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Malaria mortality in Brazil: an age-period cohort study

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Abstract

Background Malaria is a parasitic disease caused by protozoa of the genus *Plasmodium*, transmitted through the bites of *Anopheles* mosquitoes. Despite significant progress in malaria control, the disease remains a persistent public health challenge, particularly in specific Brazilian regions where environmental and socioeconomic factors contribute to its transmission. Understanding mortality trends across different age groups, periods, births cohorts, and regions is essential for developing targeted intervention strategies and optimizing resource allocation.

This study aimed to analyse malaria mortality trends in Brazil, focusing on regional differences using an age-period cohort (APC) model.

Methods This ecological study analysed malaria mortality data in Brazil from 1980 to 2024, sourced from DATASUS. Population estimates by sex were retrieved from the Instituto Brasileiro de Geografia e Estatística. Mortality data, including age, year of death, Brazillian macrorregions and admnistratvive Brazilian Amazon legal, as well as the cause of death (ICD-9: 084; ICD-10: B50—B53), were analysed using an APC model. A Poisson distribution was assumed for mortality counts, and analyses were conducted using Holford's method and its adaptations.

Results In the North region, malaria mortality showed an age-related increase, with the highest rates observed in individuals over 80 years old. A significant decline in mortality was observed over the study periods, particularly from 1980 to 1985 to 2020–2024. In the Midwest, the period effect showed fluctuations with an overall decline in recent decades. In the Northeast and Legal Amazon regions, age, period, and cohort effects highlighted clear trends of decreasing mortality over time, particularly for younger cohorts.

Conclusion Malaria mortality is influenced by age, period, cohort, and regions. The regional disparities emphasize the need for localized strategies, considering demographic shifts and epidemiological patterns. By integrating these findings into public health planning, policymakers can enhance malaria surveillance, improve healthcare access in vulnerable regions, and refine control measures to further reduce mortality. The study underscores the necessity of continuous investment in malaria prevention, particularly for older adults in endemic areas, to sustain progress and mitigate resurgence risks.

Keywords Malaria, Age-period cohort, Brazil

Background

Malaria is a parasitic disease caused by protozoa of the genus *Plasmodium*, with four main species affecting humans: *Plasmodium falciparum, Plasmodium vivax, Plasmodium malariae,* and *Plasmodium ovale* [1]. Among them, *P. falciparum* and *P. vivax* are the most prevalent worldwide [1]. The disease is transmitted

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primarily through the bites of infected *Anopheles* mosquitoes [1].

Clinically, malaria presents with a range of symptoms with variable severity [2]. The disease typically begins with fever, chills, headache, and muscle pain [2]. In more severe cases, especially those caused by *P. falciparum,* complications such as anaemia, acute respiratory distress, organ failure, and cerebral malaria can occur, which can be life-threatening if untreated [2]. Recurrent episodes are common, particularly with *P. vivax* infections, which can remain dormant in the liver and cause relapses months or years after the initial infection [2].

Globally, malaria remains a major public health issue, with an estimated 247 million cases and 619,000 deaths reported in 2021 across 84 endemic countries [3]. The disease disproportionately affects low-income regions, primarily in sub-Saharan Africa and parts of Southeast Asia, where healthcare infrastructure is often inadequate [3]. The economic costs of malaria are immense, straining healthcare systems and limiting productivity, particularly in regions heavily dependent on agricultural labour [3]. Malaria's toll extends beyond immediate morbidity and mortality, hampering economic development and perpetuating cycles of poverty [3].

In Brazil, malaria is largely confined to the Amazon Basin, which accounts for 99% of the country's cases [4]. *Plasmodium vivax* is responsible for the majority of infections (approximately 83.7%), with *P. falciparum* making up around 16.3% [4]. The epidemiology of malaria in Brazil is shaped by migration, settlement patterns, and environmental factors unique to the Amazon region [4]. The economic burden of the disease is significant, not only in terms of healthcare costs but also in the loss of productivity, which exacerbates poverty in affected communities [4]. Control efforts in Brazil are complicated by the presence of asymptomatic infections, which challenge malaria elimination strategies [4].

