Health and economic burden due to malaria in Peru over 30 years (1990−2019): Findings from the global burden of diseases study 2019

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Summary

Background Malaria is one of the biggest impediments to global progress. In Peru, it is still a major public health problem. Measures of health and economic burden due to malaria are relevant considerations for the assessment of current policies.

Methods We used estimates from the Global Burden of Diseases Study 2019 for malaria in Peru, grouped by gender and age, from 1990 to 2019. Results are presented as absolute numbers and age-standardized rates with 95% uncertainty intervals (UI). We collected economic data from the World Bank and The National Institute of Statistics and Informatics of Peru and Loreto to calculate the economic burden of productivity loss (EBPL) using the human capital approach. Economic values were presented in constant dollars, soles, and percentages.

Findings Rates of deaths, years of life lost (YLLs), years lived with disability (YLDs), and disability-adjusted life years (DALYs), as well as the EBPL, were drastically reduced from 1990 to 2019. DALYs had a greater percentage of YLDs in 2019 than in 1990. DALYs rates showed no preference between sexes, but the "< 1 year" age group had the highest DALYs values over the study period. We found that the EBPL due to malaria for Loreto was considerably higher than Peru's in terms of GDP percentage.

Interpretation Our study shows that the fight against malaria in Peru reduced remarkably the impact of the disease since 1990; however, during the last decade the estimates were stable or even increased. Our results help to measure the malaria impact on the health status of the Peruvian population as well as the economic pressure that it exerts, constituting remarkable tools for policymaking aimed at reducing the burden of this disease. Strengthening the malaria elimination program is important to achieve the elimination of the disease in the coming years.

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Introduction

Malaria remains a serious public health problem decreasing quality of life and causing economic losses. The importance of this disease is highlighted in the

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Research in context

Evidence before this study

For this health burden study, we have considered estimates from the Global Burden of Diseases Study (GBD) 2019, Peruvian Health Ministry of Health, Malaria Atlas Project, and the World Health Organization. For the economic burden of productivity loss due to malaria, we collected data from the World Bank and The National Institute of Statistics and Informatics of Peru. We reviewed mainly indexed scientific articles retrieved from PubMed or HINARI, but also checked several reports of the Peruvian Health Ministry of Health and the World Health Organization. We included only peer-reviewed articles about malaria with public health relevance if they had a reliable basis. Official documents of the World Bank, Health Ministry or World Health Organization were considered too. We read and cited relevant articles originally written in English, Spanish, and Portuguese. We performed a search of articles from July 2021 to October 2021. Some terms researched were 'Malaria, Global Burden of Diseases, Economic Burden, Public Health, Latin-America, Peru, Amazon Region, tropical diseases, and Disability-Adjusted Life Years (DALY)'. Most of the cited articles are published in Q1 journals or are official information from well-respected institutions such as WHO or the Health Ministry.

Added value of this study

We present organized and summarized information on the health burden due to Malaria from 1990–2019 in Peru, based on data from the GBD 2019. Also, we present the economic burden of productivity loss due to Malaria from 1990–2019 in Peru which, to the best of our knowledge, was not calculated ever before. Moreover, we present evidence of the positive impact of the current Malaria elimination plan "Malaria Cero" and other efforts of Peru in terms of health and economic burden over time.

Implications of all the available evidence

The available evidence organized in this study, together with other sources related to the malaria burden in Peru from 1990 to 2019 is important to understand trends; diagnose the national, regional, and local situation; build scenarios; set missions and visions of health plans and policies; and to assess the effectiveness of the past and currently implemented plans and policies. Further studies of the economic burden of malaria are recommended to complement the actual cost of the disease in Peru and to allow cost-effectiveness studies of the already taken and future measures.

2030 Agenda and the Sustainable Development Goals adopted by the United Nations, where it is established that malaria incidence is an indicator of the efforts to ensure healthy lives and promote well-being at all ages.[1] Several strategies such as the use of treated bed nets, indoor residual spray and the introduction of artemisinin-based combination therapies (ACTs) have helped to achieve an important reduction of the malaria burden worldwide. However, malaria cases started to rise again in the region of the Americas during the last quinquennium, mainly attributed to the epidemic in Venezuela.[2] Therefore, governments and international institutions ought to join efforts to control and eliminate malaria from this region.

