Original article

Time trends in mortality from intestinal infectious diseases among children under five years old, in São Paulo State, Brazil, 2000-2012*

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Abstract

Objective: to analyze time trends in mortality owing to intestinal infectious diseases (IID) among children under five years of age in São Paulo State and its Regional Health Care Networks (RRAS), from 2000 to 2012. **Methods**: this was a time series study of deaths having IID as their underlying, antecedent or contributory cause, using Mortality Information System data. **Results**: there were 2,886 deaths from IID in the state; the IID mortality rate went down by 10.5% per year (95%CI 4.8;15.8%); there was a significant decrease in the mortality rate in 13 of the 17 RRAS, with annual decrease in the range 16.6% - 8.3%. **Conclusion**: The IID mortality rate went down significantly in most RRAS, at different speeds, possibly reflecting inequalities in socio-economic conditions and health care network organization.

Key words: Time Series Studies; Diarrhea/mortality; Child Mortality; Child, Preschool; Infant.

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Introduction

Intestinal infectious diseases (IDD) are important causes of morbidity and mortality among children under five years of age throughout the world: in 2008, these diseases were responsible for 1,336 million deaths of children under five years old, and this is equivalent to, approximately, 15% of the six million deaths due to infectious diseases at this age.[1] Worldwide, the mortality rate of children under five years old decreased from 13.6 per one thousand inhabitants, according to studies published between 1955 and 1979, to 4.9 per one thousand inhabitants, according to studies published between 1992 and 2000.[2]

> *Intestinal infectious diseases are among the preventable causes of death of children under five years old.*

In Brazil, the mortality owing to intestinal infectious diseases only reduced in the second half of the twentieth century. In the period from 1985 to 1987, the intestinal infectious diseases were responsible for 17.3% of deaths among children under five years old in the country, whereas from 2003 to 2005 this proportion was of 4.2%.[3]

In the state of São Paulo and in its capital the same behavior was observed. The proportion of deaths due to infectious diseases in the city of São Paulo decreased from 45.7% of the total deaths in 1901 to 9.7% in 2000 (reduction of 78.8%). The death rate from diarrhea and gastroenteritis decreased from 321.4 deaths per 100 thousand inhabitants in 1901 to 51.2 deaths/100 thousand inhabitants in 1960 and to 2.3 deaths/100 thousand inhabitants in 2000.[4]

Intestinal infectious diseases are among the preventable causes of death of children under five years old.[5] Regarding this point of view, the preventable death can be understood as a "sentinel event", that is, the defining event of preventable situations, indicating that the quality of care should be improved, in addition to determining that the investigation of the incident must be accompanied by interventions on possible socioeconomic, environmental and cultural factors or genetic determinants of the given situation.[5]

In 2010, the Health Care Networks (*RAS*) were structured in order to (i) overcome the fragmentation of health care and management and (ii) improve the political and institutional functioning of the Brazilian National Health System (*SUS*).[6] In São Paulo State, where the *RAS* became regional, they were named Regional Health Care Networks (*RRAS*).[7] São Paulo *RRAS* are formed by horizontal organized relations: the Primary Health Care is the coordinator of care and the organizer of the networks. The way of organizing the *RRAS* is defined by the singularity of its decentralizing processes compared to other social sectors. Health services are structured in network areas of health care, with equipment of different technological densities to be distributed spatially, effectively, efficiently and with quality.[8]

Assuming that the organization of the *RRAS* can be an assistance organization strategy capable of contributing to (i) appropriate and timely detection and treatment of intestinal infectious diseases and (ii) reduction of children deaths due to this group of causes in the state, the objective of this study was to analyze time trends in mortality owing to intestinal infectious diseases among children under five years of age in São Paulo State and in its *RRAS* in the period from 2000 to 2012.

Methods

A time series study was conducted. The study area corresponded to São Paulo State and its 17 Regional Health Care Networks – *RRAS*. In 2012, São Paulo had 645 municipalities, distributed over a territorial area of 248,222.4 km² and an estimated population of 41,901,219 inhabitants.[9] The 17 *RRAS* are heterogeneous in relation to area, population and number of participant municipalities.[7]

All deaths of children under five years old, residents in the state, with underlying, antecedent or contributory cause of death from 'intestinal infectious diseases' – codes A00 to A09 of the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10) were included in the study.[10]

As data source, we used the Mortality Information System (*SIM*) to obtain data on deaths; information about the size of the population, results from the 2000 and 2010 demographic censuses and estimates for the other years were obtained from by the Brazilian Institute of Geography and Statistics (*IBGE*).

