

## Possible causes and consequences of low measles vaccination coverage: an integrative literature review study

Possíveis causas e consequências da baixa cobertura vacinal de sarampo: um estudo de revisão integrativa da literatura

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### ABSTRACT

Measles is a viral, infectious, preventable disease that requires high vaccination coverage in order for herd immunity to be achieved and for outbreaks to be prevented. This study aims to identify the possible causes and consequences of low measles vaccination coverage. This is an integrative literature review based on original articles published in electronic databases between 2015 and 2021. Said articles were identified through controlled descriptors, prepared for structural and methodological evaluation, and categorized using the thematic content analysis technique. After application of the inclusion, exclusion and checklist criteria, six publications remained. Two thematic categories were defined: “Possible causes of low measles vaccination coverage worldwide” and “Consequences of low measles vaccination coverage”. Evidenced causes included: absent, incomplete or late vaccination schedule, late implementation of mass vaccination, insufficient stock of vaccines, and increased hesitation on the part of parents. The consequences were an increase in measles cases, in the risk of mortality, and in the health expenses of the public sector. It was concluded that a reduction in measles vaccination coverage has the potential to impact the population’s health conditions, to raise morbimortality indicators and to cause losses to public coffers.

**Keywords:** Measles. Measles vaccine. Vaccination coverage. Vaccine-preventable diseases.

### RESUMO

O sarampo é uma doença viral, infecciosa, evitável, que requer alta cobertura vacinal para atingir imunidade coletiva e prevenir surtos. Este estudo objetivou identificar as possíveis causas e consequências da baixa cobertura vacinal de sarampo. Trata-se de uma revisão integrativa da literatura, elaborada a partir de artigos originais, publicados em bases de dados eletrônicas entre 2015 e 2021, identificados por meio de descritores controlados. Os artigos foram submetidos à avaliação estrutural e metodológica, categorizados por meio de técnica de análise de conteúdo temática. Após aplicação dos critérios de inclusão, exclusão e checklist, restaram seis publicações. Foram apreendidas duas categorias temáticas: “Possíveis causas da baixa cobertura vacinal de sarampo no cenário mundial” e “Consequências da baixa cobertura vacinal de sarampo”. Evidenciaram-se, como causas, esquema vacinal ausente, incompleto ou tardio, implementação tardia da vacinação em massa, estoque insuficiente de vacinas e aumento da hesitação vacinal por parte dos pais. Consequentemente, verificaram-se o aumento de casos de sarampo, risco aumentado de mortalidade e aumento das despesas de saúde do setor público. Concluiu-se, portanto, que a redução da cobertura vacinal de sarampo tem potencial para impactar as condições de saúde da população, elevar indicadores de morbimortalidade e acarretar prejuízos financeiros aos cofres públicos.

**Palavras-chave:** Cobertura vacinal. Doenças preveníveis por vacina. Sarampo. Vacina contra sarampo.

## INTRODUCTION

Measles is a highly infectious, vaccine-preventable viral disease that requires high vaccination coverage in order for herd immunity to be achieved and for outbreaks to be prevented (Lo & Hotez, 2017). It is a viral infection that mainly affects children under five years of age and is characterized as one of the main causes of mortality among children, reaching general lethality rates of 10.7 per 1,000 inhabitants in areas with a higher vaccination deficit (Lo & Hotez, 2017; Faruk et al., 2020; Gutu et al., 2020).

In order to mitigate measles lethality rates among children, in the 1960s, Brazilian researchers developed the measles vaccine, with a 95% efficacy (Fundação Oswaldo Cruz, 2014). This means that, for every 100 children vaccinated with this immunobiological, five could still develop the disease. From this perspective, aspects such as the measles virus transmission rate and the effectiveness of the available vaccine have guided the recommendation of 95% vaccination coverage to prevent the circulation of the measles virus (Lo & Hotez, 2017). Furthermore, it should be noted that vaccination is the cheapest, safest and most effective way to contain the spread of measles through herd immunity (Lo & Hotez, 2017).