A study using age-period cohort analysis on malaria mortality in Brazil may helps to understanding the temporal trends and the influence of demographic and societal changes on mortality risk. Such an approach can help clarify the roles of aging populations, shifts in exposure due to migration, and the effectiveness of control interventions over time. By identifying vulnerable cohorts and periods of increased risk, this study can inform targeted interventions and enhance public health strategies aimed at reducing malaria mortality in endemic regions. Hence, were developed a study with the aim to investigate malaria mortality in Brazil using an age-period cohort model.

Methods

Study characterization

This is an ecologic study that evaluated malaria mortality by an age-period cohort model.

Data source

All data were were provided by the Sistema de Informação de Mortalidade (SIM), that is, a Brazilian national system that controls all data regarding death causes in the country. This system feeds the DATASUS, a database that encompass data from SIM and others Brazilian data health survailence programs and present them open access to public allowing their access and analysis. The data were categorized into two groups: demographic and clinical. The demographic data refer to the total population of Brazilian macrregions evaluated along the observed period. Such data were obtained from the census and demographic projections of the Instituto Brasileiro de Geografia e Estatística available on the aforementioned platform.

The clinical data of the patients refer to the age at which they deceased, the year of their death and the cause of death. In this case, were chosen patients whose cause of death was identified by the code 084 according to the standardization of the International Classification of Diseases in its ninth edition (ICD9) and codes B50, B51, B52, and B53 according to ICD10 were evaluated. It is worth to mention that this code include all species of protozoa that cause malaria. An inclusion deaths for which the species could not be specified as there is not avaible data on the subject.

A 45 year period of time, 1980 and 2024, were evaluated since it was the period in DATASUS with all the evaluated data available.

The Brazilian macrorregions of North, Northeast and Central-West of Brazil, as well as the administrative Brazilian Legal Amazon region, were evaluated. It was decided to evaluate these regions because they concentrate practically all the country's cases related to malaria, since they are linked to the Amazon rainforest region. The focus on Legal Amazon derives as the Brazilian government consider it as an endemic region to malaria, presenting a particular enviromental, and population dinamics that contributes to malaria occurence. Futhermore, the South and Southeast regions of Brazil did not present complete data to enable their analysis (Fig. 1).

Data analysis

The data were arranged in Excel® spreadsheets according to Lexis diagram.

Birth cohorts were calculated by subtracting the patient's death year by their age at death, according

