Health in Brazil 3

Successes and failures in the control of infectious diseases in Brazil: social and environmental context, policies, interventions, and research needs

Mauricio L Barreto, M Gloria Teixeira, Francisco I Bastos, Ricardo A A Ximenes, Rita B Barata, Laura C Rodrigues

Despite pronounced reductions in the number of deaths due to infectious diseases over the past six decades, infectious diseases are still a public health problem in Brazil. In this report, we discuss the major successes and failures in the control of infectious diseases in Brazil, and identify research needs and policies to further improve control or interrupt transmission. Control of diseases such as cholera, Chagas disease, and those preventable by vaccination has been successful through efficient public policies and concerted efforts from different levels of government and civil society. For these diseases, policies dealt with key determinants (eg, the quality of water and basic sanitation, vector control), provided access to preventive resources (such as vaccines), and successfully integrated health policies with broader social policies. Diseases for which control has failed (such as dengue fever and visceral leishmaniasis) are vector-borne diseases with changing epidemiological profiles and major difficulties in treatment (in the case of dengue fever, no treatment is available). Diseases for which control has been partly successful have complex transmission patterns related to adverse environmental, social, economic, or unknown determinants; are sometimes transmitted by insect vectors that are difficult to control; and are mostly chronic diseases with long infectious periods that require lengthy periods of treatment.

Lancet 2011; 377: 1877–89

Published Online
May 9, 2011
DOI:10.1016/S0140-6736(11)60202-X

See Comment *Lancet* 2011; **377:** 1721, 1722, and 1724

See Online/Comment
DOI:10.1016/S0140-6736(11)60326-7, and
DOI:10.1016/S0140-6736(11)60437-6

This is the third in a Series of six papers on Health in Brazil

Instituto de Saúde Coletiva, Federal University of Bahia, Salvador, Brazil (Prof M L Barreto MD, M G Teixeira MD)**; Fundação Oswaldo Cruz, Rio de Janeiro, Brazil, and Brown University, Providence, RI, USA** (F I Bastos MD)**; Federal University of Pernambuco, Recife, Brazil** (R A A Ximenes MD)**; Faculty of Medical Sciences, Santa Casa de São Paulo, São Paulo, Brazil** (R B Barata MD)**; and London School of Hygiene and Tropical Medicine, London, UK** (Prof L C Rodrigues MD)

Corespondence to:
Prof Mauricio L Barreto, Instituto de Saúde Coletiva, Federal University of Bahia, Rua Basilio da Gama s/n, Canela, 40110-040 Salvador-Bahia, Brazil
mauricio@ufba.br

Introduction

Infectious diseases are still a public health problem in Brazil, despite the proportion of total deaths that are caused by infectious diseases decreasing from 50% to 5% in the past 80 years.[1] Such reductions have been more pronounced for some infectious diseases than they have for others. Figure 1 shows the proportion of deaths from all causes between 1930 and 2007, and the proportion of deaths attributable to different infectious diseases between 1980 and 2008, from which time detailed data exists.[4] A large proportion of deaths from infectious diseases in Brazil are due to respiratory infections, and respiratory infection deaths have become more common in adults than in children (figure 1). There have been some pronounced decreases in proportional mortality from specific diseases—ie, diarrhoeal diseases, vaccine-preventable diseases, and pneumonia in children. Deaths from HIV/AIDS have increased since the mid 1980s, dengue has emerged as a substantial cause of death, the number of deaths from tuberculosis and Chagas disease have remained stable, and the proportion of adult deaths due to respiratory infections is increasing (figure 1). The distribution of causes of death from infectious diseases has shifted towards one more commonly seen in high-income countries, especially in the predominance of pneumonia in the adult and elderly populations.[4] In this report, we do not give a comprehensive review of trends for all infectious diseases in Brazil, but assess the relative successes of policies and interventions for selected diseases.

The relative contribution of different diseases to overall mortality in a country is associated with its gross domestic product (table 1). The past 60 years were a time of much change in Brazil. In the 1950s, 64% of the Brazilian

Key messages

- Brazil is undergoing a rapid and sometimes unorganised urbanisation process. Cash transfer programmes for the neediest populations, the Unified Health System (SUS), and other social and environmental improvements (such as in sanitation and education) related to this rapid urbanisation are, and should continue to be, crucial for efforts to control infectious diseases.
- Successful and moderately successful public health initiatives, such as those to control vaccine-preventable diseases, diarrhoea, respiratory infections, HIV/AIDS, and tuberculosis, have provided universal and free at the point of use vaccination, access to treatment, and primary health care. Such equitable policies must be supported and reinforced in the face of existing and renewed challenges, such as less than optimum adherence to treatment regimens and the emergence and transmission of drug-resistant pathogens.
- The control of disease vectors in areas of rapid urbanisation and poor-quality housing cannot be achieved through health policies alone. Such efforts must be fully integrated into broad policies that incorporate the mobilisation of society, health and environmental education, improvements in habitation and sewerage, and attempts to avoid further deforestation.
- Scientific research in Brazil has thrived in the past 10 years, with rapid and sustained growth in applied biomedical and epidemiological research on infectious disease prevention and management. Such academic achievements must be translated into deliverable products and policies so that they can be of benefit to the Brazilian population.

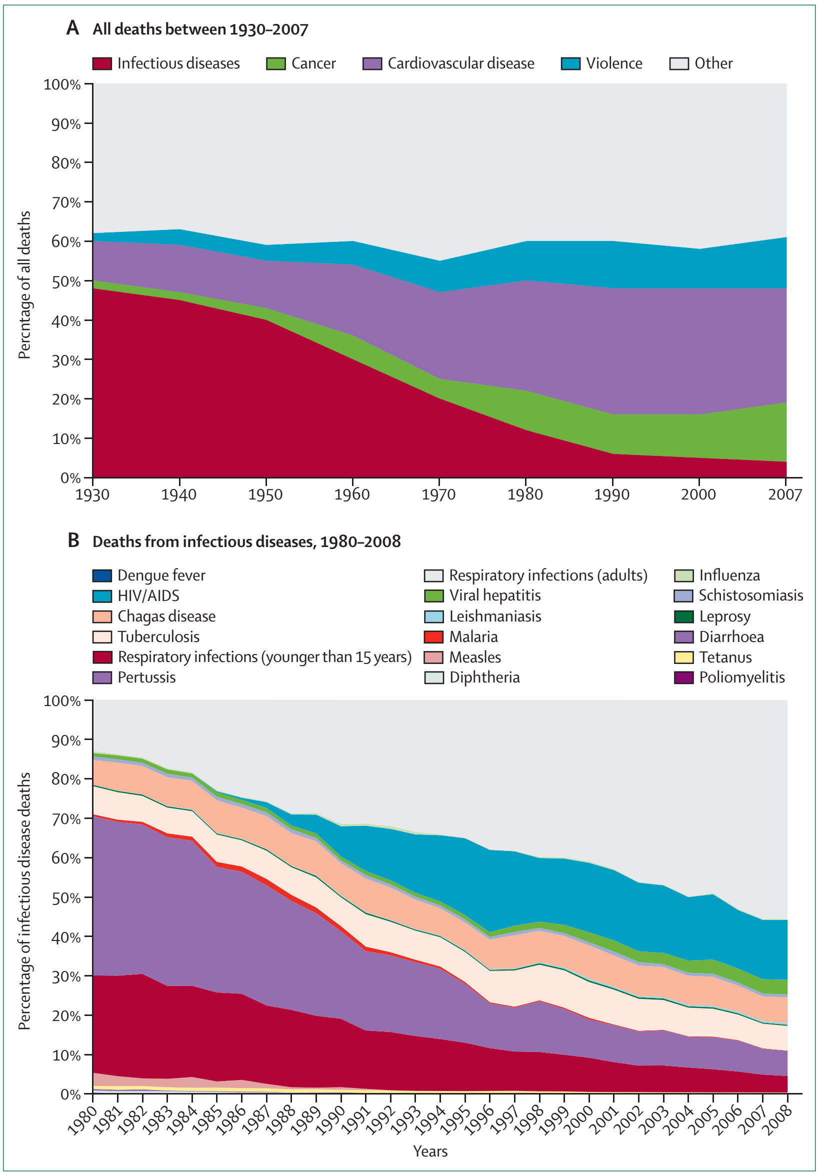


Figure 1: **Trends in the causes of death in Brazil**
(A) All deaths between 1930–2007. (B) Deaths from infectious diseases, 1980–2008.[2,3]

population lived in rural areas. Vector-borne diseases and intestinal parasitic diseases with transmission cycles that require a stage of development in soil or water were common, and diarrhoea, respiratory infections, and measles caused most deaths in children younger than 5 years. Living conditions in both urban and rural areas were poor, with restricted access to health care (including vaccines), adequate housing, and water and sanitation, fostering the transmission of tuberculosis, poliomyelitis, measles, mumps, diphtheria, typhoid, and leptospirosis.[1,6–9]

In 1953, with the creation of the Ministry of Health, a programme for rural diseases was established, which led to the systematic implementation of vector control measures.[10] In the decades after industrialisation, which started in the late 1950s, many people migrated from rural areas to urban areas, amid much urbanisation, improvements in the country's infrastructure (ie, ports, energy generation, road networks), increased access to health care, and modernisation of the state, which increased its presence in different aspects of economic and social spheres (eg, industrial development, roads and communication, housing, water and sanitation, health, and science and technology). By 2000, only 19% of the population lived in rural areas—most of the burden of infectious diseases was borne by those living in urban areas. Between 1980 and 2007 the proportion of households with piped water supply increased from 52% to 84% (93% in urban areas) and the proportion with access to sewerage or a septic tank increased from 25% to 74%.[11] These changes took place in a period of much social inequality—a common situation throughout much of Brazil's history—with a Gini coefficient of around 0·6, which, since only 2001, has begun to slowly decrease to 0·56.[12]

Such progress had some detrimental consequences. For example, much deforestation has taken place to enable agro-industrial activities, or the extraction of basic products and commodities, and increased population mobility has expanded areas of transmission for some endemic diseases (eg, yellow fever) and caused previously rural diseases to appear in urban areas (eg, visceral leishmaniasis and leprosy).[13–16] The reintroduction of *Aedes aegypti* in 1976 resulted in successive dengue epidemics since 1986.[17–19] The cholera pandemic in the 1990s and the rapid spread of the influenza A H1N1 virus in 2009 are examples of international infections that affected Brazil. Finally, changes in urban and rural environments were associated with emergence of new infectious diseases (eg, Brazilian haemorrhagic fever, hantaviruses).[20–22] Diseases that were previously well controlled were reintroduced to Brazil (dengue[17]) or underwent epidemiological changes that compromised their effective control (visceral and cutaneous leishmaniases,[13] hepatitis C[23]).[24] Reductions in mortality from some diseases were not always accompanied by reduction in incidence; tuberculosis and HIV/AIDS are still a public health problem in many regions of the country, despite substantial decreases in mortality rates since the mid-1990s.[25–27] A substantial proportion (13%) of resources allocated to health care are spent on infectious diseases.[28]

The health system: surveillance, prevention, and care

The Brazilian National System for Surveillance and Control of Diseases (SNVS) is a decentralised, hierarchical, integrated network that operates a horizontal and universal approach, as part of the Unified Health System (*Sistema Único de Saúde*, or SUS).[29] All 27 states of Brazil have public health laboratories; there are 5 National Reference Laboratories and 51 Centres for Surveillance and Strategic Information (CIEVS).[30] State Health Secretariats coordinate and assess state-level activities.[31] Teams based in the municipalities investigate individual cases and outbreaks reported by the health service and implement relevant control measures. All reported cases (from public health services or from private health providers) are included in the notification database (SINAN), which is openly accessible on the internet. When necessary, CIEVS provide technical staff, material, and financial resources needed for clinical and epidemiological investigation and implementation of control measures. CIEVS are operational 24 h a day and 7 days a week, monitoring the information received and any relevant information, including information from the press and other media.