The database with deaths of residents of São Paulo State, provided by the Department of Health Surveillance of the Ministry of Health, were obtained at the electronic

website of the IT Department of the National Health System (*Datasus*). According to the Death Certificate (DC), we selected the deaths in which the underlying cause was intestinal infectious diseases and then deaths of intestinal infectious diseases as antecedent (part I of the DC) or contributory cause (part II of the DC). The increment of the number of deaths due to intestinal infectious diseases was calculated by adding these last pieces of information.

To calculate de proportional mortality and the mortality rate, we used the total of deaths (underlying cause, antecedent cause and contributory cause) due to intestinal infectious diseases. We conducted a proportional distribution of deaths according to sex, age (under one year old, one year to four years old) and *RRAS* of residence. The proportional mortality due to ill-defined causes (chapter XVIII of ICD-10) was used as a *proxy* of data quality of *SIM* over the years for the *RRAS* and the state.

The specific annual mortality rate was calculated for intestinal infectious diseases of children under five years old (deaths/population under five years), per 100 thousand inhabitants. Line graphs were built to evaluate the patterns of mortality through time in the state and in the *RRAS*. In order to estimate the annual percentage change of the mortality rate through the studied period, linear regression models using the Prais-Winsten technique were built to control the autocorrelation of the residuals of the regression between the years analyzed.[11] The dependent variable was the base10 logarithm of the specific mortality rate in the state of São Paulo and in the *RRAS*; and the independent variable was the year. The level of statistical significance selected was $p \leq 0.05$. The data processing was performed using the Statistical Package for the Social Sciences (SPSS) version 15.0 and the statistical analyses were made with the program Stata version 11.1.

The study project was submitted to the Scientific Committee of the Department of Social Medicine of the College of Medical Sciences of Santa Casa of São Paulo and approved (Report No. 019/2013), being dismissed from appreciation of the Research Ethics Committee, because it only used secondary data, of public domain, without nominal data that would enable the identification of the individuals.

Results

In the period from 2000 to 2012, in São Paulo State, there were 128,537 deaths from all causes in children under five years old, with a reduction in the number of deaths over the years (from 13,710 in 2000 to 8,150 in 2012). The main groups of underlying causes of death were certain conditions originated in the perinatal period (49.8%), followed by congenital malformations (18.3%), diseases of the respiratory system (8.2%) and infectious and parasitic diseases (5.7%). From the 7,263 deaths due to infectious and parasitic diseases, 2,702 (28.5%) of them had intestinal infectious diseases as underlying causes.

Regarding the analyses of antecedent and contributory causes of death (part II of the DC), more than 814 deaths mentioned intestinal infectious diseases (increment of 39.0%). Thus, the number of deaths due to intestinal infectious diseases as underlying, antecedent or contributory cause was 2,886 (Figure 1).

Of the 814 deaths that mentioned intestinal infectious diseases as antecedent or contributory cause, the main chapters of ICD-10 recorded as the underlying cause were: diseases of the respiratory system (23.6%), congenital malformations (16.5%), endocrine, nutritional and metabolic diseases (15.2%), infectious and parasitic diseases (10.2%) and conditions originated in the perinatal period (9.2%) (Figure 1). Among the deaths due to respiratory diseases, 137 (71.4%) were consequence of pneumonias by unidentified microorganism; 32 (23.9%) of the 134 deaths due to congenital malformation were related to congenital heart malfunction. Among the deaths due to endocrine, nutritional and metabolic diseases, 99 (79.8%) were due to malnutrition (77 of these deaths happened until 2003; from 2010 on there were no more deaths from this cause). From the 83 deaths due to infectious and parasitic diseases, 42 (50.6%) were by non-identified septicemia and 19 (25.3%) of the 75 deaths from conditions originated in the perinatal period were by bacterial septicemia in the newborn.

There were 1,605 (55.6%) deaths of male children and 2,280 (79.0%) deaths were of infants under one year old. The largest number of deaths was in *RRAS* 6 (City of São Paulo) and in *RRAS* 2 (Alto Tietê) (Table 1). The number of deaths decreased over the years.