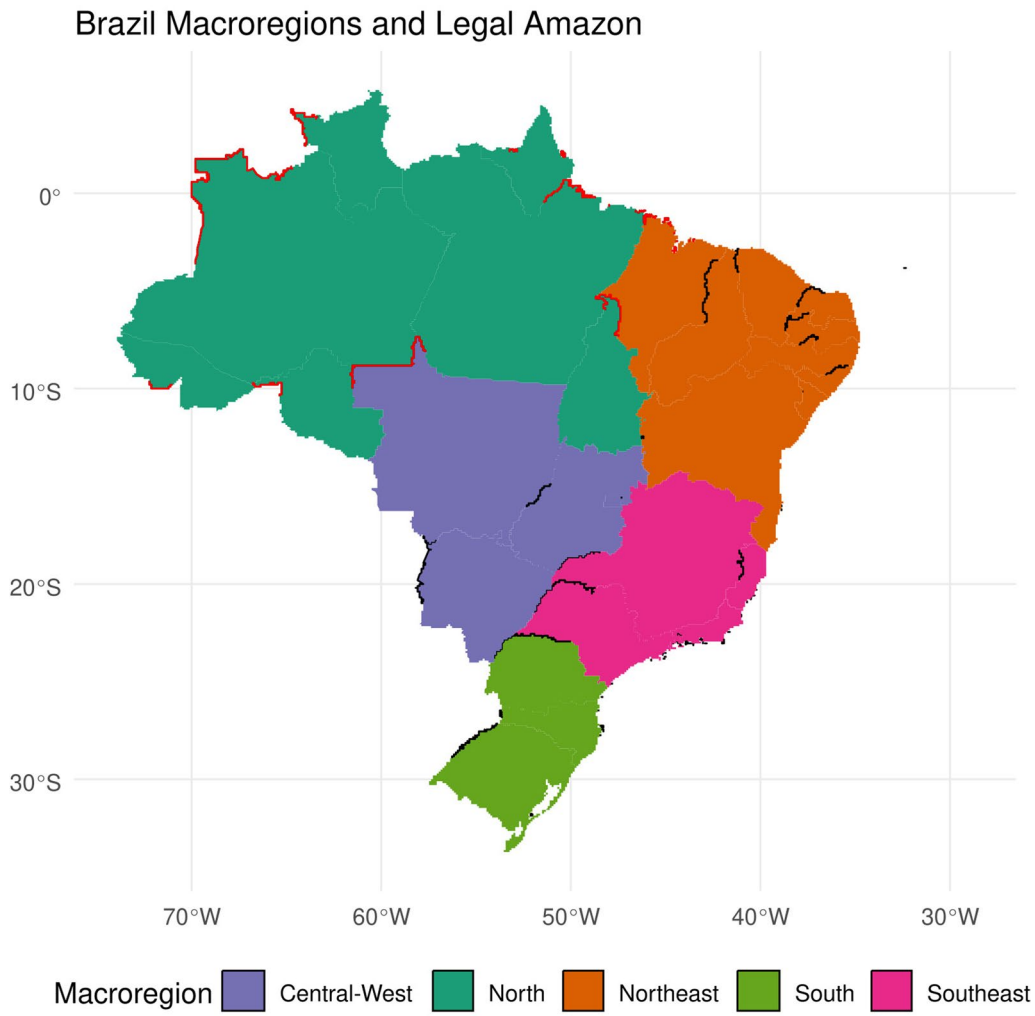

Fig. 1 Brazilian macrorregions. (Legal Amazon is highlighted by a red edges)

to the classical method. The periods were categorized as: 1980–1984; 1985–1989; 1990–1994; 1995–1999; 2000–2004; 2005–2009; 2010–2014; 2015–2019; and 2020–2024. Age was categorized in 5 years groups as: 0–4, 5–9, 10–14, 15–19, 20–24, 25–29, 30–34, 35–39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–69, 70–74, 75–79, and more than 80 years. This divisions follows the classic model for an APC analysis. In case, it divides time and periods into groups of 5 years starting from the initial time/period, regardless external factors that may influence them, which must be addressed after the analysis [5–7].

It can be assumed that the number of deaths, resulting from a counting process, follows a Poisson distribution. Hence, age-period cohort allows to assign a more satisfactory distribution for the response variable, and consider different forms for the relationship between the number of deaths and the explanatory variables (age, period, and cohort), which is often non- linear.

The effects were analysed using the age-period-cohort model proposed by Holford and adapted by Clayton and Schifflers and Carstensen [5–7]. The mortality rate (λijk) for age (i), period (j) and cohort (k) was modelled according to the formula below. The μ represents the global average mortality rate; α represents the average age effect; β represents the average period effect and γ represents the average cohort effect.

Likelihood ratio tests were used to compare different submodels objecting to assess the effects of age, period, and cohort on mortality rates. Such submodels were adjusted in a conveniently organized sequence in order to provide the tests for the mentioned effects as a comparison between them. Based on these comparisons, made by using the Akaike Information Criterion, the best

model was obtained. The adequacy of the final model fit was verified via deviance statistics. The analysis was performed using the R 4.4.2 software ® by using the function Epy.

Results

North

The analysis of mortality by age shows a distinct upward trend, with rates per 100,000 individuals increasing steadily from individuals who decease between 0 and 4 years old (1.657, 95% CI 1.476–1.861) to those whose decease with more than 80 years old (3.653, 95% CI 3.076–4.338). In terms of mortality risk across periods, a clear decline is observed when compared the period between 1980 and 1985 (Relative Risk–RR: 8.451; 95% confidence Interval–95%CI 7.973–8.958) to period between 2015 and 2019 (RR: 0.143; 95%CI 0.130–0.158). Finally, cohort analysis reveals a U-shaped pattern, with higher risks in 1950's cohorts (RR: 1.102; 95%CI 1.038–1.169), while younger cohorts demonstrate a decreasing trend, as observed for 2015's cohort (RR: 0.660; 95%CI 0.553–0.788)—Tables 1, 2, 3, and Fig. 2.

