Epidemiological Report

Surveillance and control of respiratory-transmitted diseases

Historic Series 2010 – 2021

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DOI: https://doi.org/10.57148/bepa.2022.v.19.37882

VOL. 20 • **Nº** 219 • **YEAR** 2023 • **ISSN** 1806-4272

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INTRODUCTION

Compulsory notification of respiratory-transmitted diseases is mandatory and universal, given the necessity for immediate intervention due to the speed of contamination and the potential for dissemination. In most cases, they can be characterized by outbreaks and/or epidemics and, to a lesser extent, pandemics, which always require a systemic, timely and effective action of surveillance services. Due to changes in the epidemiological profile, the establishment of other techniques for monitoring diseases, the knowledge of new diseases or the re-emergence of others, there is a need for periodic reviews of the inventory of these conditions, in the sense of pragmatic updating.

The Division of Respiratory-Transmitted Diseases of the Surveillance Centre “Prof. Alexandre Vranjac” (DDTR/CVE) has the mission of acting as a sentinel of health surveillance of the population, based on the best practices and governance culture, technological innovation, and socio-environmental responsibility. Thus, it aims to promote population health and quality of life through the prevention and control of acute respiratory transmission diseases, in partnership with health regions, cities, states and society in general. The values that orient the DDTR are based on ethics, commitment, excellence with simplicity and quality, with a focus on results, team spirit, integrity, innovation, and sustainability.

According to the expanded concept of citizen health, the Unified Health System (SUS) model includes the citizens not only as users, but also as participants in its management. The citizenship rights expansion, the concern with universality, with social justice and the role of the State in the provision of social care are common points that stand out and shape relevant items, specifically, political, economic, and social, according to the historical determinants that involve the systemic and programmatic environment in the context of collective health.

In this context, we present below a historical retrospective of the mandatory notification diseases under DDTR monitoring, which impact on São Paulo State’s (SSP) epidemiological profile. From the perspective of a universal, integral, and egalitarian health system, the contributions and actions developed in the period under consideration are also presented, in order to generate and disseminate the accumulated knowledge and to face the challenges in health, at a global level, which require a community approach to health surveillance.

Document elaborated by Telma Regina Marques Pinto Carvalhanas, Ana Lucia Frugis Yu, march 2023, Sao Paulo, Brazil.

Meningitis surveillance

BRIEF HISTORY OF THE DISEASE

Meningitis is an inflammation of the meninges, the membranes that surround the brain and spinal cord, and the viral and bacterial causes are the most important for public health, due to their potential to produce outbreaks and trigger serious clinical conditions, as well as the need for medical care as soon as possible, when symptoms are suspected.

Not all meningitis is contagious or transmissible. However, people of any age can contract the disease, with children under 5 years old being the most affected.[1,2]

The first meningitis cases in Brazil were registered, in 1906, in Portuguese immigrants coming from Madeira Island. Autopsies revealed the presence of meningococcus (*Neisseria meningitidis*), the main bacterium causing the disease. During the 20th century, the country experienced three outbreaks of meningitis - 1923, 1945 and 1970, and the latter, the largest of them, has infected several people with meningococcal serotypes C and A.[3] In 1999, with the introduction of the Hib vaccine in the official calendar, there was a reduction of 90% in the number of cases caused by this pathogen. This demonstrates the importance of adequate surveillance and diagnosis to observe the real impact of the vaccine and the epidemiological variations of the various pathogens that cause the disease.

In Brazil, the surveillance is based on the compulsory notification of suspected cases in the public and private health systems. Since the early 1990s, the Sistema de Informação de Agravos de Notificação - SINAN (Information System for Notifiable Diseases) has received epidemiological information on meningitis. This is critical for the prompt detection of epidemics and for determining the local disease burden, as well as for the rapid implementation of appropriate prevention and control strategies.[4,5]

ETIOLOGIC AGENT

According to the Ministry of Health's epidemiological surveillance guide,[2] the main etiological agent of meningitis is the *Neisseria meningitidis* bacterium, belonging to the *Neisseriaceae* family. Due to the antigenic composition of the polysaccharide capsule, meningococcus is classified into 12 different serogroups: A, B, C, E, H, I, K, L, W, X, Y and Z. The most prevalent are serogroups A, B, C, Y, W and X, and therefore cause possible epidemics and are responsible for Meningococcal Disease (MD).

Other etiological agents, such as bacteria (*Haemophilus influenzae* b - Hib, pneumococcus), viruses, protozoa, helminths, and fungi can cause meningitis, but in smaller numbers, like fungi, or be less lethal, like viruses, which have significant incidence but low lethality rates.[2,5-8] Although often caused by microorganisms, meningitis can also originate from inflammatory processes, such as cancer (metastasis to the meninges), lupus, reaction to some drugs, head trauma and brain surgeries.[2]

TRANSMISSION MODE

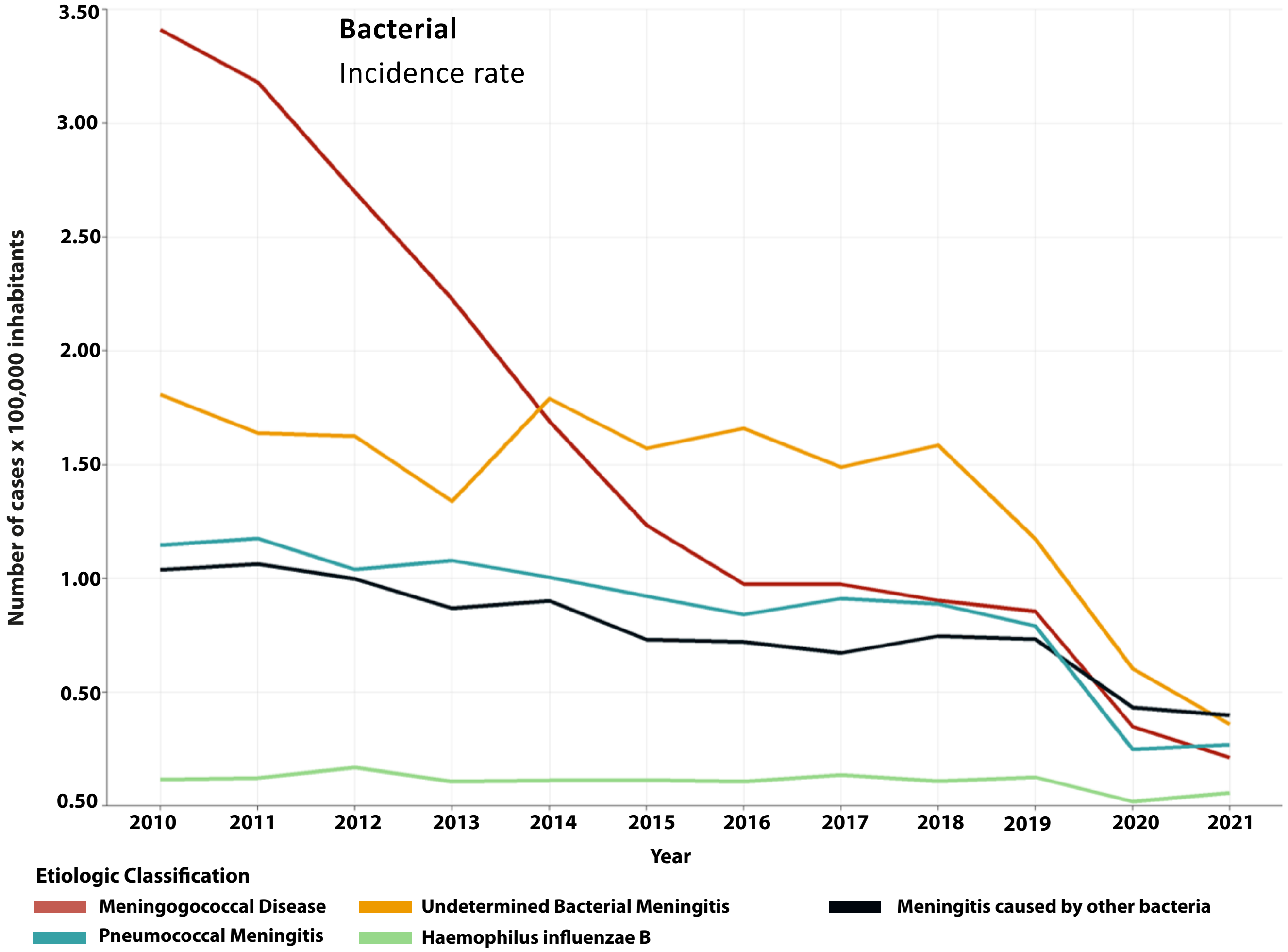
Transmission occurs by direct person-to-person contact, through respiratory secretions of infected, asymptomatic, or ill individuals. While there is a possibility of transmission through fomites (objects or substances contaminated by infectious agents), this form is not considered important.

EPIDEMIOLOGICAL SITUATION

Among the major advancements observed, we can highlight the molecular surveillance of meningitis, which allows the characterization of the etiological agent and the epidemiological monitoring of circulating strains, enabling the strengthening of control and prevention actions. The process of incorporating, validating, and decentralizing the real-time PCR (polymerase chain reaction) technique allowed a progressive reduction on the incidence of non-determined bacterial meningitis throughout the state of São Paulo (Graph 1).

Also, regarding the success in combating meningitis, the experiences related to the reduction of cases by *Haemophilus influenzae b*, from 1999 on, with the introduction of the conjugated vaccine against serotype b hemophilus are noteworthy. With this measure, the Hib incidence rate in under-5s has dropped to the level of less than one case per 100,000 population-year, remaining low in the period 2010 to 2021, with less than 0.100 cases/100,000 population-year (Graph 2).

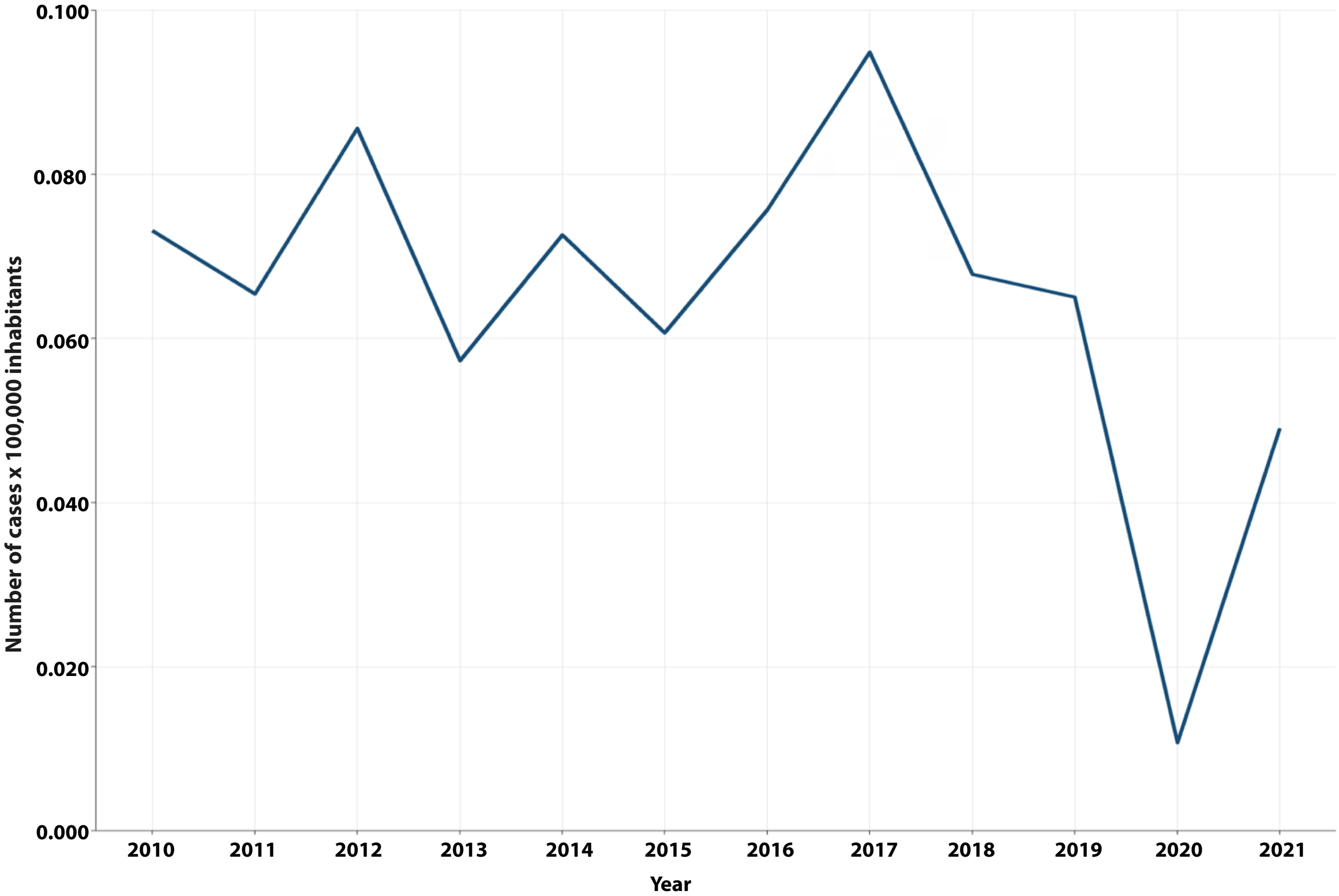
Graph 1. Bacterial meningitis: incidence rate per 100,000 person-years, according to etiology. SSP, 2010 a 2021.



Source: SINAN NET. Data collected in June/2022. *Data subject to change.

Added to this the cases of meningococcal disease, since 2010, with the introduction of the conjugate vaccine against meningococcus C (Graph 3). Similarly, after the inclusion of the 10-valent pneumococcal vaccine (conjugate) for children under 2 years of age in the national vaccination calendar, lower rates of meningitis due to this specific agent (pneumococcus) were observed. In recent years, the incidence of meningococcal disease in this age group was approximately double in serogroup B compared to serogroup C, 3.9 serogroup B cases/100,000 population-years versus 2.1 serogroup C cases/100,000 population-years.

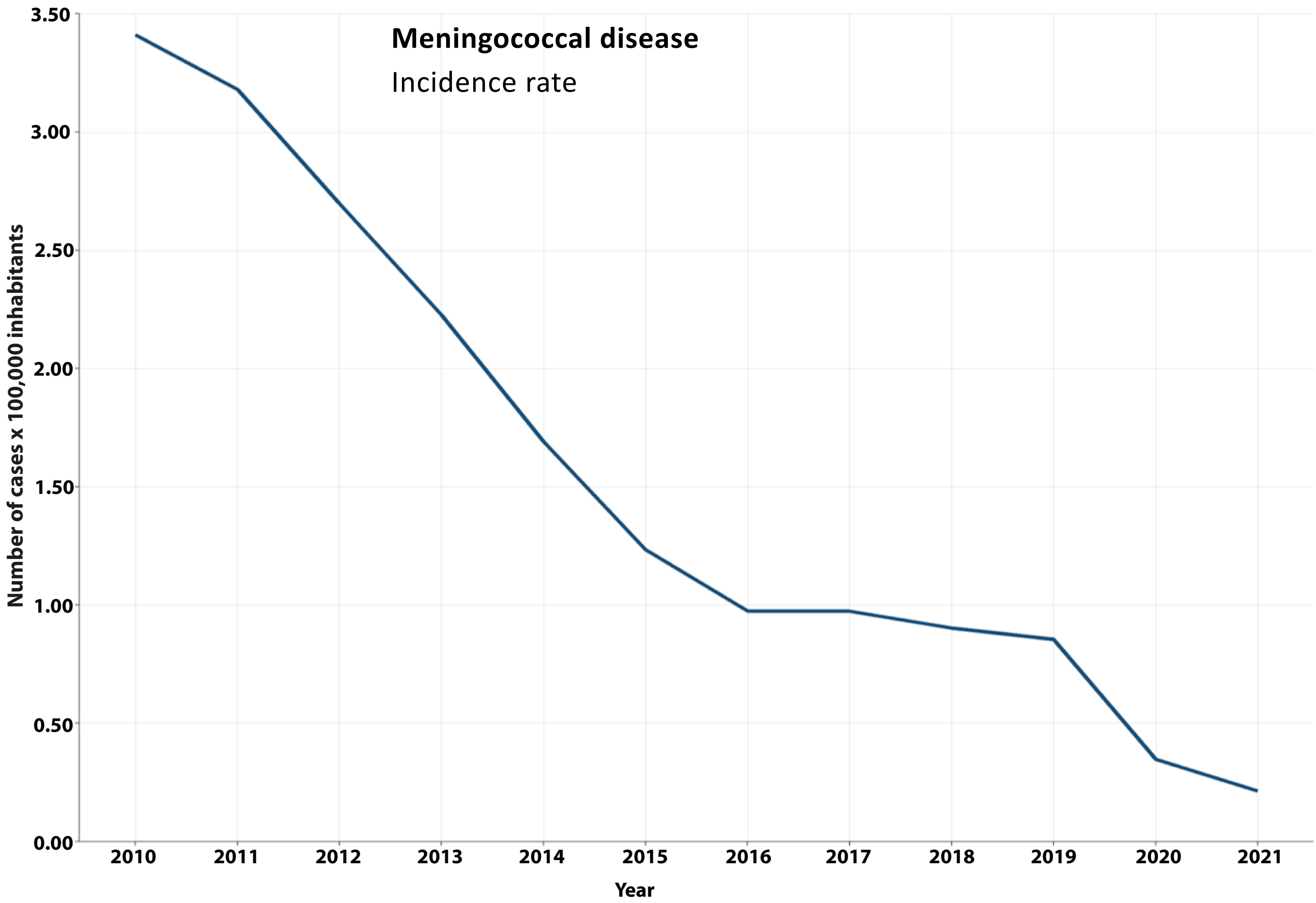
Graph 2. Meningitis caused by *H. influenzae b* in children under 5 years of age, incidence rate per 100,000 population-year. SSP, 2010 to 2021.*



Source: SINAN NET. Data collected in June/2022. *Data subject to change.

The last decade in the state of São Paulo has seen an increase in notification, clinical management, and adequate treatment of the disease, as well as the optimization of etiological diagnosis for bacterial, viral, parasitic, and fungal meningitis. This initiative was taken not only to better understand the epidemiological behavior of the agents that cause the disease in order to implement prevention and control measures, but also to reduce morbidity, mortality, and eventual sequelae.