Vaccination coverage data for 2017 suggest that many American states have achieved desirable herd immunity, reaching 95% vaccination coverage in the age group from 2 to 11 years, as recommended by the World Health Organization (WHO) (Gastañaduy et al., 2017). However, the crowding of susceptible people, that is, unvaccinated individuals, is directly linked to large measles outbreaks (Lo & Hotez, 2017). For instance, in the United States (US), between 2001 and 2017, the percentage of susceptible individuals increased, resulting in a total of 2,218 measles cases reported. Of these total reports, 68% of individuals were not immunized against measles (Gastañaduy et al., 2017).

This growing percentage of individuals susceptible to measles that affects the US is also a reality in low-income countries, such as Nigeria, Uganda and Ethiopia. These countries, in addition to dealing with the lack of financial and immunobiological resources, also suffer from low measles vaccination coverage and show a seasonal variance of this type of viral infection, with medians of 1.8, 0.7, 0.4 and 0.1, respectively, for the 1<sup>st</sup>, 2<sup>nd</sup>, 3<sup>rd</sup> and 4<sup>th</sup> quarters, in observations carried out between 2013 and 2017 (Faruk et al., 2020).

In order to transform this chaotic scenario of measles outbreaks and lethality that affects several countries, it is pertinent to reach the levels of vaccination coverage recommended by the WHO, with a view to achieving herd immunity and favoring the epidemiological control of measles. To this end, as important as guaranteeing the first dose of the measles vaccine is guaranteeing its second dose (Lo & Hotez, 2017; Cuong et al., 2019).

In Brazil, measles is an old dilemma. Faced with this relevant public health problem, the promotion of actions aimed at preventing this disease by achieving the vaccination coverage recommended by the WHO was considered effective and efficient, contributing to Brazil being given, in 2016, a measles eradication certificate, since the last cases of the disease had been reported in 2015 (Ministry of Health [MS], 2022). However, a drop in measles vaccination coverage rates was identified in subsequent years and, in 2018, 10,346 cases of this disease were confirmed in Brazil, with the free circulation of this virus throughout the national territory in less than a year, which reflected in the loss of the virus eradication title previously received. In 2019, new outbreaks were reported and 20,901 new cases were confirmed (MS, 2022).

In this context, still with the aim of highlighting the effects of low measles vaccination coverage in the Brazilian scenario, it should be noted that, between the first and 52<sup>nd</sup> epidemiological week of 2021, 2,306 suspected measles cases were reported and, of these, 668 were confirmed. Among the confirmed cases of measles in the same period, two deaths were reported in the state of Amapá, both of unvaccinated children under 1 year of age (MS, 2022).

In view of the growing percentage of individuals unvaccinated against measles that affects countries of all economic levels, including Brazil, the present study was guided by the following

question: “What are the possible causes and consequences of low measles vaccination coverage?”. As an answer to this question, this research aimed to identify the possible causes and consequences of low measles vaccination coverage.

## MATERIAL AND METHODS

This is an Integrative Literature Review (ILR) research carried out in accordance with the steps proposed for this type of study, such as: definition of the theme and elaboration of the research question, definition of inclusion and exclusion criteria, search for original research in scientific databases, application of defined inclusion and exclusion criteria, reading and review of selected studies, data extraction, interpretation and systematic organization of results, and presentation of the ILR.