Plasmodium sp. are unicellular protozoan parasites that cause malaria. Five species can infect humans, but *Plasmodium vivax* and *Plasmodium falciparum* are the main ones responsible for causing the disease worldwide as well as in Peru. Globally, in 2019, there were an estimated 229 million malaria cases and 409 000 deaths, while in the region of the Americas 0·9 million malaria cases and 551 deaths were estimated. Within this region, Peru was the fourth country with more malaria cases, after Venezuela, Brazil, and Colombia, accounting for 5 % of all the cases on its own.[2]

In Peru, in 2019, 12·8 million people live in transmission areas, of which 1·6 million are in high-transmission areas.[2] While the number of notified deaths caused directly by malaria from 2015 to 2019 has been zero or nearly so, the number of cases remained over 24 000 in 2019, even after a reduction of more than 60% from 2017, attributed to the National Program for malaria elimination "*Malaria Cero*".[3] However, these numbers represent a great reduction over time, showing a clear reductive trend in the last three decades, even though there were periodical peaks of malaria's high incidence in the late 1990s (with more than 100 000 cases per year), early 2000s and 2012–2015.[4]

The Global Burden of Disease Study (GBD) is the most comprehensive effort to study epidemiological levels and trends worldwide. Since 1990, it has been quantifying and comparing the magnitude of health losses due to diseases and injuries as well as their risk factors according to location, sex, age, and year. The GBD uses the disability-adjusted life year (DALYs) as its population's primary health metric. DALYs are composed of years lived with disabilities (YLDs) and years of life lost (YLLs) due to premature death for a given cause. They are relevant metrics for decision-makers because they help quantify health losses due to fatal and nonfatal disease burdens.[5]

Additionally, since diseases imply direct costs, productivity losses, and intangible costs, DALYs help assess the impact of diseases in economic terms. Using DALYs and macroeconomic indicators, like the gross domestic product (GDP) per capita, we can estimate the economic burden of productivity loss (EBPL), considering DALYs are years in which people cannot be productive due to diseases, which means monetary losses for these individuals and the country overall.[6] This kind of economic estimation is vital to evaluate the cost-effectiveness of health policies and to find optimal alternatives, especially for countries like Peru which has no recent report about EBPL due to malaria.

Here, we present an analysis of the malaria burden stratified by sex and age in Peru, as well as the first EBPL analysis using the human capital approach in this country. The understanding of the health and economic burdens of productivity loss due to the disease will be relevant to current and future health policies. In the present study, we analyzed the malaria burden in Peru using the data from the GBD 2019 describing the main burden metrics (DALYs, YLDs, and YLLs), as well as presenting the EBPL due to malaria for Peru and Loreto Department using the data from the World Bank and the National Institute of Statistics and Informatics.

Methods

Study area

Peru is the third-largest country in South America, with 1·29 million Km^2 and it had an estimated population of 32·5 million inhabitants in 2019.[7] In this year, it was estimated that approximately 5 % of the Peruvian population (1·6 M) lived in a high malaria transmission area (>1 case per 1000 population), 34% (12·8 M) in a high or low transmission area (0 - 1 case per 1000 population), and the rest of the population in considered "Malaria-free areas".[2] The Amazon departments are the most affected ones, especially the department of Loreto, with an estimated population of more than 1 million inhabitants in 2019. *Plasmodium vivax*, the predominant parasite species in Peru and the America region, causes more than 75% of the cases over time, followed by *P. falciparum*.[2,3,8]

Global burden of diseases study (GBD) overview

The GBD is coordinated by the Institute for Health Metrics and Evaluation (IHME) and consists of a systematic and scientific effort to quantify the comparative magnitude of health losses due to diseases, injuries, and risk factors by sex, age, and location over time, so that health systems can be improved, and disparities can be eliminated.