The mortality rate due to intestinal infectious diseases decreased in São Paulo State. Differences were noticed in the behavior of these rates over the years and between the different *RRAS*. The *RRAS* 3 (Franco da Rocha) and 4 (Mananciais) initiated the time series with the highest mortality rates (22.4 and 33.3 deaths/100 thousand

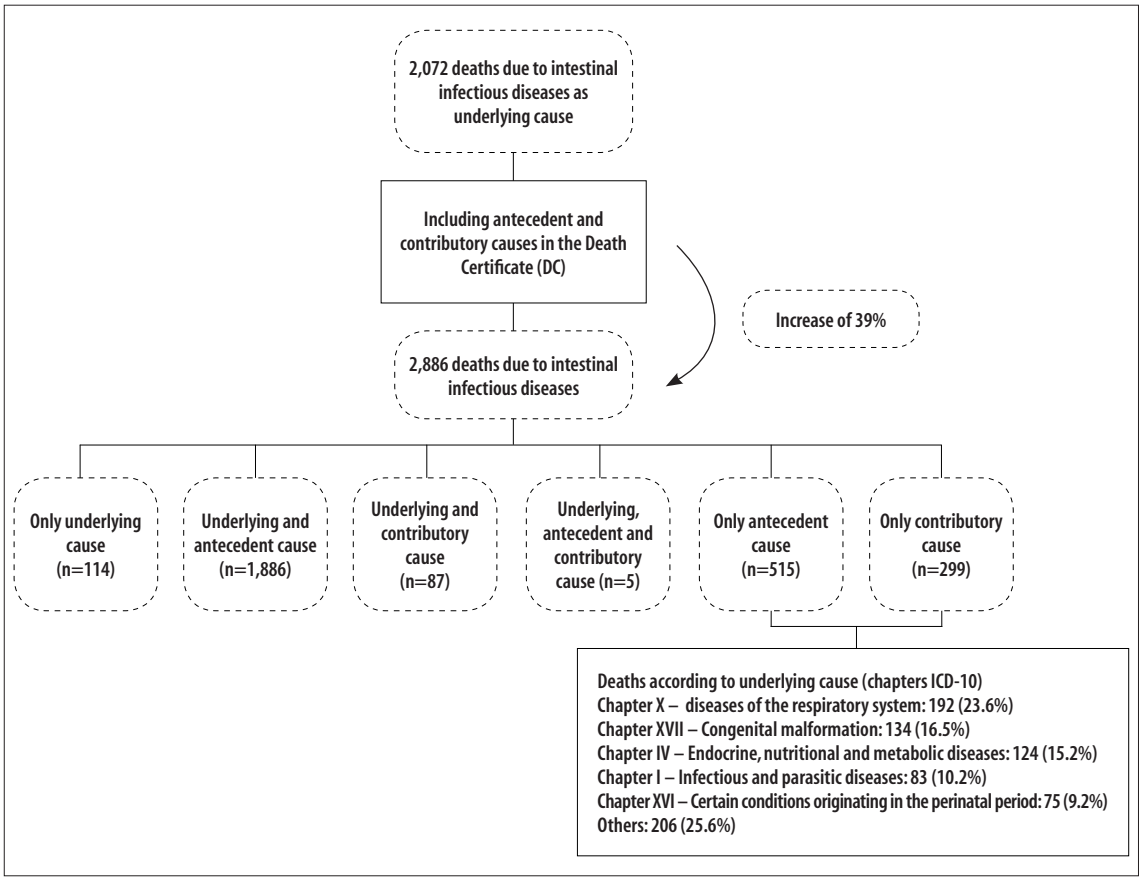

Figure 1 – Distribution of deaths from intestinal infectious diseases according to reference as underlying cause, antecedent cause or contributory cause (part II of Death Certificate) in São Paulo State, 2000-2012

inhabitants, respectively) and presented the deepest reduction (Figure 2). On the other hand, the *RRAS* 15 (Campinas) initiated the time series with the lowest rate (9.6 deaths/100 thousand inhabitants). There was a large variability in the mortality rate, especially in *RRAS* 10 (Adamantina, Tupã, Marília) and 11 (Extremo Oeste Paulista), which also presented the highest and the most variable proportions of deaths due to ill-defined causes (Figure 2).

In the period from 2000 to 2012, the mortality rate due to intestinal infectious diseases in children under five years old showed a decrease of 10.5% per year (95%CI 4.8;15.8%; p=0.002) (Table 2) in São Paulo. In 13 of the 17 *RRAS*, we could also observe significant reduction in the mortality rate (Table 2). The *RRAS* 3 (Franco da Rocha) presented the greatest annual reduction percentage of mortality for the period (16.6% per year; 95%CI 4,0;27.5%; p=0.019) (Table 2 e Figure 3). The *RRAS* 5 (Rota dos Bandeirantes), 9 (Lins, Bauru, Jaú), 10 (Adamantina, Tupã, Assis, Marília) and 11 (Extremo Oeste Paulista) did not show statistically significant reduction in the mortality rate due to intestinal infectious diseases (Table 2 and Figure 3).

