



Epidemiological burden of meningococcal disease in Brazil: A systematic literature review and database analysis

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ABSTRACT

Objectives: The aim of this study was to evaluate the epidemiological profile of invasive meningococcal disease (IMD) in Brazil, the first Latin American country to introduce the group C meningococcal conjugate vaccine (included in the vaccination schedule in 2010).

Methods: A systematic review was conducted, covering the years 2005–2017, to identify epidemiological information on IMD and *Neisseria meningitidis* carriers in Brazil. Documents from the Brazilian Ministry of Health and two public databases were analyzed to determine annual incidence rates, absolute numbers of diagnosed cases, serogroups identified, the relative distribution of cases per serogroup, and the case fatality rate (CFR).

Results: Sixteen studies were selected. The incidence rate ranged from 0.88 to 5.3 cases per 100 000 inhabitants per year. According to secondary data, the annual incidence of IMD in 2015 was highest in males <1 year old (7.1/100 000). The number of diagnosed cases declined significantly over the years. In the literature, IMD showed a CFR from 20.0% to 50.0%, and a higher CFR for serogroup W (17.8%). Secondary data showed an absolute reduction in meningitis-attributable deaths between 2007 and 2015; however, the CFR remained stable (11.1% in 2007 and 8.4% in 2015). In 2015, serogroup W showed the highest CFR (24.1%), followed by serogroups C (19.2%), B (17.7%), and Y (14.3%).

Conclusions: Despite a reduction in cases, the CFR remained stable and similar in the different age groups, even for disease caused by different serogroups. The highest CFR was found to be associated with serogroup W.

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Introduction

Despite advances in the diagnosis and treatment of infectious diseases, invasive meningococcal disease (IMD) is still a major public health concern (Cordeiro et al., 2007; Agrawal and Nadel, 2011; Sáfadi et al., 2012). In Brazil, meningococcal infection is endemic and presents in a cyclical pattern, with most cases occurring during the winter, interspersed with occasional outbreaks (Souza and Seguro, 2008; Sáfadi et al., 2012; Bastos et al., 2015). The disease still carries high case fatality rates (CFR) and the risk of serious sequelae. In this context, vaccination is

considered the best strategy for prevention and control (Bastos et al., 2015).

IMD is caused by the bacterium *Neisseria meningitidis*, which is classified into serogroups based on different capsular polysaccharides and external protein membranes. At least 13 distinct meningococcal serogroups have been defined, and six (A, B, C, W, X, Y) are responsible for the greatest clinical disease burden (Municipal Health Office, São Paulo, 2007; Sáfadi et al., 2012).

In 2010, Brazil became the first country in Latin America to introduce the group C meningococcal conjugate vaccine into its routine immunization program. Meningococcal C (MenC) vaccination was introduced for infants (at 3 and 5 months, with a booster at 12 months of age). Toddlers from 12 to 23 months of age received a single dose, with no catch-up campaign for the older age groups (Ministry of Health, Brazil, Secretariat of Health Surveillance, 2014; Sáfadi et al., 2014a; Ministry of Health, Brazil, 2017a,b). The universal childhood vaccination program with MenC has proved to be a cost-effective strategy (Soárez et al., 2011). After routine MenC

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vaccination was implemented, a significant decrease in the incidence rate of disease was observed in the age groups targeted for vaccination (Sáfadi et al., 2014a). However, no impact was observed in the other age groups, likely reflecting the lack of a catch-up program targeting adolescents, the age group responsible for carriage (Moraes et al., 2015). In January 2017, the Brazilian Ministry of Health included a dose of MenC conjugate vaccine for adolescents aged between 12 and 13 years, (Ministry of Health, Brazil, 2017a,b), which was extended in 2018 to 11–14-year-olds (Ministry of Health, Brazil, 2018).

Epidemiological data on meningococcal disease are necessary to characterize the more commonly circulating strains and to guide future prevention and control strategies. This study was conducted to evaluate the epidemiological profile of IMD and *N. meningitidis* carriers in Brazil through a systematic literature review and secondary data analysis derived from population-based data.

Methods

Systematic literature review

Electronic searches were conducted in the MEDLINE databases (via PubMed), Latin American and Caribbean Health Sciences Literature (LILACS), Centre for Reviews and Dissemination (CRD), and The Cochrane Library in January 2017. Systematic reviews and prospective or retrospective observational studies published after January 2005 and containing epidemiological information on IMD or *N. meningitidis* carriers in Brazil were included, as well as data concerning associated serogroups and their relationship with the course of disease. Abstracts, case reports, case series, letters to the editor, studies with only immunological outcomes, and those reporting results associated with other etiologies of meningitis were excluded. Any population group, including all ages, was considered. No limitation on language was applied.

Secondary data analysis

Documents available from the Brazilian Ministry of Health, as well as two different databases (the National Notifiable Diseases Information System (SINAN) and Department of Information Technology of the Unified Health System (DATASUS)) were consulted to trace the epidemiological profile of IMD (Ministry of Health, Brazil, 2017a,b; Ministry of Health, Brazil, DATASUS, 2017). In Brazil, meningitis surveillance is based on mandatory notification of suspected cases occurring in the public and private Brazilian healthcare systems. Cases are reported to SINAN with or without etiological agent identification, which guarantees greater reliability of the data presented in the country. Data on confirmed cases based on the clinical and laboratory case definition used by the Brazilian Ministry of Health were retrieved.