SNVS undertakes disease-specific surveillance and control programmes for vaccine-preventable diseases, dengue fever, malaria, HIV/AIDS, tuberculosis, leprosy, meningitis (panel 1; table 2), leishmaniasis, diarrhoea, leptospirosis, and other diseases. All drugs and immunobiological products used in such control programmes are given to individuals free of charge.

	Gross domestic product* per head (US$)	Infectious diseases (yearly mortality per 100 000 population)	HIV/AIDS (yearly mortality per 100 000 population)	Tuberculosis (yearly mortality per 100 000 population)
Brazil	10 070	139	8	3·8
Russia	15 630	71	28	15
India	2960	377	..	23
China	6020	86	3	12
Argentina	14 020	88	18	3·1
Chile	13 270	46	7	0·8
Mexico	14 271	73	10	1·4
Canada	36 220	22	<10	0·3
USA	46 970	36	7	0·3
UK	36 130	37	<10	0·7
Japan	35 010	39	<10	1·4
South Africa	9780	965	721	39
Mozambique	770	954	379	36

*Adjusted by the purchasing power parities.[5]

Table 1: **Mortality from different infectious diseases (in individuals without HIV) and gross domestic product in different countries, 2004**

Control: successes and failures

Here we examine trends from 1980 to 2007 in selected infectious diseases of public health importance—grouped according to their control being either successful, partly successful, or a failure—and look for common factors in each group. We consider the control of diseases that were eliminated, are well controlled (less than one case per 100 000 population), or for which mortality has been reduced by at least 90% as successes. Control of diseases for which incidence or mortality rates have increased we consider as failures. The control of diseases that are defined by neither of the above two definitions are considered as partly successful.

Despite their importance, respiratory tract infections and health-care acquired infections were not selected for inclusion in this report. Respiratory infections in children are discussed elsewhere in this Series.[35] In short, a pronounced decrease in child mortalities due to respiratory infections has been recorded in the past two decades—between 1991 and 2007, mortality decreased by about 80%—which was largely attributable to the increase in access to health care, including the Family Health Programme.[36] In the elderly population, evidence exists that the incidence of fatal respiratory infections is also decreasing slowly, although becoming a larger proportion of all deaths. The universal availability of influenza vaccines since 1999 for this age group has substantially reduced the proportion of mortalities in this age group that are caused by respiratory infections.[37,38] Universal access to vaccination led to a decrease in the socioeconomic disparity in number of deaths due to respiratory infections.[39] About a third of all hospital-acquired infections are pneumonia, making up a substantial proportion of the national burden of respiratory infections.[40]

Expansion of the Brazilian health system has led to an increase in the occurrence of health-care acquired infections.[41] Although there has been a national programme of monitoring and control since 1983, available data are not sufficient for an adequate assessment of trends at a national level.[42] However the little data available suggest that such infections are an important problem,[43] which will probably increase as the access to the hospital system increases and the use of high-technology, and invasive interventions becomes more frequent.

Panel 1: Meningitis in Brazil

Of all types of meningitis, meningococcal meningitis has the most public-health importance because of its epidemic potential. There were several epidemics of meningococcal disease in the 20th century in Brazilian cities. In São Paulo, the largest metropolis in the country, there were four major epidemics, the largest of which was in the 1970s, when waves of serotypes A and C spread from peripheral urban areas to all social and demographic groups. To control this epidemic, the largest mass vaccination campaign with conjugated vaccines (serotypes A and C) was done—95% of the 11 million population of São Paulo city were vaccinated in 4 days. The epidemic was during the military dictatorship and lasted 7 years. During the first 5 years of the epidemic the government banned mention of the epidemic in the media and did not disclose the number of deaths or cases, fearing that links between the epidemic and accelerated economic growth could bring attention to the poor conditions in which the working population lived.[32–34]

	Proportion	Fatality rate (per 100 cases)	Incidence rate (per 100 000 population)
Tuberculosis	1·44%	31·85	0·21
Pneumococcal	4·66%	29·84	0·67
Haemophilus influenzae type b	0·09%	16·34	0·09
Meningococcal	12·24%	20·15	1·76
Not specified	10·90%	12·94	1·57
Bacterial	21·53%	13·24	3·09
Viral	44·61%	1·57	6·41

Table 2: **Meningitis incidence, fatality rate, and cause in Brazil, 2001–09**

For the **SINAN database** see http://dtr2004.saude.gov.br/sinanweb/

> **Panel 2: Production of vaccines in Brazil**
>
> The domestic production of vaccines has increased substantially in the past 20 years. In 1992, roughly 60% of all vaccines used in the National Immunisation Programme were imported; by 2002, 70% were produced in Brazil.[44] The largest national producers are the Butantan Institute and BioManguinhos, both public laboratories that produce only immunobiologicals. The Butantan Institute is affiliated to the State of São Paulo Health Secretariat and produces vaccines against hepatitis B; diphtheria, pertussis, and tetanus (DPT); diphtheria and tetanus; rabies; and seasonal influenza A. BioManguinhos is part of the Oswaldo Cruz Foundation (FIOCRUZ), is affiliated to the Brazilian Ministry of Health, and produces yellow fever, *Haemophilus influenzae* type b (Hib), polio, and tetravalent (DPT plus Hib) vaccines.

Successful control

Vaccine-preventable diseases

The National Immunization Programme (*Programa Nacional de Imunização*; PNI) has been very successful, achieving one of the highest immunisation coverage rates worldwide, without the use of coercive strategies. All vaccines are given to individuals free at the point of use. Routine universal vaccination programmes include BCG; poliomyelitis, measles mumps, and rubella (MMR); diphtheria, pertussis, tetanus (DPT) plus *Haemophilus influenzae* type b (Hib); hepatitis B; yellow fever; rotavirus; 10-valent pneumococcal; and meningococcal C conjugate vaccines. These vaccines are provided in about 30 000 health units, and also in an additional 100 000 temporary vaccination points twice a year during national vaccination days. In 2007, the government spent R$710 million (US$373 million) on vaccines, most of which were produced in Brazil (panel 2). Vaccination against human papilloma virus is provided exclusively through private clinics, but recent public-private partnerships have increased its availability through substantial discounts offered to patients from both low-income and middle-income groups at outpatient units, with medical assistance by the charities in the Santa Casa da Misericórdia network.

For more on **Santa Casa da Misericórdia network** see www.cmb.org.br

Actions by the Pan American Health Organization, who have a prominent role in the control of vaccine-preventable diseases in South America, have contributed much to the success in control of such diseases in Brazil.[45,46] Between 1980 and 2007, the number of deaths from tetanus decreased by 81% and deaths from pertussis decreased by 95%—no deaths were registered from diphtheria, poliomyelitis, or measles in 2007.[47,48] Poliomyelitis was eliminated in Brazil in 1990 (although a few cases of vaccine-related poliomyelitis have been reported since).[47] Measles transmission was interrupted in the past decade; sporadic cases, however, been reported from cases imported from Europe and Asia.[48] As in many places with high vaccine coverage, the incidence of and mortality from meningitis caused by *H influenzae* type b in children younger than 5 years substantially decreased after the introduction of the Hib vaccine to the routine schedule in 1999.[49,50] Although, in general, vaccine coverage in Brazil is very high, it is not uniform across socioeconomic levels, with lowest coverage in the highest and lowest socioeconomic groups (figure 2).

Diarrhoea and cholera

Mortality from diarrhoea decreased substantially in the 1980s with the generalised use of oral rehydration therapy. In addition to use of oral rehydration therapy, increased access to health services[52] and especially to primary health care[36] contributed to this reduction in mortality. In children younger than 1 year, diarrhoea-related mortality decreased from 11·7 deaths per 1000 livebirths in 1980, to 1·5 deaths per 1000 livebirths in 2005, a reduction of about 95%.[53] Incidence of diarrhoea also decreased during this period,[54,55] as a result of the pronounced increase in provision of treated, piped drinking water and, to a lesser extent, of hygienic sewage disposal.[54–56] Such improvements in sanitation have caused a shift in the predominant causes of diarrhoea, from bacteria spread by faecal-oral transmission (eg, *Salmonella* spp and *Shigella* spp) to viruses spread by person-to-person transmission (mainly rotaviruses, but also adenovirus and norovirus).[57–59] In 2006, after successful efficacy trials, vaccination against rotavirus was introduced to the routine schedule.[60]

After an epidemic in mid-19th century, no new cases of cholera were recorded in South America until the end of the 20th century in Peru,[61] and was detected in the Brazilian Amazon region, close to the Peru border, in 1991.[62] The disease spread quickly through cities in the north and northeast regions, leading to an epidemic that peaked in 1993, with only 60 000 reported cases (39·8 cases per 100 000 population) and 1·1% case fatality rate;[63] the last case of cholera in Brazil was reported in 2005.[64]

