



**MENINGITIS IN THE ELDERLY POPULATION IN BRAZIL: NARRATIVE REVIEW**

**MENINGITIS EN LA POBLACIÓN MAYOR DE BRASIL: REVISIÓN NARRATIVA**

**MENINGITE NA POPULAÇÃO IDOSA NO BRASIL: REVISÃO NARRATIVA**

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**ABSTRACT**

**Objective:** To present scientific evidence, based on an integrative literature review, about meningitis in the elderly Brazilian population. **Methods:** The articles were searched in the databases SciELO, LILACS, MEDLINE (PubMed), Scopus, BIREME and Web of Science, in addition to a search for gray literature on Google Scholar. The studies were selected with a combination based on Medical Subject Headings (MeSH), conducted according to the recommendations of PRISMA. **Results:** The predominance of non-valiant pneumococcal conjugate vaccine (PCV10) serotypes is predominant in invasive pneumococcal disease in the elderly population in strains that circulate three to five years after the introduction of PCV10 in Brazil. A long interval between the onset of symptoms and the diagnosis of the disease indicates a worsening of the prognosis and an increase in lethality in the elderly Brazilian population. **Conclusion:** Meningitis in the elderly population is associated with greater diagnostic difficulties, neurological severity, clinical complications and increased mortality.

**KEYWORDS:** Aged. Meningitis. Health of the elderly. Immunization Programs.

**RESUMEN**

**Objetivo:** Presentar evidencia científica, basada en una revisión integradora de la literatura, sobre la meningitis en la población anciana brasileña. **Métodos:** Los artículos fueron buscados en las bases de datos SciELO, LILACS, MEDLINE (PubMed), Scopus, BIREME y Web of Science, además de una búsqueda de literatura gris en Google Scholar. Los estudios fueron seleccionados con una combinación basada en Medical Subject Headings (MeSH), realizados de acuerdo con las recomendaciones de PRISMA. **Resultados:** El predominio de los serotipos de la vacuna antineumocócica conjugada no valiente (PCV10) es predominante en la enfermedad neumocócica invasiva en la población anciana en cepas que circulan de tres a cinco años después de la introducción de la PCV10 en Brasil. Un largo intervalo entre el inicio de los síntomas y el diagnóstico de la enfermedad indica un empeoramiento del pronóstico y un aumento de la letalidad en la población brasileña de edad avanzada. **Conclusión:** La meningitis en la población anciana se asocia a mayores dificultades diagnósticas, gravedad neurológica, complicaciones clínicas y aumento de la mortalidad.

**PALABRAS CLAVE:** Anciano. Meningitis. Salud de las personas mayores. Programas de vacunación.

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### RESUMO

**Objetivo:** Apresentar evidências científicas, com base em uma revisão integrativa da literatura, sobre meningite na população idosa brasileira. **Métodos:** Os artigos foram pesquisados nas bases de dados SciELO, LILACS, MEDLINE (PubMed), Scopus, BIREME e Web of Science, além de uma busca por literatura cinza no Google Scholar. Os estudos foram selecionados com uma combinação baseada no Medical Subject Headings (MeSH), conduzidos de acordo com as recomendações do PRISMA. **Resultados:** Destaca-se a predominância de sorotipos da vacina pneumocócica conjugada não-10 valente (PCV10) na doença pneumocócica invasiva na população idosa em cepas que circulam três a cinco anos após a introdução da PCV10 no Brasil. Um longo intervalo entre o início dos sintomas e o diagnóstico da doença indica piora do prognóstico e aumento da letalidade na população idosa brasileira. **Conclusão:** Meningite na população idosa está associada a maior dificuldade diagnóstica, gravidade neurológica, complicações clínicas e aumento da mortalidade.