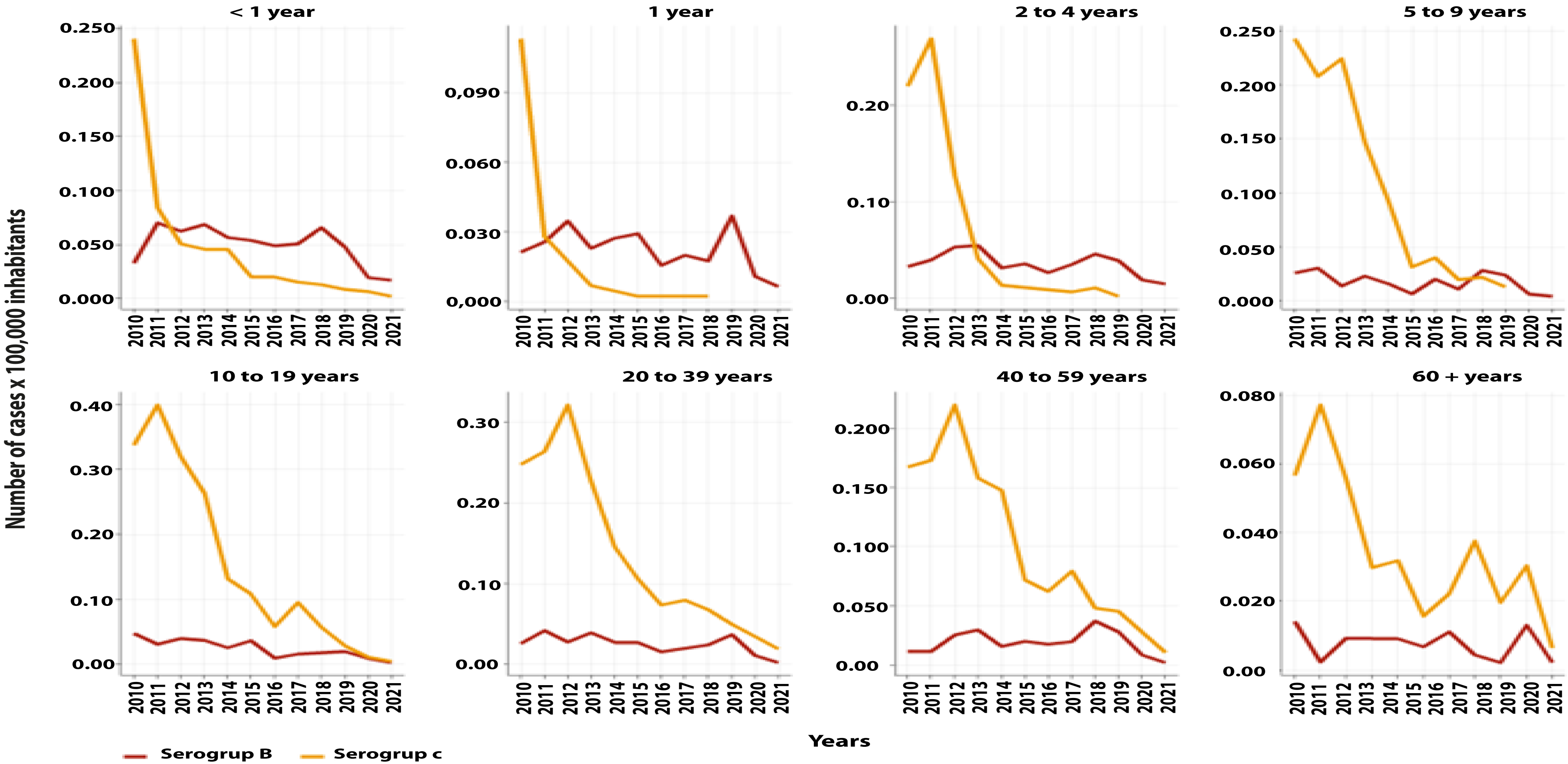
Graph 3. Meningitis due to N. meningitidis, incidence rate per 100,000 person-year. SSP, 2010 a 2021.*



Source: SINAN NET. Data collected in June/2022. *Data subject to change.

The current challenge is the occurrence of serogroup B meningococcal disease cases with incidence higher than that of serogroup C among children under 1 year, 1 year, 2 to 4 years and 5 to 9 years (Figure 1, top panels). In the state, for all other age groups the incidence of serogroup C is still higher than that of serogroup B (Figure 1, lower panels). Therefore, it is necessary to establish updated guidelines for the prevention and control of MD, including the introduction of meningococcal B vaccine in the national vaccine calendar, as well as to prevent or mitigate the occurrence of outbreaks, hospitalizations, sequelae, and mortalities.

Figure 1. Incidence rate per 100,000 population-year of meningococcal disease (meningitis due to N. meningitidis) by serogroup and age group. SSP, 2010 to 2021.*



Source: SINAN NET. Data collected in June/2022. *Data subject to change.

Document elaborated by Bernadete de Lourdes Liphaus, Ana Lucia Frugis Yu, Telma Regina Marques Pinto Carvalhanas, march 2023, Sao Paulo, Brazil.

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Pertussis surveillance: "22 years of sentinel surveillance"

BRIEF HISTORY OF THE DISEASE

Pertussis is an acute infectious disease that affects the respiratory tract (trachea and bronchi), characterized by non-productive cough paroxysms.[1,2] It is universally distributed, highly contagious and affects people of all age groups. It is more severe in infants, especially in the first six months of life, and may result in a high number of complications and even death.[1,3]

The DDTR (Division of Respiratory Tract Diseases) implemented a surveillance system for pertussis based on sentinel units in 2000.[4] The main objective of this system is the adequate triage of cases based on the definition of a suspected case and laboratorial confirmation of the disease through the appropriate collection of nasopharyngeal secretions for the culture.[4,5] Consequently, surveillance structured in the sentinel units' model has enabled a better follow-up of pertussis tendencies, providing a more assertive exclusion of other *pertussis* syndromes.[4] The Instituto Adolfo Lutz (IAL) is the reference laboratory for the disease in the state of São Paulo (SSP) and at national level.[5] In 2010, the diagnosis of pertussis was improved with the incorporation of a faster and more sensitive method of detection, RT-PCR (real-time polymerase chain reaction), a diagnostic tool adopted aiming to optimize results.[4]

Currently, there are 34 active sentinel units for disease surveillance, which are strategically distributed in the state of São Paulo. Today, the DDTR (Division of Respiratory Tract Diseases) promotes the evaluation of these units based on operational indicators and achieved targets.

ETIOLOGIC AGENT

The etiologic agent of pertussis is the *Bordetella pertussis* bacterium, a Gram-negative coccobacillus, aerobic, non-sporulated, immobile, and small (1 mm), with a capsule (pathogenic forms) and fimbriae.[1-3] Other *Bordetella* species may eventually cause illnesses that feature prolonged coughing, such as *B. parapertussis*, the *B. bronchiseptica* and *B. holmesii.*[3]

TRANSMISSION MODE

Transmission occurs by close contact with infected individuals, through respiratory droplets eliminated by speech, coughing or sneezing.[2] Indirect transmission may occur through freshly contaminated fomites;[1,3] however, this form of transmission is not frequent due to the agent's short-lived survival outside the host.[1]

In general, older children or adults are the ones responsible for introducing the disease into the family, and they may manifest the classic clinical condition or even milder, atypical forms.[4] The duration of classical pertussis is from 6 to 10 weeks;[4] and the incubation period from 5 to 21 days, with an average range between 7 and 10 days.[3]

PREVENTION AND CONTROL MEASURES

The main prevention measure against the disease is vaccination. However, infection or administration of the immunizer does not provide lifelong immunity.[2] The vaccine and chemoprophylaxis should be administered to family and other close contacts, as recommended by the Ministry of Health *Guia de vigilância em saúde* (Health surveillance guide).[1]

The Programa Nacional de Imunização - PNI/MS (National Immunization Program) calendar indicates the administration of the first dose at 2 months of age, the second at 4 months and the third at 6 months, using the combined vaccine DTP+ Hib (diphtheria, tetanus and pertussis + *Haemophilus influenzae* type b). Two DTP boosters are recommended: one at 15 months of age and another between 4 and 6 years, 11 months and 29 days.

Since 2001, pertussis is a compulsory notification disease at national level. Every suspected case should be registered in Sinan.[4]

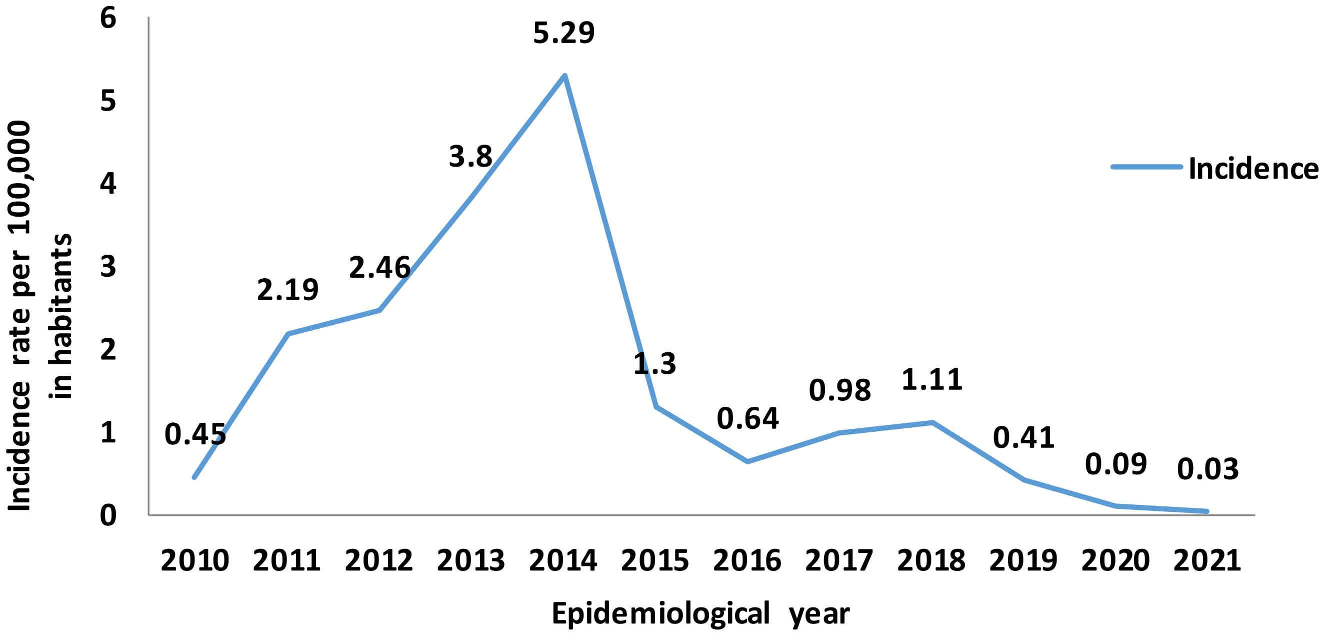
In the second half of 2014, the acellular pertussis vaccine for pregnant women (DTPa) was included in the PNI/MS, aiming to protect children under 2 months of age. This immunization should be applied, at each pregnancy, after the 20th week.[1] It is also recommended that all health workers receive a dose of DTPa, with reinforcement every ten years.[1]

EPIDEMIOLOGICAL SITUATION

Pertussis is endemic throughout the world, occurring most frequently in summer and autumn.[3] According to the epidemiological behavior of the disease, hyperendemic cycles may occur every three to five years, followed by a decline in the number of cases.[4]

In the historical series of confirmed cases of pertussis in São Paulo, an increase in its incidence in the state can be observed from 2010, reaching the highest rates in 2014, followed by a significant decrease in 2015 (Graph 1). The years 2020 and 2021 were marked by the public health emergency of Covid-19, which impacted the notifications of infectious diseases such as pertussis. It can be assumed that social distancing and other sanitary measures aimed at pandemic control have reduced the spread of respiratory droplet-borne diseases.

Graph 1. Incidence rate (100,000 person-year) of confirmed pertussis cases. SSP, 2010 to 2021.*

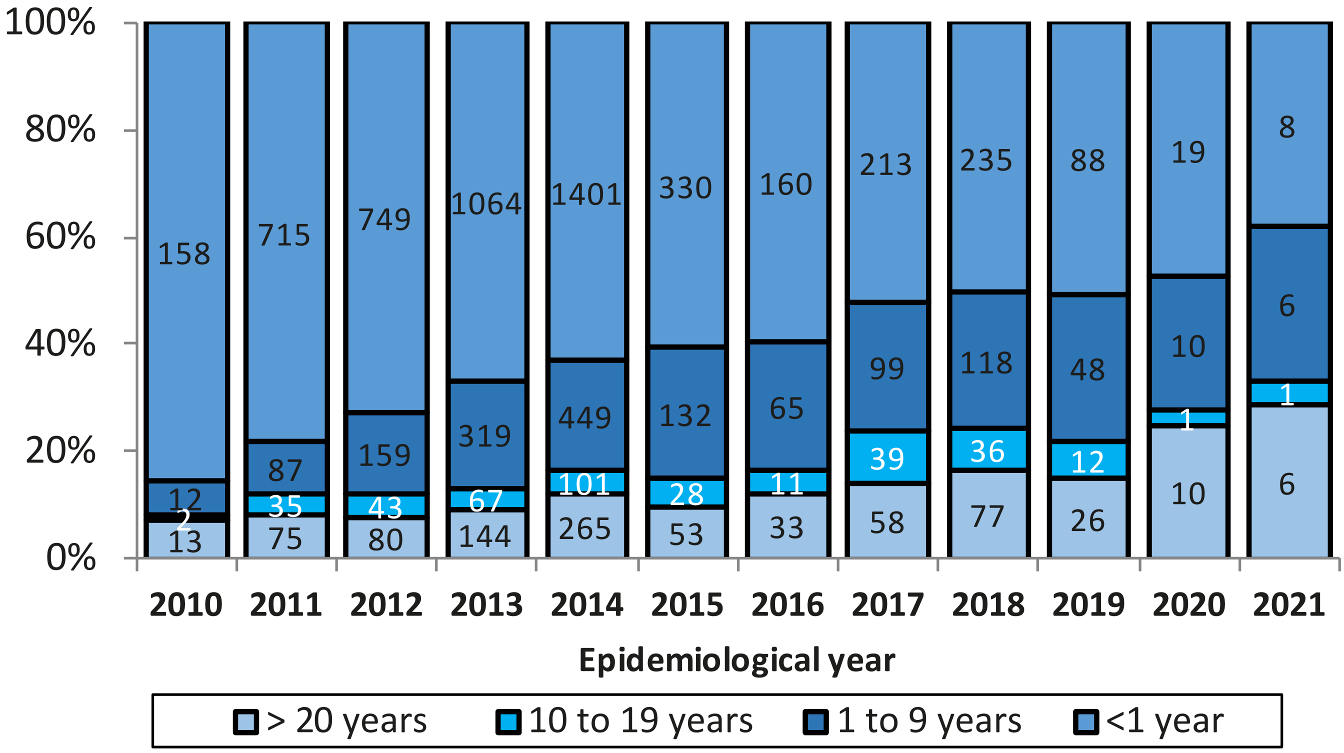


Source: SINAN NET. Data collected in June/2022. *Data subject to change.

Stratifying the cases by age group, the majority was found in children under 1 year of age (Graph 2), in agreement with the literature.[1,3]

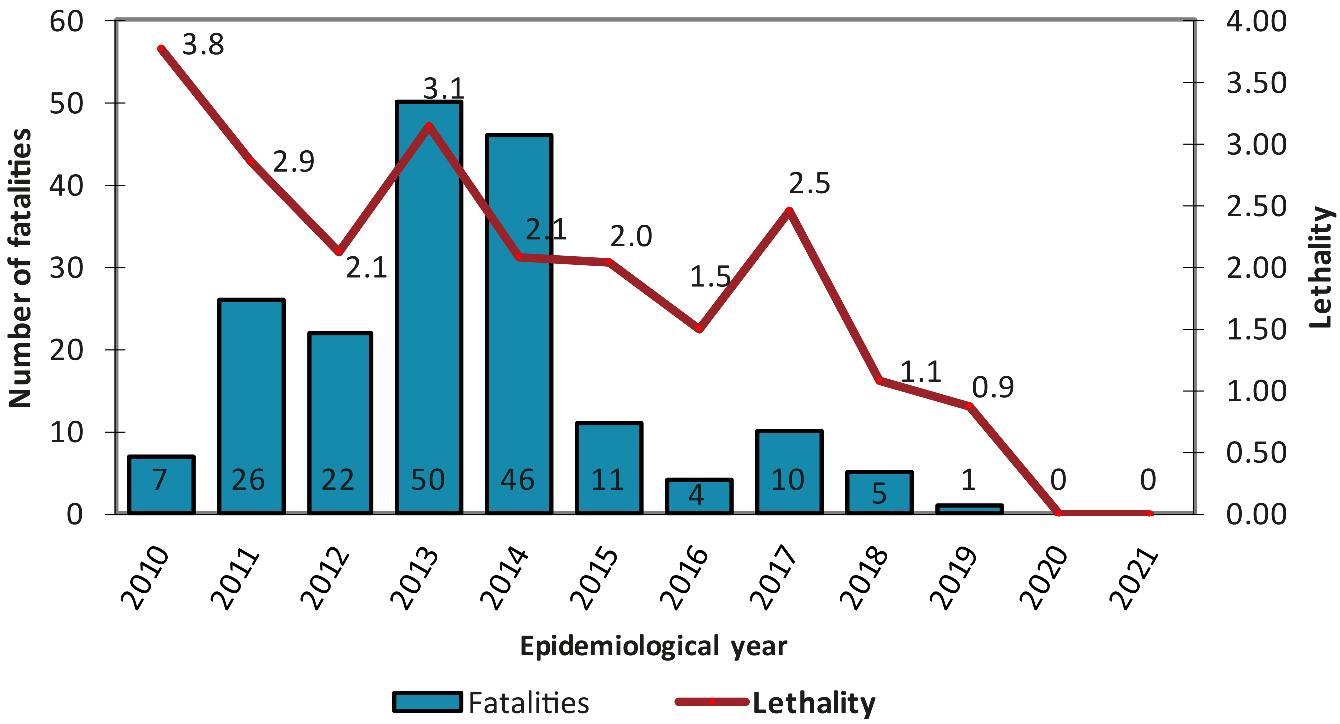
The epidemiological data indicate that the number of deaths from the disease has decreased since 2014, when compared to the first four years of the series (Graph 3). However, the lethality presented a variation in the analyzed period.