Chagas disease

The chronic form of Chagas disease presents with myocardiopathy, mega-oesophagus, or megacolon. The myocardiopathy is very severe with a high case fatality rate of 80% within 5 years of diagnosis, mostly in men aged 30–40 years. Chagas disease is caused by the protozoan parasite *Trypanosoma cruzi*, and the main insect vector in Brazil is *Triatoma infestans*, a haemophagic bug that lives mostly indoors. Infective forms of *T cruzi* are transmitted to human beings via the vector's faeces, entering through an individual's skin (at the point of a bite) or through mucosal membranes. Alternative routes of transmission are blood transfusions, mother-to-chil d transmission, and, very rarely, contaminated fresh foods. Until the 1970s, *T cruzi* transmission was intense in two-thirds of Brazil (18 states). At the end of the 1970s, an estimated 5 million people were infected with *T cruzi*,[65] although only 2% of infections progress to the severe, chronic form of Chagas disease.[66] An intensive vector control programme in Brazil, done in conjunction with other South American countries, eliminated the main vector of the disease and has thus interrupted vector-borne transmission since 2006.[67] Transmission through blood transfusions was also interrupted through mandatory screening procedures.[68] The seroprevalence of *T cruzi* infection in children younger than 5 years is presently 0·00005%, presumably a result of mother-to-child transmission before control measures were implemented.[68,69] The national programme for Chagas disease control is one of the clearest successes of Brazil's public health system. However, because of Chagas disease's long latency period, 3·5 million individuals in Brazil still have the chronic form of the disease, meaning that diagnosis and care of such individuals is a continuing burden on health services.[70] Even so, mortality due to chronic Chagas disease (mostly due to myocardiopathy) is decreasing, and most deaths are among people older than 60 years.[71,72]

Partly successful control

HIV/AIDS

The incidence of HIV-related illnesses has been stable in the past 5 years, with about 33 000 new cases registered every year.[73] An estimated 600 000 people have HIV infection in Brazil, and the mean national seroprevalence is less than 0·6%.[74] These estimates have been stable since 2000,[74] and accord with population-based studies of the general population.[75,76] Although incidence of AIDS-related illnesses has decreased substantially in large urban areas, low-level transmission still occurs in municipalities of small and medium size,[77] suggesting that resources for diagnosis and treatment in such municipalities are not sufficient and need to be increased.[78,79]

A continuing challenge is to decrease, or at least prevent the increase, of transmission in vulnerable populations, such as men who have sex with men, injecting and non-injecting drug users, and commercial sex workers.[80] Rates of HIV infection and other sexually transmitted infections are high in populations of men who have sex with men.[80] The prevalence of HIV infection in injecting drug users has decreased substantially—from about 25% to 8%,[81] presumably a result of prevention programmes implemented nationally since the mid-1990s (eg, syringe-exchange programmes, targeted condom distribution, and referral to treatment centres), and because many drug users have switched to non-injecting drugs, particularly crack cocaine.[82,83]

Because Brazil operates the largest programme of free-of-charge, highly active antiretroviral therapy in the world, the emergence of resistance to many antiviral drugs was predicted.[84] However, rates of infection with resistant strains have been consistently low, with a slow increase in resistance to first-line traditional drugs that is no higher than that seen in the USA or Europe.[84]

Free and universal access to antiretroviral treatment represents a formidable achievement by the health system in Brazil. However, the undeniable gains have been challenged by the slow but progressive increase of resistance and side-effects associated with most drugs, especially those associated with the long-term consequences of their continued use, such as metabolic

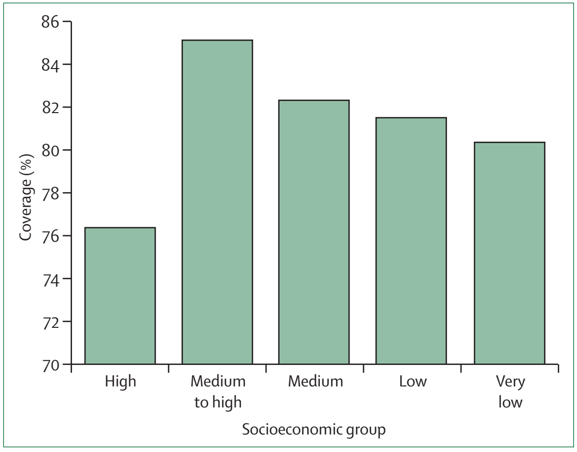


Figure 2: **National Programme of Immunization coverage, by socioeconomic group, 2007–08**
Data are for coverage of children aged 18 months in state capital cities and federal district in Brazil.[51]

(eg, insulin resistance and dyslipidaemias) and cardiovascular disorders.[85] Brazil has tackled this challenge with a well structured treatment programme, and a diverse portfolio of drugs, providing locally produced first-line generic drugs at low cost, second-line drugs produced through compulsory licences (eg, efavirenz), and drugs under patent protection bought at discount prices from other countries. Costs of antiretroviral treatment have increased in the past 5 years, before which time the progressive introduction of locally produced generic drugs caused prices to decrease (figure 3).[87]

HIV control efforts in Brazil include prevention of mother-to-child transmission (with provision of testing and prophylaxis in prenatal care) and treatment of children and adolescents with HIV/AIDS. The incidence of vertically transmitted infections has decreased over the past decade, but prenatal care is sometimes substandard and the introduction of prophylaxis can be delayed in some underserved neighbourhoods.[88] Such drawbacks are partly compensated for by the country-wide use of rapid HIV-diagnostic tests for pregnant women in peripartum who are unaware of their serostatus.[89] Substantial improvements have been made in survival and quality-of-life in children with HIV/AIDS.[90]

HIV/AIDS has been the subject of many campaigns that emphasise the need to practise safe sex and to seek prompt treatment. Such measures have had an effect on both incidence and mortality, which have decreased substantially over the past 15 years. Because mortality from and transmission of HIV/AIDS still occurs, we have categorised HIV/AIDS control efforts in Brazil as partly successful. However, such efforts have been as effective in Brazil as they have been in most developed countries.

Hepatitis A and B

In the past two decades there has been evidence of reduced transmission of hepatitis A and B,[91–93] although this

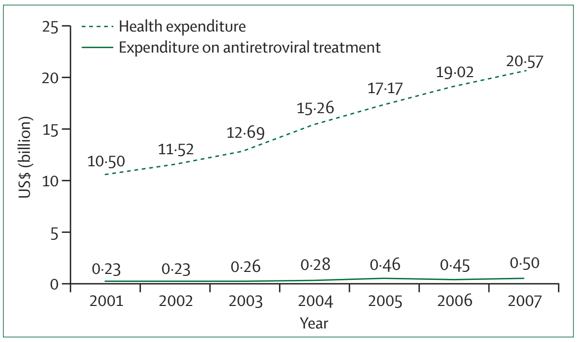


Figure 3: **Health spending by the Brazilian Government**
*Estimated costs, based on preliminary data.[86]

reduction has not been apparent in surveillance data.[94] However, data from repeated seroprevalence surveys and from death registration show a decrease in both prevalence and mortality.[91,65,96] A national survey of seroprevalence of viral hepatitis is being done in the 26 state capital cities and in the federal district (Brasilia), and will produce an accurate map of the prevalence of these infections by the end of 2011. Early findings from this survey in a large area of the country, including the northeast region, the centre-west region, and Brasilia,[92] show an overall seroprevalence of hepatitis A in children aged 5–9 years of 41·4%, which is considered medium endemicity. Earlier surveys in the same areas noted high endemicity.[97] Because hepatitis A vaccine is given to high-risk groups and not to healthy children, the decrease in prevalence rates among children was not the result of vaccination programmes, but rather of improvements in water supply and sanitation, and in hygiene and living conditions in general.

For hepatitis B, data for the same three regions show a seroprevalence of HBsAg of less than 1%,[93] an improvement from earlier findings.[98] Vaccination against hepatitis B has been part of the national basic vaccination schedule and given free at the point of use since 1989 in the western Amazon (the region with the highest prevalence of hepatitis B),[99,100] and rolled out in 2001 to the whole country as a routine schedule for children and adolescents. In the northeast and the centre-west regions, and in the Federal District (Brasilia city), the national hepatitis survey showed that 30% of people aged 10–19 years received at least one dose of the vaccine.[93] A national vaccination survey had shown that for those younger than 1 year, coverage is 86·7%.[101] To further reduce transmission and mortality, a policy was implemented in 2001 that defined the standard treatment regimens for chronic infection, with all drugs given free of charge.[102]

Leprosy

Leprosy is detected in every state of Brazil, but the highest detection rates are in the Amazon region and in a few urban centres in the northeast region; more than 50% of cases are reported in areas where 17·5% of the country's population lives.[103] In 2006, the annual new-case detection rates per 100 000 population were 70·1 in the north region, 61·8 in the centre-west region, and 32·2 in the northeast region. Because the incubation period of leprosy is long, the geographical pattern of occurrence is related to historical transmission levels and other epidemiological determinants (eg, migration patterns), which are poorly understood.[104]

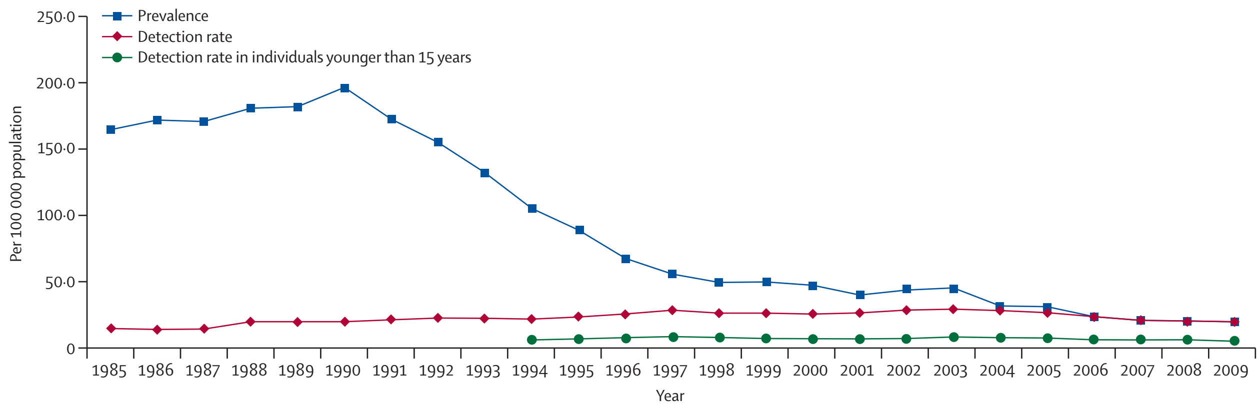
After the introduction of multidrug therapy, which is given free-of-charge to patients with leprosy by the SUS, the prevalence of leprosy in Brazil decreased substantially—from 180 cases per 100 000 population in 1988 to 26 cases per 100 000 population in 2008 (figure 4), with much reduction in disabilities associated with leprosy.[106] However, during this period incidence rates changed little, with a case-detection rate in individuals younger than 15 years staying at about 7 cases per 100 000 population every year. This finding suggests that although efforts to control leprosy by identification and treatment of cases reduced disease prevalence, this strategy had little effect on reducing transmission. Identification of new ways to control leprosy (ie, interrupting transmission) are necessary, as is keeping leprosy as a world priority on the public health and research agenda to avoid waning of interest and financial support for research, prevention, and care.[107,108]

