases could change the temporal trend. If these three analyses show similar temporal trends (upward, flat, downward), it will be plausible for a minimization of a misclassification of death certification during these three decades of observation (14, 15).

Again, to prevent some kind of bias related to chronic obstructive respiratory disease (COPD) we restricted the analysis to people aged 5–35 years old, in which the probability of a diagnosis of COPD is very unlikely in any country worldwide permitting safe comparisons among them.

The population estimate for each year was based on the National Census Data (1991, 2000, and 2010). We use

three age-strata: 5–14 years old, 15–24 years old, and 25–34 years old.

This study was not submitted to an Institutional Review Board because all data about mortality and hospitalization are of public domain, without personal identification information such as name, residence, or identification number of the index event.

A simulation was performed using the “Joint Regression Program 3.3.5” (a log-linear model using Poisson regression) to verify the peaks and trends by creating a Monte Carlo permutation test to identify points where the trend line changed significantly in magnitude or direction, disclosing the annual percent change (APC) (16). Running the model required a minimum of three observations after the first joint point, with four following the second and third points. The statistical power to determine whether an APC is different from zero is a function of the length of the interval; thus, a short segment rising at a steep rate may not be statistically significant. As the statistical power to determine whether APC is different from zero is a function of the length of the interval, a short segment rising at a steep rate may not be statistically significant. We also determined the average annual percent change (AAPC) during the last 10 years of observation. From 2000 and 2010, the quality of the death certification for the whole country was more homogenous compared with previous decades. The AAPC is an alternative analytical method that is useful for evaluating subsets, such as sex, age strata, and the region of the country only testing the direction of the temporal trend. A permutation test was applied singly for APC and AAPC after all analyses with a significance level of 0.05 (17). A statistically significant change implies a 95% CI that does not cross the zero value.

RESULTS

During the period from 1980 to 2010, we identified 6840 deaths of patients aged 5–34 years throughout Brazil with the underlying cause of asthma; 7384 additional deaths were classified as being due to bronchitis. During these three decades, deaths exclusively related to asthma ranged from 3.3 to 6.1% of all respiratory diseases cases; 56% of these cases occurred among women. Concerning race/ethnic background, the death rates (per 100,000) were 0.25 for White, 0.19 for Mixed, 0.05 for Black, and 0.01 for Asian subgroups. Three-quarters of the events occurred during hospitalization.

Figure 1 summarizes the temporal changes of asthma mortality. There were two points of inflection of the curve, yielding three different APC patterns: a decline from 1980 to 1992, followed by a nonsignificant rise until 1996, and a new significant downward trend from 1997 to 2010. Analysis of the category “asthma and bronchitis” showed a similar pattern.

Table 1 shows the annual percent change of mortality rates according to age strata. The cases of patients aged 5–14 years exhibited a flattening pattern during all periods.