Graph 2. Percent distribution of confirmed cases of pertussis by age group. SSP, 2010 to 2021.*



Source: SINAN NET. Data collected in June/2022. *Data subject to change.

Graph 3. Distribution of the pertussis number of deaths and lethality. SSP, 2010 to 2021.*



Source: SINAN NET. Data collected in June/2022. *Data subject to change.

Document elaborated by Marcela Rodrigues da Silva, Angela Tiemi Tanamachi, Ana Lucia Frugis Yu, Telma Regina Marques Pinto Carvalhanas, march 2023, Sao Paulo, Brazil.

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Diphtheria surveillance

BRIEF HISTORY OF THE DISEASE

Diphtheria is an acute toxic-infectious, immuno-preventable and potentially lethal disease that frequently colonizes the tonsils, pharynx, larynx, nose and occasionally other mucous membranes and skin. It is characterized by typical pseudomembranous plaques.[1,2]

In some countries in Asia, the South Pacific, the Middle East, and Eastern Europe, as well as in Haiti and the Dominican Republic in the Caribbean, diphtheria is considered endemic. Since 2016, outbreaks of the disease have occurred in Indonesia, Bangladesh, Myanmar, and Vietnam; Venezuela and Haiti; South Africa and Yemen.[3]

After the advent of the triple bacterial vaccine (DTP), the number of diphtheria cases became very rare in Brazil.[1] There was, however, a significant outbreak in the state of Maranhão in 2010, with 29 cases and 3 deaths.[4]

In 2021, four South American countries confirmed 38 cases of the disease, and 16 of these cases died: Brazil (1 case), Dominican Republic (18 cases, with 12 deaths), Haiti (18 cases, 3 deaths), and Colombia (1 fatal case). The Brazilian case was confirmed by laboratory criteria, with isolation of *Corynebacterium diphtheriae* by culture.[5]

In the state of São Paulo (SSP), between 2010 and 2021, 140 suspected cases of diphtheria were reported. Of this total, 8 (5.7%) were confirmed and 1 death was reported (2013). The last confirmed case in São Paulo occurred in 2019.[6]

ETIOLOGIC AGENT

The etiologic agent of diphtheria is the bacterium *C. diphtheriae,* Gram-positive, nonsporulating bacillus with claviform structures. It can produce an exotoxin of protein origin, diphtheria toxin, which is its main virulence factor.[1,7]

TRANSMISSION MODE

It occurs through direct contact between a susceptible individual and a sick person or a person carrying the bacteria, through droplets of respiratory secretion, eliminated by coughing, sneezing, or talking. In rare cases, contamination by fomites[1] can occur. In general, the incubation period is between 2 and 5 days, with a variation of 1 to 10 days.[7]

PREVENTION AND CONTROL MEASURES

The main prevention measure against diphtheria is vaccination.[7] High vaccination coverage reduces morbidity and mortality and decreases the number of persons with the disease.[1]

In the vaccination schedule of the National Immunization Program of the Ministry of Health (PNI/MS), the first dose against diphtheria is applied at 2 months of age, the second at 4 months, and the third at 6 months, using the combined vaccine DTP+ Hib (diphtheria, tetanus, and pertussis + *Haemophilus influenzae* type b). The following vaccine boosters are recommended with the DT (diphtheria + tetanus): the first should be applied within 6 to 12 months after the third dose; the second, between 4 and 6 years of age; and a booster every ten years. Properly immunized individuals neutralize the toxin produced by the diphtheria bacillus, which is responsible for the clinical manifestations of the disease.[1,8-12]

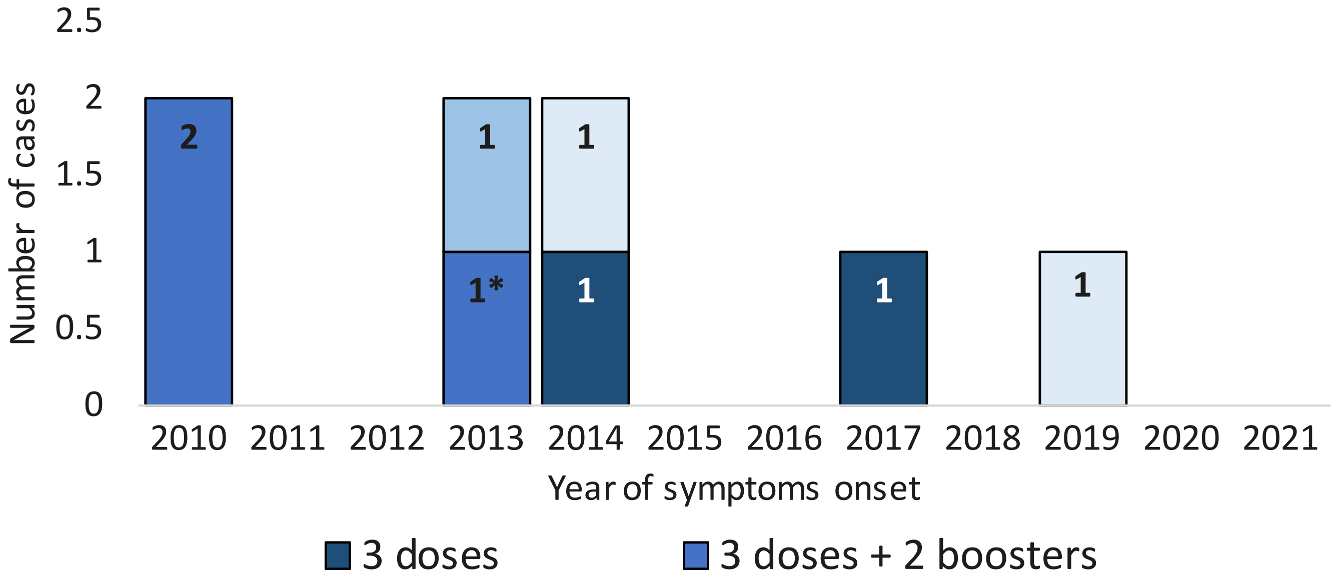
Diphtheria is a compulsory notification disease throughout the country, and any suspected case must be registered in Sinan[1,2] (The Information System of Notifiable Diseases). When a case is suspected, the main therapeutic measure is anti-diphtheria serum (SAD), which, however, has no action on the toxin impregnated in the tissue. The use of antibiotic therapy is an auxiliary therapeutic measure.[2]

Despite adequate treatment, complications (myocarditis, neuritis, and nephropathy) can occur; and approximately one in ten people who acquire diphtheria develops into death.[8] The disease does not provide permanent immunity.[2]

EPIDEMIOLOGICAL SITUATION

Between 2010 and 2021, eight cases of diphtheria were confirmed in the SSP (Graph 1). Regarding the vaccination status, three of these cases had three doses and two boosters; two cases had three doses; one case had no vaccination; and two had no information.[6]

Graph 1. Number of confirmed diphtheria cases according to vaccination schedule. SSP, 2010 to 2021.*,**



Source: SINAN NET. Data collected in June/2022. *Death. **Data subject to change.

Document elaborated by Marcela Rodrigues da Silva, Angela Tiemi Tanamachi, Ana Lucia Frugis Yu, Telma Regina Marques Pinto Carvalhanas, march 2023, Sao Paulo, Brazil.

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Surveillance of measles, rubella and congenital rubella syndrome

BRIEF HISTORY OF THE DISEASE

In Brazil, the endemic circulation of the measles virus was interrupted in 2000, and the cases recorded from that year on were imported or imported-related. Since then, a record number of the disease occurred in the country in 2013 (220 cases), 2014 (876), and 2015 (214), with the highest concentration in the states of Ceará and Pernambuco. After this period, with the implementation of effective control measures, the circulation of the virus was interrupted in July 2015. Therefore, in September 2016, the one-year interruption of viral circulation in the country has allowed the Americas region to be declared the first in the world free of measles.

In 2016 and 2017 there were no confirmed disease cases in Brazil. However, in February 2018 the virus was reintroduced in the Brazilian territory, with 9,325 cases and 12 deaths reported. That year, most of the confirmed cases were concentrated in the states of Amazonas, Roraima, and Pará. In February 2019, after 12 months of active circulation of the same viral genotype (D8) identified at the beginning of the previous year's outbreak, endemic transmission was re-established in the country, leading the country to lose its measles virus-free nation certification.

In the state of São Paulo (SSP) sporadic cases of the disease caused few and limited outbreaks between 2010 and 2018. In 2019, there was the beginning of active transmission of the measles virus in São Paulo territory, which recorded the highest number of cases in two decades, including deaths. In 2020, the containment and mitigation measures of the Covid-19 pandemic contributed to a major decrease in the number of cases and deaths from the disease in the state. Viral circulation in SSP continued and cases were confirmed in 2021.[1-7]

The epidemiological surveillance of rubella integrated with that of measles was implemented in 1992 in the SSP and in Brazil in 1999. The main objective of surveillance for rubella and congenital rubella syndrome (CRS) is to detect virus circulation in a proper and timely manner, given the risk of infection in pregnant women and the potential development of the syndrome.

With the proposal to eliminate both diseases, there was a massive investment in the decentralization of actions and in maintaining good vaccination coverage, which culminated, in 2008, with the vaccination of men and women aged between 20 and 39 years, in line with the objective of the Pan American Health Organization (PAHO) to eliminate rubella and CRS from the Americas by

2010. Thus, from that year on, there was effective control of these diseases in the country, which was officially declared free of both diseases by the World Health Organization (WHO) in 2015. The last confirmed case of rubella in SSP occurred in 2008 and of CRS in 2009.[4,8]

ETIOLOGIC AGENT

Measles is an acute, potentially serious, and highly transmissible viral disease caused by an RNA virus belonging to the genus *Morbillivirus*, family *Paramyxoviridae.*[1]

TRANSMISSION MODE

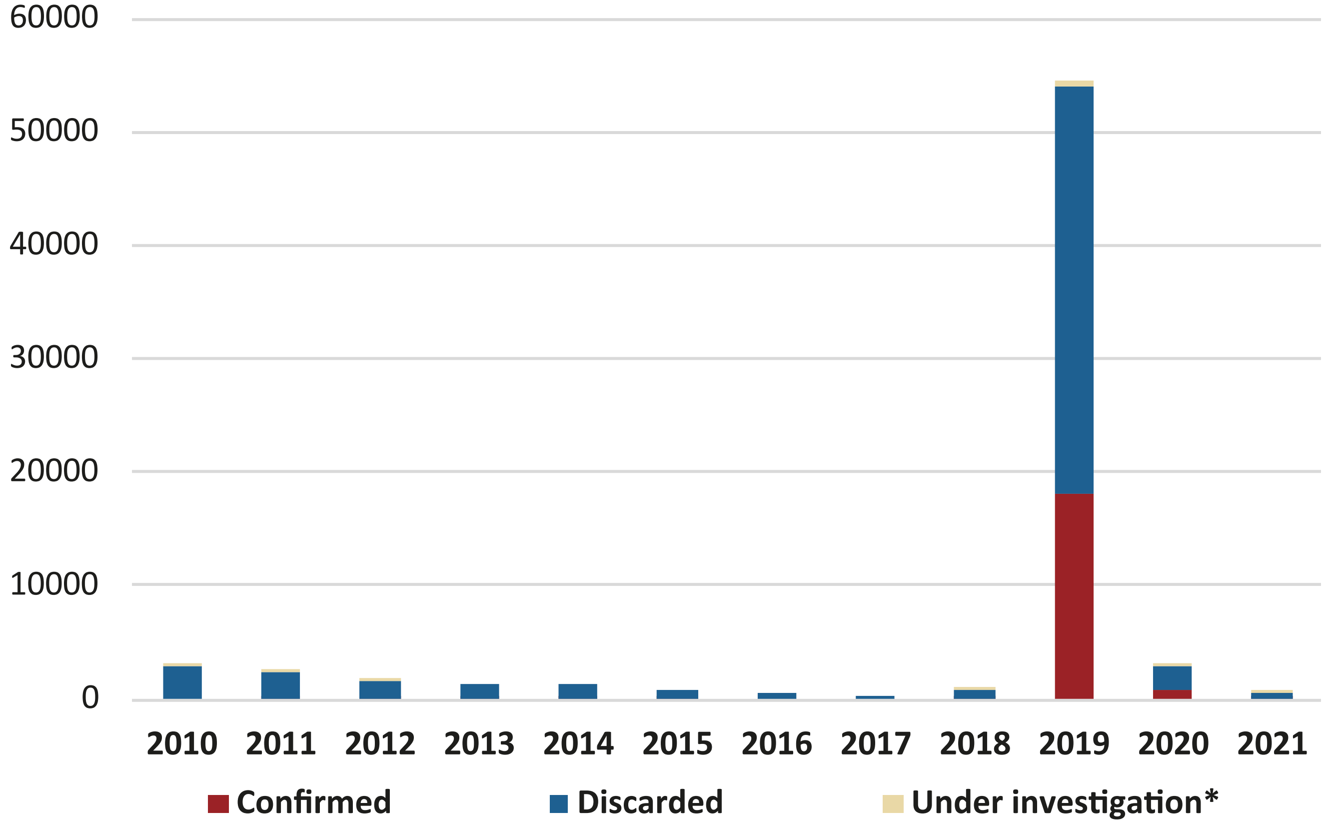
The transmission is direct, through nasopharyngeal secretions expelled by the patient when coughing, sneezing, speaking, or breathing. It is also described as being transmitted by the dispersion of aerosols with viral particles in the air in closed environments, such as schools, day care centers, clinics, and transportation.[1]

EPIDEMIOLOGICAL SITUATION

Between 2010 and 2018, 49 measles cases were confirmed, identified as imported or imported-related, which occurred on an individual basis or in limited outbreaks with small numbers of cases. Throughout the studied period, no cases were recorded in the years 2010, 2016, and 2017. Sustained circulation of the virus began in 2019 in SSP, with 18,013 cases confirmed, with active transmission of the disease remaining in 2020 and 2021.

From the 879 confirmed cases in 2020, 85% (#749) occurred until April, when the sustained circulation of SARS-CoV-2 was established in the São Paulo territory, with increasing numbers of cases and deaths by Covid-19, illustrating the impact of the pandemic on measles surveillance. Graph 1 shows the number of disease cases per year, their final classification, and the closing criteria, also shown in Table 1, along with the incidence coefficient and the lethality.

Graph 1. Measles: number of reported cases per year and final classification, SSP, 2010-2021.**



Source: SINAN NET. Data collected in June/2022. *The cases under investigation are due to problems in the national Sinan return flow. **Data subject to change.

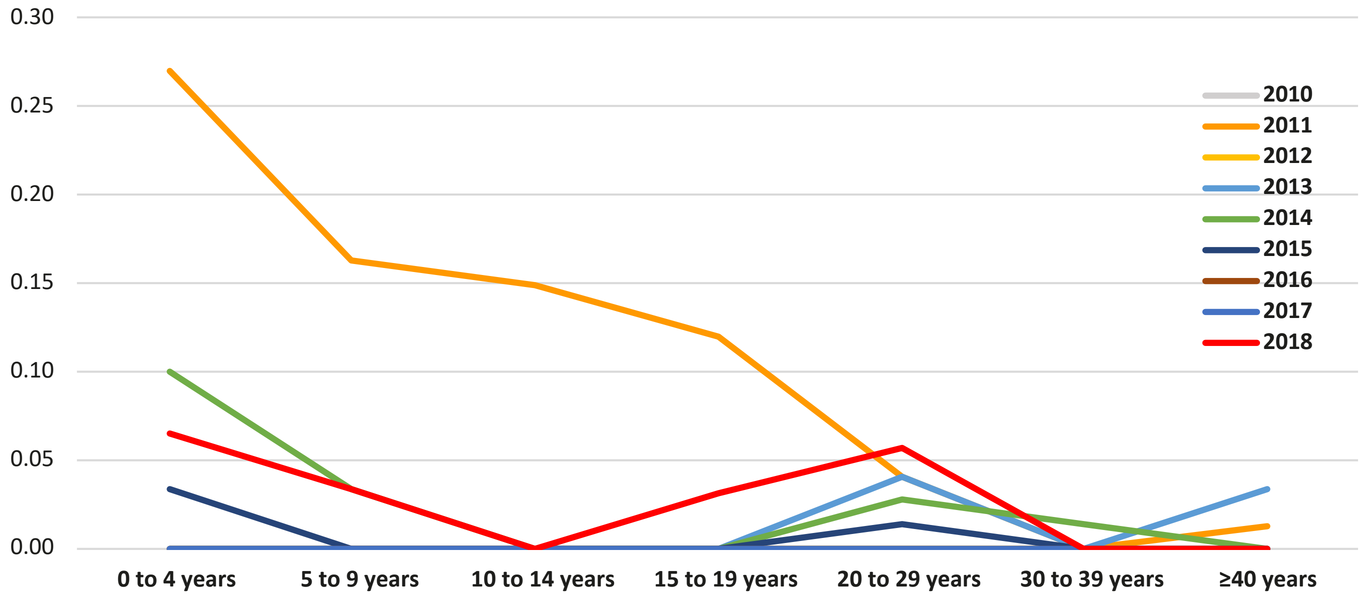
Table 1. Measles: number of cases, incidence and lethality coefficients by year, SSP, 2010-2021.*

YEAR	CASES	INCIDENCE	DEATHS	LETHALITY
2010	0	0.00	0	0
2011	27	0.07	0	0
2012	1	0.00	0	0
2013	5	0.01	0	0
2014	7	0.02	0	0
2015	2	0.00	0	0
2016	0	0.00	0	0
2017	0	0.00	0	0
2018	7	0.01	0	0
2019	18,013	40.65	18	0.1
2020	879	1.98	1	0.1
2021	9	0.02	0	0

Source: SINAN NET. Data collected in June/2022. *Data subject to change.

Evaluating the period before the 2019 epidemic (2010-2018), in this period was found that the highest incidence rates (No. of cases per 100,000 population-year) occurred between 0 and 4 years of age, followed by the age group 20 to 29 years, as noted in Graph 2.