Tuberculosis

During the 1980s, the incidence of tuberculosis was high, largely because of the high prevalence of HIV infection in the population. However, with the rollout of antiretroviral therapy programmes, tuberculosis incidence decreased from 51·4 cases per 100 000 person-years in 1990 to 38·2 cases per 100 000 person-years in 2007 (a 26% reduction)—mortality also decreased during this period, from 3·6 deaths per 100 000 person-years to 1·4 deaths per 100 000 person-years (a 32% reduction).[109] However, pronounced regional differences in incidence of and mortality from tuberculosis exist, with larger incidences in states with higher prevalences of HIV infection, such as Rio de Janeiro, and in states with restricted access to health services, such as those in the Amazon region.[110,111] Pronounced socioeconomic differences in incidence and mortality also exist within urban areas.[112] Although there are clear guidelines for tuberculosis diagnosis and treatment,[113] delays from onset of symptoms to diagnosis and treatment still vary between and within regions, and reorganisation of the health-care system has not yet resulted in uniformly early diagnosis of tuberculosis.[114]

Completion of treatment is essential for tuberculosis control and is carefully monitored and reported in the SINAN database. 63% of patients are cured with complete treatment, but 8% of patients stop treatment before completion.[109] These estimates, although improving, do not meet the Ministry of Health's targets of 85% and 5%, respectively, and are lower than needed to interrupt transmission.[109]

Because prevention of acquired resistance depends on early case finding and effective treatment, standardised



	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
Prevalence	164·0	171·0	170·0	180·0	181·0	195·0	171·0	154·0	131·0	104·0	88·5	67·2	55·5	49·3	49·4	47·1	39·9	43·3	45·2	31·6	31·0	23·7	21·1	20·6	19·9
Detection rate	14·6	13·7	14·3	19·0	19·6	20·0	21·0	22·5	22·6	21·6	23·3	25·8	28·3	26·2	26·6	25·4	26·6	28·3	29·4	28·2	26·9	23·4	21·2	20·6	19·6
Detection rate in individuals younger than 15 years	..	..	..	..	..	..	..	..	..	5·7	6·2	7·5	8·3	7·9	7·3	6·7	7·0	7·5	8·0	7·7	7·3	6·2	6·1	5·9	5·4

Figure 4: **Prevalence and detection rate of Leprosy in Brazil[105]**

treatment and the supply of drugs at no cost to the patient are crucial to avoid the development of resistance. In Brazil, multi-drug resistance seems to be largely associated with retreatment, probably because of irregular treatment schedules or patients' abandonment of treatment.[115,116] Of all individuals with tuberculosis in Brazil, an estimated 6·0% are infected with strains resistant to isoniazid and 1·4% are infected with strains resistant to both isoniazid and rifampicin.[116–118] The prevalence of such resistant strains might decrease with a decision made in 2009 to change the first-line treatment regimen, introducing ethambutol as a fourth drug during the first 2 months of treatment and the use of one pill containing the four drugs.[117] Extensive data for the prevalence of extensively drug-resistant tuberculosis are not available, but cases have been reported.[119]

The proportion of health services that offer directly supervised treatment increased from 7% in 2000 to 81% in 2006,[120] although these seem to be reaching no more than a quarter of patients in treatment.[121] Brazil has a very successful Family Health Programme, and there are plans to include tuberculosis monitoring in its activities, therefore extending the coverage of supervised treatment.

In the 1990s, 30% of individuals with HIV also had tuberculosis—this proportion decreased to 10% after the introduction of highly active antiretroviral therapy.[110] Among tuberculosis patients attending health services for treatment, the proportion of individuals also infected with HIV is roughly 20%, but only half of patients with tuberculosis are routinely tested for HIV.[122] The Ministry of Health now recommends the use of rapid diagnostic tests for HIV for all patients with tuberculosis in the first 2 weeks of treatment.[123]

Treatment of latent tuberculosis infection with isoniazid in adolescents and adults in Brazil is recommended.[124] Treatment criteria are well defined, varying according to age and comorbidities that increase the risk for developing active tuberculosis (ie, HIV infection, diabetes, use of corticosteroids, etc). Assessment of the extent to which this recommendation is being implemented and its effect on tuberculosis control, treatment completion rates, and the occurrence of adverse events is not yet possible because it was implemented in only 2009, but either the Ministry of Health or other research teams will assess it in the future.[124]

Brazil has a prison population of about 400 000 individuals (227 prisoners per 100 000 population).[125] The prevalence of active tuberculosis among prisoners in different studies has ranged from 2·5%[126] to 8·6%,[127] and a prevalence of 2·7% was recorded among inmates entering prisons from police remand centres.[126,128] Further studies are needed to assess the role of prisons in tuberculosis transmission and development of drug resistance in Brazil.

Schistosomiasis

The only schistosome species in Brazil is *Schistosoma mansoni*. In 1997, about six million people were infected.[129] Different sources of data show a decrease in schistosomiasis occurrence and severity: from 1995 to 2006, the number of hospital admissions for complications of schistosomiasis per 100 000 population per year decreased from 21 to 4 (a reduction of 80%) and deaths per 100 000 population per year decreased from 0·38 to 0·27 (a reduction of 29%).[130] Prevalence estimates from stool examinations in repeated surveys in large areas showed a decrease in positive detection rates from 8·4% in 1995 to 5·5% in 2006.[130–132]

Transmission requires specific freshwater snails as intermediate hosts and occurs mainly in the northeast region, in rural and poor peri-urban areas. The schistosomiasis control programme started in 1975 in Brazil, it was vertical and based on mass treatment.

Figure 5: **Trends in the prevalence of malaria in the Amazon region, Brazil (1960–2008)**[138]

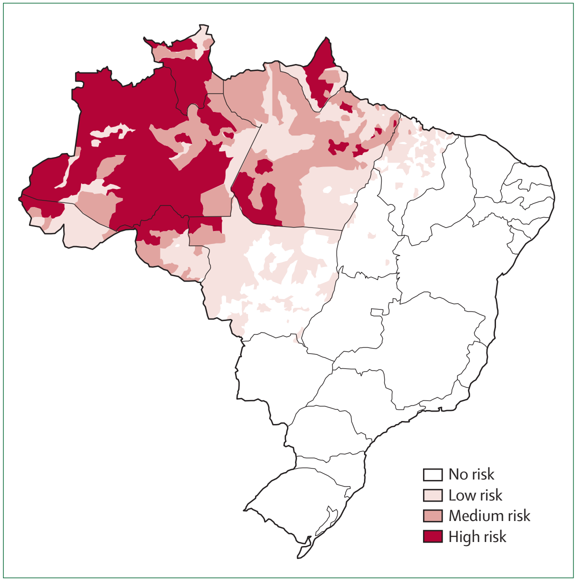


Figure 6: **Malaria transmission in Brazil, 2008**
High risk=annual parasite incidence (API) greater than 50 cases per 100 population.[138] Medium risk=API between 10 and 50 cases per 100 population. Low risk=API less than 10 cases per 100 population.

In 1993 the programme was decentralised to states, then to municipalities, and was eventually integrated into primary health care in 2007–10. Much of the reduction in schistosomiasis prevalence is attributable to improvements in access to clean water and sanitation, which has meant that individuals now have less contact with fresh water bodies; mass treatment is likely to have reduced severity of disease and could have contributed to decreased transmission.[133,134] A remaining challenge is to integrate specific control measures with more general measures (eg, expansion of the sewerage network) and to basic health care.[131]

Malaria

Malaria is a public health problem in Brazil, with roughly 300 000 new cases registered every year. Although still substantial, this incidence is much lower than it was in the 1940s and 1950s, when about 5 million new cases were registered every year.[135–137] After implementation of the malaria eradication programme in the early 1960s, the yearly number of cases decreased rapidly, to a low in 1969, when 52 469 cases were reported in the Amazon region (figure 5),[139] only to increase again as a result of a chaotic and rapid settlement process in the Amazon.[135] *Plasmodium vivax* accounts for more than 80% of cases and *Plasmodium falciparum* accounts for less than 20% of cases, unlike in 1960–88 when the prevalences of both species were much the same.[140] The case-fatality rate for malaria—which has been less than 1% since 1960—decreased substantially in the past 10 years, possibly because of improved access to diagnosis and treatment, which are given free of charge. Standardised treatment protocols kept levels of drug resistance low, and much work has been done to develop new drugs (eg, artemisinin combination therapies).[140]

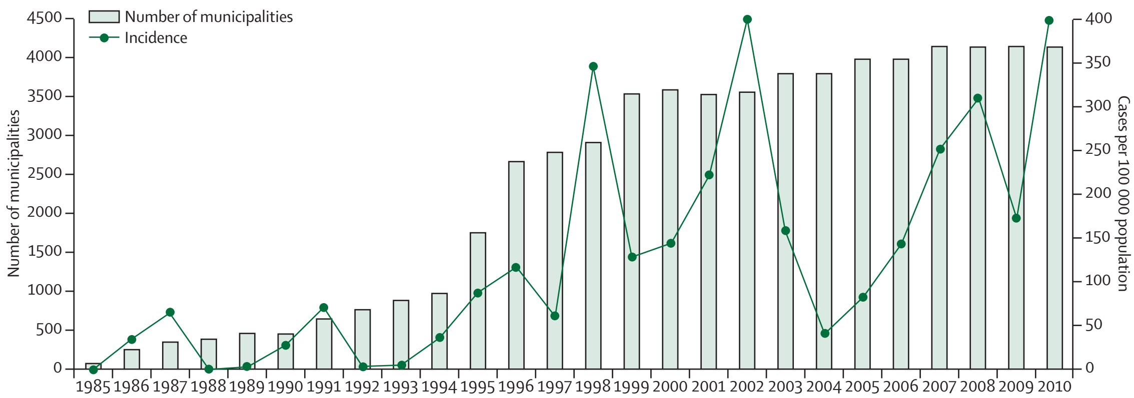
99% (315 809 cases) of all malaria cases are reported in the legal Amazon area, where geographical, economic, and social factors facilitate transmission and limit the use of standard control measures. Malaria incidence is lower in rubber extraction areas, and higher in areas that were colonised in the past 10 years and open-air mining areas. Peri-urban areas also have high incidence, largely because of migration from failed agricultural settlements in malarious areas.[135–137] Malaria transmission occurs in 67% of legal Amazon's municipalities; 49% have low endemicity (an annual parasite incidence [API] <10), 10% have moderate endemicity (an API of 10–50) and 8% have intense transmission (an API >50; figure 6).