**PALAVRAS-CHAVE:** Idoso. Meningite. Saúde do idoso. Programas de imunização.

### INTRODUCTION

Meningitis can be classified as an inflammatory disease affecting the membranes that protect the central nervous system (CNS). Common symptoms of the disease are normally fever, headache, vomits, and nausea. These are combined with the diagnostic examination with changes in the cerebrospinal fluid, which can be caused by both infectious and noninfectious agents. It must be kept in mind that meningitides are serious and evolve quickly, and their prognosis depends on early diagnosis and adequate treatment.<sup>1</sup>

The disease is usually transmitted via the respiratory pathways or contact with secretions from an infected person. The main risk factors for its development are deficient nutrition, impaired immune system, prolonged corticoid treatment, and CNS traumas.<sup>2</sup> With advancing age, the physiological changes grow increasingly worse, leading to the severity of possible infections in older adults. People older than 60 years are constantly subject to underlying diseases with associated symptoms, which may be mistaken for those of meningitis.<sup>3</sup>

The clinical diagnosis of infectious meningitis in older adults is a complex issue, and the delay in diagnosing and treating it increases lethality. In the literature, meningitis is described as a disease with high lethality rates (24% to 62%) in the older population.<sup>4</sup> From 2004 to 2020, there were 15,730 reported cases of meningitis among older people in Brazil – 3,507 of whom died.<sup>5</sup> **(Table1)**



**TABLE 1.** Deaths from meningitis by reporting region from 2006 to 2020

Reporting region	Period															Total
	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	
1 North Region	-	4	6	4	4	-	5	9	8	7	12	6	10	13	2	90
2 Northeast Region	1	25	24	36	25	33	35	24	30	28	31	34	41	33	6	406
3 Southeast Region	1	118	131	141	139	165	164	172	157	181	205	208	210	160	47	2199
4 South Region	1	48	38	48	38	35	49	48	55	62	43	66	61	50	23	665
5 Central-West Region	1	10	6	4	15	18	11	8	15	12	12	6	11	14	4	147
Total	4	205	205	233	221	251	264	261	265	290	303	320	333	270	82	3507

Given the above, the main and guiding objective of this research was to present the acuity of meningitis in the older Brazilian population, aiming to answer the following question: What is the indication of meningitis in the older Brazilian population?

## METHODS

### Protocol

This narrative review was conducted according to the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) recommendations.<sup>6</sup> The scientific articles were searched by two independent researchers in the MEDLINE (PubMed), LILACS, SciELO, SCOPUS, Web of Science, and BIREME databases, with no restriction of language, time, and place of publication. Complementarily, a manual search was conducted in the references of the articles already included in this research, as well as a search for gray literature in Google Scholar. The research was structured



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and organized in the PICOS framework, an acronym that stands for Target Population, Intervention, Comparison, Outcomes, and Study Type. The population of interest or health problem (P) corresponds to the older adults; intervention (I) is related to prevention; comparison (C) corresponds to meningitis; outcome (O) refers to the Brazilian data; and the types of the studies included (S) are descriptive study, cross-sectional study, observational study, case reports, case-control studies, controlled clinical trials, and cohort studies.

### Research Strategy

The descriptors were chosen based on the dictionary in the Health Sciences Descriptors (DeCS) and Medical Subject Headings (MeSH), considering their use by the scientific community to index articles in the PubMed database. After the search for descriptors, adjustments were made for the other databases when necessary. At the first moment, the following combination and Boolean operators were proposed for the search: (elderly) and (meningitis) and (Brazil). The search for articles took place mainly in August 2020.

### Eligibility criteria

The studies included here were designed as a descriptive study, cross-sectional study, observational study, case reports, case-control, controlled clinical trials, and cohort studies. They were included with no restriction of language, time, and place of publication. One of the inclusion criteria was that the studies had a score higher than 6 in the modified protocol by Pithon et al.,<sup>7</sup> which assesses their quality, and necessarily contained information on the older Brazilian population.

