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# Years of potential life lost and hospitalization costs associated with leptospirosis in Brazil

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## ABSTRACT

**OBJECTIVE:** To estimate costs of hospitalization and years of potential life lost associated with leptospirosis.

**METHODS:** Databases of the Brazilian Ministry of Health's information system were used to carry out probabilistic linkage of cases and hospitalizations leading to death by leptospirosis in 2007. Within the Information System for Notifiable Diseases, confirmed cases were subdivided into hospitalization and death. These were then linked to the Hospital Information System (records with primary diagnosis) and the Mortality Information System (underlying cause of death A27.0, A27.8, and A27.9) databases. The partial cost of hospitalization, deaths by disease, and years of potential life and work lost, were estimated.

**RESULTS:** Most hospitalizations leading to death occurred among males aged 18-49 years, of white ethnicity, living in urban areas, and with incomplete elementary education. Years of potential life lost amounted to 6,490, 75% of which were in the 20-49 years age group. When adjusted for the population, this loss represented 15 days of life/thousand persons. The ratio of years of potential life lost to number of deaths was on average 30 years per death. The estimated financial impact amounted to R\$ 22.9 million in non-earned wages. Hospitalization costs totaled R\$ 831.5 thousand. Estimated days of wages lost per admission period (median: 6 days) amounted to R\$ 103.0 thousand.

**CONCLUSIONS:** There was a high social cost in terms of years of potential life lost and partial hospital costs associated with leptospirosis when compared to the possibility of early treatment or prevention of infection, both of which could minimize the impact of the disease on the Brazilian population.

**DESCRIPTORS:** Leptospirosis, economics. Hospitalization. Health Care Costs. Potential Years of Life Lost.

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## INTRODUCTION

Leptospirosis is an acute febrile zoonosis of global importance and also a public health issue in Brazil. Roughly 90% of cases of leptospirosis evolve as a mild, self-limiting disease, the presentation of which includes fever, head and muscle aches, nausea, and vomiting, and which is usually misdiagnosed as viral infection.<sup>14</sup> Nevertheless, 5% to 10% of leptospirosis patients progress to the icteric form of the disease, known as Weil's syndrome, which leads to multiple organ failure and requires support treatment and high-cost hospitalization.<sup>8,17</sup>

In Brazil, leptospirosis is endemic in all geographic regions, and can become epidemic during rainy periods. Notification of suspected leptospirosis cases in the *Sistema de Informação de Agravos de Notificação* (SINAN – Notifiable Disease Information System) is mandatory, and deaths are recorded in the

*Sistema de Informação de Mortalidade* (SIM – Mortality Information System). These systems also contain patients' personal information and address, diagnosis, signs and symptoms, likely associated risk factors, and underlying and intermediate cause of death, among other information that is relevant to the epidemiological surveillance of the disease.<sup>3</sup> In addition, every case admitted to public network hospitals or to hospitals associated with the *Sistema Único de Saúde* (SUS – Brazilian Unified Health Care System) have the costs associated with hospitalization reported to the SUS' *Sistema de Informações Hospitalares* (SIH – Hospital Information System). SIH is the official system used by the Ministry of Health to process information generated by hospitals, allowing for the management and monitoring of financial ceilings and health service productivity and payment of service providers.<sup>3</sup>

Ministry of Health data show that, from 1999 to 2005, 81,897 suspected cases of leptospirosis were notified, of which 22,774 were confirmed, leading to 2,574 deaths. Incidence of the disease in this period was 1.9 per 100 thousand population. However, the International Leptospirosis Society indicates that there is underreporting of cases is extensive, due mainly to difficulties in diagnostic confirmation, frequent confusion with other diseases, and low levels of detection of mild forms.<sup>10</sup> It is therefore important to resort to more than one source of data when attempting to estimate the true scenario of the disease, or even when re-identifying records in order to ensure data quality.<sup>15</sup> Furthermore, considering that resources are ever more scarce, health care systems must evaluate the cost of their activities in order to ensure effective intervention and the proper allocation of resources.<sup>a</sup>

The lack of knowledge concerning the impact of leptospirosis in Brazil reduces our awareness of its socioeconomic importance, leading to postponement by public health managers of the implementation of more effective measures for disease control. Thus, the aim of the present study was to estimate the partial cost associated to leptospirosis (direct medical and hospital costs – hospitalization, days of work lost, and loss of income), as well as the years of potential life lost (YPLL) due to the disease.