The main health metric from GBD 2019 is the disability-adjusted life years (DALYs), which represents one year of healthy life lost due to a specific illness or injury and it results from the sum of the years of healthy life lost due to disability (YLDs) and the years of life lost due to premature death (YLLs). The GBD 2019 used the Bayesian meta-regression analytic tool DisMod-MR 2.1 to synthesize consistent estimates (with their 95% uncertainty intervals) of incidence, prevalence, remission, excess mortality, and cause-specific mortality considering a wide range of updated and standardized analytical procedures. The general methodological approaches to estimate the metrics in GBD 2019 are detailed in previous publications of the yearly series.[5]

GBD 2019 provides a comprehensive annual assessment of mortality and morbidity estimates for 369 diseases and injuries in 204 countries and territories from 1990 to 2019. Diseases and injuries were organized in 4 hierarchical levels from the broadest to the most specific causes of death and disability.[5] Malaria was defined and identified according to various revisions of the International Classification of Diseases and Injuries (ICD), which latest version was the ICD-11.[9]

The GBD data sources for Peru can be reviewed on the webpage of the Global Health Data Exchange of IHME (http://ghdx.healthdata.org/gbd-2019/data-input-sources). Mortality data and data used to generate the YLLs estimates came from the Peru Vital Registration of the WHO Mortality Database.[10] The main sources of morbidity data, used for the estimation of the YLDs, were the Malaria Atlas Project and the Peru Continuous Demographic and Health Survey.[11,12] It is noteworthy that Peruvian metrics used in this study considered the entire nation, and no stratified information for departments or Amazon areas were available. Also, it is relevant to state that the fact that less informative data was available from Peruvian official sources in the early years of 1990 may explain the wider uncertainty intervals shown.

The malaria burden was assessed by metrics of incidence, number of deaths, YLLs, YLDs, and DALYs. The YLLs express the years of life lost due to premature deaths in the population and results from the multiplication of the number of estimated deaths due to malaria at a certain age by the standard life expectancy at the age of death. GBD 2019 considered a global standard life expectancy of 73·5 (95% UI 72·8–74·3) years at birth, based on the lowest observed death rates for each 5-year age range in 2019.[13] The YLDs express the sum of the prevalence of sequelae related to malaria multiplied by the disability weight. The disability weight reflects the severity of health loss associated with a given disease and is presented on a scale varying from 0 (perfect health) to 1 (equivalent to death). The sum of the YLLs and the YLDs yields the DALYs.[5]

Herein, we present the estimates as age-standardized rates by 100 000 inhabitants. The age-standardized rates were calculated using the GBD's world population standard. The metrics are presented with their respective 95% uncertainty intervals (95% UI) and the relative percentages of change.

Economic burden of productivity loss due to malaria

To estimate the EBPL due to malaria, we use the human capital approach, a method to estimate the indirect cost due to productivity loss.[6] Following this approach, we consider individuals are productive members of the economy and their yearly economic contribution is the gross domestic product (GDP) per capita. Since DALYs correspond to years in which individuals are not productive and do not contribute to the GDP, we can estimate the productivity loss due to malaria in economic terms. Therefore, we have valued individuals only by taking into account their contributions to the Peruvian economy, considering only the economically active population (EAP), individuals between 15 and 64 years old. The EBPL due to malaria in Peru was calculated by multiplying the estimated DALYs of the EAP and their respective 95% uncertainty intervals due to malaria by the Peruvian GDP per capita, each year. Peruvian GDP per capita from 1990 to 2019 was obtained from the World Bank both in constant 2010 dollars (US$)[14] and in constant local currency (2007 soles (S/.)).[15]

For the Loreto department, we corrected the DALYs due to malaria in Peru to have Loreto's DALYs by assuming it corresponded to the proportion of national malaria cases that occurred in this department according to Peruvian Ministry of Health reported data, available since 2004.[3,8] This correction is an approximation because we are not considering the specific weight of malaria deadly cases or plasmodial species proportion, among other relevant factors; however, this assumption is made on the basis that Loreto is the most relevant department for this disease, accounting for up to 96.6% of the cases in recent years, and it shares Amazon characteristics with the other most relevant departments. Afterwards, we calculated the EBPL due to malaria in this Amazon department by multiplying the Loreto's DALYs of the EAP and their respective 95% uncertainty intervals due to malaria by the Loreto's GDP per capita from 2001 to 2019 in constant 2007 soles, obtained from The National Institute of Statistics and Informatics (INEI).[16]

Additionally, the value of DALYs lost due to malaria as a percentage of total GDP (of Peru and Loreto) was calculated for each year. DALYs used in this section of the study were not age-standardized values and were obtained from the GBD 2019.