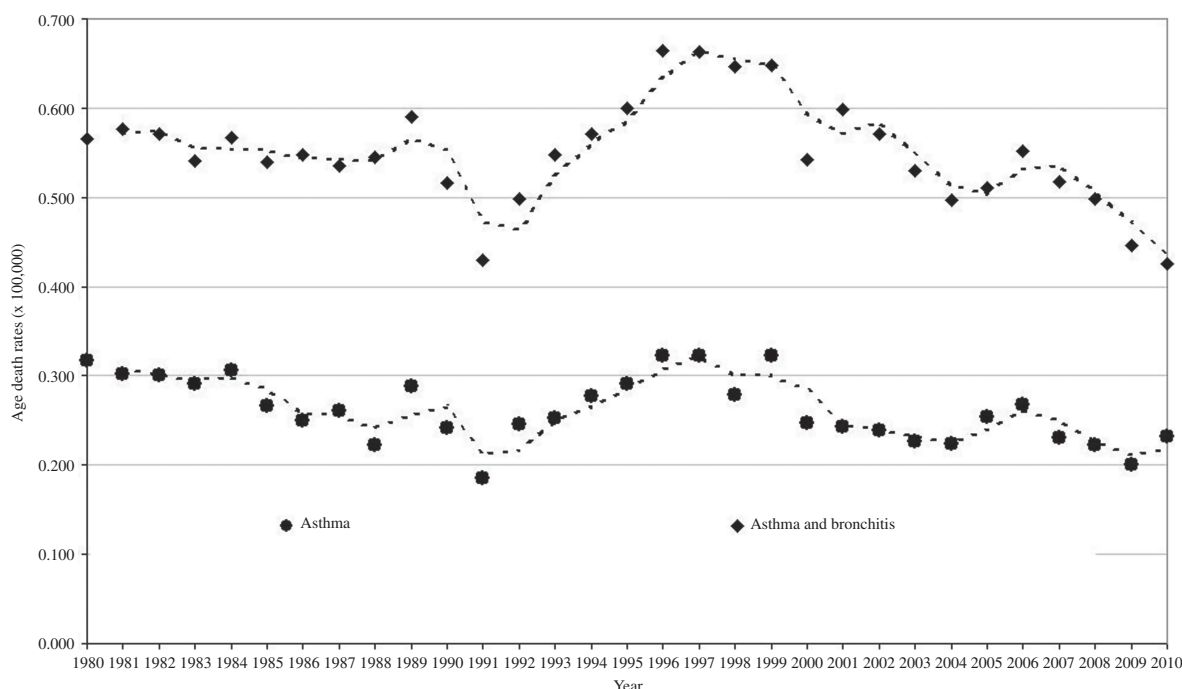


FIGURE 1.—Temporal trends of age-adjusted asthma death rates in Brazil from 1980 to 2010 for the age strata 5–34 years. Lines were created using a 2-year moving average. ICD-9 and ICD-10 mean the Ninth and Tenth Revisions of the International Classification of Diseases, respectively.

Note: APCs (95% CI) for asthma: 1980–91: -3.4 (-5.0 to -1.8); 1992–96: 6.8 (-1.4 to 15.6); 1997–2010: -2.7 (-3.9 to -1.6).

APCs (95% CI) for asthma and bronchitis: 1980–92: -1.3 (-2.4 to -0.3); 1993–96: 7.5 (-1.6 to 17.5); 1997–2010: -2.7 (-3.5 to -1.9).

Asthma means all underlying causes of death coded as ICD-9: 493 (1980–95) and ICD-10: J45-J46 (1996–2010). Asthma and Bronchitis is a category that jointly includes all underlying causes of death coded as ICD-9: 493 (1980–95) and ICD-10: J45-J46 (1996–2010) to ICD-9: 466, 490–492, 494, 496 (1980–95) and ICD-10: J20-21, J40-44, J47 (1996–2010).

TABLE 1.—Annual percent changes (APCs) and 95% confidence intervals (95% CIs) according to temporal trends of asthma, asthma/bronchitis, and all respiratory diseases from 1980 to 2010 in Brazil.

Age group (years)	Asthma		Asthma/bronchitis		All respiratory	
	Years	APC (95% CI)	Years	APC (95% CI)	Years	APC (95% CI)
5–14	1980–2010	-0.3 (-1.1 to 0.5)	1980–2010	-0.2 (-0.8 to 0.4)	1980–2007	-2.7^a (-3.0 to -2.4)
					2008–2010	5.3 (-5.0 to 16.7)
15–24	1980–1991	-2.1 (-5.0 to 0.9)	1980–1998	1.9^a (0.6 to 3.2)	1980–1996	0.2 (-0.5 to 0.8)
	1992–1996	6.8 (-6.7 to 22.2)	1999–2010	-3.6^a (-5.7 to -1.3)	1997–2007	-4.2^a (-5.5 to -2.8)
	1997–2010	-3.9^a (-5.7 to -2.0)			2008–2010	8.5 (-1.4 to 19.5)
25–34	1980–1992	-2.5^a (-4.6 to -0.3)	1980–1992	-1.6^a (-2.6 to -0.5)	1980–1996	1.0^a (0.2 to 1.8)
	1993–1995	12.0 (-21.1 to 59.1)	1993–1996	6.3 (-1.5 to 14.7)	1997–2007	-4.7^a (-6.2 to -3.3)
	1996–2010	-1.7^a (-3.0 to -0.4)	1997–2006	-1.6^a (-2.9 to -0.3)	2008–2010	5.0 (-5.1 to 16.1)
			2007–2010	-7.7^a (-912.1 to -3.2)		

Note: ^aThe tendency was significant.

The strata 15–24 years showed a nonsignificant decline and flattening pattern of asthma deaths, and a significant rise of asthma plus bronchitis deaths from 1980 to 1997/98. For cases of patients aged 25–34 years, a decline beginning in the 1980s was observed for cases described as only involving asthma.

Table 2 presents the AAPC from the last 10 years of observation (2001–2010), according to age-strata, gender, and region of the country. The decline was significant for age over 15 years, for women, and for cases occurring in the Southeast region of the country. AAPC of the combination of “asthma and bronchitis” showed a decline similar to that of asthma alone. In

contrast, the tendency measured by AAPC for all respiratory diseases was flat.