Searches for original studies were conducted in the following electronic databases: *Biblioteca Virtual em Saúde* [Virtual Health Library] (BVS), Scientific Electronic Library Online (SciELO), Library of Medicine National Institute of Health (PubMed), *Biblioteca Brasileira de Teses e Dissertações* [Brazilian Theses and Dissertations Library] (BDTD), through controlled descriptors, which were selected from the Health Sciences Descriptors database (DeCS), in Portuguese and English, namely: “cobertura vacinal”, “Doenças preveníveis por vacina”, “sarampo”, “vacina contra sarampo” and “vaccination coverage”, “vaccine-preventable diseases” “measles”, “measles vaccine”. In all databases, the descriptors were combined using the Boolean operator “AND”, for instance: “cobertura vacinal” AND “sarampo”, “Doenças preveníveis por vacina” AND “vacina contra sarampo” and “vaccination coverage” AND “measles”, “vaccine-preventable diseases” AND “measles vaccine”.

The inclusion criteria comprehended: original articles addressing the (chosen) topic, published in Portuguese, English and Spanish, from January 2015 to June 2021 and that were available in the databases in full and free of charge. Moreover, for the election of only robust and quality studies to integrate this review research, the selected articles were subjected to structural and methodological evaluation using the checklist proposed by Caldwell, Henshaw & Taylor (2011). Only original articles that obtained 80% or more of affirmative answers to said checklist were included in this review.

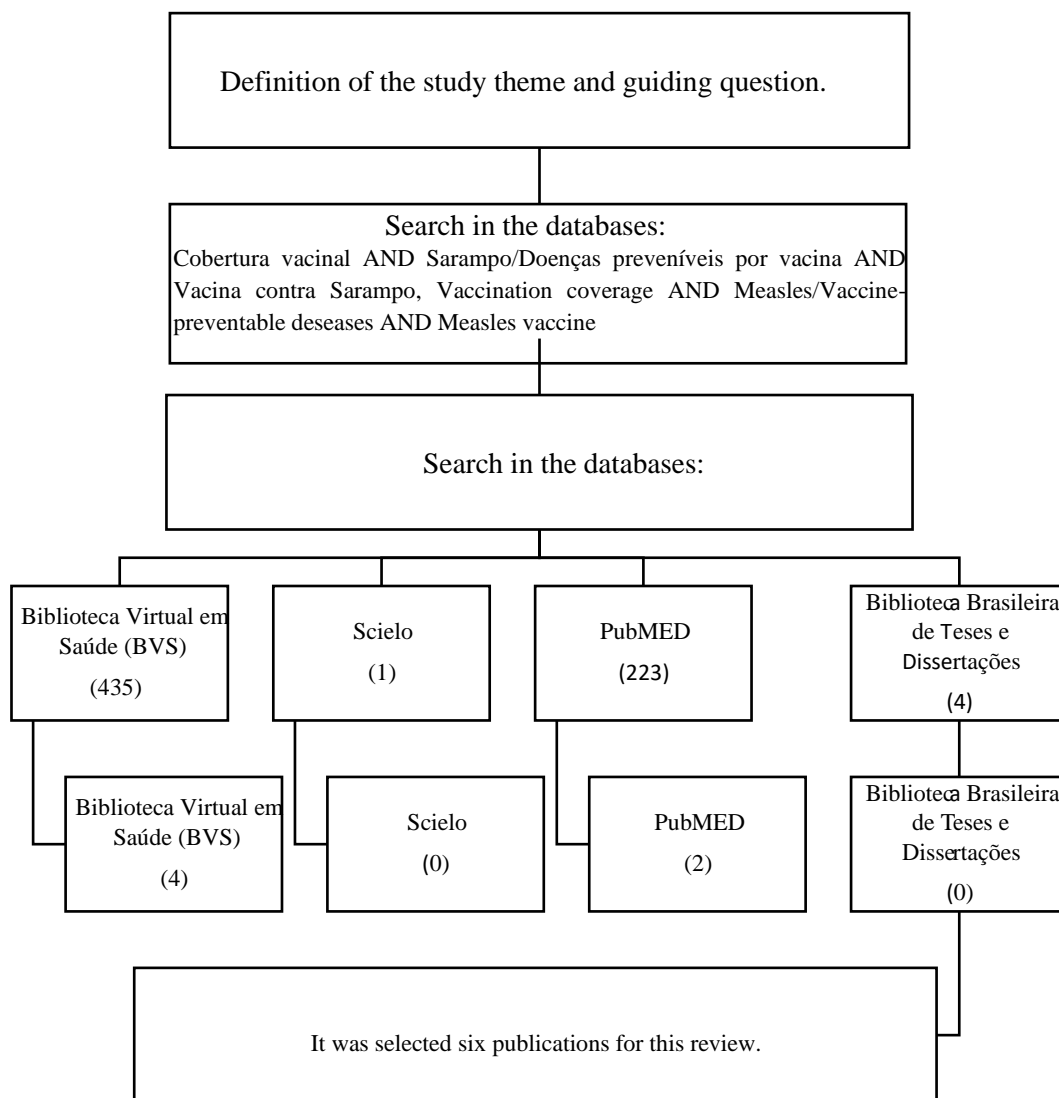
Articles belonging to the following modalities were excluded: case studies, experience reports, reflective articles, editorials, paid and/or repeated articles, and literature reviews. After titles and abstracts were read, articles that did not address the topic proposed for this study and/or were duplicated were excluded. Original studies that obtained less than 80% of affirmative answers to the checklist proposed by Caldwell et al. (2011) were excluded.