Graph 2. Measles: incidence by age group and year (100,000 hab-year), SSP, 2010-2018.*



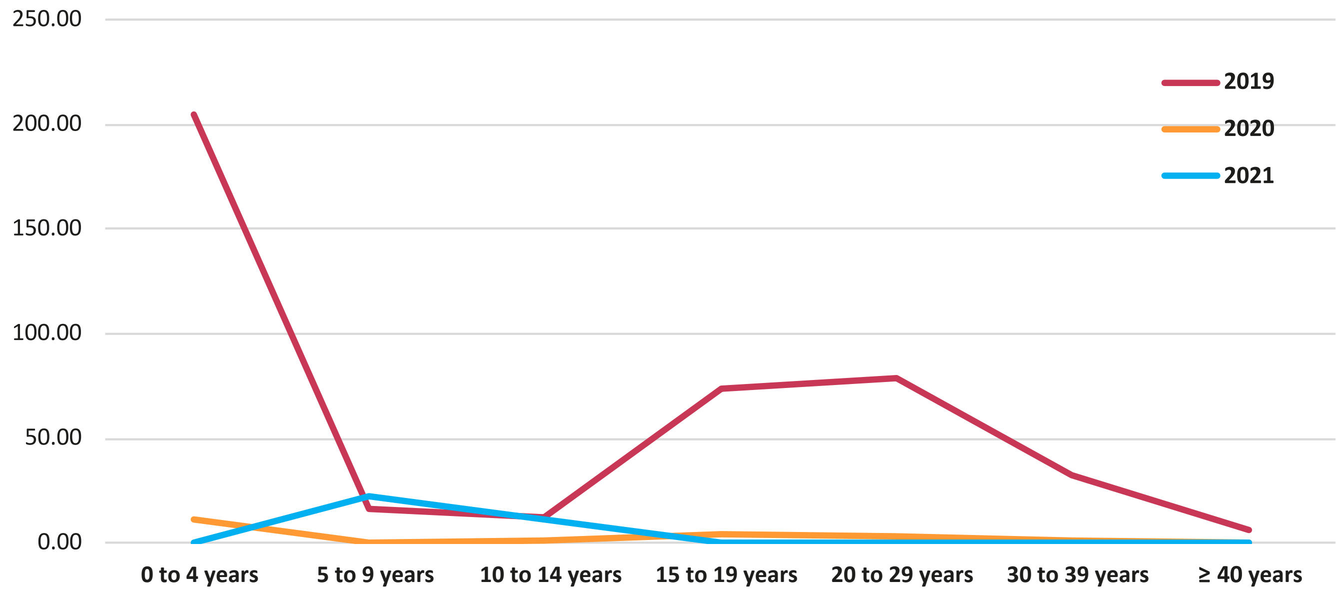
Source: SINAN NET. Data collected in June/2022. *Data subject to change.

Considering the period from 2019 to 2021, it was observed that in 2019 all age groups were affected, with the highest incidence rates occurring among those under 4 years of age, followed by those between 15 and 29 years. The impact of the Covid-19 pandemic in 2020 has caused this profile to remain at lower values. In 2021, the 5- to 9-year-old age group had the highest incidence rate (Graph 3).

Regarding rubella, there were no confirmed cases in the period. It was observed that starting in 2010 there was a decrease in suspected cases of the disease, with a slight rise in 2019, during the measles epidemic, and a further decrease in 2020 and 2021, resulting from the impact of the Covid-19 pandemic. The number of suspected rubella cases per year is shown in Graph 4.

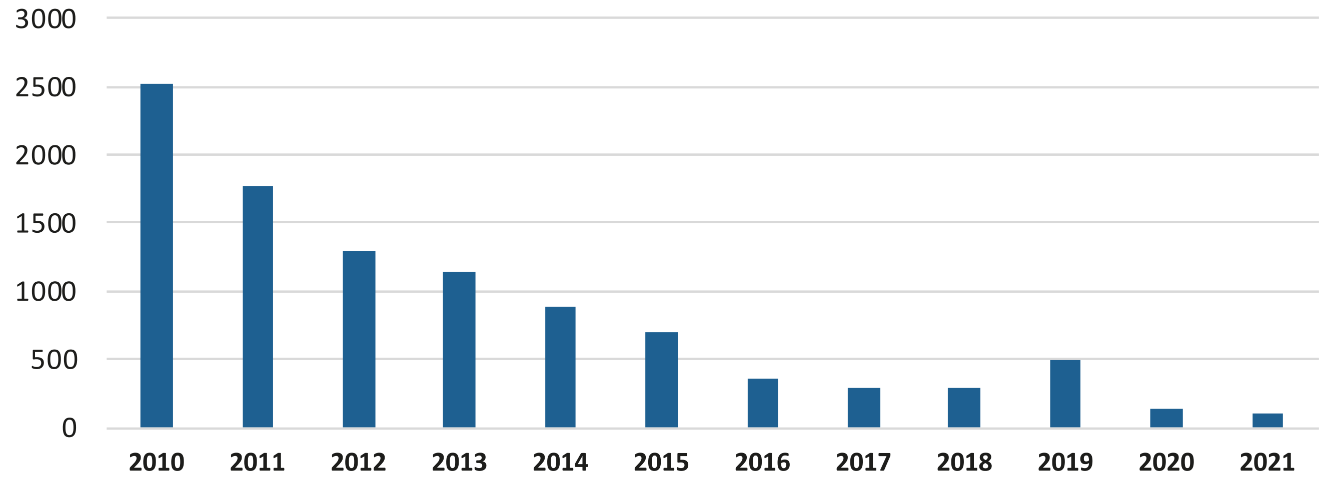
In the period from 2010 to 2021 there were no confirmed cases of congenital rubella syndrome. On the other hand, the number of suspected cases of CRS has decreased since 2013, increasing in 2021, as shown in Graph 5.

Graph 3. Measles: incidence by age group and year (100,000 hab-year), SSP, 2019-2021.*



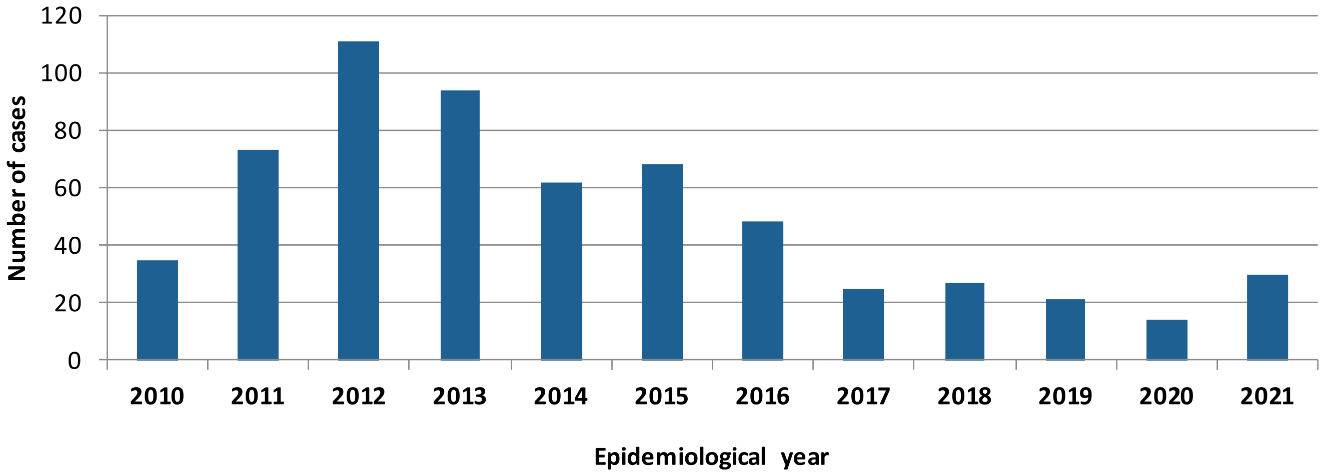
Source: SINAN NET. Data collected in June/2022. *Data subject to change.

Graph 4. Rubella: number of suspected cases per year, SSP, 2010-2021.*



Source: SINAN NET. Data collected in June/2022. *Data subject to change.

Graph 5. Congenital rubella syndrome (CRS): number of suspected cases per year, SSP, 2010-2021.*



Source: SINAN NET. Data collected in June/2022. *Data subject to change.

Vaccination is the most effective measure for the prevention, control, and elimination of measles and the sustainability of rubella elimination. The maintenance of high levels of immunity against the viruses of both diseases in the general population and of high-quality surveillance systems is critical to the interruption of circulation and sustainability of virus elimination. To achieve this, the vaccination coverage must be high (95% or more) and homogeneous in all cities, with two doses of the triple viral vaccine (measles, mumps, and rubella).

Document elaborated by Ana Lucia Frugis Yu, Juliana Akemi Guinoza Ando, Ana Paula Alves dos Santos, Telma Regina Marques Pinto Carvalhanas, march 2023, Sao Paulo, Brazil.

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Influenza: "20 years of Influenza-like illness sentinel surveillance"

INTRODUCTION

In the last 100 years, Brazil has faced six major influenza pandemics that helped organize and improve the national epidemiological surveillance system.[1] In 2000, the acute respiratory syndromes surveillance system was created to monitor the circulation of influenza viruses in the country, from a sentinel surveillance network of influenza syndrome. This system currently includes the network of sentinel units, surveillance of severe acute respiratory syndrome (SARS), deaths, and institutional outbreaks of influenza syndrome.

Universal SARS surveillance was initiated in 2009, after the World Health Organization (WHO) declared a public health emergency due to the occurrence of influenza A (H1N1) pdm09 in humans. This allowed us to identify the profile of severe cases and deaths from pandemic influenza, based on the clinical picture of SARS. The available data today comes from the Sistema de Informação de Vigilância Epidemiológica da Gripe Influenza - SIVEP-Gripe (Epidemiological Surveillance Information System of Influenza – SIVEP-Flu), managed by the Ministry of Health/Health Surveillance Department, in conjunction with the state and city health departments.[2]

BRIEF HISTORY OF THE DISEASE

Influenza, popularly known as the flu, is an acute febrile respiratory disease that occurs in annual outbreaks. In general, their epidemics and pandemics start suddenly and peak within 2 or 3 weeks, with a total duration of 5 to 8 weeks.[3] The impact of influenza epidemics reflects the interaction between viral antigenic variation, the level of immunity of the population to the circulating strains, and their degree of virulence.[4]

The virus infects the respiratory tract and has a variable clinical spectrum, and can cause common cold, pharyngitis, tracheobronchitis, and pneumonia.[5] The main upper airway symptoms are rhinorrhea, sore throat, hoarseness, and cough. Systemic symptoms associated with complications can also occur, such as malaise, chills, headache, and myalgia. The disease usually has spontaneous resolution within seven days, although cough, malaise, and fatigue may remain for a few weeks.[5]

Influenza affects people of all age groups, but the highest incidence of infection is seen among school-aged children.[6] Serious complications and deaths are most seen in children under 1 year and adults over 65 years of age,[7] and patients with chronic diseases have a higher risk of complications in all age groups.[3,4]

ETIOLOGIC AGENT

The influenza virus *Myxovirus influenzae* belongs to the *Orthomyxoviridae* family and has segmented single-stranded RNA.[4,8] Their classification into types A, B and C was based on the internal nucleoprotein antigen. Type A infects a wide variety of animal species, including humans, pigs, horses, marine animals, and birds. In humans the disease is moderate to severe. Influenza caused major epidemics, such as the one in 1918, when between 20 million and 50 million deaths occurred worldwide.[9] The influenza B virus causes mild epidemics, affecting only humans, especially children, while the influenza C virus has no expression in public health, because it is not an epidemic virus.[4]

TRANSMISSION MODE

These viruses are the only ones capable of causing recurrent annual epidemics, affecting almost all age groups in a short period of time. This is only possible due to the influenza's high genetic variability and adaptability.[4] Direct transmission (person-to-person) is the most common and occurs through droplets of the infected individual when they speak, sneeze, or cough. In addition, there is also indirect transmission through contact with surfaces contaminated with these respiratory droplets.

The disease incubation period is 1 to 4 days and transmissibility occurs mainly between the first 24 to 72 hours after the beginning of the disease. Immunosuppressed people and children can excrete the virus for weeks or months.[2,5]

EPIDEMIOLOGICAL SITUATION

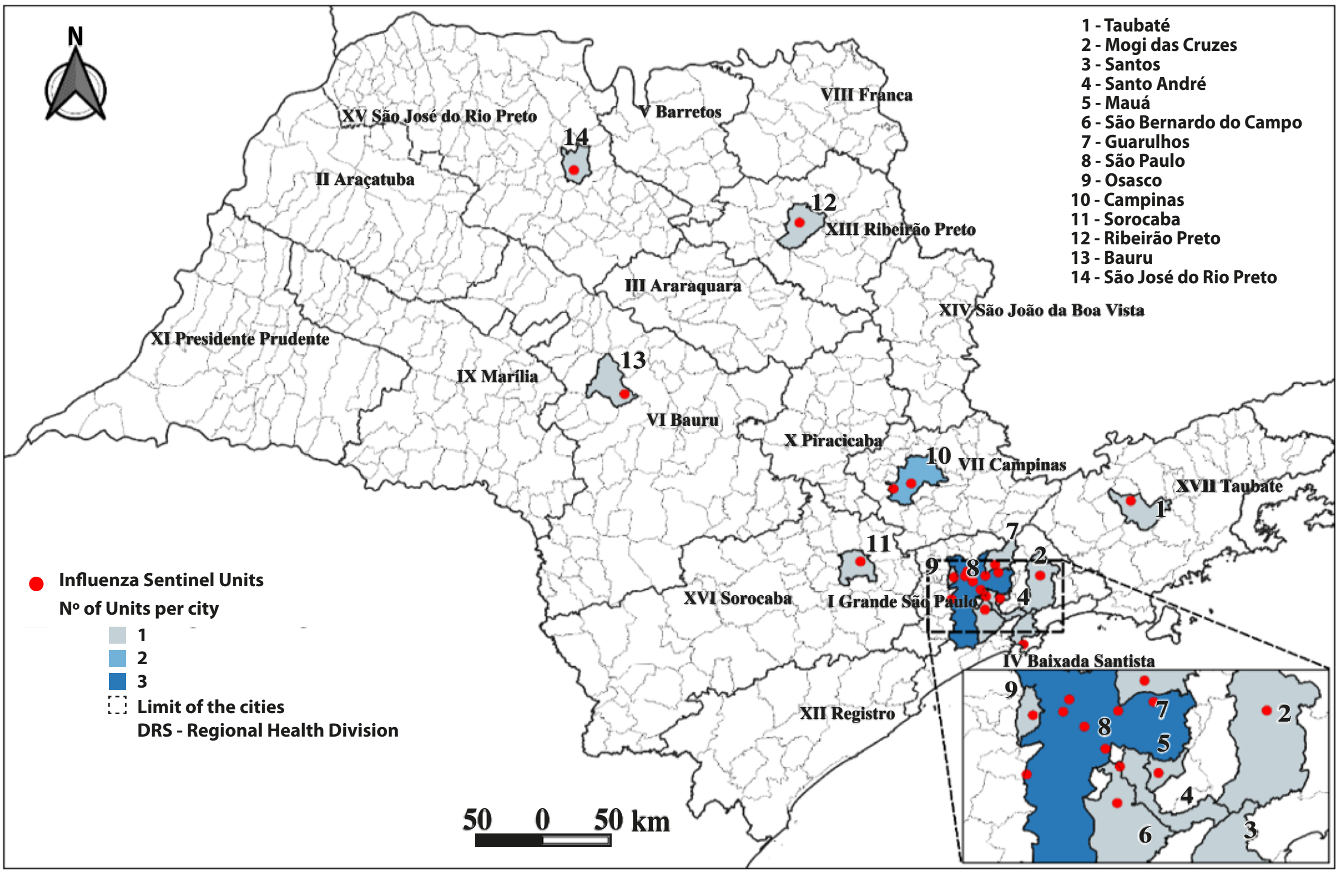
Regarding influenza surveillance, the pillars that make up the surveillance system for acute respiratory syndromes are covered below.

Network of sentinel units

Sentinel surveillance of influenza syndrome aims to strengthen the epidemiological surveillance of respiratory viruses by identifying the circulating viruses, according to their pathogenicity, their virulence in each seasonal period, the existence of unusual situations, or the occurrence of a new viral subtype. The isolation of the most prevalent viral specimens and their prompt submission to the Collaborating Center for the Americas (CDC - Atlanta/USA) and the WHO aims at the adequacy of the annual seasonal influenza vaccine recommendation in the Southern Hemisphere, as well as at monitoring the circulation of respiratory viruses. The following objectives are added: to provide timely and quality information for the planning and adjustment of treatment protocols and to establish the prevention and control measures related to influenza syndrome.

The Health Units must have characteristics of assistance for all age groups and, ideally, be 24-hour facilities (emergency and urgent care units, among others). The sentinel surveillance network of influenza syndrome in Brazil is composed of health units defined by the managers of the cities, states, and Federal District.[10] In São Paulo, this network is currently composed of 21 service units (Figure 1), distributed between the capital and the strategic macro-regions of the state, with the Instituto Adolfo Lutz (IAL/NIC - central and regional) as the reference laboratory for molecular analysis and characterization.

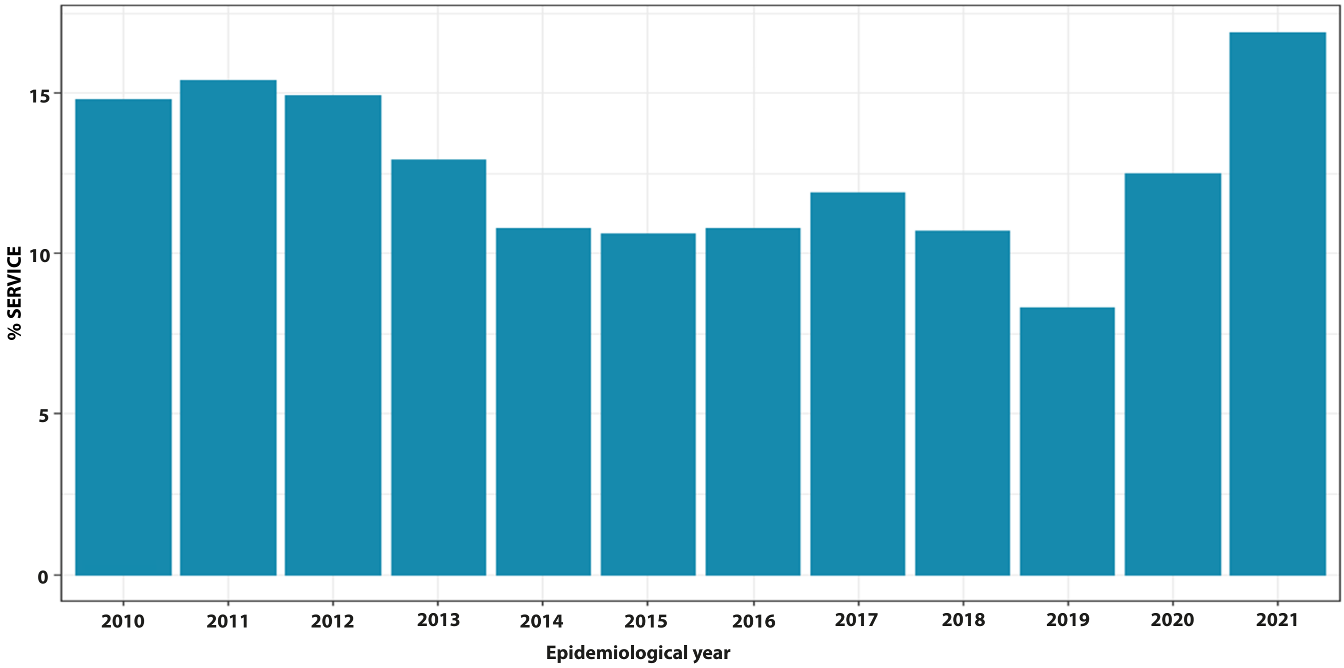
Figure 1. Distribution of influenza sentinel units in SSP, 2022.