Descriptive statistics are presented, with the annual incidence per 100 000 inhabitants by sex and age group (2007–2015), absolute number of diagnosed cases per year (2007–2015), incidence per 100 000 inhabitants by region and state (2015), absolute number of diagnosed cases per identified serogroup (2007–2015), relative distribution of diagnosed cases per identified serogroup by region and age group (2015), CFR (2007–2015), and CFR by serogroup (2015). SINAN and DATASUS data were collected for the years 2007–2015 and 2013–2015, respectively. Concerning ethical aspects, SINAN and DATASUS data are in the public domain and do not allow for subject identification, ensuring individual confidentiality and anonymity.

Results

Bibliographical research

The systematic literature review resulted in 50 bibliographical references in PubMed, 147 in LILACS, eight in CRD, and 19 in the

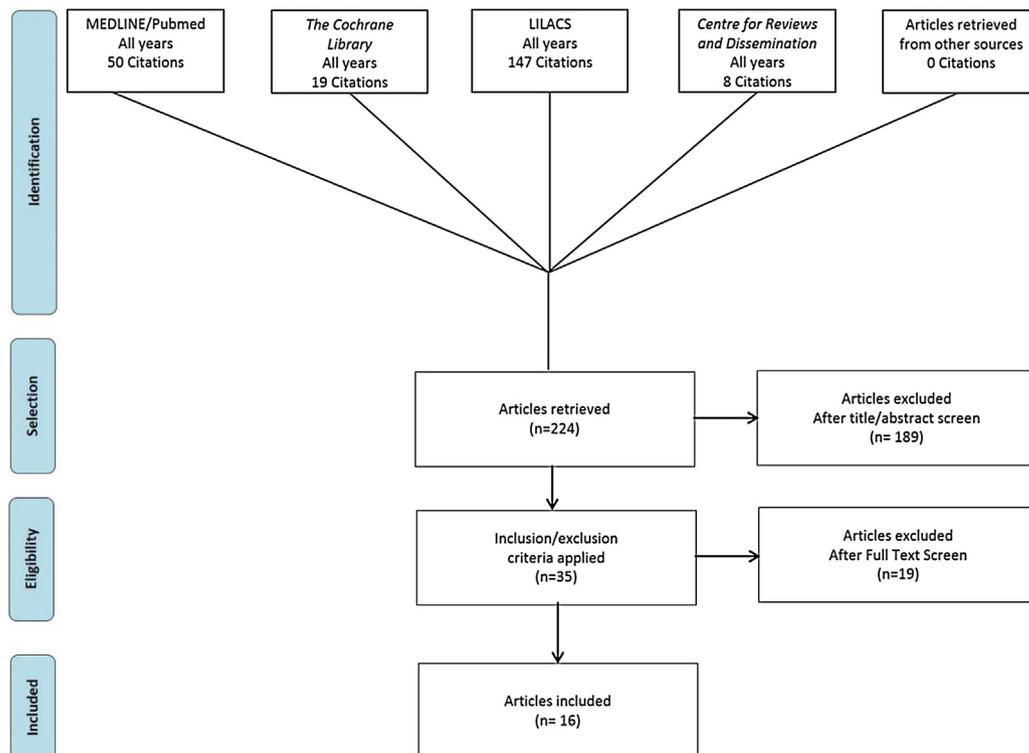


Figure 1. Flowchart of the study selection procedure.

Cochrane databases. After reading the titles and abstracts, 189 references that did not fulfill the eligibility criteria, as well as duplicate references, were excluded. Then, 35 articles were selected for detailed analysis of their content. Sixteen studies that fulfilled the inclusion criteria were considered for the review (Figure 1).

Characteristics of studies

The selected studies were published between 2005 and 2016. The study populations showed a predominance of males, except for the study by Nunes et al. (2016). Only four publications reported the median age of the participants, which ranged from 3 to 8 years.

The time period of study evaluation was wide. Moraes and Barata (2005) analyzed the epidemiological behavior of meningococcal disease in the city of São Paulo, Brazil, over the course of the 20th century and evaluated the period from 1906 to 2000. The most recent study, conducted by Nunes et al. (2016), was a cross-sectional study that took place between September and December 2014. This study estimated the prevalence of *N. meningitidis* and identified factors associated with carriage among adolescents in Salvador, Brazil. The characteristics of the included studies are described in Table 1.

Four studies evaluated the epidemiological behavior of meningococcal disease in Bahia state, one in Federal District,

one in Minas Gerais, one in Rio de Janeiro, three in Rio Grande do Sul, one in Santa Catarina, and five in São Paulo. No studies reported data for the Brazilian Northern region (Figure 2).

Epidemiological data

Incidence

Nine studies retrieved in the literature review reported incidence data. According to the results, the incidence of IMD has been cyclical and dynamic in nature and has varied geographically and over time (Table 2).

The lowest incidence rate was observed in the study conducted by Nascimento et al. (2012) in Minas Gerais state, with about 168.8 annual meningococcal disease cases from 2000 to 2009 (average incidence 0.88 cases/100 000 inhabitants/year). The highest incidence rate was described by Masuda et al. (2015) from 1986 to 2004 in São Paulo city. The average annual incidence rate was 5.3 cases/100 000 inhabitants, with a peak of 8.1 in 1995 and a minimum of 1.2 in 1986 (Masuda et al., 2015). Bertoncini et al. (2007) also showed a high incidence rate, with an average of 7.9 cases/100 000 inhabitants in Santa Catarina between 1987 and 2003.

Regarding the distribution by age group, incidence rates were 23.5 and 7 cases/100 000 inhabitants for children <1 year old and between 1 and 4 years old, respectively, in Rio Grande do Sul

Table 1
Characteristics of the studies included in the systematic review.