DISCUSSION

We determined that asthma mortality has been mainly declining in Brazil during the last 10 years. This tendency is in agreement with observations of a previous study of Sao Paulo and the most recent study of Rio Grande do Sul, as well as with the tendency of COPD deaths for people over 35 years old (11–13, 18). The decline of asthma mortality may be explained by the following factors,

TABLE 2.—Average annual percent changes (AAPCs) and 95% confidence intervals (95% CIs) according to temporal trends of asthma and all respiratory diseases from 2001 to 2010 in Brazil.

	Death rates (per 100,000)		Number of deaths (min–max)	AAPC (95% CI)
	2001–02	2009–10		
Brazil	0.229	0.217	203–263	–1.7 ^a (–3.0 to –0.4)
Age strata (years)				
5–14	0.152	0.177	37–64	–0.3 (–1.1 to 0.5)
15–24	0.178	0.156	50–81	–3.9 ^a (–5.7 to –2.0)
24–34	0.393	0.319	99–151	–1.7 ^a (–3.0 to –0.4)
Sex				
men	0.213	0.193	97–121	–0.1 (–0.6 to 0.5)
women	0.245	0.241	106–142	–2.8 ^a (–4.1 to –1.5)
Region				
North	0.139	0.125	7–19	–3.8 (–7.7 to 0.2)
Northeast	0.201	0.228	50–86	0.7 (–0.1 to 1.4)
Southeast	0.263	0.229	89–127	–3.9 ^a (–5.2 to –2.6)
South	0.275	0.257	31–48	0.1 (–0.7 to 0.8)
Center-West	0.172	0.133	5–15	–3.2 (–6.7 to 0.5)
Other conditions				
Asthma and bronchitis ^b	0.551	0.438	428–546	–2.3 ^a (–3.1 to –1.5)
All respiratory ^c	4.607	4.569	3577–5006	–0.4 (–3.0 to 2.2)

Notes: ^aThe tendency was significant. ^bAge-adjusted rates of deaths coded as the underlying causes J20–21/J40–44/J47 (ICD-10). ^cAge-adjusted rates of all deaths classified into the chapter of the respiratory disorders.

alone or in combination: an artifact of health statistics, a decline of asthma prevalence, and a reduction of case-fatality rates.

The biggest challenge to confirming the downward trend of asthma mortality lies in avoiding artifacts, which result from the imprecision of death notifications, changes in the international classification of diseases, and the improving quality of death certification in Brazil in the 2000s. In the 1970s, the quality of death certification for respiratory diseases in São Paulo was evaluated and determined to be acceptable and comparable to the observed quality of the official health statistics of cities such as Bristol (UK) and San Francisco (USA) (14, 15). However, the trend of asthma mortality in Brazil has been debated since the 1990s, when two states—São Paulo and Rio Grande do Sul—were analyzed independently and showed flat and increased rates, respectively (11, 12). In São Paulo, the category “asthma and bronchitis” was analyzed, while only deaths coded as asthma were included in the Rio Grande do Sul study. It is possible that the increase reported in Rio Grande do Sul could be due to a shift from “other respiratory diseases” to asthma codes, because the rate of deaths due to respiratory diseases did not change during the analyzed period (19). The accuracy of death certification for asthma is a challenge in Brazil as well as in other countries—due to the potential for misclassification of deaths due to asthma as deaths due to COPD, which exists mainly in patients over 40 years old (20, 21). This occurrence originates from a real diagnostic confusion between COPD and asthma; the follow-up of NHANES III showed the coexistence of COPD and asthma (when well-defined by spirometric evaluation) to be a predictor of

worse prognosis when compared to either COPD or asthma alone (22). To prevent this problem, we restricted our sample population to up to 35 years old, and we analyzed the category of “asthma and bronchitis.” Comparison of annual percent changes for asthma solely and “asthma and bronchitis” revealed relatively parallel trends from 1980 to 2010 (Table 1).

The ICD-10 creates two new codes: J45 for deaths attributable to asthma and J44 for those attributable to COPD. Under the ICD-9 rules, the code 493.0 included deaths from asthma and COPD. In the United States, the comparability ratio between the ICD-10 and ICD-9 was 0.8938 (23), but in Brazil (in São Paulo of the Southeast region), it was close to 1.0 (24). We considered that the sharp fall of asthma death rates beginning in 1997 may have been due to the implementation of the ICD-10. However, when we calculated the AAPC from 2001 to 2010 under only the ICD-10, the decline of asthma death rates was constant (Table 2).