Source: prepared by Division of Respiratory Tract Diseases/ESC/DCC/SHD-SP.

Graph 1 shows the percentage of flu cases seen in influenza sentinel units from 2010 to 2021. The year 2019 had the lowest percentage of attendances, while 2021 was above 15%.

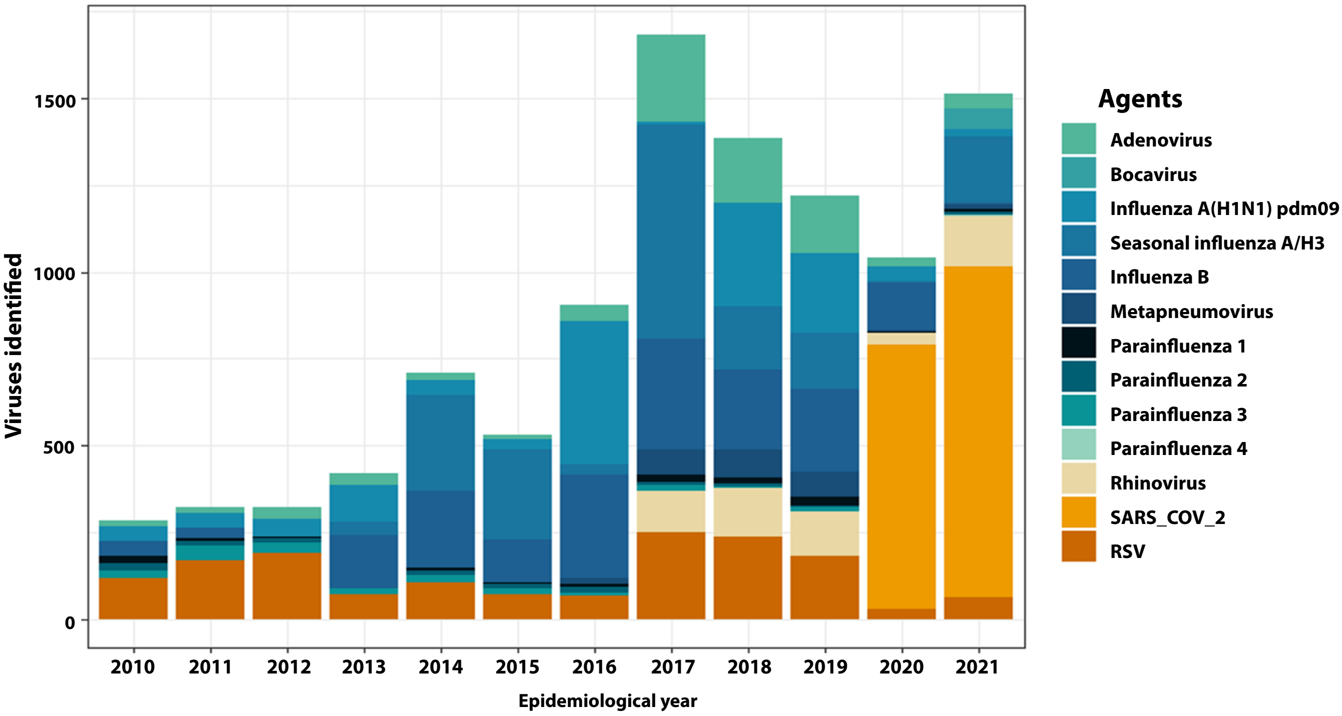
Graph 1. Percentage of influenza syndrome care in influenza sentinel units per epidemiological year, SSP, 2010 to 2021.*



Source: SIVEP-Gripe. Data consulted in June/2022. *Data subject to change.

The cases of influenza syndrome with weekly samples collected in the sentinel units follow the flows established by the surveillance of influenza and other respiratory viruses and are registered in SIVEP-Gripe(Flu). Since 2020, due to the pandemic scenario (Covid-19), cases of influenza syndrome seen in the state's Health Units and those of SARS are also tested for SARS-CoV-2 and respiratory syncytial virus (RSV) (Graph 2).

Graph 2. Distribution of respiratory viruses in influenza sentinel units in SSP, 2010-2021.*



Source: SIVEP-Gripe. Data consulted in June/2022. *Data subject to change.

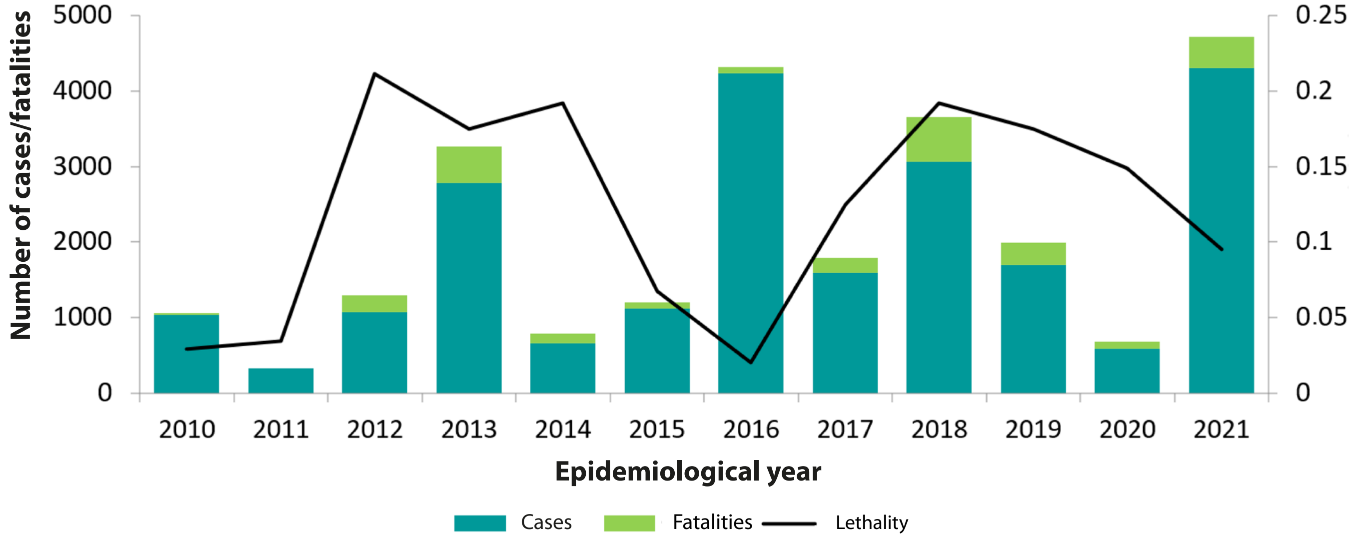
Severe acute respiratory syndrome

Since the 2009 pandemic of influenza A (H1N1) pdm09, epidemiological surveillance of the disease has had universal reporting of SARS of hospitalized cases and related deaths, as well as of Covid-19 and other respiratory viruses. This notification occurs, first, in the Information System of Notifiable Diseases - Sinan Influenza Web and, from 2019, in SIVEP-Gripe(Flu).

SARS surveillance is carried out in all hospitals in the country, public and private. The collection of clinical samples must occur on a universal basis, following the flows established for the surveillance of acute respiratory syndromes.

In Brazil, influenza seasonality generally begins in epidemiological week 13 (early April) and extends into the winter period, in epidemiological week 30 (early August). Analyzing the influenza SARS data from previous years, it is possible to observe an oscillation in the number of cases and deaths (Graph 3). The ones with the most cases were 2016, 2018, and 2021. It is important to note that there were changes to the SIVEP-Gripe(Flu) system and forms starting in 2013, which may have influenced the recording of cases during this transition. By 2020, with the emergence of the SARS-CoV-2 pandemic and due to the implementation of health measures such as social distancing, the influenza virus transmission may also have been impacted, with evidence of low viral activity.

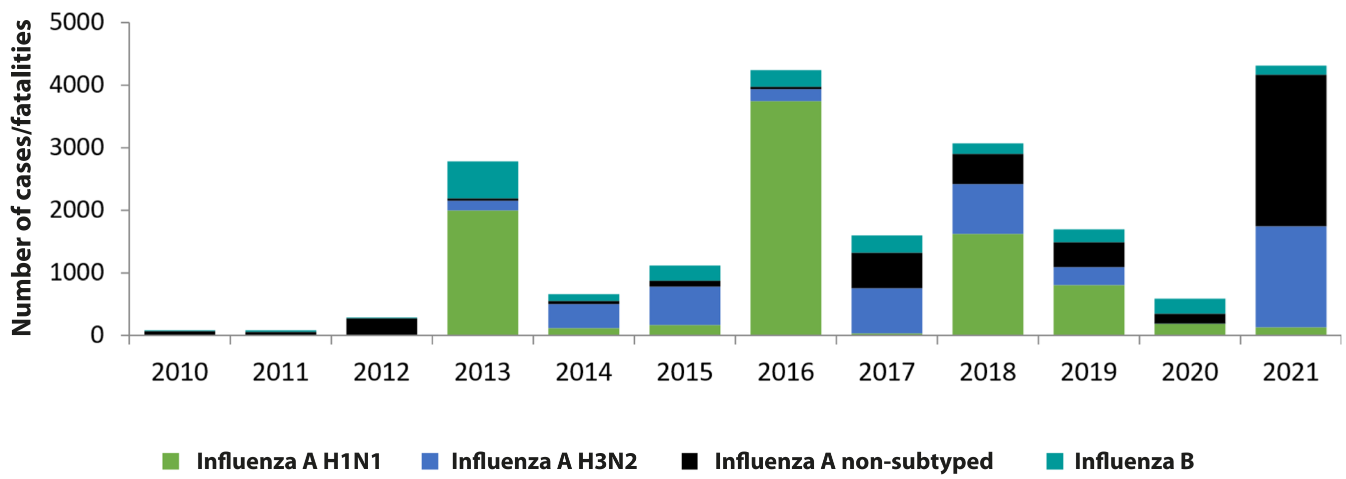
Graph 3. Number of confirmed cases and deaths and lethality of SARS Influenza. SSP, 2010 a 2021.*



Source: SIVEP-Gripe. Data consulted in June/2022. *Data subject to change.

Regarding viral subtypes, the cases recorded in 2013, 2016 and 2018 were mostly due to influenza A (H1N1) pdm09, and those recorded in 2015, 2017 and 2021 were caused by influenza A (H3N2) virus (Graph 4). The influenza B virus was circulating in all years, but with few related cases.

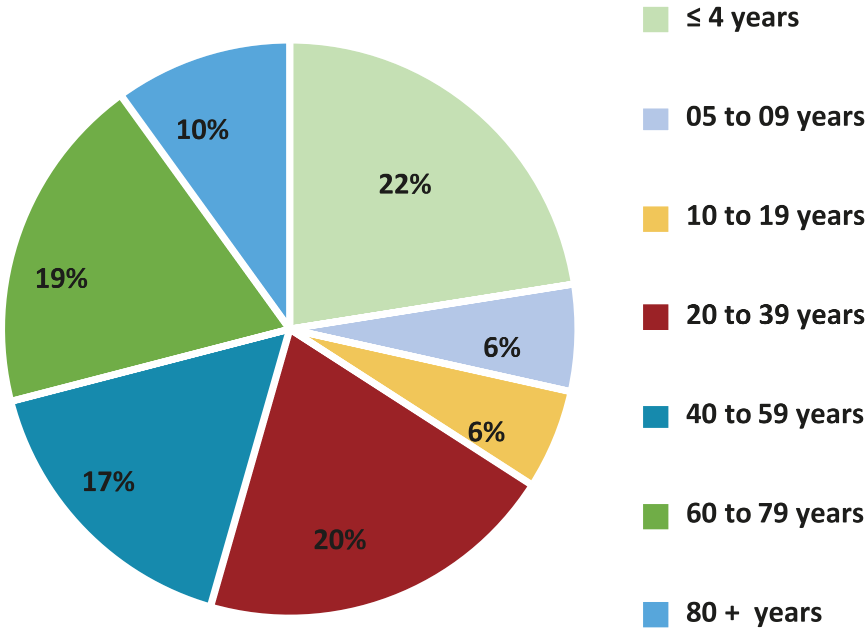
Graph 4. Number of confirmed cases of influenza SARS, according to type and/or viral subtype. SSP, 2010 a 2021.*



Source: SIVEP-Gripe. Data consulted in June/2022. *Data subject to change.

Graph 5 shows the age groups most affected by the disease: those under 4 years old (22%) and those over 60 (29%). In Brazil, the official recommendation for influenza vaccination has been directed to groups at higher risk of developing severe conditions, complications, and deaths attributed to the virus.

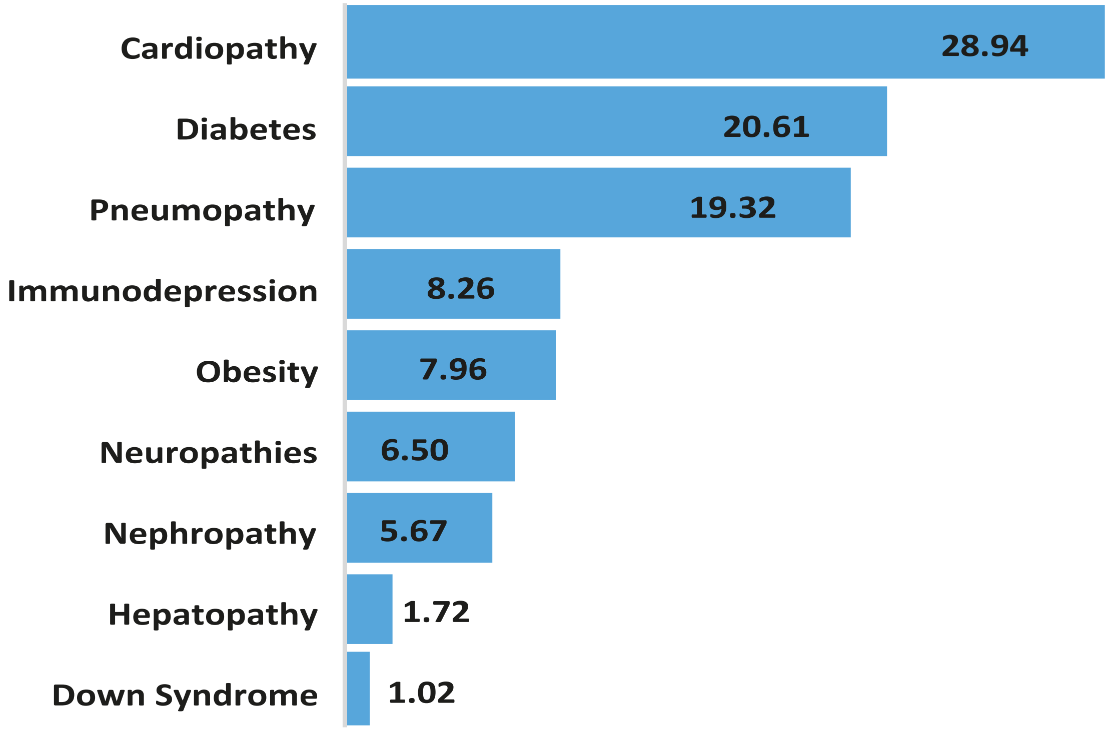
Graph 5. Percentage of confirmed SARS influenza cases by age group. SSP, 2010 a 2021.*



Source: SIVEP-Gripe. Data consulted in June/2022. *Data subject to change.

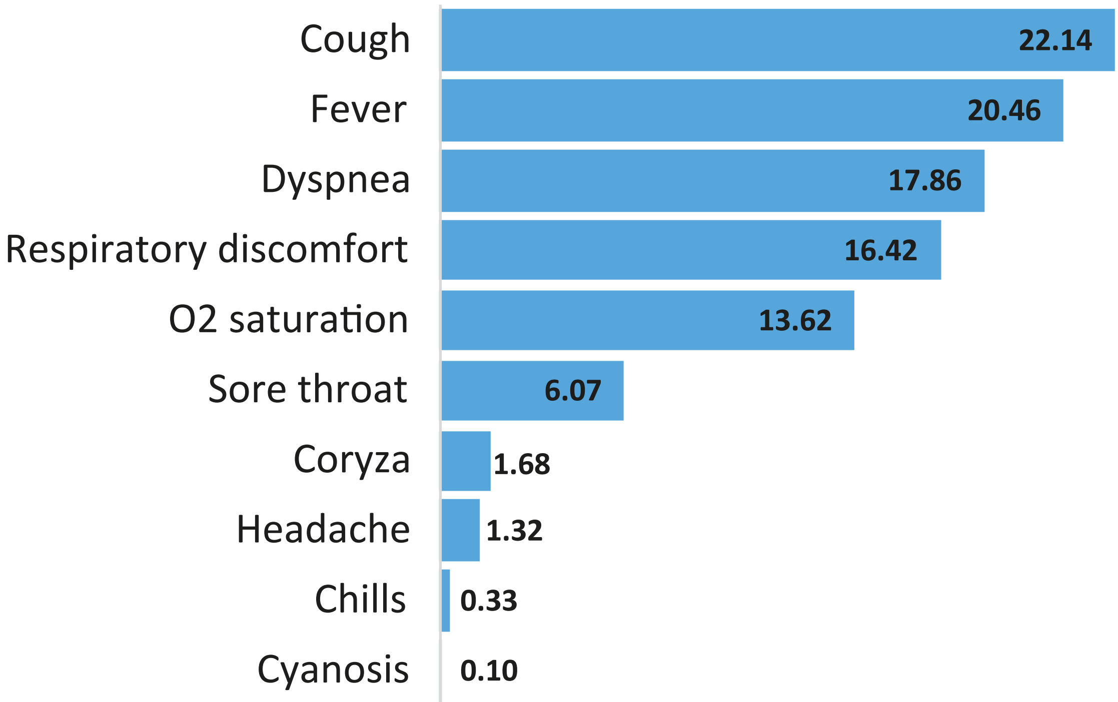
The main risk conditions (Graph 6) related to severe cases and deaths from influenza were in individuals with heart diseases (28.94%), diabetes (20.61%), and pneumopathies (19.32%), which is in agreement with the literature.[3,6,8,9] Among the most frequent signs and symptoms (Graph 7), the most severe cases have reported cough (22.14%), fever (20.46%), and dyspnea (17.86%). Although vaccination is the main tool for prevention and control of the disease,[4] specific antivirals are also of great importance. The oseltamivir phosphate is licensed in Brazil for the treatment of infection.[5]

Graph 6. Percentage distribution of risk conditions present in influenza SARS cases. SSP, 2010 to 2021.*



Source: SIVEP-Gripe. Data consulted in June/2022. *Data subject to change.