Ethical approval
This work has used country-level published data from GBD, INEI, and World Bank. It does not deal with any individual or personal sensitive data. Therefore, this study does not require any ethical permissions.

Role of the funding sources
This work was funded by project: Contract No. 09-2019-FONDECYT-BMINC.INV and FONDECYT-BM, Perú (Program INCORPORACIÓN DE INVESTIGADORES E038-2019-01, Registry Number: 64007). Grants were used for data collection, analysis and interpretation; researchers' salaries (JRT, CC-O, EES-C, SCH and RTL) and to pay the cost of publication. Funders had no role in study design, data collection, data analysis, interpretation, writing of the report or decision to submit.

Results

GBD estimates at national level
The main metrics on malaria burden and relative change from 1990 to 2019 in Peru are presented in Table 1. In 2019, the malaria incidence rate was 261·9 cases per 100 000 inhabitants (95% UI 104·1 – 583·6), and the mortality rate was 0·057 deaths per 100 000 inhabitants (95% UI 0·001 – 0·323), representing a reduction of 90·55% and 97·98%, respectively, in comparison with 1990. The DALYs rate also decreased in the country, going from 167·9 DALYs per 100 000

Metrics	Absolute number N (95 % UI)		Relative change (%)	Rate per 100,000 inhabitants (95% UI)		Relative change (%)
	1990	2019		1990	2019	
Incidence	572757 (266430 – 1250116)	90340 (35935 – 201209)	−84,23	2771,3 (1311,3 – 5899,0)	261,9 (104,1 – 583,6)	−90,55
Deaths	571 (53 – 2163)	19 (0,4 – 109)	−96,63	2,813 (0,0262 – 10,570)	0,057 (0,001 – 0,323)	−97,98
YLLs	36076 (3352 – 136587)	937 (19 – 5399)	−97,40	150,8 (14,0 – 571,5)	2,7 (0,1 – 15,7)	−98,19
YLDs	4098 (2166 – 7865)	1032 (558 – 1749)	−74,81	17,2 (9,1 – 33,2)	3,1 (1,7 – 5,2)	−82,15
DALYs	40173 (6717 – 141995)	1969 (752 – 6328)	−95,10	167,9 (28,2 – 594,2)	5,8 (2,2 – 18,4)	−96,55

***Table 1*: Incidence rates, number of deaths, years of life lost due to premature death (YLLs), years lived with disability (YLDs), and disability-adjusted life years (DALYs) for malaria in Peru in 1990 and 2019.**
Absolute numbers and age-standardized rates per 100,000 inhabitants are presented along with relative change 1990 – 2019. N: Absolute vale of the metric, 95 % UI: Uncertainty interval of 95%, %: Percentage, YLL: Years of life lost due to premature death, YLDs: Years lived with disability, DALYs: Disability-adjusted life years.

inhabitants (95% UI 28·2 – 594·2) in 1990 to 5·8 DALYs per 100 000 inhabitants (95% UI 2·2 – 18·4) in 2019 representing a reduction of 96·55% (Table 1).

In 1990, the YLLs rate [150·8 per 100 000 inhabitants (95% UI 14·0 – 571·5)] accounted for 89·8% of the DALYs, while the YLDs rate [17·7 (95% UI 9·1 – 33·2) per 100 000 inhabitants] corresponded to 10·2% of the total DALYs due to malaria. Over the years, the contribution of YLLs and YLDs to the total DALYs of malaria changed. In 2019, 46·6% of the DALYs rate corresponded to YLLs [2·7 (95% UI 0·1 – 15·7) per 100 000 inhabitants], and 53·4% corresponded to YLDs [3·1 per 100 000 inhabitants (95% UI 1·7 – 5·2)] (Figure 1).