Study	Year of publication	State	Number	Sex distribution (%)	Age group (median)	Study period
Moraes and Barata (Moraes and Barata, 2005)	2005	São Paulo	NR ^a	NR ^a	NR ^a	1906–2000
Bertoncini et al. (Bertoncini et al., 2007)	2007	Santa Catarina	1269 ^b	Male: 53 Female: 47	NR	1987–2003
Cordeiro et al. (Cordeiro et al., 2007)	2007	Bahia	408 ^{c,d}	Male: 56	8 years	1996–2001
Baethgen et al. (Baethgen et al., 2008)	2008	Rio Grande do Sul	2215 ^b	NR	NR	1995–2003
Weidlich et al. (Weidlich et al., 2008)	2008	Rio Grande do Sul	493 ^b	NR	NR	2003–2005
Barroso et al. (Barroso et al., 2010)	2010	Rio de Janeiro	2413 ^b	Male: 55 Female: 45	6 years	1990–1996
Nunes et al. (Nunes et al., 2011)	2011	Bahia	2070 ^b	NR ^f	NR	1998–2007
Cardoso et al. (Cardoso et al., 2012)	2012	Bahia	2000–2006: 281 ^b 2007–2011: 437 ^b	NR	NR	2000–2011
Leme and Zanetta (Leme and Zanetta, 2012)	2012	São Paulo	490 ^b	NR	NR	1999–2008
Nascimento et al. (Nascimento et al., 2012)	2012	Minas Gerais	1690 ^b	Male: 54.7 ^g Female: 45.1 ^g	NR	2000–2009
Sáfadi et al. (Sáfadi et al., 2014b)	2014	São Paulo	104 ^e	NR	NR	2010
Tauil et al. (Tauil et al., 2014)	2014	Distrito Federal	309 ^b	Male: 52.1	2005–2009: 3 years 2010: 5 years 2011: 4 years	2005–2011
Coch Gioia et al. (Coch Gioia et al., 2015)	2015	Rio Grande do Sul	18 ^e	Male: 55.5 Female: 44.4	NR	2011
Moraes et al. (Moraes et al., 2015)	2015	São Paulo	120 ^e	Male: 52.5 Female: 47.5	NR ^h	2012
Masuda et al. (Masuda et al., 2015)	2015	São Paulo	10 087 ^b	Male: 53.8	4 years	1986–2004
Nunes et al. (Nunes et al., 2016)	2016	Bahia	59 ^e	Female: 61.8	NR	2014

NR, not reported.

^a The age and sex distribution remained unaltered during all endemic periods, showing an increased risk associated with younger age. Not possible to extract a value.

^b Cases of meningococcal disease.

^c Cases of meningococcal meningitis.

^d Epidemiological data were available for 397 (97%) cases.

^e Colonized by *Neisseria meningitidis*.

^f Slightly higher proportion in males.

^g Sex was not reported for three (0.2%) cases.

^h Participants were divided into three groups according to age: A (11–13 years), B (14–16 years), and C (17–19 years).



Figure 2. Geographical coverage of eligible studies in Brazil.

(Weidlich et al., 2008). Similarly, Cordeiro et al. (2007) showed that infants <1 year old presented the highest incidence (14.7 cases/100 000 inhabitants) in Bahia. In the southern region, the mean incidence (\pm standard deviation) of meningococcal disease in infants <1 year old during the years 1995–2003 was 31.3 ± 5.7 cases/100 000 inhabitants, higher than the rate observed for those aged 1–4 years (11.3 ± 3.4 cases/100 000 inhabitants; $p < 0.001$) (Baethgen et al., 2008). The results of Nascimento et al. (2012) correlate with those described previously, with reported highest incidence among children aged <1 year, followed by the 1–4 years and 5–9 years age groups in Minas Gerais.

The MenC conjugate vaccine strategy implemented in Brazil in 2010 has been shown to be highly effective and has had a strong direct impact on the target population. Tauil et al. (2014) assessed the direct impact of the MenC conjugate vaccine by age group. From 2005 to 2009 and in 2010 and 2011, the average annual incidence rates in children <1 year old were 30.6, 13.3, and 13.1/100 000 inhabitants/year, respectively, and in children 2 years of age the rates were 14.4, 10.8, and 2.7/100 000 inhabitants/year, respectively.

According to secondary data on the annual incidence of IMD per 100 000 inhabitants in 2015 from the Brazilian Ministry of Health, which is available by sex and age group, the highest incidence occurred in male patients <1 year old (male: 7.1/100 000; female: 5.8/100 000) (IBGE, 2013; Ministry of Health, Brazil, DATASUS, 2017) when compared with the other age groups.

In 2007 and 2015, 2469 and 1292 cases of IMD, respectively, were diagnosed. A significant reduction in diagnosed cases was observed over the years, which was most significant (26%) between 2011 and 2012. The reduction was proportional in all age groups (Ministry of Health, Brazil, DATASUS, 2017).

In 2015, the south (0.68/100 000 inhabitants) and southeast (0.91/100 000 inhabitants) regions presented the highest incidences of IMD. Other regions had equivalent incidences (north: 0.48/100 000 inhabitants; midwest: 0.42/100 000 inhabitants). The Northeast region presented the lowest incidence of IMD (0.29/100 000 inhabitants) (Figure 3). Furthermore, also in 2015, São Paulo state presented the highest incidence rate of IMD in the country (1.24/100 000 inhabitants), followed by Rio Grande do Sul and Rio de Janeiro, as shown in Table 3.