Data were extracted through completion of an instrument adapted and validated for Brazil, containing the following variables: year/country/database; article title; objective; main results and conclusions (Ursi & Galvão, 2006). In response to the guiding question and the research objective, the findings were organized and categorized using the thematic content analysis technique, in accordance with the following steps: pre-analysis, material exploration, treatment and inference/interpretation of results (Bardin, 2016).

With regard to ethical matters, because this is an ILR study without the involvement of human beings, submission to the Standing Committee on Ethics in Research Involving Human Beings [*Comitê Permanente de Ética em Pesquisas Envolvendo Seres Humanos*] (COPEP) was waived.

## RESULTS AND DISCUSSION

The searches in the databases identified 663 publications related to the theme, which, after application of the inclusion and exclusion criteria, reading of titles, abstracts, full texts, and application of the checklist, resulted in a set of six publications, as shown in Figure 1.



*Figure 1.* Flowchart of the selection of original articles by database.  
Source: The authors.

Regarding the language of the selected articles, there was a predominance of English ( $n=6$ ), with most articles coming from Africa ( $n=4$ ) and North America ( $n=2$ ). It is noteworthy that, in the period investigated in this study, no primary studies of Brazilian origin were identified, which may suggest a gap in Brazilian scientific research and the relevance of promoting investigations on the subject nationwide. As for the type of research, one article with a quantitative approach, one article with a qualitative approach and four articles with a mixed-method approach were found. Furthermore, it is noted that most of the selected articles were the result of searches conducted in the BVS database ( $n=4$ ), as shown in Table 1.

Concerning the year of publication, it is noteworthy that 50% of the articles selected to compose this ILR are recent and were published in 2020 ( $n=3$ ). However, no primary studies published from January to June 2021 that obtained 80% or more of affirmative answers to the checklist adopted in this investigation were identified. This finding may indicate that robust original studies on this topic have not yet been published in said period, and this lack of publications on measles in this period may be a consequence of the implementation and promotion of efforts in scientific investigations aimed at the prevention, control, and effects on health, society and economy of a new serious disease, the Coronavirus disease 2019, SARS-Cov-2, better known as COVID-19 (Costa et al., 2020).

Table 1 presents the main information extracted from the publications selected for this ILR.

Table 1  
Summary of the original articles included in this ILR (n=6).