Discussion

In the period from 2000 to 2012, the mortality rate related to intestinal infectious diseases in children under five years old presented significant decline in São Paulo State and in 13 of the 17 *RRAS*. However, there were differences on the speed of mortality rate reduction between the *RRAS*.

A similar trend was observed in other studies conducted in Brazil[4,12-17] and in other parts of the world.[2,18] The highest proportion of deaths occurred with infants under one year old as observed in some studies conducted in Brazil[12,15] and in other parts of the world.[18,19]

Several factors may have contributed for this decline. Among them, we can mention the improve in sanitation coverage,[20,21] which was already high in São Paulo in the early 1980s, the expansion of health services coverage,[14,16] the decrease of child malnutrition and the increase of vaccination coverage,[15,19] breastfeeding and maternal education.[22]

Vaccination against rotavirus is one of the factors related to health services that helps reducing hospitalizations[23] and the mortality due to intestinal infectious diseases.[24] However, in this study it was observed a decrease in the mortality rate since the beginning of the time series (prior to 2006 – the year of introduction of rotavirus vaccine in Brazil) and after 2006 the rate reached stability. Therefore, it is not likely that the rotavirus vaccine, explains by itself the reduction of the mortality rate from intestinal infectious diseases in the state of São Paulo, as it was observed in a study that compared mortality and hospitalizations due to this group of causes before and after the vaccination start in Brazil.[25]

Some studies have shown that the expansion of Primary Health Care is one of the possible explanations for the reduction in the mortality rate due to intestinal infectious diseases in Brazil. Macinko et al.[16] conducted a study with the aim of evaluating the impacts of the Family Health Program (*FHP* at the time of the study, currently called Family Heath Strategy – *FHS*) in infant mortality due to diarrhea and pneumonia in the 26 Brazilian States and the Federal District , in the period from 1999 to 2004. The results suggested that as the coverage of *FHP* increased,

Table 1 – Distribution of deaths from intestinal infectious diseases according to sex, age and Regional Health Care Network (*RRAS*) in São Paulo State, 2000-2012

Variables	N	%
Sex [a]		
Male	1,605	55.6
Female	1,280	44.4
Age (in years)		
<1	2,280	79.0
1-4	606	21.0
RRAS [b]		
RRAS 1 – Grande ABC	142	4.9
RRAS 2 – Alto Tietê	235	8.2
RRAS 3 – Franco da Rocha	35	1.2
RRAS 4 – Mananciais	155	5.4
RRAS 5 – Rota dos Bandeirantes	130	4.5
RRAS 6 – Município de São Paulo	917	31.8
RRAS 7 – Baixada Santista, Vale do Ribeira	127	4.4
RRAS 8 – Itapeva, Itapetininga, Sorocaba	191	6.6
RRAS 9 – Lins, Bauru, Jaú	116	4.0
RRAS 10 – Adamantina, Tupã, Assis, Marília	63	2.2
RRAS 11 – Extremo Oeste Paulista	52	1.8
RRAS 12 – São José do Rio Preto, DRSII [c]	96	3.3
RRAS 13 – Sul de Barretos, Central do DRS III [c]	217	7.5
RRAS 14 – Araras, Limeira, Piracicaba	80	2.8
RRAS 15 – Rio Pardo, Campinas	140	4.9
RRAS 16 – Bragança Paulista, Jundiaí	68	2.4
RRAS 17 – Vale do Paraíba, Litoral Norte	119	4.1

a) One death without information on sex.
b) n=2,883 (in three registers of death there was no record of municipality of residence)
c) *DRS*: Regional Health Departments