Case fatality rate

From the literature review, the CFR was estimated using the total number of deaths from IMD as the numerator and the total number of confirmed cases of IMD as the denominator. Nine studies described the required epidemiological data (Table 2).

The CFR attributable to meningococcal disease showed a significant annual variation. The epidemiological behavior of meningococcal disease in São Paulo city over the 20th century showed a CFR ranging between 20.0% and 50.0% (Moraes and Barata, 2005).

In São Paulo state, Sorocaba region showed a CFR of 21.8% (range 8.1–34.8%) from 1999 to 2008. In an analysis by age group, the following rates were found: 26.4% for those 0–4 years, 10.6% for those 5–9 years, 18.2% for those 10–19 years, 21.8% for those 20–29 years, and 28% for those ≥ 30 years of age (Leme and Zanetta, 2012).

The overall CFR in São Paulo city from 1986 to 2004 was 20.5%, with major differences identified according to age and serogroup. The CFR was 27.4% in children under 2 years of age, reaching 32.8% in the age group over 40 years. A higher CFR was found for cases associated with serogroup W (17.8%), followed by serogroups B (12.1%) and C (11.0%). The high CFR associated with serogroup W

Table 2

Annual incidence rate of invasive meningococcal disease and case fatality rate from the included studies.

Study	Annual incidence rate (cases per 100 000 inhabitants per year)	CFR (%)
Bahia		
Cordeiro et al. (2007)	1.71	8.1
Nunes et al. (2011)	0.9–1.8	19–31
Cardoso et al. (2012)	NR ^a	NR ^a
Distrito Federal		
Tauil et al. (2014)	2008–2009: 2.0 2010: 1.8 2011: 0.8	20.7
Minas Gerais		
Nascimento et al. (2012)	0.88	26.8
Rio de Janeiro		
Barroso et al. (2010)	NR ^b	2 (meningitis) 9 (sepsis + meningitis) 33 (sepsis)
Rio Grande do Sul		
Baethgen et al. (2008)	2.5 ± 0.6 (Range 1.8 in 2003 to 3.5 in 1995)	22.2 ^c
Weidlich et al. (2008)	1.54	NR
Santa Catarina		
Bertoncini et al. (2007)	2.5–11.1 (average 7.9)	NR
São Paulo		
Moraes and Barata (2005)	NR	20.0–50.0
Leme and Zanetta (2012)	1999 and 2000: >3 2001: around 2 2008: 5.5	21.8 (range 8.1–34.8)
Masuda et al. (2015)	1986 to 2004: 5.3 1995 (peak): 8.1 1986 (minimum): 1.2	20.5 (range 15–24.6)

CFR, case fatality rate; NR, not reported.

^a Reported only for serogroup C. The cumulative incidence of serogroup C meningococcal disease in the city of Salvador was 0.1 cases per 100 000 inhabitants per year from 2000 through 2006, with one death (CFR, 5%). In 2007, 13 cases (0.45 cases/100 000 inhabitants) of serogroup C meningococcal disease were identified, with two deaths (CFR, 15%); in 2008, 53 cases (1.8 cases/100 000 inhabitants) were identified, with four deaths (8%); in 2009, 69 cases (2.3 cases/100 000 inhabitants) were identified, with 10 deaths (14.5%).

^b Incidence was reported according to the period. It was not possible to extract a value.

^c Information about the outcome was not available for 515 cases. Thus, the CFR was 22.2% for cases with known outcome information.

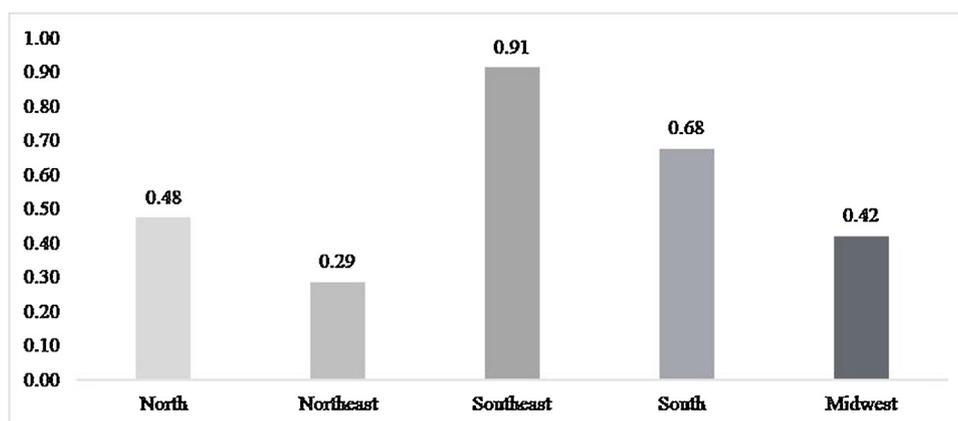


Figure 3. Incidence per 100 000 inhabitants of invasive meningococcal disease by geographical region, Brazil, 2015. (Source: Ministry of Health, Brazil; DATASUS – Department of Information Technology of the Unified Health System, 2017; Brazilian Institute of Geography and Statistics (IBGE), 2013).

was found in all age groups, especially in those ≥ 40 years old (33.3%) (Masuda et al., 2015). In the state of Rio Grande do Sul, a retrospective cohort study reported a CFR of 22% for the years 1995–2003 (Baethgen et al., 2008).