Midwest

The age-specific mortality rates show a growing trend between individuals who decease between 0 and 4 years old (RR: 0.116; 95%CI 0.086–0.157) to those who decease with more than 80 years (RR: 0.355; 95%CI 0.219–0.575). The period presents fluctuations in its effects. There is a escalating tend between 1980 and 1984 (RR: 5.917; 95%CI 4.995–7.009) till 1985 and 1989 (RR: 15.786; 95%CI 13.746–18.130). Since then, a marked decline was observed till 2015 to 2019 period (RR: 0.029; 95%CI 0.023–0.037). Most of the cohorts evaluated did not

Table 1 - Mortality rate by 100.000 individuals by age

Age (years)	North	Midwest	Northeast	Legal amazon
0–4	1.657 (1.476–1.861)	0.116 (0.086–0.157)	0.003 (0.002–0.005)	1.137 (1.023–1.263)
5–9	0.617 (0.554–0.687)	0.114 (0.088–0.146)	0.006 (0.005–0.009)	0.577 (0.525–0.635)
10–14	0.471 (0.428–0.518)	0.112 (0.089–0.142)	0.012 (0.009–0.015)	0.394 (0.359–0.432)
15–19	0.607 (0.564–0.655)	0.113 (0.091–0.141)	0.022 (0.018–0.027)	0.437 (0.406–0.470)
20–24	0.867 (0.813–0.925)	0.118 (0.098–0.142)	0.039 (0.032–0.046)	0.630 (0.595–0.668)
25–29	0.987 (0.932–1.044)	0.129 (0.111–0.150)	0.053 (0.045–0.061)	0.630 (0.595–0.668)
30–34	0.943 (0.891–0.997)	0.149 (0.128–0.173)	0.050 (0.043–0.059)	0.865 (0.821–0.912)
35–39	0.875 (0.817–0.937)	0.182 (0.155–0.215)	0.043 (0.036–0.052)	0.773 (0.723–0.826)
40–44	0.886 (0.819–0.959)	0.226 (0.185–0.275)	0.038 (0.031–0.048)	0.753 (0.695–0.815)
45–49	0.980 (0.903–1.064)	0.268 (0.211–0.340)	0.038 (0.029–0.049)	0.813 (0.748–0.883)
50–54	1.150 (1.059–1.248)	0.292 (0.228–0.374)	0.040 (0.031–0.052)	0.939 (0.865–1.020)
55–59	1.388 (1.272–1.515)	0.304 (0.238–0.388)	0.045 (0.039–0.057)	1.123 (1.033–1.222)
60–64	1.685 (1.528–1.857)	0.314 (0.241–0.408)	0.050 (0.039–0.064)	1.351 (1.233–1.480)
65–69	2.044 (1.826–2.288)	0.323 (0.239–0.438)	0.056 (0.042–0.074)	1.625 (1.466–1.801)
70–74	2.480 (2.176–2.827)	0.334 (0.234–0.476)	0.063 (0.045–0.086)	1.955 (1.737–2.200)
75–79	3.010 (2.589–3.500)	0.344 (0.227–0.522)	0.070 (0.048–0.102)	2.351 (2.053–2.692)
More than 80	3.653 (3.076–4.338)	0.355 (0.219–0.575)	0.007 (0.051–0.120)	2.828 (2.424–3.300)

Table 2 - Relative risk between periods

Period	North	Midwest	Northeast	Legal amazon
1980–1984	8.451 (7.973–8.958)	5.917 (4.995–7.009)	3.968 (3.327—4.731)	7.351 (6.973–7.749)
1985–1989	9.746 (9.211–10.312)	15.786 (13.746–18.130)	10.405 (9.018—12.006)	10.122 (9.634–10.635)
1990–1994	4.427 (4.260–4.601)	9.860 (8.594–11.313)	4.230 (3.850—4.647)	4.830 (4.661–5.004)
1995–1999	1.957 (1.903–2.012)	3.257 (2.998–3.538)	1.738 (1.621—1.863)	2.076 (2.023–2.131)
2000–2004	–	–	–	–
2005–2009	0.524 (0.507–0.541)	0.307 (0.283–0.334)	0.608 (0.561—0.659)	0.491 (0.477–0.506)
2010–2014	0.274 (0.257–0.292)	0.094 (0.080–0.111)	0.370 (0.315–0.434)	0.241 (0.227–0.256)
2015–2019	0.143 (0.130–0.158)	0.029 (0.023–0.037)	0.225 (0.177–0.286)	0.118 (0.108–0.129)
2020–2024	0.125 (0.115–1.35)	0.037 (0.019–0.045)	0.139 (0.105–0.183)	2.107 (1.820–2.439)