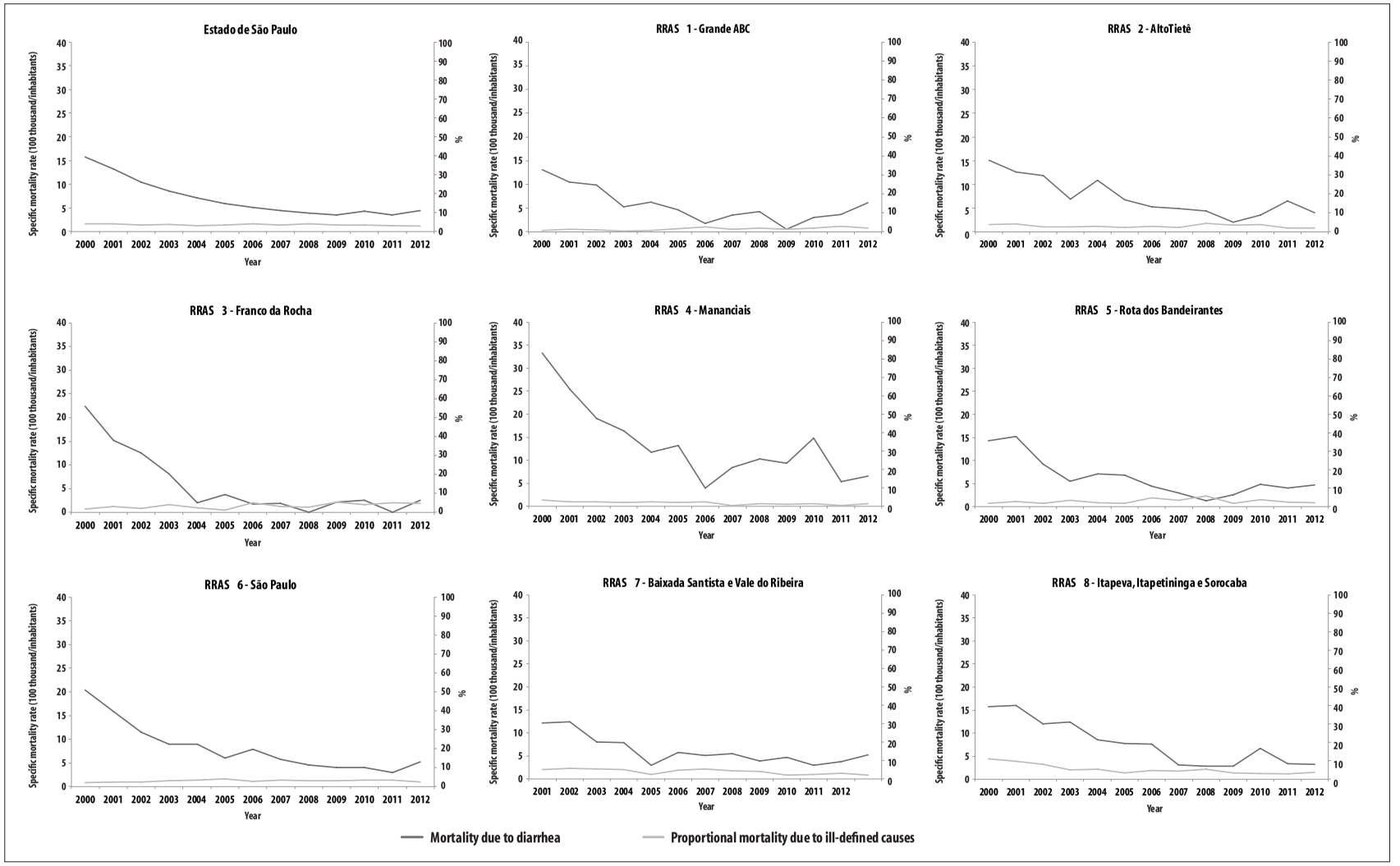

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Figure 2 – Mortality rate from intestinal infectious diseases of children under five years old per 100 thousand inhabitants and number of deaths due to ill-defined causes, according to Regional Health Care Networks (RRAS), in São Paulo State, 2000-2012