Failures

Dengue fever

Dengue fever is a major public health problem in Brazil. Since 1986, incidence has increased with successive epidemics (figure 7),[17,18] and an increasing proportion of patients are presenting with severe disease (0·06% of patients in the 1990s rising to 0·38% in 2002–08).[17] Three serotypes (DENV1–3) circulate throughout the country; DENV4 was isolated in the north region of Brazil in 2010.[141] Three in four Brazilian municipalities are densely populated with *A aegypti* mosquitoes, the main vector of dengue fever.[17] Between 2000 and 2009, 3·5 million cases of dengue fever were reported, 12 625 of which were dengue hemorrhagic fever, with 845 reported deaths.[142] The annual incidence between 1986 and 2009 varied between 40 cases per 100 000 population and 400 cases per 100 000 population, with incidence peaking in 2008 and remaining stable since—a high proportion of severe cases are in children.[17] The causes and mechanisms involved in progression from dengue fever to dengue hemorrhagic fever are not completely understood.[18,143–145]

Prospects for future control are not encouraging. Reduction in density of *A aegypti*, the most targetable link in the transmission chain, remains a challenge. Even with



	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
Number of municipalities	81	258	348	384	456	454	640	767	892	969	1752	2673	2780	2910	3535	3592	3529	3569	3794	3794	3977	3977	4137	4137	4140	4142
Incidence	0	34·5	64·6	1·1	3·8	27·3	71·1	2·5	4·9	36·8	87·7	117·0	60·9	345·7	127·7	144·4	221·9	399·7	158·9	40·5	81·9	143·2	251·0	308·9	171·8	428·9

Figure 7: **Incidence of dengue fever and number of municipalities with high a high density of *Aedes aegypti* mosquitoes, 1985–2010**[17]

more than half a billion US dollars (about R$900 million) dollars invested by the government every year in vector control, vector densities low enough to effectively limit or reduce the spread of dengue fever have not been achieved in a sustained manner.[146,147] Such difficulties in controlling *A aegypti* populations also exist in other countries, such as Singapore, where *A aegypti* control is very efficient but dengue epidemics still occur.[148] No safe vaccine is available and there is little prospect for one in the near future. During epidemics, public health efforts in Brazil are directed towards increasing awareness of symptoms to improve early presentation to health services and to enable early diagnosis and treatment of severe forms.

Visceral leishmaniasis

In Brazil, incidence of visceral leishmaniasis, also known as kala-azar, is high, with an average of two cases per 100 000 population per year. The increase in incidence and the expansion of transmission areas are both causes for concern. Nearly 70% of all cases of visceral leishmaniasis in South America are in Brazil, where the geographical reach of the disease is substantial—between 1999 and 2008, more than a third of Brazilian municipalities have reported autochthonous cases.[149,150] The disease has severe manifestations and is sometimes lethal in children. The case-fatality rate of visceral leishmaniasis in Brazil has varied between 3·2% and 6·9% in the past 10 years.[151]

Visceral leishmaniasis is a disease caused by the protozoan parasite *Leishmania chagasi* and is transmitted by phlebotomine sandflies. The transmission cycle of *L chagasi*, formerly restricted to rural areas, has changed since the 1980s, spreading to urban areas. Small, medium-sized, and large cities have been affected, including state capitals such as Teresina (in the northeast region), Belo Horizonte (in the southeast region), and Campo Grande (in the centre-west region).[149,150] Rapid urban expansion has brought domestic dog populations into contact with zoonotic cycles in rural areas and, as a consequence, they have become a major reservoir for the disease in the urban environment.[149,150] Furthermore, the main vector, *Lutzomiya longipalpis*, has adapted well to the peri-domiciliary environment.

Visceral leishmaniasis control in Brazil has focused on vector control and elimination of animals that are reservoirs for the disease, but available strategies and technologies have so far had little effect.[51,152] Available treatment for the disease is lengthy, expensive, and must be taken under medical supervision because it is highly toxic, limiting access, especially in isolated rural areas.

Conclusion

A pressing need exists to develop new treatments and vaccines for those diseases which have proved difficult to control. In Brazil, biomedical and epidemiological research is thriving,[153,154] as is public health research into infectious diseases, with much collaboration with developing and developed countries.[155–158]

Several major bottlenecks in public health research exist: biomedical and public health research centres are concentrated in the southeast region of Brazil, which does not have the highest burden of disease; administrative procedures are lengthy for the importation of research equipment; private companies invest little into research; little research in Brazil generates international patents or translates into implementable interventions such as new medicines, vaccines, and diagnostic kits.[159]

Further research is needed in the following areas: biomedical research for the development of vaccines, better treatments, fast diagnostics, and innovative vector-control methods; population based research to assess new technologies before adoption in the health system and to investigate the social determinants of diseases such as leprosy and tuberculosis; health-service research to develop and assess new strategies to deliver efficient diagnostics and treatment for chronic infectious diseases (such as

HIV, tuberculosis, leprosy, and visceral leishmaniasis) or outbreaks of severe acute disease such as dengue fever.

The substantial reorganisation of the Brazilian health system has had notable effects on the structure and functioning of initiatives to control infectious diseases. The previous vertical control structure has been replaced by horizontal actions at the municipality level. Even though successful actions have been implemented by local administrations (eg, vaccination programmes and schistosomiasis and dengue control measures), the provision of support and expertise from the federal government and state administrations is crucial. For instance, the series of dengue fever epidemics in Brazil's major urban centres has repeatedly challenged the health system to provide quality care to a growing number of severe cases, to be managed in specialised units staffed by well-trained professionals. Maintenance of such channels of communication and help will require preparedness studies and pilot projects to address emergent questions and renewed challenges.

Another key issue is the need to harmonise broad social and economic policies and specific demands and needs for the effective control of infectious diseases. Since 1970, access to clean water has increased substantially, and in the past 10 years access to sewage systems has become a priority of public policies. The full attainment of such goals will be key to the sustainable control of faecal transmitted diseases.

In the past 10 years, cash transfer programmes for the neediest populations in Brazil have helped reduce poverty and, albeit only marginally, reduce social and economic inequalities for the first time in Brazil's history.[12] More substantial improvements in education and actions to reduce socioeconomic inequalities might improve the control of diseases such as tuberculosis and leprosy. However, despite improvements recorded in the past decade, living conditions in urban slums create an ideal environment to maintain the transmission of many infectious diseases.[160] Initiatives such as the *Programa de Aceleração do Crescimento* (PAC) have been implemented to provide such underserved areas with proper sewage, running water, health centres, and schools. But much remains to be done and local infrastructure remains far from acceptable in many parts of Brazil. Challenges for the future include further reduction of individual and regional differentials in wealth, improvement of infrastructure and social services, and further expansion of programmes that support better prevention and care. Furthermore, the fast growth in medical research in Brazil must be sustained—efforts must go towards identification of new treatments (eg, for leishmaniasis), new vaccines (eg, for dengue), and more effective ways to deliver specific care.

Contributions

All authors contributed to the planning, review of data and evidences and writing of this manuscript. All authors read and approved the final version.

Conflicts of interest

We declare that we have no conflicts of interest.

References

1 Monteiro CA. Contribuição para o estudo do significado da evolução do coeficiente de mortalidade infantil no município de São Paulo, SP (Brasil) nas três últimas décadas (1950–1979). *Rev Saude Publica* 1982; **16:** 7–18.

2 Rede Interagencial de Informações para a Saúde (RIPSA). http://www.ripsa.org.br/php/index.php (accessed Feb 3, 2011).

3 Ministerio da Saúde. Departamento de Informatica do SUS (DATASUS). http://www2.datasus.gov.br/DATASUS/index.php?area=0205 (accessed Feb 3, 2011).

4 Datasus, Ministerio da Saude. Mortalidade Brasil. http://tabnet.datasus.gov.br/cgi/deftohtm.exe?sim/cnv/obt10uf.def (accessed Feb 3, 2011).

5 WHO. World Health Statistics 2010. Geneva: World Health Organization, 2010.

6 Silva LJ. Desbravamento, agricultura e doença: a doença de Chagas no Estado de São Paulo. *Cad Saude Publica* 1986; **2:** 124–40.

7 Barata RB. Cem anos de endemias e epidemias. *Cienc Saude Col* 2000; **5:** 333–45.

8 Moraes JC, Barata RB. A doença meningocóccica em São Paulo, Brasil, no século XX: características epidemiológicas. *Cad Saude Publica* 2005; **21:** 1458–71.

9 Schramm JMA, Oliveira AF, Leite IC, et al. Transição epidemiológica e o estudo de carga de doença no Brasil. *Cienc Saude Col* 2004; **9:** 897–908.

10 Tauil P. Perspectivas de controle de doenças transmitidas por vetores no Brasil. *Rev Soc Bras Med Trop* 2006; **39:** 275–77.

11 FUNDAÇÃO IBGE. Séries estatísticas & Séries históricas. http://www.ibge.gov.br/series_estatisticas/ (accessed Feb 4, 2011).

12 Hoffmann R, Ney MG. A recente queda da desigualdade de renda no Brasil: análise dos dados da PNAD, dos censos demográficos e das contas nacionais. *Economica* 2008; **10:** 7–39.

13 Werneck G. Fórum: geographic spread and urbanization of visceral leishmaniasis in Brazil. *Cad Saude Publica* 2008; **24:** 2937–40.

14 Tatem AJ, Hay SI, Rogers DJ. Global traffic and disease vector dispersal. *PNAS* 2006; **103:** 6242–47.

15 Stoddard ST, Morrison AC, Vazquez-Prokopec GM, et al. The role of human movement in the transmission of vector-borne pathogens. *PLoS Negl Trop Dis* 2009; **3:** e481.

16 Ministério da Saúde (Brasil), Secretaria de Vigilância em Saúde. Febre Amarela: aspectos epidemiológicos (2009). http://portal.saude.gov.br/portal/saude/profissional/visualizar_texto.cfm?idtxt=31620 (accessed Feb 4, 2011).

17 Teixeira MG, Costa Mda C, Barreto F, Barreto ML. Dengue: twenty-five years since reemergence in Brazil. *Cad Saúde Publica* 2009; **25** (suppl 1): S7–18.