RR (CI955); *RR* Relative risk, *CI95%* Confidence interval 95%

Table 3 - Relative risk between cohorts

Cohort	North	Midwest	Northeast	Legal amazon
1900	0.469 (0.390–0.564)	0.612 (0.356–1.053)	0.222 (0.130–0.378)	0.390 (0.327–0.464)
1905	0.515 (0.438–0.607)	0.640 (0.399–1.027)	0.283 (0.178–0.449)	0.442 (0.380–0.515)
1910	0.566 (0.490–0.653)	0.669 (0.446–1.005)	0.360 (0.242–0.536)	0.502 (0.440–0.573)
1915	0.621 (0.549–0.703)	0.700 (0.495–0.989)	0.459 (0.328–0.643)	0.570 (0.509–0.638)
1920	0.682 (0.614–0.757)	0.732 (0.546–0.980)	0.586 (0.440–0.780)	0.647 (0.587–0.713)
1925	0.749 (0.686–0.818)	0.765 (0.595–0.983)	0.747 (0.581–0.959)	0.734 (0.675–0.799)
1930	0.822 (0.763–0.886)	0.800 (0.636–1.006)	0.952 (0.750–1.207)	0.833 (0.772–0.899)
1935	0.903 (0.845–0.965)	0.837 (0.665–1.054)	1.204 (0.940–1.542)	0.943 (0.875–1.017)
1940	0.988 (0.926–1.055)	0.883 (0.698–1.116)	1.455 (1.130–1.873)	1.048 (0.971–1.132)
1945	1.062 (0.995–1.134)	0.944 (0.765–1.166)	1.603 (1.289–1.993)	1.125 (1.045–1.211)
1950	1.102 (1.038–1.169)	1.021 (0.884–1.178)	1.550 (1.342–1.791)	1.145 (1.079–1.215)
1955	1.082 (1.042–1.123)	1.061 (0.994–1.133)	1.313 (1.200–1.436)	1.093 (1.061–1.127)
1960	–	–	–	–
1965	0.907 (0.879–0.936)	0.832 (0.763–0.909)	0.772 (0.696–0.858)	0.900 (0.881–0.920)
1970	0.843 (0.805—0.884)	0.688 (0.575–0.822)	0.675 (0.579–0.787)	0.818 (0.780–0.858)
1975	0.804 (0.750–0.862)	0.635 (0.510–0.791)	0.655 (0.558–0.770)	0.762 (0.706–0.824)
1980	0.778 (0.709–0.854)	0.646 (0.516–0.808)	0.670 (0.565–0.793)	0.735 (0.674–0.802)
1985	0.758 (0.687–0.837)	0.689 (0.548–0.865)	0.690 (0.566–0.842)	0.723 (0.663–0.788)
1990	0.741 (0.671—0.817)	0.740 (0.575–0.953)	0.712 (0.557–0.909)	0.714 (0.653–0.780)
1995	0.724 (0.652—0.803)	0.796 (0.594–1.067)	0.734 (0.543–0.990)	0.705 (0.639–0.776)
2000	0.707 (0.629–0.795)	0.856 (0.606–1.209)	0.756 (0.528–1.084)	0.695 (0.623–0.776)
2005	0.691 (0.604–0.790)	0.920 (0.614–1.379)	0.780 (0.511–1.190)	0.686 (0.606–0.778)
2010	0.675 (0.578–0.788)	0.990 (0.620–1.579)	0.804 (0.494–1.308)	0.677 (0.587–0.781)
2015	0.660 (0.553–0.788)	1.064 (0.624–1.814)	0.828 (0.477–1.440)	0.669 (0.569–0.786)
2020	0.629 (0.573–0.721)	1.029 (0.658–1.349)	0.909 (0.535–1.549)	0.701 (0.549–0.729)