Year / Country / Database	Article title	Objective	Main results	Conclusions
2017 United States PubMed	<i>Public health and economic consequences of vaccine hesitancy for measles in the United States.</i> (Lo & Hotez, 2017).	To estimate potential public health and economic consequences of the decline in childhood immunization, result of a growing movement of vaccine hesitancy, using the case example of vaccination against measles, mumps and rubella (MMR) and the measles virus.	The reduction in MMR vaccination coverage due to growing vaccine hesitancy increased the annual incidence of measles. A 5% decline in MMR vaccination coverage in US children would result in a threefold increase in national measles cases in this age group, for a total of 150 cases.	The economic and health consequences have resulted in an additional \$2.1 million in economic costs for the public sector and a threefold increase in national measles cases related to low vaccination coverage, which raises the question of whether measles is really no longer a threat in the United States.
2019 United States PubMed.	<i>Factors associated with measles Transmission in the United States during the postelimination Era.</i> (Gastañaduy et al., 2017)	To discern the factors associated with measles virus transmission in the United States after elimination.	From 2010 to 2017, 2,218 measles cases were confirmed – 490 were single cases, 90 were two chains, and 116 were outbreaks of three or more cases. The average size was five cases. Of the confirmed measles patients, 68.0% were not vaccinated and 19.3% had an unknown vaccination status. Among the factors associated with high transmission, unvaccinated individuals stand out, who were 2 to 4 times more infectious. Lack of vaccination, school-age children, due to the number of people in direct contact with the patient, and individuals with a history of only one vaccine dose.	Results show predominantly subcritical measles transmission and maintenance of elimination in the United States over the past 17 years. The importance of having high targets for 2-dose measles vaccine coverage is emphasized, especially among school-age children.
2019 Vietnam <i>Biblioteca Virtual em Saúde (BVS)</i>	<i>Gap in measles vaccination coverage among children aged 9 months to 10 years in Ho Chi Minh City, Viet Nam, 2014.</i> (Cuong, et al., 2019)	To describe measles vaccination coverage in children aged 9 months to 10 years, living in HCMC, and to identify personal factors for non-vaccination.	The proportion of measles for people with no previous vaccination was 3%, and for those with unknown history, it was 5%. The total vaccination coverage was 54.9%, and the unvaccinated accounted for 45.06%. The proportion of children $\geq 18$ was 14.08%, thus showing that there was a large gap in vaccination. The most common reason reported by parents for not vaccinating was a lack of awareness of the importance of a second vaccine dose. Other less mentioned reasons were: Busy parents or caregivers, parents' reluctance to vaccinate during illness, fear of adverse effects, and children not at the age to be vaccinated.	While 85% of children over 18 months had received the first dose. In addition, 38% of children aged 9-18 months had not even had their first dose of the vaccine. This shows the critical importance of increasing vaccination coverage for both the first and second doses.

Cont. Table 1

2020 Ethiopia  <i>Biblioteca Virtual em Saúde (BVS)</i>	<i>Epidemiology of measles in Oromia region, Ethiopia, 2007-2016.</i> (Gutu <i>et al.</i> , 2020).	To assess measles epidemiology in the region and describe its distribution in Oromia from 2007-2016, review the MCV1 vaccination coverage and assess variables associated with death.	Reviewing 10 years of measles surveillance database, a total of 26,908 suspected measles cases reported was found. The vaccination status of 12,495/26,908 (46%) cases were considered to be unknown, while another 7,814/26,908 (29%) individuals were not vaccinated; on this finding, no strong association was observed. Some variables associated with death presented were age, closed-environment treatment, vaccination status and study period.	Despite efforts, measles is still a public health problem, and some of the factors that were associated with a higher risk of mortality were inpatient treatment and non-vaccination status.
2020 Madagascar  <i>Biblioteca Virtual em Saúde (BVS)</i>	<i>Madagascar 2018-2019 measles outbreak response: main strategic areas.</i> (Sodjinou <i>et al.</i> , 2020).	To describe the coordination, case management, vaccination response and epidemiological surveillance during the response to the measles outbreak.	From September 2018 to May 2019, a total of 146,277 measles cases were reported, including 1,394 (1%) laboratory-confirmed cases and 144,883 (99%) cases confirmed by epidemiological link. A total of 97,713 (67%) individuals were not vaccinated.	A total of 100% of the districts were affected, and some factors, such as late implementation of the mass vaccination response, poor vaccination coverage of routine immunization, high population mobility (migration) and high measles transmission rate may explain this rapid expansion of the outbreak. It is concluded that the elimination of measles in Madagascar will be a challenge, due to the low routine coverage and absence of the second dose of the vaccine in the routine immunization schedule.
2020 Nigeria  <i>Biblioteca Virtual em Saúde (BVS)</i>	<i>Temporal trend of measles cases and impact of vaccination on mortality in Jigawa State, Nigeria, 2013-2017: a secondary data analysis.</i> (Faruk <i>et al.</i> , 2020)	To determine the magnitude of measles in Jigawa State, identify its trend, and determine factors associated with mortality.	There were 6,214 cases, of which 52.3% are men. The most affected age group was that from 1 to 5 years old. The study shows that those who have never been vaccinated are more likely to die compared to those who have received at least one dose of the measles vaccine.	Vaccination coverage was unsatisfactory, and laboratory investigation, low. Children with no vaccination history were shown to be more likely to die; therefore, the state, the government must renew routine immunization and ensure that all eligible children are reached.