### Risk of bias

The quality of the methods used in the studies included in this research was independently assessed by the reviewers (PH and LFG), following the PRISMA recommendations. The assessment gave priority to clearly described information. At this point, the review was blind, masking the names of authors and journals and avoiding any potential bias and conflict of interests.

### Exclusion criteria

Studies published as letters to the editor, guidelines, literature reviews, narrative reviews, systematic reviews, meta-analyses, and abstracts were excluded. Studies with unclear or deficient information, or yet, with unavailable full text were also excluded.

### Data Analysis

The data for the studies' eligibility process were extracted with a suitable sheet for narrative reviews, developed by two researchers on Excel®, where the extracted data were first inserted by one of the researchers and then checked by another one. The studies were selected by their title; then, the



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abstracts were analyzed, and only the potentially eligible ones were selected for the following screening stage. Based on the abstracts, the articles were selected to be read in full, and those that met all the pre-established criteria were included.

### Study selection method

Initially, the eligibility reviewers (PH and LFG) were calibrated. After the calibration, and having their doubts answered, the titles and abstracts were independently examined by the two eligibility reviewers (PH and LFG). Those whose title was within the context but whose abstract was unavailable were also retrieved and analyzed in full. Afterward, the eligible studies had their full text retrieved and evaluated. In specific cases that a potentially eligible study had incomplete data, the authors could be contacted via e-mail for further information; however, that was not necessary for this research.

### Collected data

After the screening, the text of the selected articles was reviewed and extracted in a standardized way by two authors (PH and LFG), identifying the year of publication, place of the research, language of publication, type of study, sample, method, result, and conclusion of the study.

### Clinical result

The clinical result of interest consisted of verifying the acuity of meningitis in the older Brazilian population. Those who did not have this approach were not included in the sample of the literature review.

### RESULTS

Initially, 491 articles were selected and identified; 10 were repeated, and 479 were excluded by the analysis of their title and abstract. Lastly, two potential articles<sup>3,8</sup> were included, as they met the guidelines proposed for the present systematic research. Based on the chosen descriptors, the scientific data banks were consulted to extract the information made available in **Table 2**.



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**TABLE 2.** Classification of the references obtained from the MEDLINE, SciELO, LILACS, Web of Science, and Scopus databases.

Descriptors	No. of articles	Excluded references	Pretext	Selected	Database
(elderly) and (meningitis) and (Brazil)	5	5	Excluded by title (5);	-	SciELO
(elderly) and (meningitis) and (Brazil)	19	18	Excluded by title (7), excluded by abstract (11);	1	LILACS
(elderly) and (meningitis) and (Brazil)	23	23	Excluded by title (23);	0	BIREME
(elderly) and (meningitis) and (Brazil)	0	0	0	-	Scopus
(elderly) and (meningitis) and (Brazil)	0	0	0	-	Web of Science
(elderly) and (meningitis) and (Brazil)	444	443	Duplicated (10); Excluded by title (400); excluded by abstract (33);	1	MEDLINE
Total	491	489	489	2	LILACS and MEDLINE

Source: Developed by the authors

The first article included here<sup>3</sup> reports a sample number with 64 older patients aged 60 years or older and mean age 69.4 years. The diagnosis of meningitis was confirmed with the laboratory examination of the cerebrospinal fluid, collected with a lumbar or suboccipital puncture, depending on the patient's clinical condition. The sample comprised 64 patients, 25 of whom were women (39.06%) and 39 were men (60.94%). The fatal cases were more frequent among the unspecified bacterial



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meningitides (65.21%), whose mortality rate was 35.9% of the patients thus diagnosed. In addition, the study points out what was most observed in 98.4% of the cases at the moment when the patient was being attended, besides fever and mental changes, as the main clinical manifestations to analyze the occurrence of deaths. The most prevalent infectious meningitides were the unspecified bacterial (64.02%), the pneumococcal (14.06%), and the viral ones (12.5%), followed by the fungal (4.68%), tuberculous (3.12%), and meningococcal (1.56%).<sup>3</sup>