## METHODS

We carried out a partial evaluation study of the cost-of-illness type, from the economic perspective of both public financing organs and society. The study population was identified by probabilistic linkage of records from the Brazilian databases SINAN (for notified cases), SIM (for registered deaths), and SIH (for hospital

information). Data retrieved included date of onset of symptoms and date of death and hospitalization in the period from 1 January to 31 December 2007. This period was chosen because it is covered by data from SINAN, SIM and SIH presently in final form and available for analysis. It is also the first year after the implementation of the most current electronic version for identification of leptospirosis cases in SINAN, the major system for leptospirosis surveillance in the country.

For purposes of database linkage, we considered only those SINAN cases that had been confirmed by laboratory or clinical-epidemiological methods, excluding repeated entries. From this subset, we selected records progressing to hospitalization, which we included in a database called SINAN-hospitalization, as well as records progressing to death, which were included in a database called SINAN-death. From SIH and SIM, we selected records in which major diagnosis upon admission or underlying cause of death, respectively, were leptospirosis icterohemorrhagica (A27.0), other forms of leptospirosis (A27.8), and leptospirosis, unspecified (A27.9), according to the International Classification of Diseases, Tenth Revision (ICD-10)

Some of the variables studied after linkage were obtained only from SINAN. These included race/skin color, place of residence, and schooling.

Probabilistic record linkage was carried out using RecLink III software, which operates based on three major processes: record standardization, parsing, and pairing.<sup>2</sup> We used a strategy comprising multiple steps (five in total) in order to increase the chance of finding true pairs. In each step, we established specific cutoff scores to define true and false pairs.<sup>4</sup>

When linking SINAN-death and SIM, we used as comparison variables patient's name (soundex of first and last names), mother's name, sex, date of birth, date of death and notification, full address, and state and region of residency. When linking SINAN-hospitalization and SIH, we used date of admission in addition to the same variables used for SIM, with the exception of mother's name (which is absent from SIH) and date of death.

For the cost-of-illness analysis we measured the direct sanitary cost, which comprised the cost of hospital admission (using values specified in the SUS procedures table), as well as indirect costs (morbidity and mortality), calculated in YPLL (non-monetary valuation) and using the human capital method (monetary valuation). To calculate the cost of hospital admission, we used the records found through linkage of SINAN-hospitalization and SIH. From the SIH database, we

<sup>a</sup> Polanczyk CA, Toscano CM. Avaliação econômica em saúde. Desafios para gestão no Sistema Único de Saúde. Brasília: Ministério da Saúde; 2008[cited 2009 Jun 05]. Available from: [http://portal.saude.gov.br/portal/arquivos/pdf/livro\\_aval\\_econom\\_saude.pdf](http://portal.saude.gov.br/portal/arquivos/pdf/livro_aval_econom_saude.pdf)

obtained the total duration of hospitalization in days, including length of stay in intensive care units (ICU), for all patients with leptospirosis.

For indirect costs (morbidity and mortality) expressed in YPLL, we used the pairs found upon linkage of SINAN-death and SIM, as proposed by Romeder & McWhinnie (1977).<sup>13</sup> We assumed a life expectancy of 70 years, according to projections for the Brazilian population by sex and age from 1980 to 2050 generated by the Brazilian Institute for Geography and Statistics [*Instituto Brasileiro de Geografia e Estatística*] (IBGE) for both men and women. YPLL was calculated using the following mathematical equation:  $YPLL = \sum a_i d_i$ , where  $a_i$  corresponds to the difference between the assumed upper age limit and age at death when this occurred between ages  $i$  and  $i+1$  year, and  $d_i$  represents the total number of deaths between ages  $i$  and  $i+1$  year.