18 Teixeira MG, Costa MCN, Barreto ML, Mota E. Dengue and dengue hemorrhagic fever epidemics in Brazil: what research is needed based on trends, surveillance, and control experiences? *Cad Saúde Pública* 2005; **21:** 1307–15.

19 Degallier N, Favier C, Boulanger J-P, Menkes C. Imported and autochthonous cases in the dynamics of dengue epidemics in Brazil. *Rev Saúde Pública* 2009; **43:** 1–7.

20 Donalísio MR, Vasconcelos CH, Pereira LE, Ávila AMH, Katz G. Aspectos climáticos em áreas de transmissão de hantavirose no Estado de São Paulo, Brasil. *Cad Saúde Pública* 2008; **24:** 1141–50.

21 Silva LJ. Public Health challenges and emerging diseases: the case of São Paulo. *Cad Saúde Pública* 2001; **17** (suppl 1): S141–46.

22 Kerr-Pontes LRS, Ruffino-Netto A. Estudo epidemiológico da febre purpúrica brasileira: epidemia em localidade do Estado de São Paulo (Brasil) 1986. *Rev Saúde Pública* 1991; **25:** 375–80.

23 Penna G, Pinto LF, Soranz D, Glatt R. High incidence of diseases endemic to the Amazon region of Brazil, 2001–2006. *Emerg Infect Dis* 2009; **15:** 626–32.

24 Ximenes RA, Pereira LM, Martelli C, et al. Methodology of nationwide cross-seccional survey of prevalence and epidemiological patterns of hepatitis A, B and C infections in Brazil. *Cad Saúde Pública* 2010; **26:** 1693–1704.

25 Barreto ML, Camargo EH, Santos CAS, Ferreira LDA. Emergentes, re-emergentes e permanecentes: tendências recentes das doenças infecciosas e parasitárias no Brasil. *Informe Epidemiológico do SUS* 1996; **3:** 7–17.

26 Barata RCB. O desafio das doenças emergentes e a revalorização da epidemiologia descritiva. *Rev Saude Publica* 1997; **31:** 531–37.

27 Waldman EA. Doenças infecciosas emergentes e reemergentes. *Revista da USP* 2001; **51:** 128–37.

28 Ministério da Saúde (Brasil). Datasus. http://tabnet.datasus.gov.br/cgi/deftohtm.exe?sih/cnv/nruf.def (accessed Feb 4, 2011).

29 Paim J, Travassos C, Almeida C, Bahia L, Macinko J. The Brazilian health system: history, advances, and challenges. *Lancet* 2011; published online May 9. DOI:10.1016/S0140-6736(11)60054-8.

30 Carmo EH, Penna G, Oliveira WK. Emergências de saúde pública: conceito, caracterização, preparação e resposta. *Estudos Avancados* 2008; **22:** 19–32.

31 Ministério da Saúde, Brasil. Portaria Nº 1.399, de 15 de dezembro de 1999. http://www.rebidia.org.br/novida/port1399.html (accessed Feb 4, 2011).

32 de Moraes JC, José Cássio, Barata RB. A doença meningocócica em São Paulo, Brasil, no século XX: características epidemiológicas. *Cad Saúde Pública* 2005; **21:** 1458–71.

33 Barata RB. Epidemia de doença meningocócica, 1970/1977: aparecimento e disseminação do processo epidêmico. *Rev Saúde Pública* 1988; **22:** 16–24.

34 Barata RB. Impacto da vacinação em massa contra a doença meningocócica na epidemia da década de 70. *Cad Saúde Pública* 2004; **20:** 1762–63.

35 Victora CG, Aquino EML, Leal MdC, et al. Maternal and child health in Brazil: progress and challenges. *Lancet* 2011; published online May 9. DOI:10.1016/S0140-6736(11)60138-4.

36 Rasella D, Aquino R, Barreto ML. Reducing childhood mortality from diarrhea and lower respiratory tract infections in Brazil. *Pediatrics* 2010; **126:** e534–40.

37 Donalisio MR. Brazilian policy for influenza vaccination and its impact on the health of the elderly. *Cad Saude Publica* 2007; **23:** 494–95.

38 Francisco PM, Donalisio MR, Lattorre M do R. Impact of influenza vaccination on mortality by respiratory diseases among Brazilian elderly persons. *Rev Saude Publica* 2005; **39:** 75–81.

39 Antunes JL, Waldman EA, Borrell C, Paiva TM. Effectiveness of influenza vaccination and its impact on health inequalities. *Int J Epidemiol* 2007; **36:** 1319–26.

40 Sociedade Brasileira de Pneumologia e Tisiologia. [Brazilian guidelines for treatment of hospital acquired pneumonia and ventilator associated pneumonia]. *J Bras Pneumol* 2007; **33** (suppl 1)**:** S1–30.

41 Salomão R, Rosenthal VD, Grimberg G, et al. Device-associated infection rates in intensive care units of Brazilian hospitals: datos de la Comunidad Científica Internacional de Control de Infecciones Nosocomialesfindings of the International Nosocomial Infection Control Consortium. *Rev Panam Salud Publica* 2008; **24:** 195–202.

42 Conselho Regional de Medicina do Estado de São Paulo. O Controle da Infecção Hospitalar no Estado de São Paulo. São Paulo: CREMESP, 2010.

43 Prade SS, Oliveira ST, Rodrigues R, et al. Estudo brasileiro da magnitude das infecções hospitalares em hospitais terciários. *Rev Contr Infect Hosp MS* 1995; **2:** 11–24.

44 Ministerio da Saúde. Programa Nacional de Imunização. http://portal.saude.gov.br/portal/saude/default.cfm (accessed Feb 3, 2011).

45 Olivé JM, Risi JB Jr, de Quadros CA. National immunization days: experience in Latin America. *J Infect Dis* 1997; **175** (suppl 1)**:** S189–93.

46 de Quadros CA, Tambini G, DiFabio JL, Brana M, Santos JI. State of immunization in the Americas. *Infect Dis Clin North Am* 2000; **14:** 241–57.

47 Teixeira-Rocha ES, Carmo EH, Tavares-Neto J. Ocorrência de poliomielite associada à vacina no Brasil, 1995–2001. *Rev Panam Salud Publica* 2005; **18:** 21–24.

48 Coordenadoria de Controle de doenças, Divisão de doenças de transmissão respiratória. Secretaria de Estado da Saúde de São Paulo. Investigação de casos de sarampo no estado de São Paulo na era pós-controle. *Rev Saude Publica* 2005; **39:** 857–860.

49 Miranzi SSC, Moraes AS, Freitas ICM. Impact of the *Haemophilus influenza* type b vaccination program on Hib meningitis in Brazil. *Cad Saude Publica* 2007; **23:** 1689–95.

50 Ribeiro GS, Lima JB, Reis JN, et al. Haemophilus influenzae meningitis 5 years after introduction of the *Haemophilus influenzae* type b conjugate vaccine in Brazil. *Vaccine* 2007; **25:** 4420–28.

51 Luna EJ, Veras MA, Flannery B, Moraes JC. Household survey of hepatitis B vaccine coverage among Brazilian children. *Vaccine* 2009; **27:** 5326–31.

52 Victora CG, Olinto MT, Barros FC, Nobre LC. Falling diarrhoea mortality in northeastern Brazil: did ORT play a role? *Health Policy Plan* 1996; **11:** 132–41.

53 Ministério da Saúde. Série histórica de casos de cólera. http://portal.saude.gov.br/portal/arquivos/pdf/tabela_casos_obitos_colera_1991_2010_ok.pdf (accessed Feb3, 2011).

54 Sastry N, Burgard S. The prevalence of diarrheal disease among Brazilian children: trends and differentials from 1986 to 1996. *Soc Sci Med* 2005; **60:** 923–35.

55 Benicio MHD, Monteiro CA. Tendência secular da doença diarréica na infância na cidade de São Paulo (1984–1996). *Rev Saude Publica* 2000; **34** (suppl 6)**:** 83–90.

56 Barreto ML, Genser B, Strina A, et al. Effect of city-wide sanitation programme on reduction in rate of childhood diarrhoea in northeast Brazil: assessment by two cohort studies. *Lancet* 2007; **370:** 1622–28.

57 Barreto ML, Milroy CA, Strina A, et al. Community-based monitoring of diarrhea in urban Brazilian children: incidence and associated pathogens. *Trans R Soc Trop Med Hyg* 2006; **100:** 234–42.

58 Ferrer SR, Strina A, Jesus SR, et al. A hierarchical model for studying risk factors for childhood diarrhoea: a case-control study in a middle-income country. *Int J Epidemiol* 2008; **37:** 805–15.

59 Moreno AC, Filho AF, Gomes Tdo A, et al. Etiology of childhood diarrhea in the northeast of Brazil: significant emergent diarrheal pathogens. *Diagn Microbiol Infect Dis* 2010; **66:** 50–57.

60 Correia JB, Patel MM, Nakagomi O, et al. Effectiveness of monovalent rotavirus vaccine (Rotarix) against severe diarrhea caused by stereotypically unrelated G2P[4] strains in Brazil. *J Infect Dis* 2010; **201:** 363–69.

61 Guthmann JP. Epidemic cholera in Latin America: spread and routes of transmission. *J Trop Med Hyg* 1995; **98:** 419–27.

62 Gerolomo M, Penna MLF. Os primeiros cinco anos da sétima pandemia de cólera no Brasil. *Inf Epidemiol Sus* 1999; **8:** 49–58.

63 Toledo LM. O cólera nas Américas e sua produção no Brasil. *Informe Epidemiológico do SUS* 1993; **2:** 8–38.

64 Ministério da Saúde. Secretaria de Vigilância em Saúde http://portal.saude.gov.br/portal/arquivos/pdf/clipping_26_10_2010.pdf (accessed Feb3, 2011).

65 Silveira AC, Vinhaes M. Doença de Chagas: aspectos epidemiológicos e de controle. *Rev Soc Bras Med Trop* 1998; **31** (suppl 2)**:** 15–60.

66 Prata A. Clinical and epidemiological aspects of Chagas disease. *Lancet Infect Dis* 2001; **1:** 92–100.

67 Moncayo A, Silveira AC. Current epidemiological trends for Chagas disease in Latin America and future challenges in epidemiology, surveillance and health policy. *Mem Inst Oswaldo Cruz* 2009; **104** (suppl 1)**:** 17–30.

68 Massad E. The elimination of Chagas' disease from Brazil. *Epidemiol Infect* 2008; **136:** 1153–64.

69 Dias JC. Elimination of Chagas disease transmission: perspectives. *Mem Inst Oswaldo Cruz* 2009; **104** (suppl 1)**:** 41–45.