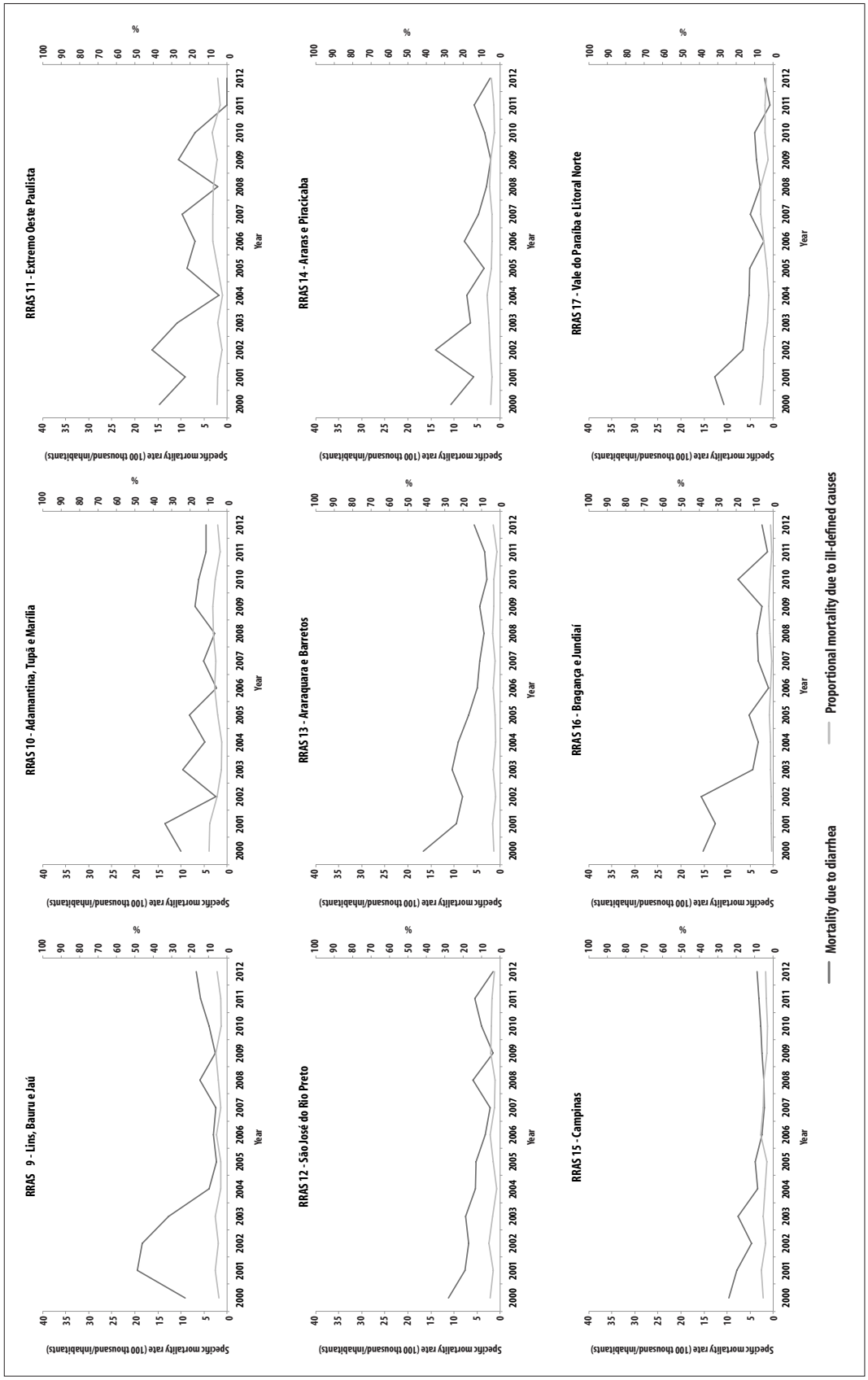

Figure 2 – Conclusion

Table 2 – Annual percentage reduction of mortality from intestinal infectious diseases according to Regional Health Care Networks (*RRAS*) in São Paulo, 2000-2012

State of São Paulo and *RRAS*	Annual Reduction (%)	IL [a]	SL [b]	p-value	R [c]
State of SP	-10.5	-15.8	-4.8	0.002	0.87
RRAS 1	-11.5	-21.3	-0.4	0.044	0.33
RRAS 2	-11.3	-16.8	-5.3	0.002	0.66
RRAS 3	-16.6	-27.5	-4.0	0.019	0.58
RRAS 4	-11.0	-17.4	-4.0	0.006	0.57
RRAS 5	-10.5	-20.8	1.2	0.072	0.52
RRAS 6	-12.8	-15.4	-10.1	< 0.001	0.88
RRAS 7	-8.3	-13.3	-3.1	0.005	0.54
RRAS 8	-13.7	-19.2	-7.9	< 0.001	0.74
RRAS 9	-6.5	-20.7	10.3	0.389	0.26
RRAS 10	-4.6	-10.1	1.3	0.112	0.16
RRAS 11	-7.2	-17.2	4.0	0.182	0.11
RRAS 12	-10.3	-14.9	-5.5	0.001	0.60
RRAS 13	-10.7	-15.1	-6.0	0.001	0.73
RRAS 14	-10.3	-12.7	-7.8	0.001	0.62
RRAS 15	-8.9	-16.5	-0.6	0.039	0.57
RRAS 16	-14.0	-22.3	-4.8	0.008	0.47
RRAS 17	-15.4	-19.6	-10.9	< 0.001	0.81

a) Inferior limit of the 95% confidence interval of the annual percentage reduction
b) Superior limit of the 95% confidence interval of the annual percentage reduction
c) Determination coefficient of the line

the number of deaths due to diarrhea decreased in relation to the total of infant deaths.