GBD estimates by sex and age groups

DALYs rate trends by sex are shown in Figure 2. DALYs rates were similar between genders in Peru over the years. In general, females presented slightly higher DALYs values than males. A marked decrease was observed in the metric from 1990 to 2019, especially from 1994 to 1995. The DALYs rates for both sexes were less than 20 per 100 000 inhabitants from the year 2005 onwards.

While DALYs rate values were drastically reduced from 1990 to 2019, the highest DALYs rate was found in the age group of "< 1 year old" and the lowest in the age group of "80-plus years" for both sexes, every year

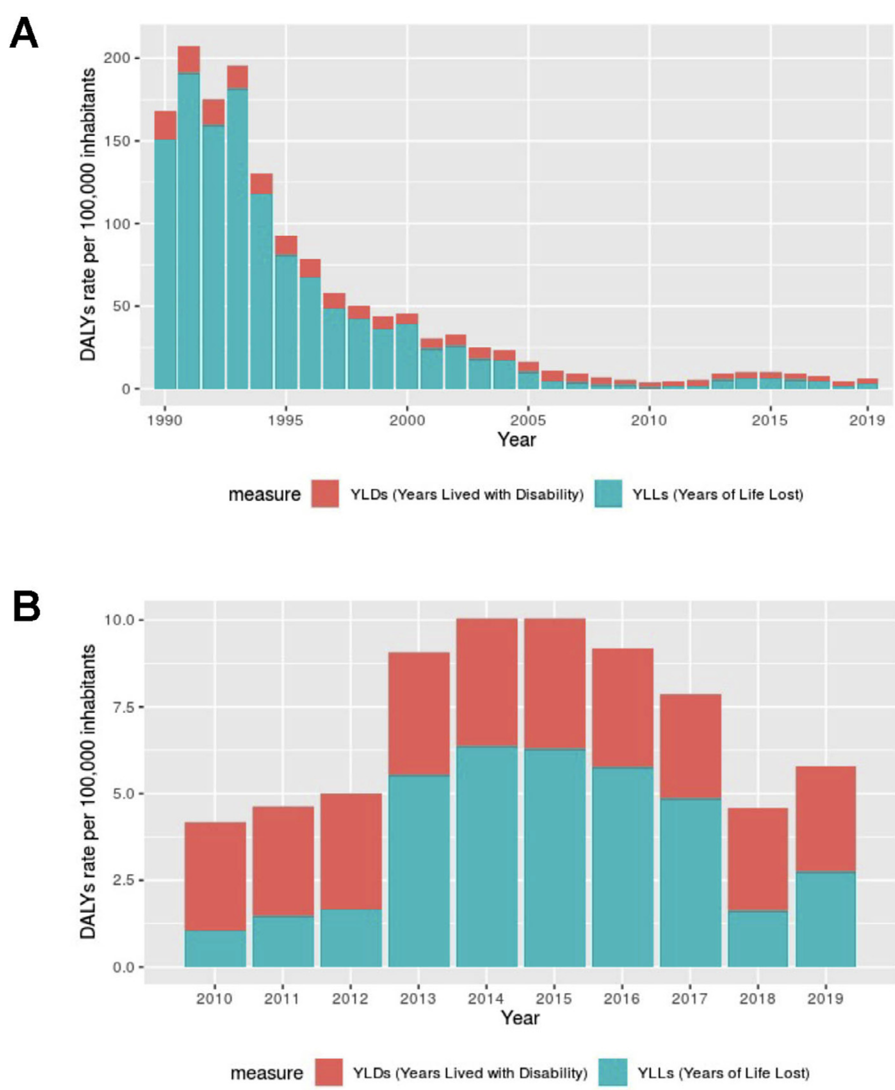

Figure 1. Disability-adjusted life years (DALYs) for malaria. Age-standardized rates per 100 000 inhabitants are presented, along with the contribution of the rates of years of life lost due to premature death (YLLs) and years lived with disability (YLDs). **(A)** Data for all years covered by the study, Peru, 1990–2019; **(B)** Data corresponding to a zoom of the data for the last decade shown in panel A, which makes it easier to visualize by changing the scale, Peru, 2010–2019.