In the state of Bahia, active hospital-based surveillance of meningococcal meningitis identified 408 cases between February 1996 and January 2001, with a CFR of 8% (Cordeiro et al., 2007). Also in Bahia, in the study conducted by Nunes et al. (2011), the CFR

ranged from 19% to 31%, reaching its highest value (31%) in 2007. However, in the Federal District, the average CFR from 2005 to 2011 was 20.7%, with no significant variation (Tauil et al., 2014).

Data from Brazilian Ministry of Health showed an absolute reduction in the number of deaths attributable to meningitis between 2007 and 2015; however, the CFR remained relatively stable during this period (11.1% in 2007 and 8.4% in 2015). In 2015, a higher CFR was seen with serogroup A (33.3%). However,

Table 3
Incidence rate of invasive meningococcal disease by state, Brazil, 2015.

Brazilian state	Incidence rate (Cases per 100 000 inhabitants)
North region	0.48
Rondônia	0.11
Acre	0.12
Amazonas	0.81
Roraima	0.59
Pará	0.51
Amapá	0.26
Tocantins	0.07
Northeast region	0.29
Maranhão	0.09
Piauí	0.34
Ceará	0.25
Rio Grande do Norte	0.55
Paraíba	0.08
Pernambuco	0.32
Alagoas	0.45
Sergipe	0.27
Bahia	0.33
Southeast region	0.91
Minas Gerais	0.35
Espírito Santo	0.33
Rio de Janeiro	0.89
São Paulo	1.24
South region	0.68
Paraná	0.57
Santa Catarina	0.41
Rio Grande do Sul	0.94
Midwest region	0.42
Mato Grosso do Sul	0.49
Mato Grosso	0.49
Goiás	0.33
Distrito Federal	0.48

Source: Ministry of Health, Brazil; DATASUS – Department of Information Technology of the Unified Health System, 2017; Brazilian Institute of Geography and Statistics (IBGE), 2013.

considering the low number of cases (one death in three cases of IMD associated with serogroup A), this value may not be representative. With the exclusion of serogroup A, serogroup W presented the higher CFR (24.1%; 13 deaths in 54 cases), followed by serogroups C (19.2%; 69 deaths in 360 cases), B (17.7%; 28 deaths in 158 cases), and Y (14.3%; two deaths in 14 cases) (Ministry of Health, Brazil, DATASUS, 2017).

Serogroup distribution

Fourteen studies in the literature review reported serogroup distribution data. Serogroup B was the most prevalent in nine studies and serogroup C in five. The geographical distribution according to the literature is presented in Table 4.

Four studies were conducted in Bahia state (Cordeiro et al., 2007; Nunes et al., 2011; Cardoso et al., 2012; Nunes et al., 2016) and showed serogroup B as the most prevalent, with rates varying from 11.8% to 83%. However, in the Federal District, the only study presenting serogroup data showed serogroup C to be the most prevalent (Taulil et al., 2014). Similarly, in Minas Gerais 57% of the patients were classified as having serogroup C disease (Nascimento et al., 2012).

In the most recent studies, an increase in serogroup W prevalence was observed, with a significant increase from 2003 to 2005 (17.8%), compared to 3.2% from 1995 to 2002 ($p < 0.001$) (Weidlich et al., 2008).

Four studies described the serogroup distribution from the colonization point of view. Moraes et al. (2015) evaluated the prevalence of meningococcal carriage in adolescents. Among *N. meningitidis* specimens, 16 (13.4%), 12 (10.0%), nine (7.5%), six (5.0%), three (2.5%), and one (0.8%) were geno/serogroup C, B, E, Y, W, and Z, respectively. Seventy-three isolates (60.8%) could not be classified by serogroup. Recently, another study evaluated 59

colonized participants: 36 (61.0%) carried non-groupable *N. meningitidis*, while seven (11.8%) carried genogroup B, five (8.5%) genogroup Y, four (6.7%) genogroup E, three (5.1%) genogroup Z, two (3.4%) genogroup C, and two (3.4%) genogroup W (Nunes et al., 2016). In a study conducted in two oil refineries in São Paulo to determine the serogroup of positive samples, 48.2% were serogroup C, 16.1% were serogroup B, 14.3% were serogroup E, 12.5% were serogroup Y, and 8.9% were serogroup W (Sáfadi et al., 2014b). In Rio Grande do Sul, 16.6% of carriers presented serogroup B (Coch Gioia et al., 2015).

Secondary data analysis using the Brazilian Ministry of Health database for IMD showed that most patients had serogroup C disease. It is important to note that in 2015, serogroup identification was presented for only 44.97% of patients (Figure 4). A gradual decrease in serogroup identification was observed starting in 2010: 50.23%, 53.05%, 54.34%, 49.41%, 48.61%, and 44.97% (2010–2015) (Ministry of Health, Brazil, DATASUS, 2017). In 2015, serogroup C was the most prevalent in all regions of the country (Figure 5). Regarding age groups, in the same year, serogroup B was the most prevalent in patients up to 5 years old. From this age, serogroup C became the most prevalent in the diagnosed population (Figure 6).

Discussion

This study is novel in performing a systematic review and secondary data collection in order to evaluate the epidemiological profile of IMD and *N. meningitidis* carriers in Brazil. As surveillance of meningitis is based on mandatory notification of suspected cases to SINAN with or without etiological agent identification, it is estimated that the real incidence of meningococcal disease is greater than that routinely reported because of the large proportion of reported cases without etiological identification (Azevedo et al., 2013). Since the mandatory notification is national, regional differences in data reports in the databases are not expected.