The *RRAS* 3 (Franco da Rocha), which initiated the time series with high mortality rate from intestinal infectious diseases, had the highest annual percentage reduction of this type of mortality in the studied period. It is possible that this behavior reflects a delay in the mortality reduction due to IID, what could explain the observed fast decrease in that *RRAS*. On the other hand, the *RRAS* 15 (Campinas) initiated the time series with a lower mortality rate, showing that their rate had presented reduction prior to 2000. In São Paulo State, the mortality rate in 2000 was of 15.7 deaths/100 thousand inhabitants, similar to the decline pattern observed for Brazil since the late 1970s,[13,17,19] when policies of sanitation expansion implemented in the country had a major impact in reducing infant mortality, mainly through the decrease in mortality from intestinal infectious diseases.

The differences in the magnitude of the mortality rate from intestinal infectious diseases observed in the first year of the studied historical series may reflect the socioeconomic inequalities between the *RRAS*. Although the average municipal human development index (MHDI) of São Paulo State was 0.702 in 2000, there was a high variation in the MDHI among the municipalities in that year, from 0.820 (high human development) in São Caetano do Sul (*RRAS* 1) to 0.462 (low human development) in Ribeirão Branco (*RRAS* 8).[26] By 2010, all the municipalities of the state presented an increase in their MDHI and this improve in the human development may be associated to the reduction in the mortality rate from intestinal infectious diseases among children under five years old. However, the development growth was heterogeneous among the municipalities, which may contribute to the persistence of inequalities in the epidemiological profile of the *RRAS*: for instance, despite the deep reduction in mortality in *RRAS* 4 (Mananciais), its mortality rate in 2012 (6.6 deaths/100 thousand inhabitants) was the highest of all *RRAS*.

Among the criteria for implementation of the Regional Health Care Networks (*RRAS*), we can cite the installed

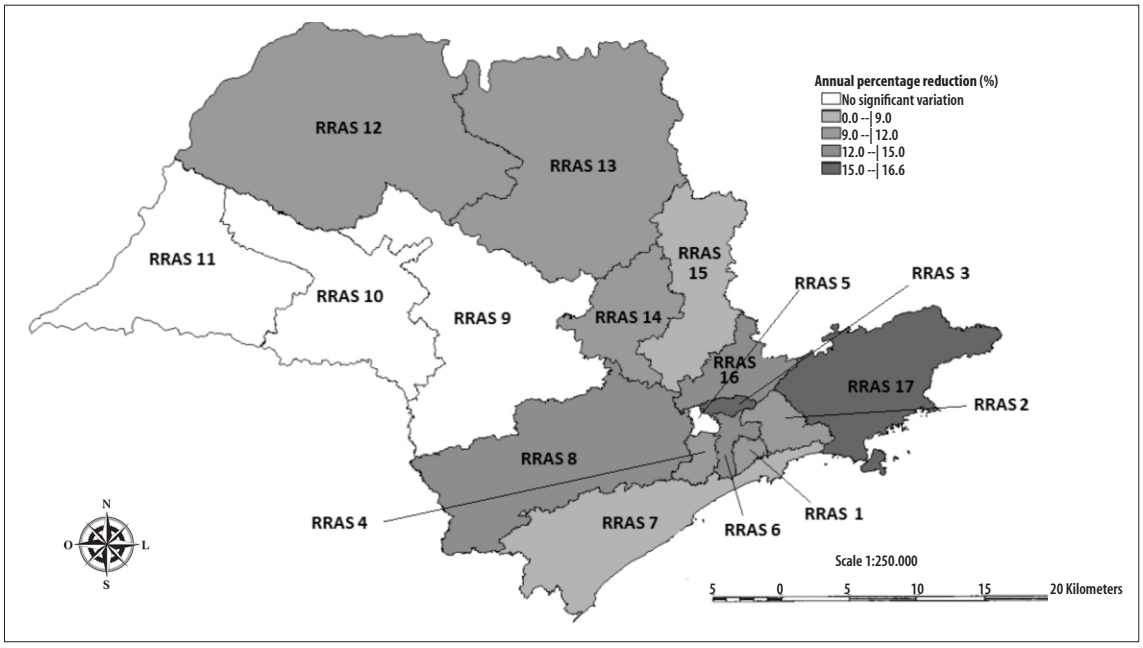

Figure 3 – Annual percentage reduction of mortality from intestinal infectious diseases according to Regional Health Care Networks (*RRAS*), in São Paulo State, 2000-2012