In the second study,<sup>8</sup> 102 cases of pneumococci were analyzed in patients with invasive pneumococcal disease (IPD). The analyses included the extraction of DNA and the antimicrobial susceptibility test for penicillin, meropenem, ceftriaxone, trimethoprim/sulfamethoxazole, levofloxacin, erythromycin, tetracycline, and vancomycin. The patients' mean age was 66 years (ranging from 50 to 90 years), and 81.4% (n = 83) of them were males. As for the diagnosis, 86.3% (n = 88) were reached with a complete blood count, followed by cerebrospinal fluid analysis in 7.8% (n = 8), pleural fluid analysis in 2.9% (n = 3), and ascites, pericardium, and joint fluid (1.0%). The authors report a predominance of non-PCV10 serotypes in IPD in the older population in strains circulating three to five years after PCV10 was introduced in Brazil (**Table 3**).

**TABLE 3.** Summary of the included articles.

Author/ Year/ Place of publication	Objective	Sample size	Examinations	Results	Conclusion
Alvarenga et al., 2013 Brazil	To assess the clinical/epidemiological aspects of the infectious meningitides in patients admitted to a reference hospital in the municipality of Goiânia.	Total of 64; 39.06% of women, and 60.94% of men.	cerebrospinal fluid examination	The most prevalent infectious meningitides were the unspecified bacterial (64.02%), pneumococcal (14.06%), and viral (12.5%), followed by the fungal (4.68%), tuberculous (3.12%), and meningococcal (1.56%). The overall mortality was high (35.9%). There was a long period between the onset of the symptoms and the	The study showed an excessively long time between the onset of meningitis symptoms and its diagnosis, which can worsen the prognosis and increase lethality.



				diagnosis (mean: 6.6 days) in the patients.	
Christophe et al., 2018 Brazil	To characterize isolations of <i>S. pneumoniae</i> obtained ca. 3 to 5 years after the PCV10 was introduced, due to invasive pneumococcal diseases in people older than 50 years	Total of 102; 83 were men, and 19 were women	DNA extraction Antimicrobial susceptibility test Sequential multiplex PCR Quellung reaction	Of the 102 isolated pneumococci, the most frequent serotypes were 19A, 13 of 102 (12,7%) and 22F, 10 of 102 (9,8%). 98 pneumococci were tested for antimicrobial susceptibility. Intermediate resistance to penicillin was present in 2/98 (2.0%), ceftriaxone in 7/98 (7.1%), and meropenem in 7/95 (7.4%) of the isolations. Resistance to penicillin was observed in 31/98 (31.6%) of the pneumococci.	The predominance of non-PCV10 serotypes in the invasive pneumococcal disease (IPD) in the older population in strains circulating ca. 3 to 5 years after the PCV10 was introduced in Brazil.