Source: The authors.

In response to the research question and the purpose of this study, the findings were analyzed in detail and fitted into two thematic categories, namely: “Possible causes of low measles vaccination coverage worldwide” and “Consequences of low measles vaccination coverage”.

### Possible causes of low measles vaccination coverage worldwide

The analysis of the results allowed for the identification of possible causes of the low measles vaccination coverage worldwide in four of the six articles selected for this ILR: Gastañaduy *et al.* (2017); Lo & Hotez (2017); Cuong *et al.* (2019); and Sodjinou *et al.* (2020). Among the evidenced causes, the following stand out: absent, incomplete or uninitiated routine measles vaccination

schedule for children aged between nine and 18 months (Gastañaduy et al., 2017; Cuong et al., 2019). In addition, the selected studies also point to late implementation of mass vaccination, insufficient stock of measles vaccines and increased vaccine hesitancy on the part of parents or guardians as being the main reasons for the unsatisfactory measles vaccine coverage in the world (Lo & Hotez, 2017; Cuong et al., 2019; Sodjinou et al., 2020).

This low measles vaccination coverage, resulting from the absent, incomplete or uninitiated routine measles vaccination schedule, among children aged between nine and 18 months, may be the result of a lack of awareness of parents or guardians about the severity of this morbidity for humans and about the protective relevance of vaccination. This is because studies evidence that parents' perception of vaccines and knowledge about their importance or lack thereof have a direct influence on the start and completion of the vaccination schedule, besides denoting those children of less educated parents are less likely to be fully immunized against measles (Cuong et al., 2019).

Another major reason for low measles vaccination coverage is the lack of the second dose of the vaccine in the routine immunization schedule. This result is consistent with the finding, hypothesis and inference presented in the previous paragraph and may also contribute to the accelerated spread of the disease, causing measles outbreaks all around the world. This fact corroborates with other studies, which indicate measles outbreaks resulting from the crowding of unvaccinated individuals or those with incomplete measles vaccination schedule (Gastañaduy et al., 2017; Lo & Hotez, 2017).

A study conducted in Madagascar evidenced late implementation of mass vaccination as one of the main explanations for the unsatisfactory measles vaccine coverage, which may contribute to an increased susceptibility for the individual to be affected by the disease due to the delay in vaccine protection (Sodjinou et al., 2020). In this context, North American researchers reveal that unvaccinated patients are three to four times more infectious compared to vaccinated ones (Gastañaduy et al., 2017). Thus, lack of vaccination or late mass vaccination, in addition to impairing vaccination coverage, can be seen as triggers for large measles outbreaks or epidemics.