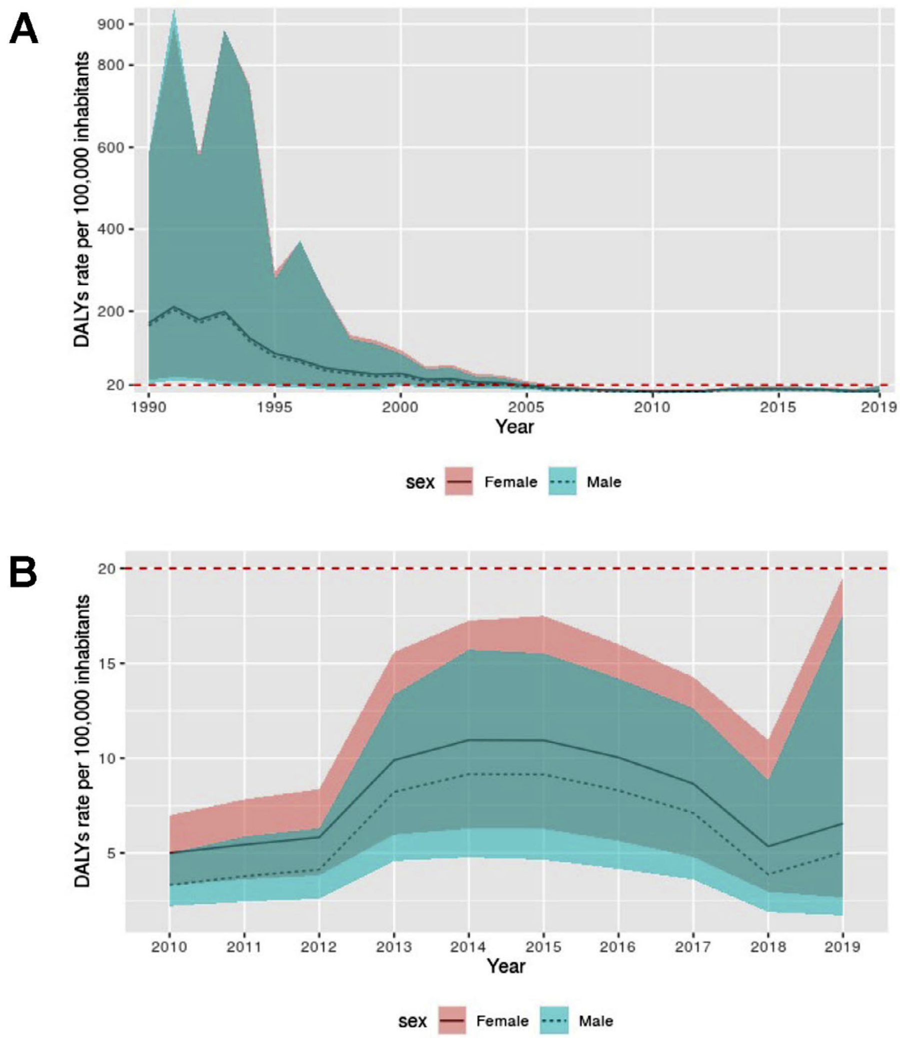

Figure 2. Age-standardized rates per 100 000 inhabitants of disability-adjusted life years (DALYs) for malaria according to sex. (A) Data for all years covered by the study, Peru, 1990–2019; **(B)** Data corresponding to a zoom of the data for the last decade shown in panel A, which makes it easier to visualize by changing the scale, Peru, 2010–2019. Shadow areas show 95% uncertainty intervals (UI). The dashed red line marks 20 DALYs rate per 100 000 inhabitants.

(Figure 3). Similar patterns were presented in 1990 and 1999 where the burden of malaria was accumulated in the younger age groups of "< 1-year-old" and "01 to 04 years" (Figures 3a and b). This accumulation was less pronounced in 2009 and 2019 (Figure 3c and d).