**Source:** Alvarenga et al., 2013; Christophe et al., 2018.

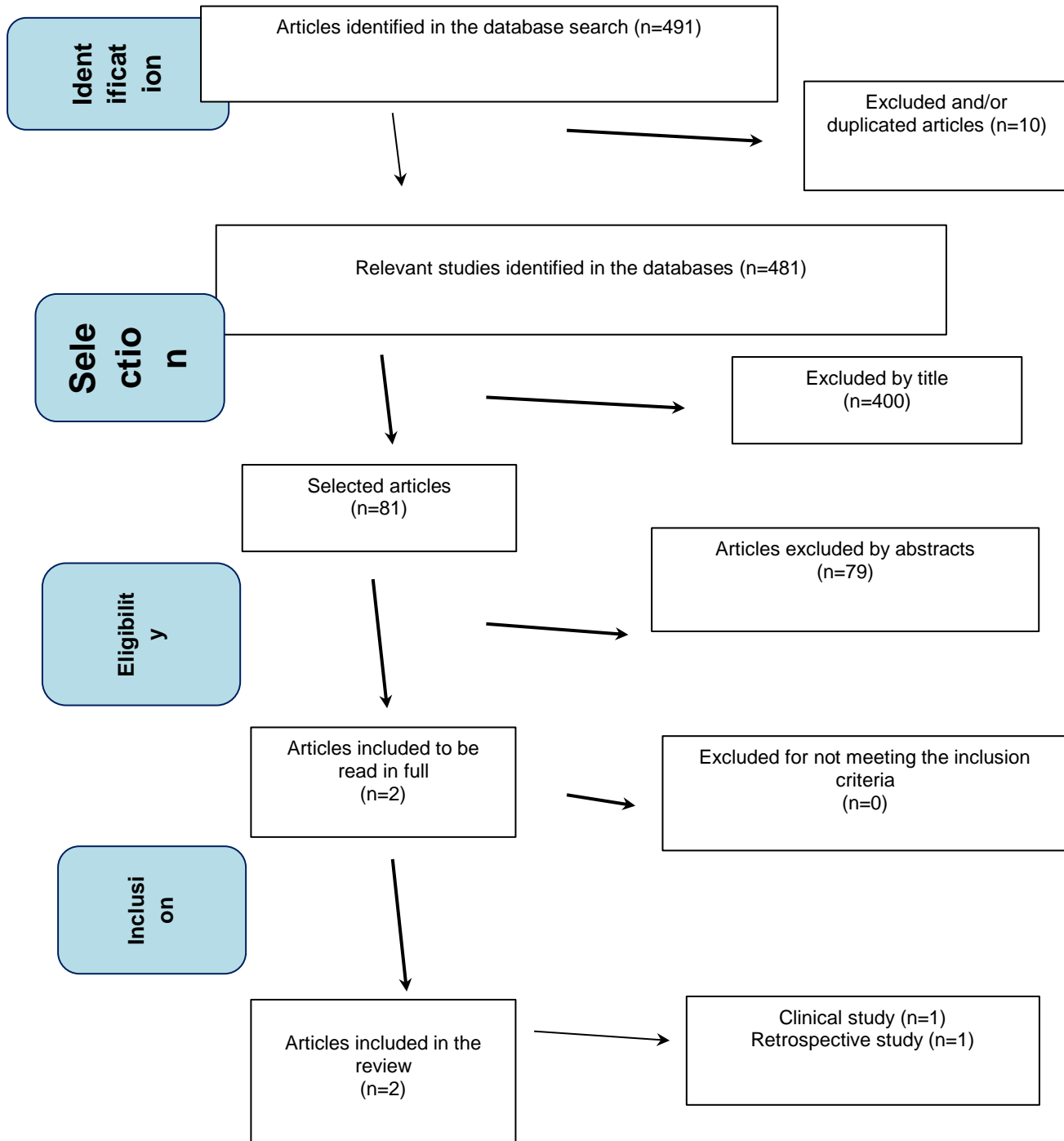
**Legend:** PCV-10: 10-valent pneumococcal conjugate vaccine; IPD: invasive pneumococcal disease

The type of articles included in the research were retrospective and clinical studies. The data obtained from the eligible studies were also transported to a spreadsheet in the same program to organize the results, as described in **Figure 1**.





**Figure 1.** Flowchart of the article search and analysis process



Source: Developed by the authors.



## DISCUSSION

The present research aimed to verify the acuity of meningitis in the older Brazilian population. In the analyzed research,<sup>3,8</sup> it was verified that an extended time between the onset of symptoms and the diagnosis of meningitis can worsen the prognosis and increase the lethality of the older adults – who are at greater risk of acquiring meningitis than younger adults. In older adults, the disease has comorbid conditions, is clinically subtler, and has a longer admission interval with antibiotic therapy. Furthermore, it is associated with an earlier and higher mortality rate than in younger patients.<sup>9</sup>

In the study,<sup>3</sup> the authors used the cerebrospinal fluid examination to confirm the diagnosis of meningitis. According to Comar et al.,<sup>10</sup> the cerebrospinal fluid (CSF) is an aqueous fluid that circulates in the intracranial space, representing most of the extracellular fluid of the CNS. This liquid has various functions, such as supplying the essential nutrients to the brain, removing the products of neuronal activity in the CNS, and mechanically protecting the brain cells.