For purposes of comparison with populations of different sizes, we calculated a YPLL rate (YPLLR) per 1,000 population, stratified by sex, according to the following formula:  $YPLLR = \sum a_i d_i \times (1,000/n)$ , where  $n$  is the studied population aged 1 to 70 years. We calculated the mean YPLL per death (YPLL/death), stratified by sex and age group.

Using data from YPLL, we also estimated the years of potential work lost and the consequent unearned wages, calculated using the human capital method. For this, we assumed 18 years as the age of entry into the workforce, retirement age of 65 years for men and 60 years for women, 40 hours of work per week for 249 days for the year of 2007, which lead to a post-tax yearly income of R\$ 4,966.67 (US\$ 2,627.87), including vacation time, 13<sup>th</sup> salary, and social security/labor rights, as specified in the Brazilian Consolidation of Labor Regulations (Government Decree no. 5,425, of 1 May 1943).

For the cost of the days of work lost due to hospitalization, not including the potential cost of any companions, we divided the mean minimum wage in 2007 (R\$ 372.50 = US\$ 197.90) by the mean number of days of work per month (20.75 days), which totaled R\$17,95 per day (US\$ 9.50). For this calculation, we considered only the population aged 18 years or older, and multiplied the number of days lost by R\$ 17.95. All values are expressed in *reais* with the value in US dollars in parentheses, using the exchange rate of August 2007 according to the Central Bank of Brazil (US\$1.00 = R\$1.89).

Data processing and analysis were carried out using Microsoft Excel and EpiInfo v.3.5.1.

The study protocol was approved by the National Research Ethics Committee under process no. 067/10.

## RESULTS

In 2007, 13,810 suspected cases of leptospirosis were registered in SINAN, of which 3,212 (23%) were confirmed (incidence of 1.8/100 thousand population). Of these, 2,742 (85%) were confirmed by laboratory testing and 436 (14%) by clinical-epidemiological criteria, whereas 34 (1%) contained no information on mode of diagnosis. Excluding the latter resulted in 331 (10%) of cases of leptospirosis progressing to death and 2,249 (71%) cases progressing to hospitalization.

In SIM, in 2007, 391 deaths were recorded for which leptospirosis was the underlying cause (mortality of 0.2/100 thousand). SIH recorded 2,903 cases of hospital admission for which the major cause was leptospirosis.

**Table 1.** Profile of cases in the Notifiable Disease Information System and those obtained through database linkage. Brazil, 2007.

Characteristics	SINAN		S1		S2	
	n	%	n	%	n	%
Sex	3,178	100	817	100	226	100
Male	2,504	79	719	88,0	187	82,7
Female	674	21	98	12,0	39	17,3
Age	3,178	100	817	100	226	100
1 to 14	292	9	47	6	5	2
15 to 17	198	6	63	8	8	4
18 to 29	878	28	229	28	52	23
30 to 49	1,218	38	336	41	89	39
50 to 94	592	19	142	17	72	32
Zone	3,079	100	793	100	220	100
Urban	2,514	82	651	82	197	90
Rural	512	17	123	16	20	9
Periurban	53	2	19	2	3	1
Ethnicity	2,746	100	720	100	175	100
White	1,698	62	425	59	82	47
Brown	828	30	238	33	68	39
Black	177	6	46	6	22	13
Yellow	28	1	5	1	2	1
Indigenous	15	1	6	1	1	1
Schooling	2,068	100	561	100	104	100
Illiterate	39	2	9	2	5	5
Elementary	1,241	60	442	79	80	77
Secondary	538	26	100	18	13	13
University	207	10	4	1	3	3
Does not apply	43	2	6	1	3	3

SINAN: Notifiable Disease Information System

S1: linkage, SINAN-hospitalizations and Hospital Information System

S2: linkage, SINAN-deaths and Mortality Information System

The majority of cases recorded in SINAN (79%), SIH (83%) and SIM (82%) were males. Median age of cases was 33 (1 to 94) years in SINAN, 43 (2 to 94) years in SIH, and 32 years (1 to 92) years in SIM. In SINAN and SIM, 92% and 87% of cases, respectively, had white or light brown skin color, and 60% of cases in SINAN and 68% in SIM had no more than elementary schooling (Table 1).