The epidemiological data for IMD differ in the systematic review and secondary data analysis. Factors such as population displacement, poor access to healthcare services, and interruption of ongoing treatment or control programs, which may increase the disease burden, explain the possible differences in incidence between regions, and may also lead to an underestimate of the importance of each serogroup.

The results of this study showed that the incidence of IMD has been declining steadily in recent years, but is still important, particularly in key age groups such as infants. The southern and southeastern regions presented the highest incidence of meningitis compared to the rest of the country, which is consistent with data reported in a literature review. The CFR remained constant despite the falling incidence, with serogroup W being a particularly important contributor to high mortality in all age groups. Currently, serogroups C and B represent the etiological agent in a substantial proportion of cases in Brazil. However, in a more recent analysis, serogroup W was also found to contribute significantly to the disease burden. The rise of serogroup W in Brazil has taken place recently and unexpectedly when compared with the long-term continued dominance of serogroups B and C disease (Abad et al., 2014). It is important to note that serogroup identification was done for only 44.97% of patients, which could lead to an underestimate of the prevalence panorama for each serogroup. The first reported serogroup W135 disease in Brazil occurred in 1983 in São Paulo state, with an incidence rate of 0.1/100 000 inhabitants. Starting in 2004, Brazil was the first country in Latin America with an increase in the percentage of cases associated with serogroup W, which was evident in Rio Grande do Sul (incidence rate 1.5/100 000) (Weidlich et al., 2008) and in Rio de Janeiro (Barroso et al., 2010). In fact, in the southern region, the

Table 4
Meningococcal serogroup distribution according to Brazilian state.

Study	B n (%)	C n (%)	W n (%)	Y n (%)	A n (%)
Invasive meningococcal disease					
Bahia					
Cordeiro et al. (2007)	309 (82)	60 (16)	7 (2)	1 (0.3)	NR
Nunes et al. (2011)	327 (71.9)	121 (26.6)	^a	^a	^a
Cardoso et al. (2012)	2000–2006: 105 (83) 2007–2011: NR	2000–2006: 20 (16) 2007–2011: NR	2000–2006: 1 (<1) 2007–2011: NR	NR	2000–2006: 1 (<1) 2007–2011: NR
Distrito Federal					
Tauil et al. (2014)	2005–2009: 25 (20.7) 2010: 2 (11.1) 2011: 2 (20.0)	2005–2009: 85 (70.2) 2010: 14 (77.8) 2011: 6 (60.0)	2005–2009: 7 (5.8) 2010: 1 (5.6) 2011: 1 (10)	2005–2009: 4 (3.3) 2010: 1 (5.6) 2011: 1 (10)	NR
Minas Gerais					
Nascimento et al. (2012)	189 (37.8)	285 (57)	14 (2.8)	3 (0.6)	9 (1.8)
Rio Grande do Sul					
Baethgen et al. (2008)	229 (79)	41 (14.1)	18 (6.2)	2 (0.7)	
Weidlich et al. (2008)	(64)	(18)	(17)	(1)	Not detected
Santa Catarina					
Bertoncini et al. (2007)	933 (73.5)	328 (23.8)	NR ^b	NR ^b	NR ^b
São Paulo					
Leme and Zanetta (2012)	(45.7)	(47.3)	(3.7)	(1.5)	NR
Masuda et al. (2015)	(51.5) ^c	(26.1) ^c	(4.8) ^c	(0.2) ^c	–
<i>Neisseria meningitidis</i> carriers					
Nunes et al. (2016)	7 (11.8)	2 (3.4)	2 (3.4)	5 (8.5)	NR
Coch Gioia et al. (2015)	3 (16.6)	NR ^d	NR ^d	NR ^d	NR ^d
Sáfadi et al. (2014b)	9 (16.1)	27 (48.2)	5 (8.9)	7 (12.5)	NR
Moraes et al. (2015)	(10.0) ^e	(13.4) ^e	(2.5) ^e	(5.0) ^e	–

NR, not reported.

^a Serogroups A, Y, and W: seven cases.^b 0.7% of cases were due to other serogroups.^c Serogroup data were available for 27% of deaths (505/8669): 51.5% (260/505) associated with serogroup B, 26.1% (132/505) with serogroup C, 4.8% (24/505) with serogroup W, 0.2% (1/505) with serogroup Y; 17.4% (88/505) of *N. meningitidis* was not typable.^d Of 18 isolated meningococcal strains, 14 were non-groupable (NG), three corresponded to serogroup B and one to serogroup 29E.^e Among the 120 detected *N. meningitidis* specimens, 16 (13.4%) were geno/serogroup C, 12 (10.0%) were geno/serogroup B, nine (7.5%) were serogroup E, six (5.0%) were geno/serogroup Y, three (2.5%) were geno/serogroup W, and one (0.8%) was serogroup Z. There were 73 non-groupable isolates (60.8%).

serogroup W strains increased from 3.2% during 1995–2003 to 17.8% in 2003–2005, with an incidence rate around 2 cases/100 000 inhabitants (López and Debbag, 2012). The literature shows a greater presence of serogroup W in young adults. An increase in the presence of serogroup W in the elderly population has not been seen in Brazil.

IMD is a rapid and unpredictable illness, with substantial morbidity and mortality among those affected. A second peak of disease occurs in young adults worldwide, despite the higher incidence in infants (Pelton, 2016). In the present analysis, the second peak of disease was not noticed in young adults, perhaps because of the endemic disease characteristic from early ages to around 20 years old.