70 Costa-Lima MF, Barreto SM, Guerra HL, Firmo JO, Uchoa E, Vidigal PG. Ageing with *Trypanosoma cruzi* infection in a community where the transmission has been interrupted: the Bambuí Health and Ageing Study (BHAS). *Int J Epidemiol* 2001; **30:** 887–93.

71 Drumond JA, Marcopito LF. Internal migration and distribution of Chagas disease mortality, Brazil, 1981–1998. *Cad Saude Publica* 2006; **22:** 2131–40.

72 Santo AH. Tendência da mortalidade relacionada à doença de chagas, estado de São Paulo, Brasil, 1985 a 2006: Estudo usando causas múltiplas de morte. *Rev Panam Salud Publica* 2009; **26:** 299–309.

73 Brazilian Ministry of Health. Boletim Epidemiológico AIDS-DST. http://www.aids.gov.br/publicacao/boletim-epidemiologico-2010 (accessed March 3, 2011).

74 Bastos FI, Nunn A, Hacker MA, Malta M, Szwarwald CL. AIDS in Brazil: the challenge and the response. In: Celentano DD, Beyrer C, eds. Public health aspects of HIV/AIDS in low and middle income countries—Epidemiology, prevention and care. New York: Springer, 2008: 629–654.

75 Dourado I, Milroy CA, Mello MA, et al. HIV-1 seroprevalence in the general population of Salvador, Bahia State, Northeast Brazil. *Cad Saude Publica* 2007; **23:** 25–32.
76 Costa ZB, Machado GC, Avelino MM, et al. Prevalence and risk factors for Hepatitis C and HIV-1 infections among pregnant women in Central Brazil. *BMC Infect Dis* 2009; **9:** 116.
77 Grangeiro A, Escuder MM, Castilho EA. Magnitude and trend of the AIDS epidemic in Brazilian cities, from 2002 to 2006. *Rev Saude Publica* 2010; **44:** 430–40.
78 Reis CT, Czeresnia D, Barcellos C, Tassinari WS. Decentralization of the HIV/AIDS epidemic and inter-municipal flow of hospital admissions in the Zona da Mata, Minas Gerais State, Brazil: a spatial analysis. *Cad Saude Publica* 2008; **24:** 1219–28.
79 Nemes MI, Melchior R, Basso CR, Castanheira ER, de Britto e Alves MT, Conway S. The variability and predictors of quality of AIDS care services in Brazil. *BMC Health Serv Res* 2009; **9:** 51.
80 Malta M, Magnanini MM, Mello MB, Pascom AR, Linhares Y, Bastos FI. HIV prevalence among female sex workers, drug users and men who have sex with men in Brazil: a systematic review and meta-analysis. *BMC Public Health* 2010; **10:** 317.
81 Bastos FI, Bongertz V, Teixeira SL, Morgado MG, Hacker MA. Is human immunodeficiency virus/acquired immunodeficiency syndrome decreasing among Brazilian injection drug users? Recent findings and how to interpret them. *Mem Inst Oswaldo Cruz* 2005; **100:** 91–96.
82 Hacker MA, Leite I, Friedman SR, Carrijo RG, Bastos FI. Poverty, bridging between injecting drug users and the general population, and interiorization may explain the spread of HIV in southern Brazil. *Health Place* 2009; **15:** 514–19.
83 Inciardi JA, Surratt HL, Pechansky F, et al. Changing patterns of cocaine use and HIV risks in the south of Brazil. *J Psychoactive Drugs* 2006; **38:** 305–10.
84 Baggaley RF, Petersen ML, Soares MA, Boily M-C, Bastos FI. Human Immunodeficiency Virus: resistance to antiretroviral drugs in developing countries. In: de J Sosa A, Byarugaba DK, Amábile-Cuevas CF, Hsueh PR, Kariuki S, Okeke IN, eds. Antimicrobial resistance in developing countries. New York: Springer, 2009: 75–94.
85 Palella FJ Jr, Baker RK, Moorman AC, et al. Mortality in the highly active antiretroviral therapy era: changing causes of death and disease in the HIV outpatient study. *J Acquir Immune Defic Syndr* 2006; **43:** 27–34.
86 Transparência Pública. Execução Orçamentária. http://www3.transparencia.gov.br/TransparenciaPublica/jsp/execucao/execucaoTexto.jsf?consulta=1&consulta2=0&CodigoOrgao=36000 (accessed March 11, 2011).
87 Nunn AS, Fonseca EM, Bastos FI, Gruskin S, Salomon JA. Evolution of antiretroviral drug costs in Brazil in the context of free and universal access to AIDS treatment. *PLoS Med* 2007; **4:** e305.
88 Barcellos C, Acosta LM, Lisboa E, Bastos FI. Surveillance of mother-to-child HIV transmission: socioeconomic and health care coverage indicators. *Rev Saude Publica* 2009; **43:** 1006–14.
89 Veloso VG, Bastos FI, Portela MC, et al. HIV rapid testing as a key strategy for prevention of mother-to-child transmission in Brazil. *Rev Saude Pub* 2010; **44:** 803–11.
90 Matida LH, Ramos AN Jr, Heukelbach J, et al. Continuing improvement in survival for children with acquired immunodeficiency syndrome in Brazil. *Pediatr Infect Dis J* 2009; **28:** 920–22.
91 Vitral CL, Souto FJD, Gaspar AMC. Changing epidemiology of hepatitis A in Brazil: reassessing immunization policy. *J Viral Hepat* 2008; **15** (suppl 2)**:** 22–25.
92 Ximenes RAA, Martelli CMT, Merchan-Hamann E, et al. Multilevel analysis of hepatitis A infection in children and adolescents: a household survey in the Northeast and Central-west regions of Brazil. *Int J Epidemiol* 2008; **37:** 852–61.
93 Pereira LM, Martelli CMT, Merchán-Hamann E, et al. Population-based multicentric survey of hepatitis B infection and risk factor differences among three regions in Brazil. *Am J Trop Med Hyg* 2009; **81:** 240–47.
94 Ministério da Saúde (Brasil) Secretaria de Vigilância em Saúde. Influenza A (H1N1). Informe Epidemiológico no 2, 2009. http://portal.saude.gov.br/portal/arquivos/pdf/situacao_epidemiologica.pdf (accessed Feb 4, 2011).
95 Vitral CL, Yoshida CFT, Lemos ER, Teixeira CS, Gaspar AMC. Age-specific prevalence of antibodies to hepatitis A in children and adolescents from Rio de Janeiro, Brazil, 1978 and 1995—relationship of prevalence to environmental factors. *Mem Inst Oswaldo Cruz* 1998; **93:** 1–5.
96 Oliveira LHS, Yoshida CFT, Monteiro SS, Câmara FP. Seroepidemiologic survey for hepatitis A and B markers in health care students from a public university of Rio de Janeiro, Brazil. *Rev Microbiol Sao Paulo* 1991; **23:** 226–31.
97 Wasley A, Fiore A, Bell BP. Hepatitis A in the Era of Vaccination. *Epidemiol Rev* 2006; **28:** 101–11.
98 Mast EE, Weinbaum CM, Fiore AE, et al. A comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP) Part II: immunization of adults. *MMWR Recomm Rep* 2006; **55:** 1–33.
99 Echevarria JM, Leon P. Epidemiology of viruses causing chronic hepatitis among populations from the Amazon Basin and related ecosystems. *Cad Saude Publica* 2003; **19:** 1583–91.
100 Viana S, Parana R, Moreira RC, et al. High prevalence of hepatitis B virus and hepatitis D virus in the western Brazilian Amazon. *Am J Trop Med Hyg* 2005; **73:** 808–14.
101 Luna EJ, Veras MA, Flannery B, et al. Household survey of hepatitis B vaccine coverage among Brazilian children. *Vaccine* 2009; **27:** 5326–331.
102 Ministério da Saúde, (Brasil). Protocolo Clínico e Diretrizes Terapêuticas para o Tratamento da Hepatite Viral Crônica B e Coinfecções. Brasilia: Ministerio da Saude, 2009.
103 Ministério da Saúde, (Brasil). Ministério da Saúde. Vigilancia da Saude: Situacao Epidemiologica da Hanseniase no Brasil. Brasilia: Ministerio da Saude, 2008.
104 Kerr-Pontes LR, Montenegro AC, Barreto ML, Werneck GL, Feldmeier H. Inequality and leprosy in northeast Brazil: an ecological study. *Int J Epidemiol* 2004; **33:** 262–69.
105 SINAN/SVS-MS. http://dtr2004.saude.gov.br/sinanweb/ (accessed March 4, 2011).
106 Ministério da Saúde Hanseníase (Brasil). Informações Técnicas. http://portal.saude.gov.br/portal/saude/profissional/visualizar_texto.cfm?idtxt=31205 (accessed Feb 4, 2011).
107 Martelli CMT, Stefani MMA, Penna GO, Andrade ALSS. Endemias e epidemias brasileiras, desafios e perspectivas de investigação científica: hanseníase. *Rev Bras Epidemiol* 2002; **5:** 273–85.
108 Penna ML, de Oliveira ML, Penna GO The epidemiological behaviour of leprosy in Brazil. *Lepr Rev* 2009; **80:** 332–44.
109 Situação da Tuberculose no Brasil. Programa Nacional de Controle da Tuberculose. DEVEP/SVS/MS. http://portal.saude.gov.br/portal/arquivos/pdf/apresentacao_tb_2009.pdf (accessed Feb 4, 2011).
110 Ministério da Saúde (Brasil) SINAN (Sistema Nacional de Agravos de Notificação). Taxas de incidência de tuberculose. http://portal.saude.gov.br/portal/arquivos/pdf/taxa_incidencia_tuberculose.pdf (accessed Feb 4, 2011).
111 Ministério da Saúde (Brasil). Série histórica da Taxa de Mortalidade de Tuberculose. Brasil, Regiões e Unidades Federadas http://portal.saude.gov.br/portal/arquivos/pdf/taxa_mortalidade_tuberculose.pdf (accessed Feb 4, 2011).
112 de Alencar Ximenes RA, de Fátima Pessoa Militão de Albuquerque M, Souza WV, et al. Is it better to be rich in a poor area or poor in a rich area? A multilevel analysis of a case-control study of social determinants of tuberculosis. *Int J Epidemiol* 2009; **38:** 1285–96.
113 Ministério da Saúde, Brasil. Secretaria de Vigilância em Saúde. Programa Nacional de Controle da Tuberculose. Manual de Recomendações para o Controle da Tuberculose no Brasil. 2010. http://portal.saude.gov.br/portal/arquivos/pdf/manual_de_recomendacoes_controle_tb_novo.pdf (accessed March 03, 2011).
114 Scatena LM, Villa TCS, Netto AR, et al. Difficulties in the accessibility to health services for tuberculosis diagnosis in Brazilian municipalities. *Rev Saude Publica* 2009; **43:** 389–97.
115 Souza MB, Antunes CMF, Garcia GF. Multidrug-resistant *Mycobacterium tuberculosis* at a referral center for infectious diseases in the state of Minas Gerais, Brazil: sensitivity profile and related risk factors. *J Bras Pneumol* 2006; **32:** 430–37.