The CNS diseases that cause meningoencephalitis are caused by various etiologic agents, such as viruses, bacteria, fungi, parasites, endocrinopathies, metabolic changes, obstructive processes. They have certain characteristics, including fever, nausea, vomits, headache, irritation of the meninges, and physical, chemical, and laboratory changes in the cerebrospinal fluid.<sup>11</sup> It is utterly important to examine this fluid, as it aids in a more assertive diagnosis of the disease.<sup>12</sup> The laboratory aspects of the cerebrospinal fluid are analyzed – i.e., its cellularity, biochemical aspects, antigen research, and polymerase chain reaction (PCR). Other complementary examinations, such as the complete blood count and C-reactive protein are also useful in the diagnosis of the disease.<sup>13</sup>

The second study included here<sup>8</sup> verified cases of pneumococci isolated from patients with invasive pneumococcal disease (IPD). Older adults who acquire pneumococcal infections make up a particularly vulnerable group to complications such as pneumonia, bacteremia, and meningitis, considering the possible physiological fragility. These are the usual consequences of IPD, representing a major cause of morbidity in people 65 years old or more. In Europe, the IPD has an incidence of approximately 45% in this age group.<sup>14</sup>

Regarding lethality due to meningitis, Alvarenga, Almeida, and Reimer, 2013,<sup>3</sup> report that the cases were more frequent among unspecified bacterial meningitides (65.21%). The overall mortality was 35.9%, which depicts an important index of that population. The study indicates that mental changes and awareness conditions were observed in 98.4% of the cases at the moment when the patient was being attended, which points to their specificity in terms of clinical assessment. The clinical characteristics, etiologies, evolution, and prognostic factors of meningitis acquired by older patients in the community require an important broadening of the scientific discussion. Meningitis in older patients is associated with greater diagnostic difficulties, neurologic severity, and greater complications, as well as an increase in mortality<sup>15</sup> – factors that must be clinically discussed and established.

Christophe, Mott, Cunha et al.<sup>8</sup> presented analyses of serotypes included in the PCV10, represented in 30.4% by pneumococci. The authors mention a prevalence of non-PCV10 serotypes in IPD in the older



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population in strains circulating three to five years after the PCV10 vaccine was introduced in Brazil – important information that points directly to the effective coverage of the vaccination in this population. The anti-pneumococcal vaccination is an effective strategy to decrease the indexes of diseases associated with the pneumococcus, particularly in the older population.<sup>16</sup> In a global scenario of older population growth, an important advancement is verified in technological vaccine development innovation. Even considering that age interferes with an efficient immune response, vaccination is one of the most important medical guidelines in the effort to decrease the morbidity and mortality caused by various infectious diseases. The importance of an effective vaccination is clear when the numbers of older people admitted to public hospitals in Brazil are analyzed. These are victims of infectious diseases that could be often avoided by broadening the effectiveness of the immunizations.<sup>17</sup>

### CONCLUSION

There may be multiple clinical characteristics and prognostic factors of meningitis in older patients. The various causes of change in their mental state, combined with the less frequency of other signs and symptoms that may suggest meningitis, makes the diagnosis more complex. When this disease affects older people, there are comorbid, clinically subtler conditions, possibly with a longer admission interval. It is important to highlight that the anti-pneumococcal vaccination is an effective strategy to decrease the indexes of the diseases associated with the pneumococcus, particularly in the older population, and that the vaccination coverage is an essential strategy to public health. Considering that age interferes with the effective immune response, vaccination is one of the most important procedures to prevent the morbidity and mortality caused by various infectious diseases, including the older population.

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