RR (CI955); *RR* Relative Risk, *CI95%* Confidence interval 95%

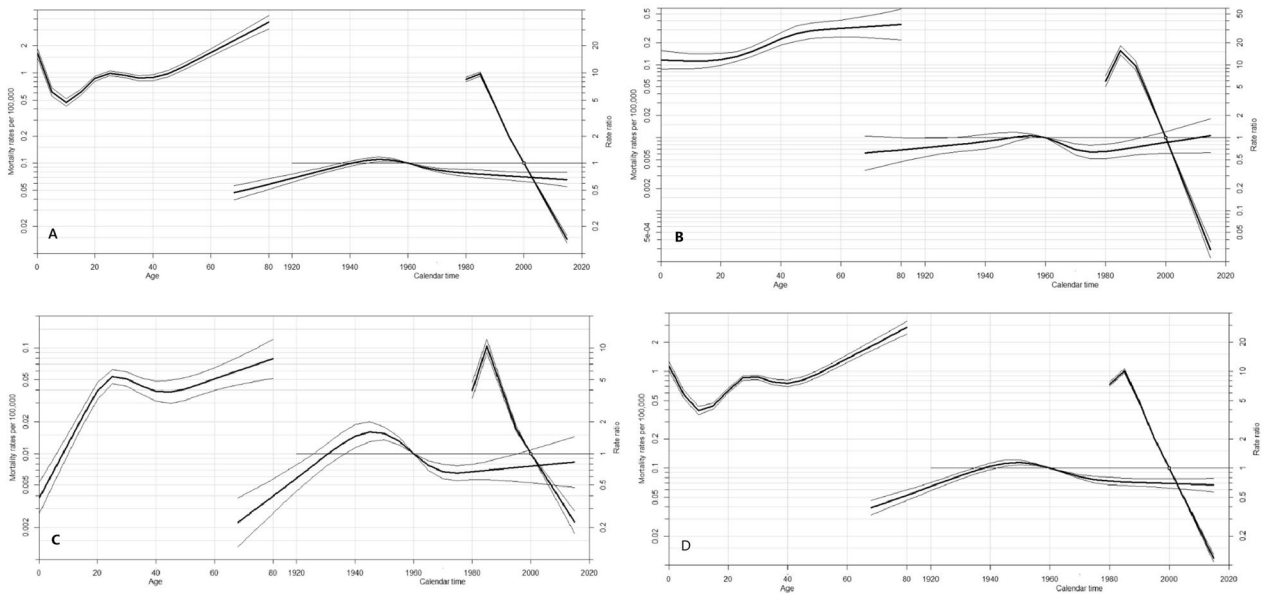

Fig. 2 - Summary of key findings for each assessed region. (**A** refers to North region; **B** refers do Midwest region; **C** refers to Northeast region; **D** refers to legal Amazon region)

demonstrate statistical significance of their effect on mortality from malaria—Tables 1, 2, 3, and Fig. 2.

Northeast

Age's effect under mortality demonstrated a increasing pattern, among individuals who decease between 0 and 4 years old (0.003; 95%CI 0.002–0.005) and those who decease with more than 80 years (0.007; 95%CI 0.051–0.120). Period's effect showed a growing tendency between 1980 and 1984 (RR: 3.968; 95%CI 3.327–4.731) till 1985 and 1989 (RR: 10.405; 95%CI: 9.018–12.006), followed by a sharp decline over time, reaching a low peak between 2015 and 2019 (RR: 0.225; 95%CI 0.177–0.286). Cohort trends reveal a gradual rise in relative risk, with cohorts born in 1945 reaching a peak (RR: 1.603, 95% CI 1.289–1.993) before gradually declining for later birth cohorts—Tables 1 to 3, and Fig. 2.

Legal amazon

A peak in mortality rate between deceased individuals with 0 to 4 years (1.137; 95%CI 1.023–1.263) with a decreasing pattern till individuals who deceased between 10 and 14 years (RR: 0.394; 95%CI 0.359–0.432) and a growing pattern since then till the rates for deceased individuals with more than 80 years (2.828; 95%CI 2.424–3.300). Period effects shoes a growing tendency between 1980 and 1984 (RR: 7.351; 95%CI: 6.973–7.749) till 1985 and 1989 (RR = 10.122; 95%CI 9.634–10.635) and significantly decreased over time, with the lowest risk observed period between 2015 and 2019 (RR = 0.118; 95% CI 0.108–0.129). Cohort trends highlight an increase in mortality risk for those born between 1900 and 1945, with the highest relative risk observed for the 1950 cohort (RR = 1.145; 95% CI 1.079–1.215). After 1960, the risk declined steadily, reaching minor values for 2015 cohort (RR: 0.669; 95%CI 0.569–0.786)—Tables 1, 2, 3, and Fig. 2.

Supplementary material

In order to provide better information and make the readers'assessment more complete, the link below contains 4 supplementary figures that translate with greater specificity the regional assessment of the effects of age, period, and cohort on malaria mortality: https://docs.google.com/document/d/1mXyTNvgh-SLFU1N23zk5o6HnQ1eu1GQ9jPX7MaDwEKI/edit?tab=t.0.