The records in Brazil show an impressive reduction of death notifications reported as due to “ill-defined cause of death” (ICD-10: chapter XVIII), from 14% in 1996 to 4% in 2009 for the age strata 5–34 years. We hypothesized that this improvement could inflate some mortality rates due to the higher percentage of precise death notifications. Such an effect was not detectable for asthma solely, nor for “asthma and bronchitis.” However, this is a possible explanation for the flattening pattern of the AAPC of respiratory deaths for all of Brazil from 2001 and 2010 (Table 2), and for the lack of change of the annual percent change for every age strata after 2008 (Table 1).

From data reported by the International Study of Asthma and Allergies in Childhood (ISAAC), in the early 1990s, it was possible to identify a worldwide mixed pattern with upward, stable, and downward asthma prevalence rates. The prevalence rates of asthma are high in Brazil, like in the United States, but the results of sequential surveys of ISAAC in Brazilian six towns did not reveal rising tendencies (25, 26). We reviewed the literature for empirical evidence that changes in the prevalence of asthma and/or outdoor and indoor pollution might be primary explanatory factors for the decline in asthma mortality. Despite the impressive decline of current smokers in Brazil, indoor pollution does not play a relevant role in the asthma mortality (27). Similarly, there is no evidence of an impact of outdoor pollution in reducing fatal asthma cases, although the association with particulate matter and asthma symptoms has been evident in Brazil (28). Prevalence of asthma and risk factors for asthma deaths apparently do not interfere with the mortality trends in Brazil. Instead, we think that the decline is likely related to a reduction of the case-fatality rate, resulting from improvements of medical care over the last years.

Since 1990, Brazil has implemented substantial political and social improvements, with a National Health System and an overall better quality of medical care (10). In 2002, a comparison between the control of asthma in São Paulo, Brazil, and Uppsala, Sweden, revealed worse control in São Paulo, with less use of long-acting beta

2-agonists solely or in combination with inhaled corticosteroids (29). Subsequently, several town- and state-based programs for asthma control were launched, including free-delivery of long-acting beta 2-agonists and inhaled corticosteroids. One open trial was performed in Londrina (in Southern Brazil) and showed a one-third reduction of hospitalizations in 2004–05 compared to 2 years before the introduction of free asthma medicines (30). Another intervention program for severe asthma control was carried out in 2003 in Salvador (in the Northeast region of Brazil); it yielded a 74% reduction of the hospitalization rate in 2006 compared to that in 2003. The rate of hospitalization in Salvador (2.3 per 10,000 inhabitants) was significantly lower when compared to that of Recife (17.1 per 10,000), a city in Northeast Brazil of the same socioeconomic level as Salvador (31). In 2005, the National Health System issued Act 2577, stating that long-acting beta 2-agonists and inhaled corticosteroids must be delivered, without any reimbursement, for patients enrolled in asthma programs at primary care settings and teaching hospitals. This led to impressively increased proportions of asthma patients receiving inhaled corticosteroids, as observed in the city of Curitiba in Southern Brazil, which experienced a rise from 28% of asthma patients using corticosteroids in 2000 to 82% in 2008 (32). Associations between wider distribution of long-acting beta 2-agonists and inhaled corticosteroids and the decline of fatal asthma cases have previously been described in five European countries (7), as well as in Israel (33), Hong Kong (34), and Argentina (35).

Our study has all of the limitations of a mortality study with secondary data, including possible inaccuracies of death certification by the physicians, and the change of the international classification of diseases during the period of evaluation (20, 21). However, we cautiously avoided some bias by analyzing not only the asthma deaths but a broad spectrum of “asthma and bronchitis,” and comparing these data with all deaths due to respiratory diseases. We did not find any empirical data that explained the significant reduction of fatal asthma observed among women but not among men.

CONCLUSIONS

We have found that asthma mortality rates have been declining in Brazil by approximately 2 percent each year since 2001, mainly for people over 15 years of age, women, and those living in the Southeast region. These data will be useful for case-control studies concerning fatal cases of asthma (4, 8). One of several plausible factors to explain the observed decline is a reduction of case-fatality rates due to increased availability of better medical care and free medicine. Our hypothesis is that an intensive therapeutic approach including inhaled corticosteroids has been a decisive factor in reducing asthma lethality and, therefore, we propose that successful public respiratory health programs should be adopted for the subsets of population with no reduction of fatal asthma.

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DECLARATION OF INTEREST

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