Researchers reveal that the late implementation of the vaccine response in Madagascar was due to the country's insufficient stock of measles vaccines (Sodjinou et al., 2020). Moreover, in addition to contributing to low vaccination coverage, this fact led to the fractionation of vaccination campaigns and, consequently, extended the incidence time of the disease (Sodjinou et al., 2020).

Vaccine hesitancy on the part of parents is another relevant barrier to achieving high measles vaccination coverage. Increased hesitancy to vaccinate or parents' refusal to vaccinate their children against measles contributes to the fact that, over time, children are no longer at the age to be vaccinated, and this may also be related to misinformation about the safety of the vaccine and the low perceived risk of measles, busy parents or caregivers, parents' reluctance to vaccinate when the child has a disease, and fear of adverse reactions from vaccination. This explanation is attuned to other studies that point to a higher incidence of vaccine hesitancy in less educated parents (Lo & Hotez, 2017; Cuong et al., 2019).

### Consequences of low measles vaccination coverage

The analysis of the results revealed the consequences of low measles vaccination coverage in three of the six articles selected for this ILR: Lo & Hotez (2017); Faruk et al. (2020); Gutu et al. (2020). Among the evidenced consequences, the following stand out: increase in the number of measles cases, in the risk of mortality resulting from non-vaccination, and in the health expenses of the public sector (Lo & Hotez, 2017; Faruk et al., 2017; Gutu et al., 2020).

North American researchers reveal that a 5% decline in measles vaccination coverage has increased the number of measles cases in the United States threefold, from 48 cases per year to a total of 150 cases (Lo & Hotez, 2017). This may be due to the relationship between lack of vaccination and the individual's susceptibility to contracting the disease. This idea is reinforced by studies showing that most individuals infected by the measles virus during an outbreak had no vaccination history, or an unknown history (Gastañaduy et al., 2017).

Another important consequence of the low measles vaccination coverage identified in the analysis of the results was a higher risk of measles mortality in individuals who were unvaccinated, under five years old, hospitalized for treatment of the disease (Faruk et al., 2020; Gutu et al., 2020). Lack of vaccination renders the individual susceptible to the disease, and school-age children can be considered a primary channel of measles transmission as a consequence of the longer chain of contacts (Lo & Hotez, 2017; Gastañaduy et al., 2017; Faruk et al., 2020). Linked to this, it is emphasized that parents' vaccine hesitancy becomes a potential engine of this transmission chain, as already mentioned in the previous category.

Among the results analyzed, it was evidenced that low measles vaccination coverage is a relevant public health problem worldwide. This is because researchers reveal that a 5% reduction in measles vaccination coverage, in the younger age group, over 10 years, would increase the total number of cases of this disease by two times and increase health expenses by 7.9 million dollars during that same period (Lo & Hotez, 2017). As an example, to manage the measles outbreak that took place in Madagascar in 2018, more than 12 million dollars were mobilized for the implementation of response interventions, such as: hospitalizations, vaccines, communication, among other disease prevention and control measures (Sodjinou et al., 2020).

## CONCLUSION

This study allowed for the identification of possible causes and consequences of low measles vaccination coverage. It also evidenced that reduced vaccination coverage has the potential to impact the population's health conditions, the indicators of measles morbimortality, and cause financial losses to the public coffers.

In the investigated period, no primary studies of Brazilian origin addressing the possible causes and consequences of low measles vaccination coverage in Brazil were identified, and this may suggest a gap in Brazilian scientific research and the relevance of promoting investigations on the subject nationwide.

Among the results, there was a lack of knowledge about the effectiveness of measles vaccine protection, as well as about its importance in preventing outbreaks and reducing measles morbimortality in children under five years of age. Linked to this, parents' resistance to vaccinate their children against measles can contribute to unsatisfactory vaccination coverage.

It is therefore necessary to monitor measles more effectively, make the population more aware so that immunization campaigns reach children who, for some reason, are not vaccinated by the routine schedule, and thus progressively eliminate the existing gaps in vaccination.

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