Linkage of the SINAN-hospitalization and SIH (S1) databases yielded 817 pairs classified as true. For SINAN-death and SIM (S2), 226 true pairs were detected. Median age of hospitalized pairs was 35 (5 to 84) years and of deceased pairs was 42 (2 to 94) years. The majority of hospitalized pairs was in the 18 to 49 years age group, lived in urban areas, had white skin color, and incomplete elementary schooling, which is similar to the characteristics obtained when the databases were analyzed individually (Table 1).

Years of potential life lost totaled 6,490; of these, 4,243 were in the 20-49 years age group, representing 75% of the total. When adjusted to the population, there was a loss of 15 days of life (0.04 years) per thousand population. The proportion of years lost was on average 30 for each leptospirosis death (Table 2).

A comparison of the proportion of YPLL between men and women showed that the 20-49 years age group was the most affected in both sexes. The YPLL rate for males was 0.06 (22 days of life per thousand men) and 0.01 for females (4 days per thousand women) (Table 2).

Analysis by years of work lost (YWL) in cases that progressed to death showed that, in absolute numbers, R\$ 22,931,116.00 (US\$ 11,847,151.32) were lost to the disease (Table 3).

Of the 817 cases with registered hospitalization, 164 were placed under intensive care (20% ICU admission rate). Median length of hospitalization per patient was six (1 to 67) days. The cost of hospitalization was R\$ 588,244.16 (US\$ 311,229.95) for normal care and R\$ 243,293.12 (US\$ 128,726.52) for intensive care. Public expenditures with the disease amounted to R\$ 831,517.73 (US\$439,956.47), most of which was related to procedures classified as "medical clinic" (Table 4).

Still with regard to the duration of hospitalization, the mean daily earning lost was R\$ 19.35 (US\$10.24) (Table 5). For all patients aged 18 years or older, total wage loss amounted to R\$ 103,014.00 (US\$ 54,504.76) for the duration of admission.

**Table 2.** Years of potential life lost, rate, percentage, and mean. Brazil, 2007.

Age group (years)	Male				Female				Total			
	YPLL	YPLLR <sup>a</sup>	%	Mean <sup>b</sup>	YPLL	YPLLR <sup>a</sup>	%	Mean <sup>b</sup>	YPLL	YPLLR <sup>a</sup>	%	Mean <sup>b</sup>
1 to 4	68	0.01	1	68	0	0.00	0	0	68	0.01	1	68
5 to 9	64	0.01	1	64	0	0.00	0	0	64	0.00	1	64
10 to 14	171	0.02	3	57	0	0.00	0	0	171	0.01	3	57
15 to 19	1,150	0.13	21	52	54	0.01	5	54	1,204	0.07	19	52
20 to 29	1,250	0.07	23	45	400	0.02	40	44	1,650	0.05	25	45
30 to 39	942	0.07	17	35	181	0.01	18	36	1,123	0.04	17	35
40 to 49	1,228	0.11	22	26	242	0.02	24	27	1,470	0.06	23	26
50 to 59	487	0.06	9	16	111	0.01	11	16	598	0.04	9	16
60 to 69	122	0.03	2	7	20	0.00	2	5	142	0.01	2	7
Total	5,482	0.06	100	31	1,008	0.01	100	29	6,490	0.04	100	30

YPLL: years of potential life lost

<sup>a</sup> YPLLR: rate per 1 000 population.

<sup>b</sup> Mean=YPLL/death

**Table 3.** Unearned wages due to years of work lost, according to age group and sex of deaths with leptospirosis as the underlying cause. Brazil, 2007.