Despite the increase in serogroup W cases following the introduction of the MenC vaccination, all IMD-related outbreaks have decreased. Outbreaks continue to occur in many regions. There are various potential causes involved in these events, including low vaccination uptake rates, poor surveillance and control systems, lack of standardized case definitions and diagnostic assessments, lack of herd protection, failure to vaccinate those currently at risk, strain changes, increases in serogroups not covered by current vaccines, and the general unpredictability of IMD epidemiology (Borrow et al., 2017).

Vaccination remains the key method for prevention. The main desired effects of vaccination are to protect those vaccinated from developing IMD when exposed, as well as to reduce acquisition and carriage (Borrow et al., 2017). The immunization of adolescents

and young adults in catch-up campaigns could reduce the carriage rates of MenC in the vaccinated age group and may prevent transmission of the organism and acquisition by other individuals (Sáfadi et al., 2014a). In Europe, the success of the MenC vaccination program has been attributed to the combined vaccine efficacy against both disease and carriage (Sáfadi et al., 2014a).

Moraes et al. showed high rates of serogroup C carriage among adolescents, reinforcing the importance of targeting both cohorts in order to achieve herd effects and maximize the benefits of the current MenC vaccination program in Brazil (Moraes et al., 2015). In 2017 and 2018, the Brazilian Ministry of Health expanded the vaccination target to reach the age groups of 12–13 years and 11–14 years of age, respectively (Ministry of Health, Brazil, 2018).

Conclusions

The analysis of the published literature and Brazilian national databases was similar and consistent in many ways, drawing attention to the unpredictability of meningococcal circulation in different regions of a country.

Overall, serogroup C is prevalent in all Brazilian regions, with a rise of serogroup B up to 5 years of age and serogroup W in young adults, alerting to a possible second peak of incidence in this age group.

Despite the reduction in number of cases reported both in the literature review and in the Brazilian database analysis, the CFR associated with IMD remained stable. It is of note that the CFR was

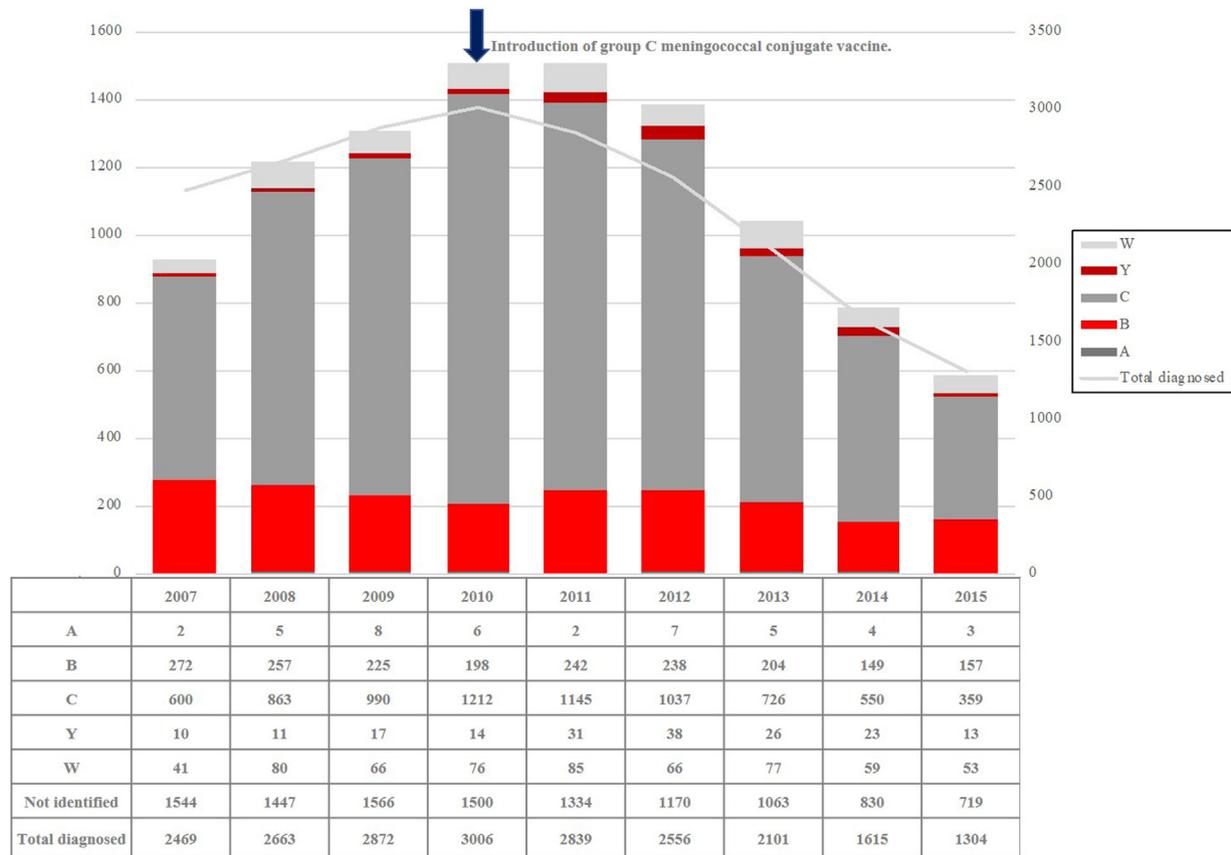


Figure 4. Number of diagnosed cases of invasive meningococcal disease over the years by serogroup, Brazil. (Source: Ministry of Health, Brazil; DATASUS – Department of Information Technology of the Unified Health System, 2017). The group C meningococcal conjugate vaccine was introduced into the routine Brazilian immunization program in 2010.