Graph 7. Proportion of signs and symptoms of influenza SARS cases, SSP, 2010 to 2021.*



Source: SIVEP-Gripe. Data consulted in June/2022. *Data subject to change.

When analyzing the spatial distribution of cases of SARS influenza, we notice a relevant concentration in the city of São Paulo former Capital ESG (Epidemiological Surveillance Group) and in the ESG Santo André and Osasco (Table 1). This is expected due to the large population in these areas

Table 1. Proportion of influenza SARS cases by municipality of residence grouped by GVE, ESP, 2010 to 2021.*

ESG	% of Influenza SARS cases
CAPITAL (City of SP)	44.92
SANTO ANDRÉ	10.55
OSASCO	6.82
CAMPINAS	6.47
MOGI DAS CRUZES	4.28
SÃO JOSÉ DO RIO PRETO	3.87
SOROCABA	3.50
RIBEIRÃO PRETO	3.09
PIRACICABA	2.02
SÃO JOSÉ DOS CAMPOS	1.89
SANTOS	1.84
TAUBATÉ	1.73
BAURU	1.10
ARARAQUARA	1.03
FRANCA	0.87
SÃO JOÃO DA BOA VISTA	0.85
JALES	0.67
FRANCO DA ROCHA	0.65
CARAGUATATUBA	0.58
BOTUCATU	0.56
ARAÇATUBA	0.52
MARÍLIA	0.49
BARRETOS	0.47
PRESIDENTE PRUDENTE	0.35
REGISTRO	0.33
ASSIS	0.30
PRESIDENTE VENCESLAU	0.21
ITAPEVA	0.03

Source: SIVEP-Gripe. Data consulted in June/2022. *Data subject to change.

Institutional outbreaks of influenza syndrome

The surveillance system for acute respiratory syndromes also includes the detection, reporting, investigation, and control of institutional outbreaks of influenza syndrome, independent of the sentinel network. The collection of clinical specimens occurs by sampling, and its processing is performed by the ALI (Adolfo Lutz Institute). This subject will be covered again in the chapter referring to institutional outbreaks.

Document elaborated by Pamella Cristina de Carvalho Lucas, Angela Tiemi Tanamachi, Camila Lorenz, Lucca Nielsen, Raquel Giardini Sanches Palasio, Ana Lucia Frugis Yu, Telma Regina Marques Pinto Carvalhanas, march 2023, Sao Paulo, Brazil.

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Surveillance of SARS/deaths Covid-19

INTRODUCTION

On January 30, 2020, the World Health Organization (WHO) announced the new coronavirus infection (SARS-CoV-2) as a Public Health Emergency of International Concern (PHEIC) and shortly thereafter named the disease Covid-19.[1] On February 26 of the same year, the Brazilian Ministry of Health confirmed the first case of the disease in Latin America: a 61-year-old Brazilian man living in the city of São Paulo who had traveled to northern Italy, in the Lombardy region, where an outbreak of Covid-19[2-4] was occurring. The virus spread rapidly in the following months worldwide, reaching 545 million cases and 6.5 million deaths by June 2022.[3]

The pandemic disease has a broad clinical spectrum, with patients presenting only mild symptoms and a subclinical pattern in the initial phase up to severe manifestations, with unfavorable outcomes, including hospitalization, the need for ICU use, and death. Elderly people and individuals with a history of subjacent chronic diseases are at greater risk of illness, complications, and deaths.[5]

ETIOLOGIC AGENT

SARS-CoV-2 is a beta coronavirus identified in bronchoalveolar lavage samples obtained from patients with pneumonia of unknown cause in Wuhan City, Hubei Province, China in December 2019.[1] Belonging to the subgenus Sarbecovirus of the family *Coronaviridae*, it constitutes the seventh coronavirus known to infect humans.

TRANSMISSION MODE

According to the most recent evidence,[1,5] like other respiratory viruses, Covid-19 is transmitted mainly by contact, droplets, and particles or aerosols. Transmission by direct contact occurs from one infected person to another healthy person (for example, during a handshake followed by touching the eyes, nose, or mouth) or by contaminated objects and surfaces (fomites).[1]

Droplet transmission happens through exposure to respiratory droplets containing the virus that are expelled by an infected person when they cough, talk, or sneeze, especially if they are less than one meter away from another person.[1] Airborne transmission also occurs through contaminated respiratory droplets and smaller particles (aerosols), which can remain suspended in the air for distances greater than one meter and for longer periods (usually hours).[1]

EPIDEMIOLOGICAL SITUATION

From the beginning of the Covid-19 pandemic in Brazil (February 2020) until December 31, 2021, 536,849 severe cases and 158,464 deaths have been reported in the state of São Paulo (SSP). Most were confirmed by RT-qPCR laboratory criteria (76%) (Table 1).

Table 1. Number and proportion of severe cases of covid-19 SARS, according to clinical course and confirmation criteria. SSP, 2020 to 2021.*

Closing criteria	Death, N = 158.464**	Death from other causes, N = 827**	Recovered, N = 359.080**	In open, N = 18.478**
Clinical	1,214 (0,8%)	24 (2,9%)	2,315 (0,6%)	629 (3,4%)
Clinical epidemiological	1,016 (0,6%)	9 (1,1%)	1,890 (0,5%)	121 (0,7%)
Clinical imaging	6,945 (4,4%)	60 (7,3%)	16,136 (4,5%)	522 (2,8%)
In open	12,033 (7,6%)	214 (26%)	31,124 (8,4%)	2,226 (12%)
Laboratory RT-qPCR	120,097 (76%)	438 (53%)	273,379 (76%)	13,052 (71%)
Laboratory TR-Ag	17,159 (11%)	82 (9,9%)	34,236 (9,5%)	1,928 (10%)

Source: SIVEP-Gripe. Data collected in September/2022. *Data subject to change. **N (%).

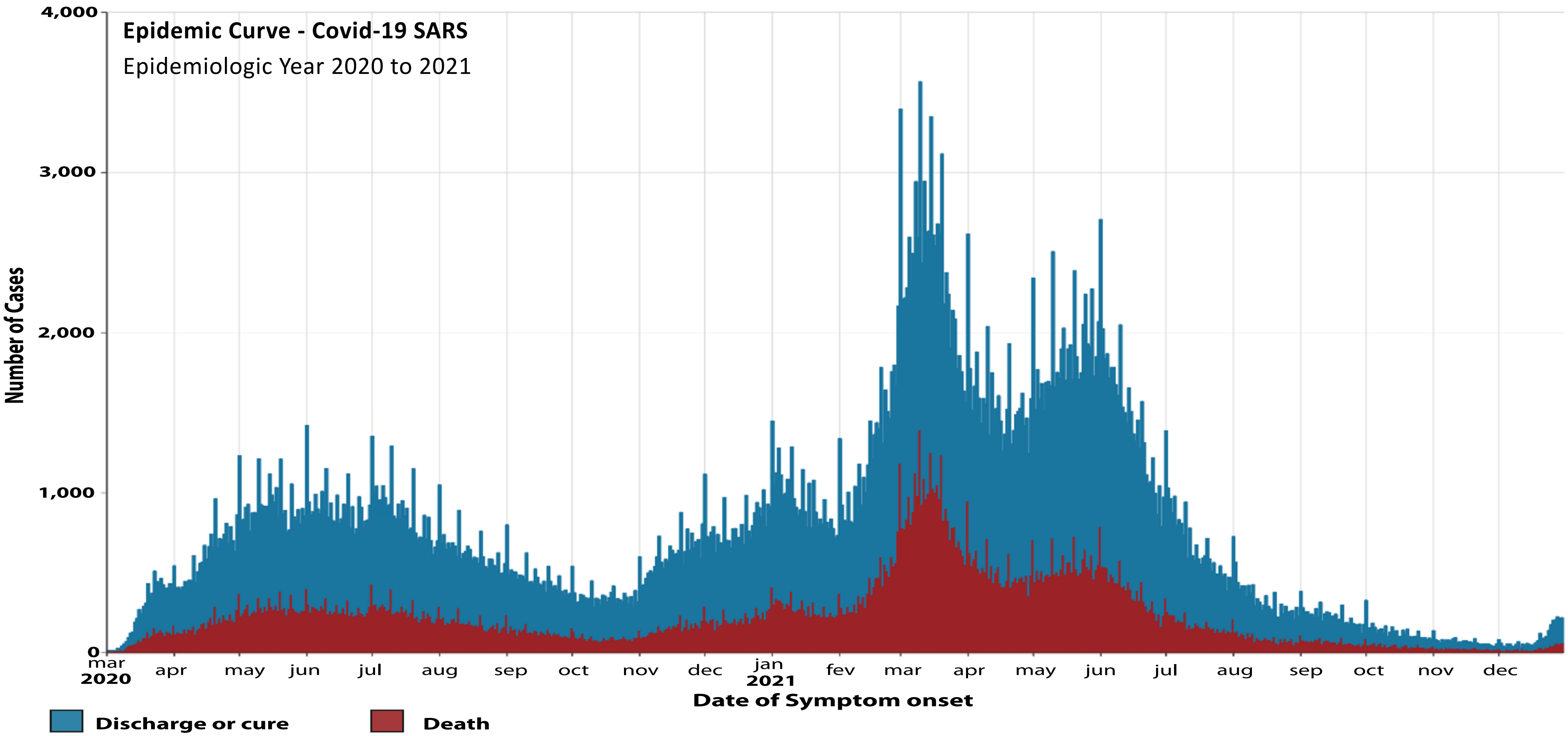
In the analyzed period, two more expressive peaks of severe cases and deaths were observed, both in 2021: the first between March and April, and the second between May and July (Graph 1).

Men were more affected than women (Graph 2), while the age groups with the highest number of hospitalizations were those in the intermediate range (<40 years). Deaths were concentrated in individuals over 60 years of age, which is consistent with the findings available in the literature.[1,4]

The spatial distribution of severe cases and deaths from the disease was heterogeneous in the São Paulo territory, with the highest numbers observed in regions of high population concentration: the capital and Greater São Paulo (Table 2).

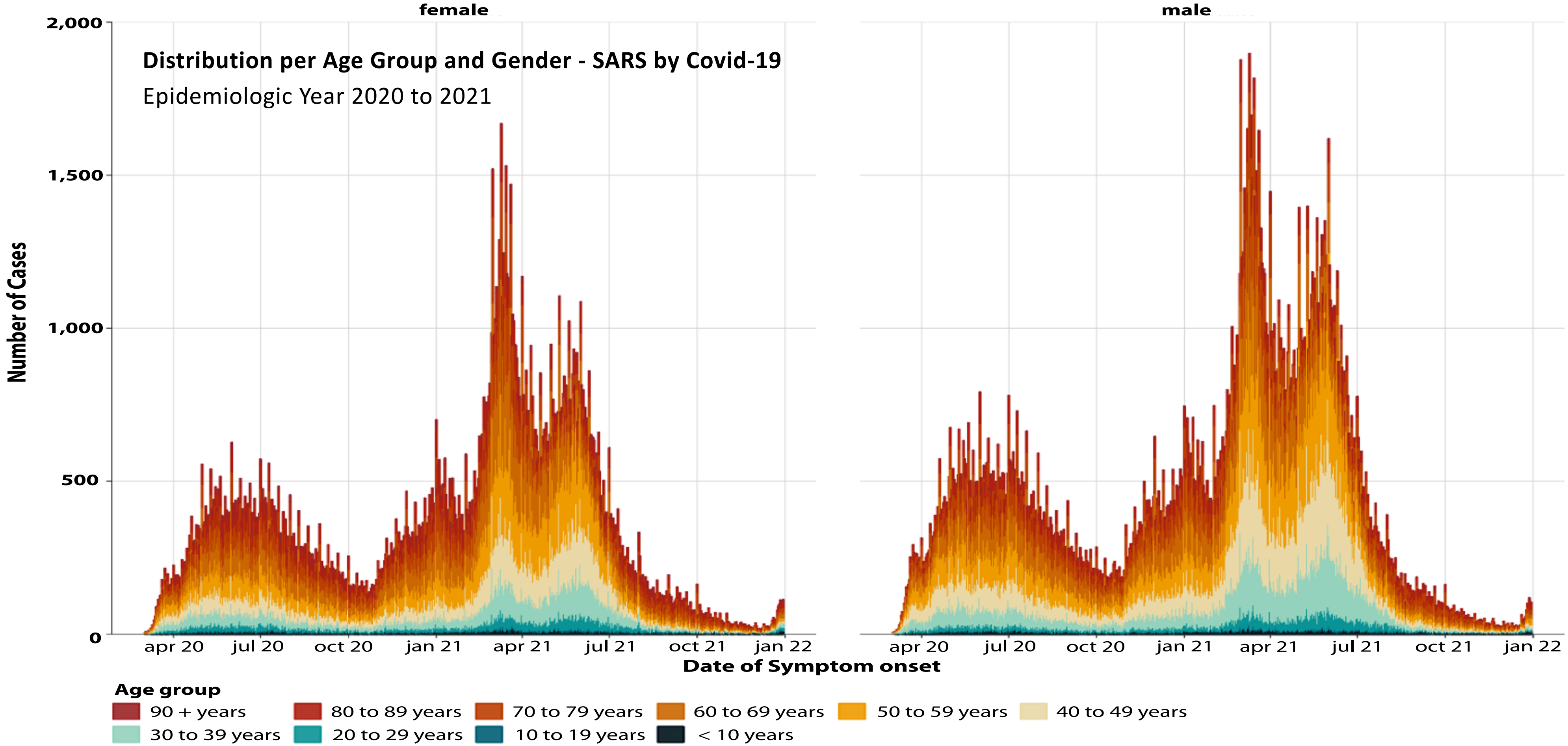
The highest cumulative incidences (per 100,000 population-year) were observed in the Regional Health Departments (DRS) of São José do Rio Preto, Araçatuba, and Greater São Paulo, while the highest cumulative mortality rates (per 100,000 population-year) were also seen in São José do Rio Preto and Araçatuba (Figures 1 and 2).

Graph 1. Number of severe cases and deaths from covid-19 SARS, by clinical course, SSP, 2020 to 2021.*



Source: SIVEP-Gripe. Data consulted in June/2022. *Data subject to change.

Graph 2. Number of severe cases of SARS covid-19 by gender and age group, SSP, 2020 to 2021.*



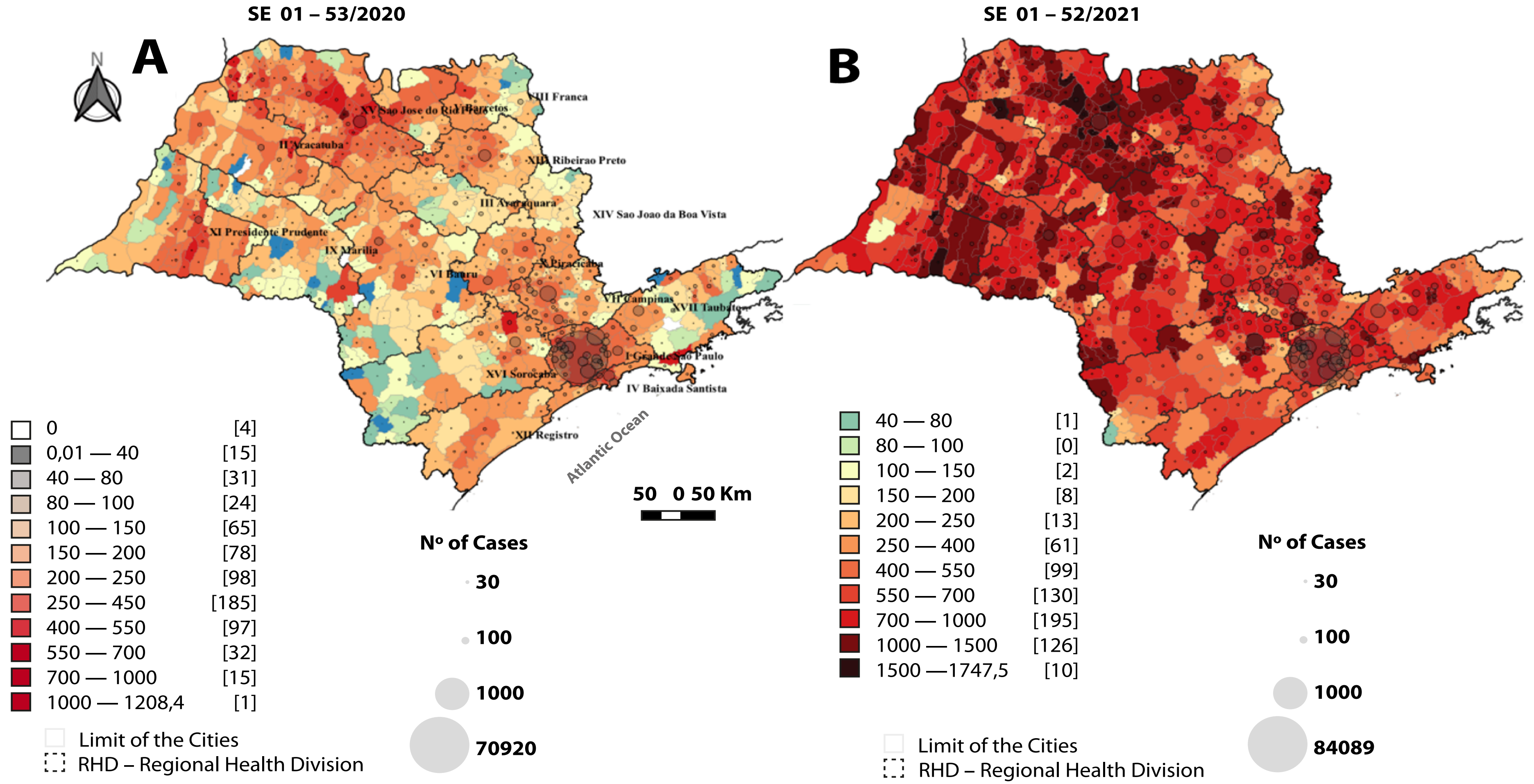
Source: SIVEP-Gripe. *Data subject to change. Data consulted in June/2022.