Age group (years)	Male				Female			
	n	%	YWL	Amount (R\$)	n	%	YWL	Amount (R\$)
18 to 29	43	27	1,808	8,979.739	9	30	310	1,539.668
30 to 49	75	46	1,795	8,915.173	14	46	283	1,405.568
50 to 65	44	27	380	1,887.335	7	24	41	203.633
Total	162	100	3,983	19,782.247	30	100	634	3,148.869

YWL: years of work lost

**Table 4.** Total cost of listed procedures carried out during hospitalization. Brazil, 2007.

Listed procedure	n	%	Total cost (R\$)
Leptospirosis, medical clinic	773	94	815,633
Leptospirosis, pediatrics	30	4	13,781
Diagnosis or 1 <sup>st</sup> medical clinic visit	17	2	1,982
Clinical care, hospitalization regimen, adults in intensive care unit	1	1	120

**Table 5.** Unearned wages due to hospitalization. Brazil, 2007.

Hospitalization (days)	n	%	Amount (R\$)
1 to 2	76	11	1,890
3 to 5	234	33	16,578
6 to 9	212	30	28,494
10 to 13	84	12	17,244
14 to 17	43	6	11,808
18 to 21	24	3	8,406
22 to 67	34	5	18,594
Total	707	100	103,014

## DISCUSSION

Leptospirosis affected mostly males living in urban areas, with low level of schooling, and in the economically active age group, which suggests that the disease is typical of a more socially vulnerable population that demands greater attention from sanitary authorities. In addition, the high number of YPLL and of minimum wages not earned highlight part of the financial impact from the perspective of society. The YPLL ratios stratified by sex and age group reveal the magnitude of mortality among the young, economically active population due to leptospirosis.

Reports in the literature show that leptospirosis affects predominantly men, both with regard to disease severity and need for hospitalization, and in terms of mortality.<sup>5,9</sup> The difference in severity between men and women is not well understood. However, it is generally attributed to environmental and occupational factors, although this tends to disappear when exposures are similar.<sup>19</sup> On the other hand, one potential explanation for the difference found in our study could be the use only of confirmed cases. This reflects a surveillance system that captures mostly severe cases of the disease, which consequently require hospitalization and may or may not have led to death of the patient.<sup>16</sup> Another behavioral hypothesis is that men may tend to seek medical care at later stages of the disease when compared to women.

Our data also show that the majority of leptospirosis cases originate from urban areas. This is in contrast to

the profile of the disease in North India, where 77% of cases occurred in rural areas, and the disease is found mainly in rural producers and workers.<sup>14</sup> This difference may be explained by the possibility that exposures in Brazil are related to poor housing and sanitation conditions that affect a substantial part of the population living in slums and in the outskirts of large cities.<sup>8</sup> According to IBGE, of the 5,564 Brazilian municipalities, roughly 33% reported the presence of slums; however, if only municipalities with population between 100 and 500 thousand are considered, this proportion rises to 85%, corroborating our finding that 64% of cases of leptospirosis come from cities in this population range.<sup>16</sup>

Leptospirosis was less frequent among children aged up to 14 years and in adults older than 50 years, which is in agreement with findings from Barbados,<sup>6</sup> Trinidad,<sup>7</sup> Seychelles,<sup>19</sup> North India,<sup>14</sup> and New Caledonia.<sup>9</sup> It has been suggested that children under five years of age have limited contact with soil and water contaminated with *Leptospira*, even though the prevalence of intestinal parasites among children in this age range suggests the opposite, and children under ten years of age have a less severe reaction to the infection.<sup>6,7</sup> As to the absence of cases among older adults, it has been hypothesized that this is associated with less contact with contaminated soil and water and the development of a certain level of immunity in endemic areas due to prior exposure.<sup>9,10</sup>

Our data indicate that the economically active population, in the 20-49 years age group, lost the greatest number of years of potential life in 2007. Death at a stage of life associated with high creativity and productivity is not only a loss to the individual and his or her close ones, but also deprives the society from this individual's economic and intellectual potential.<sup>12</sup> For example, loss of income to leptospirosis was estimated at R\$ 22,931,116.00 (US\$ 11,847,151.32) in unearned minimum wages (assuming that every individual's work potential was only the minimum wage), without including other financial costs.