Discussion

A Brazilian study, along with an analysis from the Global Burden of Disease, highlighted that children under four face a disproportionately higher risk of malaria-related mortality compared to other age groups [8, 9]. This vulnerability likely stems from the immaturity of their immune system, which limits their ability to mount an effective response against the parasite [8, 9]. Additionally, factors such as higher parasite loads, delayed diagnosis, and limited access to prompt treatment further contribute to the increased mortality in this age group [8, 9].

In parallel, as proposed by another studies, were observed a notable burden of malaria mortality in children [10, 11]. However, significant death rates were observed among adults, particularly those over 50 years old [10, 11]. This trend is likely driven by the presence of comorbidities such as cardiovascular disease, diabetes, and impaired renal function, which are more prevalent with aging and can exacerbate malaria's effects [10, 11]. Moreover, the natural decline of immune function with age, known as immunosenescence, diminishes the body's ability to effectively clear infections [10, 11]. This deterioration not only weakens the immune response to malaria but also heightens the risk of severe complications, including multi-organ failure, which is more frequently observed in older populations [10, 11].

As noted in the performed analysis and supported by others Brazilian, Indian and African studies, malaria mortality has been steadily declining over the past decades [8, 12, 13]. In Brazil, a large-scale vector control campaigns—such as insecticide spraying and swamp drainage—were implemented to reduce mosquito breeding sites since 1980 s [8, 14, 15]. Furthermore, the establishment of the National Malaria Control Programme (NMCP) in the 1990 s marked a turning point, introducing widespread early diagnosis, improved treatment protocols, and expanded healthcare access in remote areas [8, 14]. The introduction of artemisinin-based combination therapy (ACT) in 2006, alongside the expansion of rapid diagnostic tests (RDTs), further accelerated progress by ensuring faster and more effective treatment [8, 15]. Additionally, large-scale distribution of insecticide-treated mosquito nets (ITNs) and indoor residual spraying (IRS) significantly reduced transmission [14, 15]. In the 2010 s, efforts shifted toward addressing the environmental and socioeconomic drivers of malaria, particularly in the Amazon Basin, where deforestation and land-use changes fueled outbreaks [14, 15].

Globally, a similar decline in malaria mortality has been observed, driven by strengthened international cooperation and advancements in disease management [12, 13, 16, 17]. The Roll Back Malaria (RBM) initiative, launched in 1998 by the WHO, UNICEF, UNDP, and the World Bank, provided a coordinated framework for malaria control, prioritizing access to essential tools, such as insecticide-treated nets and antimalarial medications [12, 16]. In high-burden regions, investments in healthcare infrastructure, vaccination

research, and community-based intervention programs have contributed to reducing mortality rates [13, 16]. The widespread implementation of ACT, particularly in sub-Saharan Africa, has dramatically improved survival rates for *Plasmodium falciparum* infections [16, 17]. Additionally, novel approaches, such as genetically modified mosquitoes and malaria vaccines like RTS,S/AS01, represent promising strategies for long-term control [16, 17].

Temporal factors, including shifts in economic activities, have a profound influence on malaria transmission and mortality across birth cohorts [18–20]. Over the past decades, Brazil and many other regions worldwide have undergone significant transformations, such as urbanization, industrialization, and improved healthcare systems [18–20]. These changes have led to a general decline in malaria incidence and mortality, particularly in urban centers where vector control measures, sanitation, and access to medical care have improved [18–20].

However, these advancements have not been equitably distributed. Many rural and remote communities, especially in the Amazon and sub-Saharan Africa regions, continue to experience high malaria burdens due to persistent socioeconomic disparities, limited healthcare infrastructure, and environmental conditions favorable to vector proliferation [18, 19]. While industrialization and economic development have reduced malaria risk in some areas, they have also led to deforestation and migration patterns that create new vulnerabilities to transmission [20]. Globally, similar trends have been observed. Countries that have successfully industrialized and urbanized often exhibit lower malaria mortality rates, while regions with slow economic growth and persistent inequalities continue to struggle with high transmission levels [18, 19].