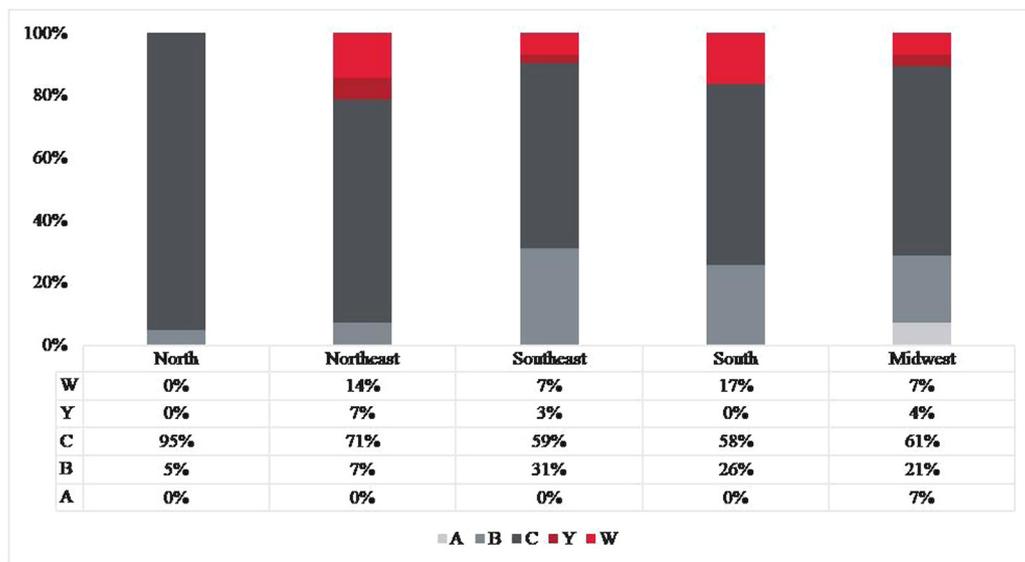


Figure 5. Relative distribution of meningococcal serogroups by geographic region, Brazil, 2015. (Source: Ministry of Health, Brazil; DATASUS – Department of Information Technology of the Unified Health System, 2017).

similar among children under 1 year of age and among adults between 30 and 40 years of age, despite the difference in serogroups causing the disease in these age groups. The highest CFR seems to be associated with serogroup W.

Future studies should analyze possible gaps, such as healthcare access, notification failures, and availability of diagnostic methods in

Brazilian regions, since the difference between the number of reported cases, together with the progressive decrease in serogroup identification over the years, could underestimate the true burden of disease and the weight of each serogroup in that context.

Finally, a country's vaccination strategy should be based on epidemiological disease analysis and, in this scenario, Brazil, which

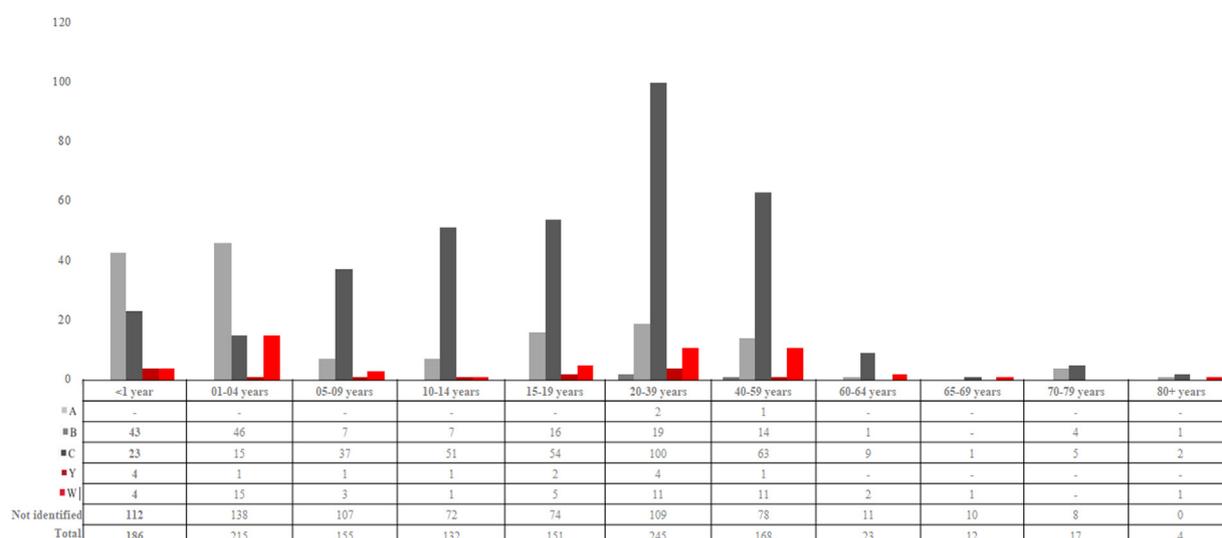


Figure 6. Relative distribution of meningococcal serogroups by age group, Brazil, 2015. (Source: Ministry of Health, Brazil; DATASUS – Department of Information Technology of the Unified Health System, 2017).

has already started vaccination for children under 1 year of age, has now started to adopt an adolescent vaccination strategy, reinforcing the need to investigate the epidemiological evolution that may occur in the subsequent years.

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Conflict of interest

Jéssica Vespa Presa: Pfizer Inc. employee; Rodrigo Sini de Almeida: Pfizer Vaccines Brazil employee; Júlia Regazzini Spinardi: Pfizer Vaccines Brazil employee; Alejandro Cane: Pfizer Vaccines Argentina employee.

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