Our findings with regard to YPLL (6,490 years) were similar to numbers reported in Cuba by Perez et al (1998)<sup>11</sup> (6,238 years), which corresponded to 2% of YPLL due to all infectious diseases. We were unable to find other Brazilian studies dealing exclusively with YPLL due to leptospirosis. However, a study carried out in the state of Rio de Janeiro (Southeastern Brazil) reports that infectious and parasitic diseases are the sixth greatest cause of YPLL. In a retrospective cohort evaluated for the period between 1991 and 2007 in New Caledonia, leptospirosis directly accounted for 0.6% of all YPLL, corresponding to 14% of all deaths due to infectious diseases.<sup>9</sup> Prevention and control of leptospirosis are relatively cheap (basic sanitation,

rodent control, cleaning of vacant lots, among others) and minimize exposure to other infectious diseases as well, especially when compared to other diseases that are difficult to control and that are chronic in character, such as AIDS (YPLL=6,464) and hypertension (YPLL=3,379).<sup>1</sup> We therefore conclude that the number of years of potential life lost in Brazil to leptospirosis was high.

Regarding patient hospitalization, the mean length of stay (six days) detected in our study was slightly lower than that reported in New Caledonia (seven days)<sup>9</sup> and São Paulo (nine days).<sup>b</sup> As to the cost of hospitalization, although the values found in our study (US\$ 439,956.47) were lower than those reported for New Caledonia (US\$ 771,696.45),<sup>9</sup> Suputtamongkol et al (2010)<sup>18</sup> propose that it is more advantageous to invest in early treatment of the patient, such as by doxycycline administration (100 mg orally every 12 hours for 5-7 days) (R\$ 0.76/day or US\$0.40/day, not taking into account other direct sanitary costs) – even prior to the confirmation of leptospirosis infection –, than to resort to late treatment, which places patients at risk of more severe disease, prolonged hospitalization, and premature death.<sup>19</sup>

Limitations of the present study include potential errors in YPLL estimation due to the assumption of a 70-year life expectancy. Since this limit is not homogeneous between men and women, this assumption could lead to an overestimation of YPLL among males. However, since we used only the intersection of the records found by database linkage to calculate YPLL, we believe that these values are in fact an underestimate.

The elimination of a given cause of death does not necessarily imply survival to the limit of life expectancy, there being the possibility of an individual dying by other causes that were obviously not accounted for. This may lead to an overestimation of the impact

caused by that death, given that the individual may not have gained the number of years of life assumed in the calculation.

Hospital costs may have been underestimated, since they were estimated based only on the perspective of the health care manager and on the only ICD-10 codes available for this disease. We believe, therefore, that other procedures may be administered to patients with leptospirosis in addition to those predefined in the present study.

The high social cost in terms of YPLL and hospital expenditures could have been minimized if early detection and treatment of suspect cases were available.

YPLL reflect part of the impact generated by an ancient, neglected disease, whose risk factors are related to close exposure to rat excretions, especially near the patient's home. Resolving these ancient problems will require definition of priorities in terms of health care, with emphasis on the importance of measures aimed at preventing untimely death due to leptospirosis. The fact that such measures can extend beyond the reach of the health care sector, points towards the need for greater multidisciplinary and social mobilization in order to redirect efforts, as exemplified by improvements in basic sanitation.

Unfortunately, due to the lack of similar studies in Brazil, we were unable to compare the impact of leptospirosis in our study to that of previous years. Thus, we suggest that other studies of morbidity, mortality and economic impact be conducted in order to estimate the true burden of this disease in the country. In this manner, such studies could help target resources to education and training of health personnel for early detection of potential cases, rapid laboratory confirmation of true cases, and necessary improvements in infrastructure and basic sanitation and environmental policies.

<sup>b</sup> Valentim LS, Quitério LAD. Qualidade de vida e saúde na bacia hidrográfica do alto Tietê: uma aproximação através das internações hospitalares por doenças relacionadas às condições sanitárias e ambientais. São Paulo: Centro de Vigilância Sanitária; 1998[cited 2010 May 20]. Available from: [http://www.cvs.saude.sp.gov.br/pdf/artigtec\\_vidasaude.pdf](http://www.cvs.saude.sp.gov.br/pdf/artigtec_vidasaude.pdf)

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