Interestingly, studies from 2000 s predominantly suggested that older individuals were more susceptible to malaria-related mortality [10, 11]. However, 2020 s research has shifted focus toward younger cohorts, indicating that those born in later decades may now face a heightened risk of severe disease and death [8, 9]. Several hypotheses could explain this trend, including waning population-level immunity, shifts in vector-host interactions, and broader changes in epidemiological patterns [10, 11].

For instance, in recent eras, a shift in climatic patterns has been increasingly documented, with reports of malaria cases and fatalities emerging in subtropical and temperate regions [20, 21]. This expanding geographic distribution of malaria underscores the complex interplay between environmental changes and vector dynamics, raising concerns about the disease's potential resurgence in areas previously considered at low risk [20–22].

Additionally, the impact of co-infections has gained attention, as diseases such as COVID-19 and H1 N1 influenza have been shown to compromise immune responses, potentially exacerbating malaria severity in previously lower-risk groups [23, 24]. These findings call for further investigation into the evolving landscape of malaria mortality and the multifaceted factors driving its demographic shifts [23, 24].

Comparing across regions, the North and Legal Amazon exhibit the highest malaria mortality rates, whereas the Midwest and Northeast show lower but still significant trends [25, 26]. This is possibly due to the fact that the Northeast and Midwest regions have higher urbanization rates, which correlate with greater healthcare coverage, ensuring timely treatments [25]. At the same time, the Legal Amazon, which largely overlaps with the North, has healthcare services concentrated in major urban centers, such as state capitals [26]. This geographic distribution hinders access to preventive measures and delays treatment for patients requiring intensive care, ultimately contributing to worse prognoses [26].

The period effect highlights nationwide improvements in malaria control over the decades, though the decline has been more pronounced in urbanized and non-Amazonian regions [26, 28]. This likely reflects the impact of public policies and regional health measures implemented by the Brazilian government in recent decades, as previously discussed [27]. Moreover, the more dispersed population distribution in the North and Legal Amazon, along with the unique characteristics of riverine and Indigenous communities in these areas, difficulties the adaptation and implementation of similar policies [27].

The cohort effects suggest that older generations faced higher malaria-related mortality risks, likely due to historically limited healthcare access and less effective control measures [25, 28]. However, other factors may have contributed to this pattern [25]. Shifts in occupational and migratory patterns may also be relevant, as past generations were more frequently engaged in high-exposure activities, such as agriculture and extractives, in endemic regions [28]. Indeed, Brazil observed an extensive populational migration towards Midwest and North along 1960 s to 1980 s, which may increased the local population, which supplements and house conditions may be not adequate to avoid malaria infection [28]. In parallel, the Northwest observed a individual's migration towards Brazilian Southeast region, which reduced its population, and possible, malaria transmition and mortality [27, 28].

This study is limited by the ecological design, which may not capture individual-level risk factors. Incomplete data from the South and Southeast regions of Brazil also restricted a nationwide analysis. Additionally, the analysis relied on public health databases, which may have reporting inaccuracies.

Nonetheless, this study has some valuable strengths that must be recognized. Indeed, after a literature review, this study observed the largest time range, a 45-year approach, regarding malaria mortality. Furthermore, over the years an improvement in notification system have been documented, which improved data quality and reliability. By focusing on regions with the highest malaria burden, it offers relevant findings for public health strategies, as well as evaluating specific effects of age, period, and cohort, it contribute to understanding the dynamics of malaria mortality in Brazil.

Conclusions

The study provides a comprehensive analysis of malaria mortality in Brazil from 1980 to 2024, evaluating the impact of age, period, and birth cohort across different regions. The findings reveal a consistent pattern in age-specific mortality, with higher rates observed in the older population across all regions. Period effects consistently showed a significant reduction in malaria mortality over time across all regions. Cohort analyses highlighted region-specific trends, with earlier birth cohorts (especially those born around the 1940 s and 1950 s) experiencing higher risks, particularly in the Legal Amazon and Northeast. However, a steady decline in risk was observed for more recent cohorts, reflecting the impact of improved malaria control measures on younger generations.

Overall, the results indicate significant progress in malaria control in Brazil, marked by substantial reductions in mortality over time. Despite these advancements, the persistent age-related risk suggests a need for targeted strategies to protect vulnerable age groups, particularly the elderly, to achieve further reductions in malaria-related deaths.

Supplementary Information

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Supplementary material 1

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Declarations

Competing Interests
The authors declare no competing interests.

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