capacity in primary health care for medium complexity and part of the high complexity. There are differences in the number of doctors from different specialties between the *RRAS*.[27] In 2011, the *RRAS* 3 (Franco da Rocha) presented one of the lowest number of *SUS* doctors per inhabitant (1.11 *SUS* doctors/one thousand inhabitants) and a high percentage of occupations for primary health care areas (55.0%). In contrast, the *RRAS* 6 (municipality of São Paulo) had the highest number of *SUS* doctors per inhabitants (2.17 *SUS* doctors/one thousand inhabitants) and the lowest percentage of health professionals in primary health care (38.7%).[27] The highest number of health care professionals in primary health care may be related to higher reduction in the mortality rate from intestinal infectious diseases in *RRAS* 3.

The *RRAS* 5 (Rota dos Bandeirantes), 9 (Lins, Bauru, Jaú), 10 (Adamantina, Tupã, Assis, Marília) and 11 (Extremo Oeste Paulista) did not present annual significant reduction of mortality due to intestinal infectious diseases. The mortality rate in these *RRAS* showed great variability, probably related to the variation in the annual frequency of deaths in municipalities with small populations. In addition, the *RRAS* 10 and 11 had an annual proportion of deaths by ill-defined causes higher than the others, which might indicate fragility in the quality of their Mortality Information System – *SIM*.

The reliability of information on the underlying cause declared for infant deaths, especially in the case of infectious diseases, has been studied by several authors.[28,29] The findings of Mendonça et al. have shown little reliability of underlying cause declaration of infant deaths, mainly due to malnutrition, diarrhea and pneumonias, possibly related to major difficulty of defining underlying causes and contributory causes in those cases in which the infection-malnutrition relation is strong. For these cases, it is difficult to follow the principle of underlying cause of death, especially because in many cases, the etiology and sequence of the development of the diseases could not be determined.[28] In this study, to address this issue and broaden the sensibility of capturing deaths due to intestinal infectious diseases, it was decided to use deaths from intestinal infectious diseases whether they appeared as underlying cause, antecedent cause or contributory cause of death.

In deaths that mentioned intestinal infectious diseases only as antecedent or contributory cause, the main underlying causes registered were the respiratory diseases, congenital malformation, endocrine, nutritional and metabolic diseases, infectious and parasitic diseases and conditions originated in the perinatal period. The relation infection-malnutrition could be observed in the conditions of malnutrition, diarrhea and pneumonias,

known in some study as 'complex diarrhea-pneumonia-malnutrition':[30] among deaths due to respiratory diseases, pneumonia represented 71.4% of underlying causes of death, and malnutrition represented 79.8% of deaths from endocrine, nutritional and metabolic diseases.

This study presented some limitations. The analysis of a time series restricted to 13 years made it difficult to detect secular or seasonal patterns. We chose to perform the analysis per year and no per months so we could study and compare a pattern observed in São Paulo State and in its *RRAS*. Moreover, the great variability in the mortality rates in some *RRAS*, due to their small population, compromised the adjustment of models (the coefficient of determination – R^2 – obtained ranged from 0.33 to 0.85). Still, it was possible to translate different behaviors of the *RRAS* throughout time. The use of a wide range of diagnoses (intestinal infectious diseases) instead of specific diagnoses increased the number of deaths captured, although it has compromised its specificity: it was not possible to evaluate the behavior of deaths due to rotavirus or other specific agents. It is likely that the deaths from intestinal infectious diseases as antecedent or contributory causes are different in terms of socioeconomic or clinical characteristics. However, it was deemed important to include them in the analyses to estimate the magnitude of this problem among death causes in this age group in a more reliably way.

The reduction in mortality owing to intestinal infectious diseases in children under five years of age may reflect improve in life conditions of the population and in the access to health services and technologies. The inequalities in the reduction of mortality seen between the Regional Health Care Networks suggest the need to special attention in death surveillance due to this preventable cause of death, especially in the *RRAS* located in the western of São Paulo State. Integrating health promotion actions, articulated in the context of primary health care services, and surveillance of intestinal infectious diseases may contribute to reducing even more the mortality due to these preventable causes of death which are sensible to Primary Health Care.

Authors' Contributions

Martins RS and Nascimento AF contributed to the conception and design of the study, analyses and interpretation of data, drafting and critical revision of the manuscript and approval of the final version to be published.

Eduardo MBP contributed to the conception and design of the study, critical revision of the manuscript's intellectual content and approval of the final version to be published.

All authors declared to be responsible for all aspects of the study, ensuring its accuracy and integrity.

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