116 Baliza M, Bach AH, Queiroz GL, et al. High frequency of resistance to the drugs isoniazid and rifampicin among tuberculosis cases in the city of Cabo de Santo Agostinho, an urban area in northeastern Brazil. *Rev Soc Bras Med Trop* 2008; **41:** 11–16.

117 Ministério da Saúde, Brasil. Secretaria de Vigilância em Saúde. Departamento de Vigilância Epidemiológica. Programa Nacional de Controle da Tuberculose. Nota técnica sobre as mudanças no tratamento da tuberculose no Brasil para adultos e adolescentes. http://portal.saude.gov.br/portal/arquivos/pdf/nota_tecnica_versao_28_de_agosto_v_5.pdf (accessed Feb 4, 2011).

118 Aguiar F, Vieira MA, Staviack A, et al. Prevalence of anti-tuberculosis drug resistance in an HIV/AIDS reference hospital in Rio de Janeiro, Brazil. *Int J Tuberc Lung Dis* 2009; **13:** 54–61.

119 Araújo-Filho JA, Vasconcelos-Jr AC, Sousa EM, et al. Extensively drug-resistant tuberculosis: a case report and literature review. *Brazil J Infect Dis* 2008; **12:** 447–52.

120 Santos J. Brazilian response to tuberculosis control. *Rev Saude Publica* 2007; **41** (suppl 1)**:** 89–93.

121 Bierrenbach AL, Gomes AB, Noronha EF, Souza Mde F. Tuberculosis incidence and cure rates, Brazil, 2000–2004. *Rev Saude Publica* 2007; **41** (suppl 1)**:** 24–33.

122 Ministério da Saúde, Brasil. Co-infecção HIV / TB: resposta nacional e integração das agendas. http://portal.saude.gov.br/portal/arquivos/pdf/painel3_aids_mariangela_draurio.pdf (accessed Feb 4, 2011).

123 Programa Nacional de DST/AIDS, Programa Nacional de Controle da Tuberculose. Implantação Do Teste Rápido Como Diagnóstico Da Infecção Pelo Hiv. http://www.saude.ba.gov.br/divep/arquivos/COAGRAVOS/GT%20Tuberculose/Cursos%20-%20Capacita%C3%A7%C3%B5es%20-20Treinamentos/Teste%20R%C3%A1pido%20de%20HIV%20-%20mar%C3%A7o%202008/Teste%20R%C3%A1pido%20em%20portadores%20de%20TB.pdf (accessed Feb 4, 2011).

124 Ministério da Saúde, Brasil. Secretaria de Vigilância em Saúde. Departamento de Vigilância Epidemiológica. Guia de vigilância epidemiológica/Ministério da Saúde/, Secretaria de Vigilância em Saúde, Departamento de Vigilância Epidemiológica. 7 ed. Brasília: Ministério da Saúde, 2009.

125 Secretaria Nacional de Segurança Pública. Rede INFOSEG. Brasil é oitavo do mundo em populacão de detentos. http://www.infoseg.gov.br/infoseg/destaques-01/brasil-e-oitavo-do-mundo-em-populacao-de-detentos (accessed Feb 4, 2011).

126 Lemos ACM, Matos ED, Bittencourt CN. Prevalence of active and latent TB among inmates in a prison hospital in Bahia, Brazil. *J Bras Pneumol* 2009; **35:** 63–68.

127 Sánchez AR, Massari V, Gerhardt G, et al. Tuberculosis in Rio de Janeiro prisons, Brazil: an urgent public health problem. *Cad Saúde Pública* 2007; **23:** 545–52.

128 Sanchez A, Larouzé B, Espinola AB, et al. Screening for tuberculosis on admission to highly endemic prisons: The case of Rio de Janeiro State prisons. *Int J Tuberc Lung Dis* **13:** 1247–52.

129 Katz N, Peixoto SV. Análise crítica da estimativa do número de portadores de esquistossomose mansoni no Brasil. *Rev Soc Bras Med Trop* 2000; **33:** 303–08.

130 Carmo EH. Prevenção e controle da morbidade da esquistossomose no Brasil. www.medtrop2009.com.br/.../Esquistossomose_Eduardo%20Hage_11.03.ppt (accessed Feb 4, 2011).

131 Farias LMM, Resendes APC, Sabroza PC, Souza-Santos R. Preliminary analysis of the Information System in the Brazilian Schistosomiasis Control Program,1999-2003. *Cad Saúde Pública* 2007; **23:** 235–39.

132 Amaral RS, Tauil PL, Lima DD, Engels D. An analysis of the impact of the Schistosomiasis Control Programme in Brazil. *Mem Inst Oswaldo Cruz* 2006; **101** (suppl 1)**:** 79–85.

133 Ministério da Saúde (Brasil). Datasus. http://tabnet.datasus.gov.br/cgi/idb2008/Com_F17.pdf (accessed Feb 4, 2011).

134 Carmo EH, Barreto ML. Esquistossomose mansônica no Estado da Bahia: tendências históricas e medidas de controle. *Cad Saude Publica* 1994; **10:** 4225–39.

135 Barata RCB. Malária no Brasil: panorama epidemiológico na última década. *Cad Saude Publica* 1995; **11:** 128–36.

136 Loiola CCP, Silva CJM, Tauil PL. Controle da malária no Brasil: 1965 a 2001. *Rev Panam Salud Publica* 2002; **11:** 235–44.

137 Katsuragawa TH, Gil LHS, Tada MS, Silva LHP. Endemias e epidemias na Amazônia—malária e doenças emergentes em áreas ribeirinhas do rio Madeira. *Estudos Avançados* 2008; **22:** 111–41.

138 Brazilian Ministry of Health. National Malaria Control Programme.

139 Barata RB. Technologic organization of malaria control in Sao Paulo, Brazil, 1930–1990. *Pan Am J Public Health* 1998; **3:** 102–10.

140 Oliveira-Ferreira J, Lacerda MV, Brasil P, Ladislau JL, Tauil PL, Daniel-Ribeiro CT. Malaria in Brazil: an overview. *Malar J* 2010; **9:** 115.

141 Ministério da Saúde. Nota técnica CGPNCD/DEVEP/SVS/MS CGVS/SES-RR/SVS/SMS-BV/Atualização em 23/08/2010 http://portal.saude.gov.br/portal/arquivos/pdf/nt_denv_5_revisada_23_08_2010.pdf (accessed March 3, 2011).

142 Brasil, Ministério da Saúde, Dengue. http://portal.saude.gov.br/portal/saude/profissional/area.cfm?id_area=1525 (accessed Feb 4, 2011).

143 Figueiredo MAA, Rodrigues LC, Barreto ML, et al. Allergies and diabetes as risk factors for dengue hemorrhagic fever: results of a case control study. *PLoS Negl Trop Dis* 2010; **4:** e699.

144 Blanton RE, Silva LK, Morato VG, et al. Genetic ancestry and income are associated with dengue hemorrhagic fever in a highly admixed population. *Eur J Hum Genet* 2008; **16:** 762–65.

145 Silva LK, Blanton RE, Parrado AR, et al. Dengue hemorrhagic fever is associated with polymorphisms in the JAK1 gene. *Eur J Hum Genet* 2010; **18:** 1221–27.

146 Newton EA, Reiter P. A model of the transmission of dengue fever with and evaluation of the impact of ultra-low volume (ULV) insecticide applications on dengue epidemics. *Am J Trop Med Hyg* 1992; **47:** 709–20.

147 Teixeira MG, Barreto ML, Ferreira L D A, Vasconcelos P F C, Cairncross S. Dynamics of dengue virus circulation: a silent epidemic in a complex urban area. *Trop Med Int Health* 2002; **7:** 757–62.

148 Ooi EE, Goh KT, Gubler DJ. Dengue prevention and 35 years of vector control in Singapore. *Emerg Infect Dis* 2006; **12:** 887–93.

149 Maia-Elkhoury ANS, Alves WA, Sousa-Gomes ML, et al. Visceral leishmaniasis in Brazil: trends and challenges. *Cad Saúde Pública* 2008; **24:** 2941–47.

150 Gontijo CMF, Melo MN. Leishmaniose visceral no Brasil: quadro atual, desafios e perspectivas. *Rev bras epidemiol* 2004; **7:** 338–49.

151 Ministério da Saúde. Letalidade de Leishmaniose Visceral. Brasil, Grandes Regiões e Unidades Federadas, 2000 a 2009 http://portal.saude.gov.br/portal/arquivos/pdf/4_lv_letalidade_14_10_10.pdf (accessed Feb 2, 2011).

152 Desjeux P. Leishmaniasis: current situation and new perspectives. *Comp Immunol Microbiol Infect Dis* 2004; **27:** 305–18.

153 Guimarães JA. A pesquisa médica e biomédica no Brasil. Comparações com o desempenho científico brasileiro e mundial. *Ciênc Saúde Coletiva* 2004; **9:** 303–27.

154 Barreto ML. [Growth and trends in scientific production in epidemiology in Brazil]. *Rev Saude Publica* 2006; **40:** 79–85.

155 Ministry of Health, Brazil. Flows of financial resources for health research and development in Brazil 2000–2002. Brasilia: Ministry of Health, 2006.

156 Hill DL. Latin America shows rapid rise in S and E articles. Arlington: National Science Foundation, 2004.

157 Morel CM, Serruya SJ, Penna GO, Guimarães R. Co-authorship network analysis: a powerful tool for strategic planning of research, development and capacity building programs on neglected diseases. *PLoS Negl Trop Dis* 2009; **3:** e501.

158 Dujardin JC, Herrera S, do Rosario V, et al. Research priorities for neglected infectious diseases in Latin America and the Caribbean region. *PLoS Negl Trop Dis* 2010; **4:** e780.

159 Regalado A. Science in Brazil. Brazilian science: riding a gusher. *Science* 2010; **330:** 1306–12.

160 Riley LW, Ko AI, Unger A, Reis MG. Slum health: diseases of neglected populations. *BMC Int Health Hum Rights* 2007; **7:** 2.