Table 2. Number of covid-19 SARS cases by ESG and clinical evolution. ESP, 2020 to 2021.*

ESG	Death , N = 158,464**	Death from other causes, N = 827**	Recovered, N = 359,080**	In open, N = 18,478**
ARAÇATUBA	3,310 (2,1%)	20 (2,4%)	6,757 (1,9%)	98 (0,5%)
ARARAQUARA	2,794 (1,8%)	11 (1,3%)	6,379 (1,8%)	176 (1,0%)
ASSIS	1,930 (1,2%)	8 (1,0%)	3,013 (0,8%)	61 (0,3%)
BARRETOS	1,896 (1,2%)	19 (2,3%)	3,371 (0,9%)	353 (0,9%)
BAURU	3,702 (2,3%)	11(1,3%)	10,020 (2,8%)	174 (0,9%)
BOTUCATU	1,858 (1,2%)	24 (2,9%)	3,730 (1,0%)	124 (0,7%)
CAMPINAS	15,430 (9,7%)	54 (6,5%)	36,026 (10%)	1,590 (8,6%)
CAPITAL	40,506 (26%)	165 (20%)	109,570 (31%)	5,289 (29%)
CARAGUATATUBA	841 (0,5%)	8 (1,0%)	2,353 (0,7%)	425 (2,3%)
FRANCA	2,095 (1,3%)	11 (1,3%)	2,588 (0,7%)	1,226 (6,6%)
FRANCO DA ROCHA	1,696 (1,1%)	4 (0,5%)	2,963 (0,8%)	247 (1,3%)
ITAPEVA	1,235 (0,8%)	2 (0,2%)	1,036 (0,3%)	7 (<0,1%)
JALES	1,320 (0,8%)	5 (0,6%)	1,901 (0,5%)	242 (1,3%)
MARÍLIA	2,336 (1,5%)	1 (0,1%)	5,726 (1,6%)	6 (<0,1%)
MOGI DAS CRUES	10,71 (6,8%)	53 (6,4%)	22,505 (6,3%)	961 (5,2%)
OSASCO	9,927 (6,3%)	47 (5,7%)	24,153 (6,7%)	1,400 (7,6%)
PIRACICABA	5,294 (3,3%)	55 (6,7%)	11,690 (3,3%)	301 (1,6%)
PRESIDENTE PRUDENTE	1,689 (1,1%)	28 (3,4%)	5,274 (1,5%)	94 (0,5%)
PRESIDENTE VENCESLAU	1,25 (0,6%)	10 (1,2%)	1,920 (0,5%)	41 (0,2%)
REGISTRO	957 (0,6%)	10 (1,2%)	1,837 (0,5%)	40 (0,2%)
RIBEIRÃO PRETO	5,548 (3,5%)	13 (1,6%)	11,136 (3,1%)	455 (2,5%)
SANTO ANDRÉ	11,165 (7,0%)	130 (16%)	22,553 (6,3%)	1,812 (9,8%)
SANTOS	7,735 (4,9%)	14 (1,7%)	9,680 (2,7%)	374 (2,0%)
SÃO JOÃO DA BOA VISTA	2,911 (1,8%)	32 (3,9%)	5,364 (1,5%)	242 (1,3%)
SÃO JOSÉ DO RIO PRETO	6,776 (4,3%)	10 (1,2%)	17,257 (4,8%)	168 (0,9%)
SÃO JOSÉ DOS CAMPOS	3,225 (2,0%)	14 (1,7%)	6,370 (1,8%)	1,883 (10%)
SOROCABA	7,654 (4,8%)	56 (6,8%)	17,017 (4,7%)	384 (2,1%)
TAUBATÉ	2,899 (1,8%)	12 (1,5%)	6,891 (1,9%)	305 (1,7%)

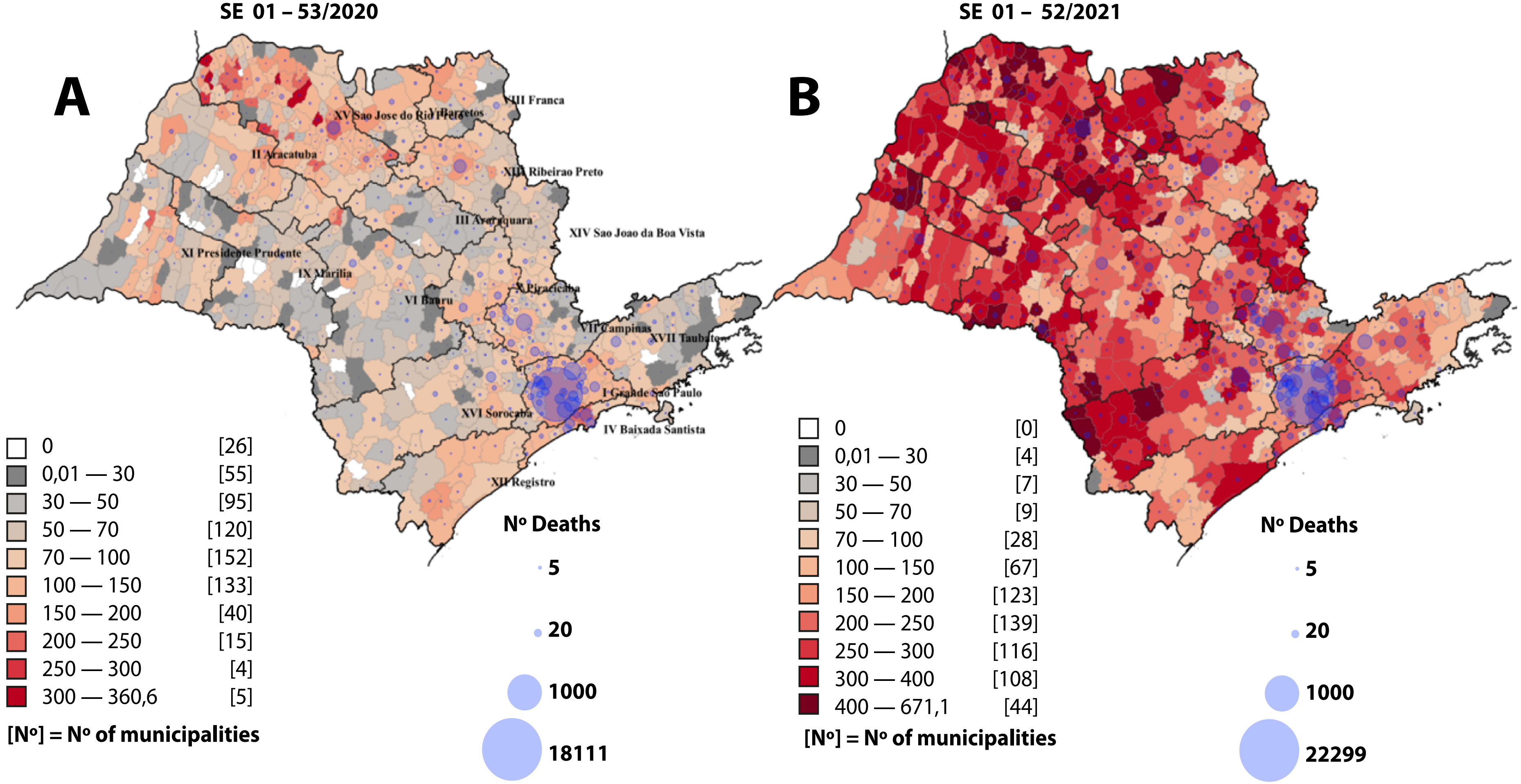
Source: Sivep-Gripe. Data consulted in September/2022. *Data subject to change. **n (%).

Figure 1. Covid-19 SARS incidence rate (per 100,000 person-year), according to the city of residence and date of symptom onset. SSP. A: SE 01-52/2020; B: SE 01-52/2021.



Source: SIVEP-Gripe. Data consulted in June/2022. *Data subject to change.

Figure 2. Covid-19 SARS mortality rate (per 100,000 person-year), according to the city of residence and date of symptom onset. SSP. A: SE 01-52/2020; B: SE 01-52/2021.



Source: SIVEP-Gripe. Data consulted in June/2022. *Data subject to change.

Pediatric/adult multisystemic inflammatory syndrome

Since April 2020 cases have been reported of a severe rare syndrome in children and adolescents aged 0-19 years, which was temporally associated with Covid-19. The first reports occurred in Europe and North America, and then spread to several Latin American countries.

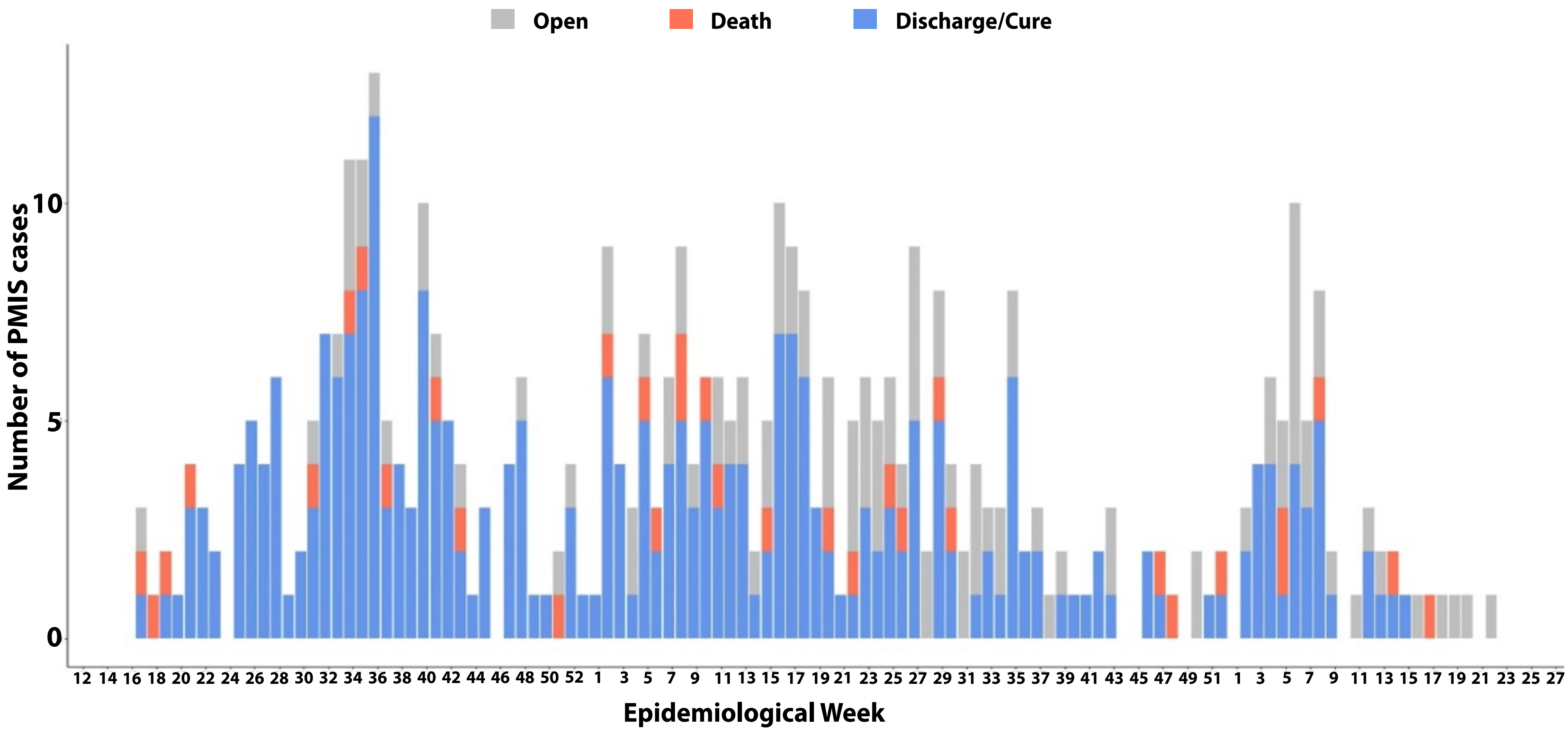
Named pediatric multisystemic inflammatory syndrome (PMIS), it occurs days to weeks after acute infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Its clinical features are similar to Kawasaki syndrome, macrophage activation syndrome, and toxic shock syndrome. Patients with PMIS may have criteria for complete or incomplete Kawasaki syndrome. It usually occurs in older children, schoolchildren, and adolescents, with elevated inflammatory markers and cardiac injury.

Evidence shows, however, that rare cases among adults (above the recommended age range PMIS - 0 to 19 years) may develop a similar syndrome associated with SARS-CoV-2 infection. The term multisystem inflammatory syndrome in adults (MIS-A) has been proposed to define these cases and has been adapted to Portuguese by the Ministry of Health as *síndrome inflamatória multissistêmica em adulto*s (SIM-A). The disease is characterized by a broad spectrum of signs and symptoms that include cardiovascular, gastrointestinal, dermatological, and neurological changes, and an association with recent SARS-CoV-2 infection, diagnosed by RT-PCR, rapid antigen test (RAT), and/or serology. Because it is a rare condition, few cases have been reported in the literature, so information about MIS-A is still scarce. To this date, the SSP has no record of cases in the notification system.

In the period from SE 01/2020 to SE 22/2022, the São Paulo state government confirmed 417 cases of PMIS, of which 278 evolved to discharge/healing, 32 to death, and 107 remained with an open outcome (Graph 3). Of these cases, 154 occurred in the period SE 01-53/2020 (11 deaths, 126 discharges and 17 open cases) and 206 in SE 01-52/2021 (17 deaths, 123 discharges and 66 open cases). Between SE 01 and SE 22/2022 there were 57 cases (4 deaths, 29 discharges and 24 open cases).

Of the total number of cases, 240 (57.6%) occurred in males and 177 (42.4%) in females. The mean and median age were 6.1 and 6 years, respectively. Regarding the health conditions of the cases, 72 (17.3%) had a history of previous morbidities, with a predominance of neurological disease, pneumopathy, obesity, genetic syndrome, heart disease, hematological disease, oncological disease, and immunodepression. Among the 278 PMIS cases that progressed to discharge/cure, 22 had sequelae: cardiac, motor, neurological, vascular, and pulmonary impairment.[6]

Graph3. Number of cases and deaths from PMIS temporally associated with covid-19. SSP, 2020 a 2021.*



Source: RedCap. Data consulted in June/2022. *Data subject to change.

The 32 PMIS deaths occurred in individuals between the ages of 0 and 19 years (Figure 2), with the mean and median age among them being 8.5 and 8.7 years, respectively. As for gender, 16 individuals were female and 16 were male. Among these cases, 11 had a history of previous chronic illness. The deaths occurred in the cities of São Paulo (7), Campinas (3), Araçatuba (2), Guarulhos (2), Ribeirão Preto (2), Cotia (1), Guapiaçu (1), Guaratinguetá (1), Holambra (1), Indaiatuba (1), Itajobi (1), Jardinópolis (1), Mogi Mirim (1), Paulínia (1), Pontalinda (1), Presidente Prudente (1), Santo André (1), Santos (1), São Caetano do Sul (1), São José do Rio Preto (1) and São Vicente (1).[6]

Document elaborated by Pamella Cristina de Carvalho Lucas, Camila Lorenz, Camila Martins Trevisan, Rafael Lopes Paixão da Silva, Tatiana Portela Zenker, Raquel Giardini Sanches Palasio, Lucca Nielsen, Guillermo Leonardo Flores-Montero, Ana Lucia Frugis Yu, Telma Regina Marques Pinto Carvalhanas, march 2023, Sao Paulo, Brazil.

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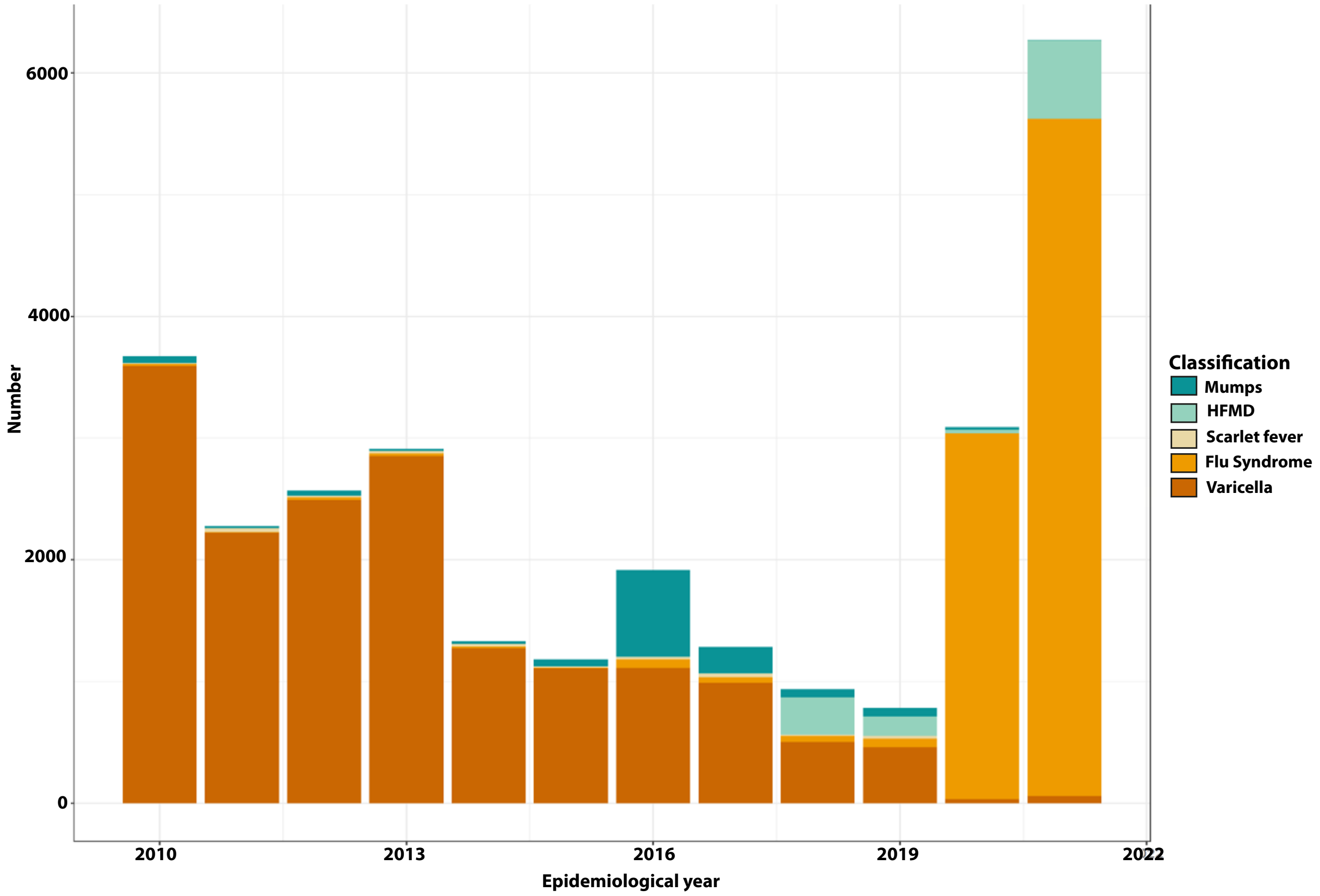
Surveillance and control of outbreaks of respiratory diseases

INTRODUCTION

The respiratory diseases that are on the national list of compulsory notification have great potential for dissemination and rapidity of transmission. Thus, they can trigger outbreaks and/or epidemics, requiring early detection, rapid response, and application of effective control measures by epidemiological surveillance.[1,2]

A retrospective of institutional outbreaks, according to viral identification and epidemiological year of notification in the state of São Paulo (SSP) is presented below (Graph 1).

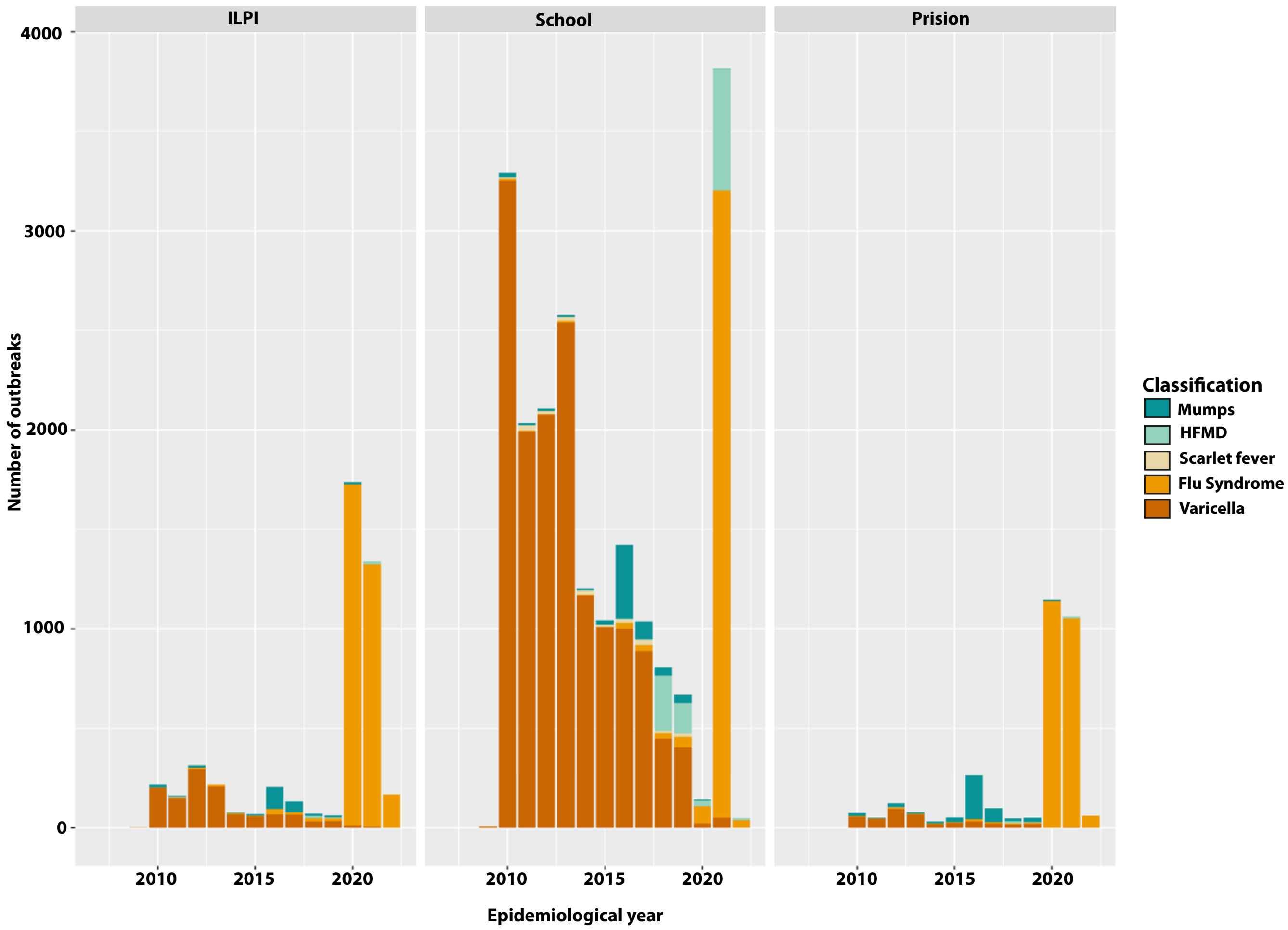
Graph 1. Distribution of institutional outbreaks of respiratory diseases, according to the virus identified. SSP, 2010 a 2021.*



Source: SINAN NET. Data collected in June/2022. *Data subject to change.

The distribution of institutional outbreaks, in terms of the number of cases and viral identification, is not homogeneous in São Paulo, given the state's population diversity and loco-regional susceptibilities. Graph 2 shows the concentration of outbreaks, according to the place of occurrence, in the three institutions with the highest number of cases.

Graph 2. Distribution of outbreaks of respiratory diseases, according to place of occurrence. SSP, 2010 to 2021.*



Source: SINAN NET. Data collected in June/2022. *Data subject to change.

FLU SYNDROME

Flu syndrome (influenza syndrome) is the clinical condition in which the individual presents an acute respiratory condition characterized by at least two of the following signs and symptoms: fever (even if referred), chills, sore throat, headache, cough, and runny nose.[1,3]

Observations:

- in children, besides the previous items, nasal obstruction is also considered, in the absence of another specific diagnosis;
- in the elderly, one should also consider specific worsening criteria such as syncope, mental confusion, excessive sleepiness, irritability, and inappetence;
- in suspected Covid-19, fever may be absent (especially in the elderly) and gastrointestinal symptoms (diarrhea) may be present, as well as changes in smell and taste; and
- in suspected influenza, myalgia, arthralgia, prostration, and fatigue may be present.

An outbreak of influenza syndrome is considered to be the occurrence of two or more suspected or confirmed cases that are related, have similar signs and symptoms, in the same institution, and within a period of up to 14 days.[1,2]

ETIOLOGIC AGENT

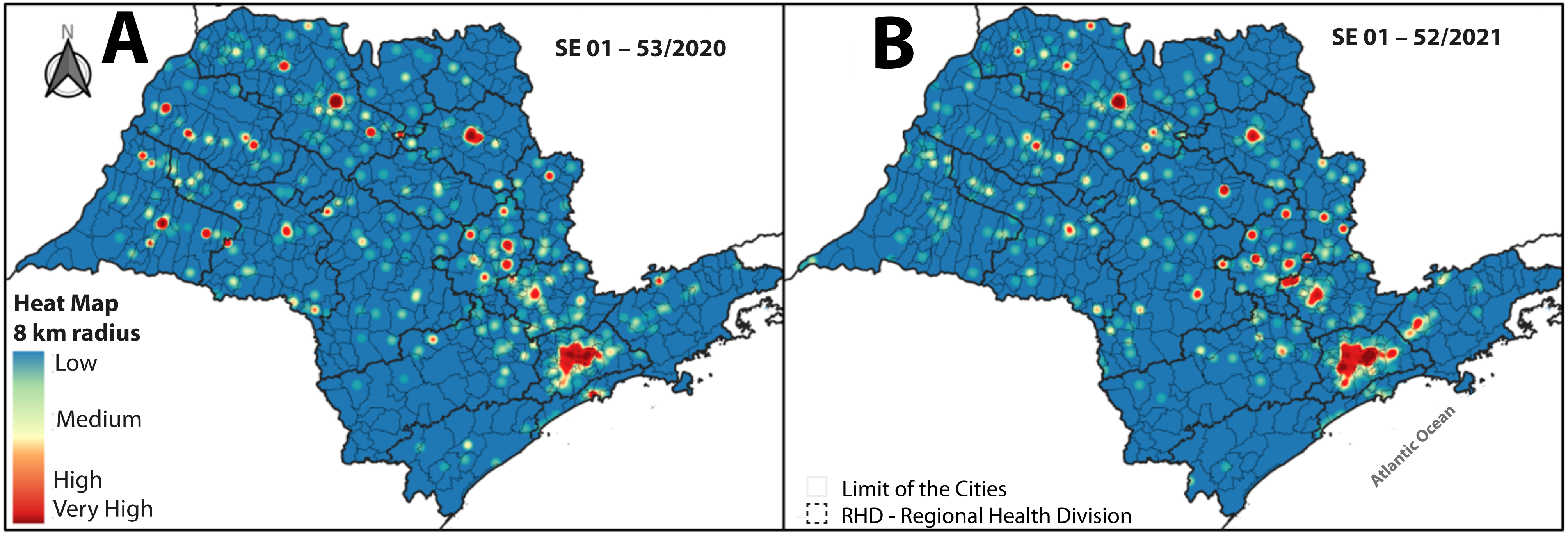
The influenza syndrome can be caused by influenza virus, rhinovirus, coronavirus, human respiratory syncytial virus, adenovirus, and human parainfluenza virus, among others.

EPIDEMIOLOGICAL SITUATION

Starting in 2020, due to the emergence of the Covid-19 pandemic, institutional outbreak surveillance began to consider SARS-CoV-2 virus in its routine. Throughout this period, it was observed that, initially, Long-Term Care Institutions for Elderly were the most affected by outbreaks of influenza syndrome, notably those of Covid-19. In mid-2021 an increase in the number of notifications in school units was observed.

Figure 1 shows the concentration of cases related to influenza syndrome outbreaks in SSP. It can be seen that the largest concentration of cases is in Greater São Paulo, followed by the regions of Araçatuba, São José do Rio Preto and Ribeirão Preto, which concentrate the largest number of universities, Long-Term Care Institution, and prisons.

Figure 1. Spatial distribution of cases related to influenza syndrome outbreaks, according to city of residence and date of symptom onset. SSP. A: SE 01-52/2020; B: SE 01-52/2021.



Source: SINAN NET, outbreak module. Data collected in June/2022. *Data subject to change.

HAND, FOOT AND MOUTH DISEASE

Hand-foot-mouth disease (HFMD) is an acute, usually self-limited, exanthematous viral illness that mainly affects children under 5 years of age in outbreaks. Its main clinical manifestations are fever, rashes on hands and feet, and mouth ulcers. The lesions heal spontaneously, without leaving marks.[4]

The most common clinical complication associated with HFMD is dehydration, the result of inadequate fluid intake secondary to odynophagia (pain when swallowing) caused by painful mouth ulcers. Secondary bacterial skin infections are uncommon. Cases that affect the central nervous system can trigger severe systemic complications and/or pulmonary edema, sometimes fatal, particularly in children under 5 years of age.[4]

ETIOLOGIC AGENT

HFMD is mainly caused by human enterovirus A (HEV-A), in particular *Coxsackie A16* and *Enterovirus 71*, which are responsible for more severe conditions in children, although other HEV-A serotypes, such as *Coxsackievirus A6* and *Coxsackievirus A10*, are also associated with the disease. These belong to the family *Picornaviridae*, genus Enterovirus.[4]

TRANSMISSION MODE

Direct transmission occurs by the fecal-oral route - feces and possibly vomit -, by airway secretions, such as mucus, saliva, and droplets, and by contact with skin lesions. Indirect transmission occurs through contaminated surfaces and fomites since enteroviruses can remain at room temperature without losing viability.[5]

EPIDEMIOLOGICAL SITUATION

The geographical distribution of the HFMD is variable and it can occur throughout the year, but there is a seasonal pattern of increased cases due to environmental (summer and rainy season related), socioeconomic, and immunological factors. A high attack rate is also observed in daycare centers (30%), with a reduction in incidence during school vacations.

In SSP, in the first quarter of 2018, 58% of cases reported in Sinan NET required hospitalization, highlighting the need for reorganization of health surveillance. Thus, the Division of Respiratory

Tract Diseases (DDTR) started to monitor the outbreaks and cases of HFMD in a systematic way, with flows and guidelines defined in state normative instruction.[5]

VARICELLA

Varicella is an acute, highly contagious primary viral infection, whose main clinical feature is the polymorphism of skin lesions (macules, papules, vesicles, pustules, and crusts), accompanied by pruritus. In children it is often benign and self-limited, while in adolescents and adults the clinical picture is more exuberant, with a more compromised general state, higher and more prolonged fever, and more pronounced exanthema, which can lead to death.[6]

Varicella is also associated with other clinical cases, such as shingles due to reactivation of the varicella virus, which remains latent in the nervous system after a primary reinfection and is more common in people with immunodepression. In addition, the disease is associated with Reye's syndrome, occurring especially in children and adolescents who take acetylsalicylic acid during the acute phase, which results in liver impairment, followed by brain impairment. Maternal infection during the first trimesters of pregnancy can result in embryopathy, with a risk of serious injury to the fetus, such as low birth weight, malformations of the extremities, skin scars, microphthalmia, cataracts, and mental retardation.

ETIOLOGIC AGENT

It is caused by the varicella-zoster virus ("VZV"), also known as shingles, and human herpesvirus 3 (HHV3). It is a member of the family *Herpesviridae*, subfamily *Alphaherpesvirinae*, and genus *Varicellovirus.*[6] The reservoir is man.

TRANSMISSION MODE

The transmission of varicella is person to person, through direct contact with skin lesions or respiratory secretions (airborne spread of viral particles/aerosols). There is no evidence of the virus spreading by fomites (objects or substances contaminated by infectious agents), since it is extremely labile and unable to survive for long in the environment.

Infection with varicella in one family member usually results in infection of almost all susceptible persons in the household.[1,6]

SCARLET FEVER

Scarlet fever is an acute infectious disease caused by the beta hemolytic streptococcus group A. Bacteria of this genus are also causative agents of throat infections (tonsillitis) and skin infections (impetigo, erysipelas). The appearance of scarlet fever does not depend on a direct action of the streptococcus, but on a hypersensitivity reaction (allergy) to the substances it produces (toxins). Thus, the same bacteria can cause different diseases in each individual it infects.[7]

The importance of group A streptococcal infections is mainly related to their suppurative manifestations, such as necrotizing fasciitis, streptococcal toxic shock syndrome, cervical lymphadenitis, retropharyngeal or peritonsillar abscess, mastoiditis, bacteremia, endocarditis, pneumonia, and otitis media. In the case of scarlet fever, its importance is directly related to the non-suppurative sequelae: rheumatic fever and acute diffuse glomerulonephritis. Post-streptococcal glomerulonephritis may occur after impetigo or other skin lesions.[7]

ETIOLOGIC AGENT

Scarlet fever is caused by ß-hemolytic Streptococcus group A (*Streptococcus pyogenes*), possibly group C, D, and G.[7]

TRANSMISSION MODE

Transmission usually occurs through saliva or nasal secretions of an infected person. Sick people are much more likely to transmit the bacteria to other individuals than asymptomatic carriers. Crowded conditions - such as those in schools, day care centers, or military training facilities - facilitate transmission. Although rare, the spread of group A streptococcal infections can also occur through food, due to improper handling.[7,8]

MUMPS

Mumps is an acute viral disease characterized by the enlargement of one or more salivary glands, usually the parotid glands. After the widespread implementation of vaccination, the incidence of the disease decreased substantially.[3,6]

The clinical picture of mumps can have mild symptoms or no symptoms at all, which contributes to the spread of the disease. Generally benign, there may be more severe cases, rarely leading to death.

Susceptibility to mumps is general. Those with the greatest complications are adolescents (puberty) and adults, particularly males, in whom orchitis (inflammation of the testicles) is commonly reported, occurring in approximately 30% of unvaccinated post-pubertal males and 6% of vaccinated males. This condition can lead to testicular atrophy, impotence, or sterility.[3,6]

ETIOLOGIC AGENT

The disease is caused by *Paramyxoviruses* belonging to the *Rubulavirus* family. Its reservoir is the human being.[6]

TRANSMISSION MODE

The mumps virus replicates in the upper respiratory tract and is transmitted from person to person through contact with respiratory tract secretions, saliva, or infected respiratory droplets. The greatest transmissibility occurs from two days before to five days after the onset of parotitis.[6]

Document elaborated by Pamella Cristina de Carvalho Lucas, Pedro de Campos Mello Monteiro, Camila Lorenz, Guillermo Leonardo Flores-Montero, Raquel Giardini Sanches Palasio, Marcela Rodrigues da Silva, Ana Lucia Frugis Yu, Telma Regina Marques Pinto Carvalhanas, march 2023, Sao Paulo, Brazil.

ACKNOWLEDGEMENTS

To the technical and administrative teams and collaborators of DRTDE/ESC/DCC/SHD-SP, for their cooperation in data analysis, technical contributions, content construction, referenced literature review, support, trust, and dedication to this informative multi-thematic tool.

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Publication

May 2023

Open access

How to cite

Yu ALF, Santos APA, Tanamachi AT, Liphaus B de L, Ando JAG, Rodrigues M, Lucas PCC, Carvalhanas TRMP, Lorenz C, Trevisan CM, Montero GLF, Nielsen L, Monteiro PCM, Palasio RGS, Silva RLP, Zenker TP. Epidemiological report of the surveillance and control of respiratory-transmitted diseases. Bepa [Internet]. 2023 Apr 1 ;20(220):1-56. Available in: https://periodicos.saude.sp.gov.br/BEPA182/article/view/37882