Economic burden of productivity loss due to malaria

In 1990, the EBPL due to malaria in Peru (considering the GDP of the entire country) was 44·5 million dollars (95% UI 8·2 – 14·7) or 115·6 million soles (95% UI 21·2 – 382·0), corresponding to 0·0762% of the national GDP. However, in 2019, the economic burden decreased to 8·3 million dollars (95% UI 2·9 – 30·4) or 21·4 million soles (95% UI 7·5 – 79·0) (Figure 4), corresponding to 0·0039% of the national GDP (Figure 5). Moreover, the EBPL due to malaria in Peru was less than 15 million dollars of GDP from the year 2003 onwards (Figure 4) and less than 0·09% of the national GDP during the period 1990 – 2019 (Figure 5).

Using the GDP of the department of Loreto, the most relevant Amazon region for malaria in Peru, the EBPL due to malaria in 2004 was 4·0 million dollars (95% UI 2·1 – 7·0) or 10·4 million soles (95% UI 5·4 – 18.2) corresponding to 0·2287% of the Loreto's GDP. In 2019, the economic burden slightly increases to

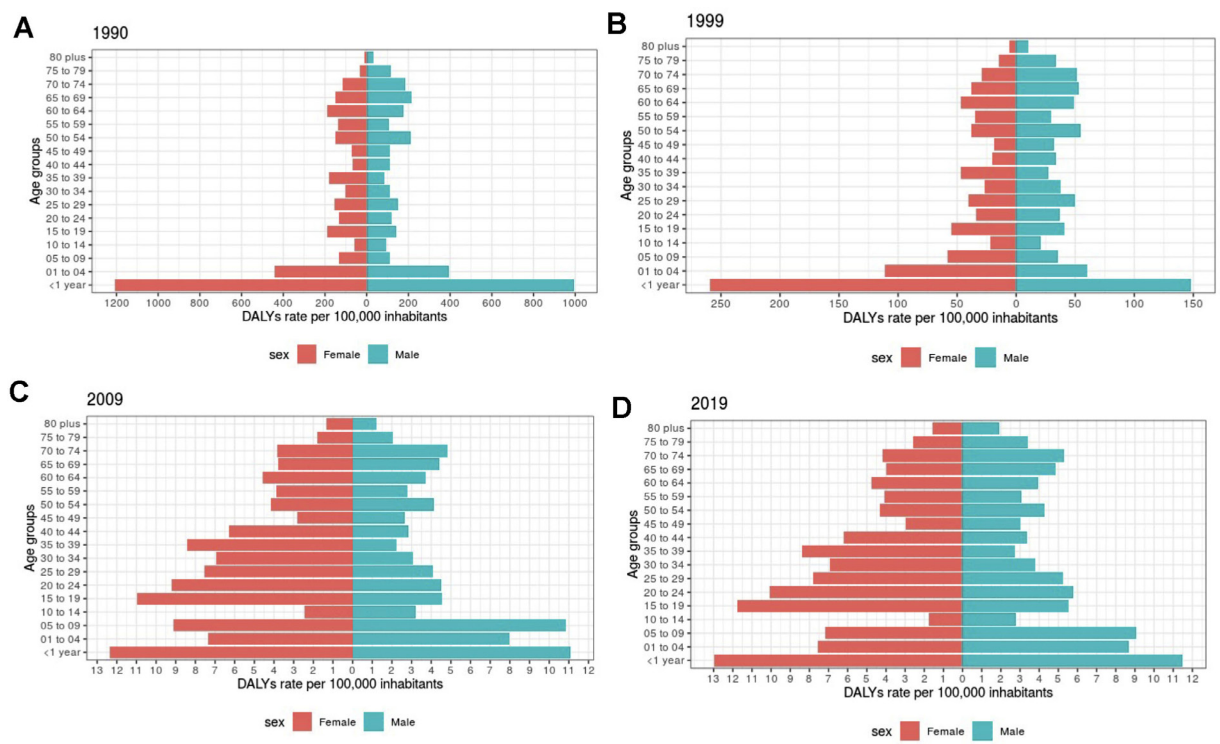

Figure 3. Disability-adjusted life years (DALYs) rates per 100 000 inhabitants for malaria according to age groups in Peru. (A) 1990; **(B)** 1999; **(C)** 2009; **(D)** 2019. Each panel presented an auto-adjusted X-scale to clearly show the distribution of the DALYs rates.

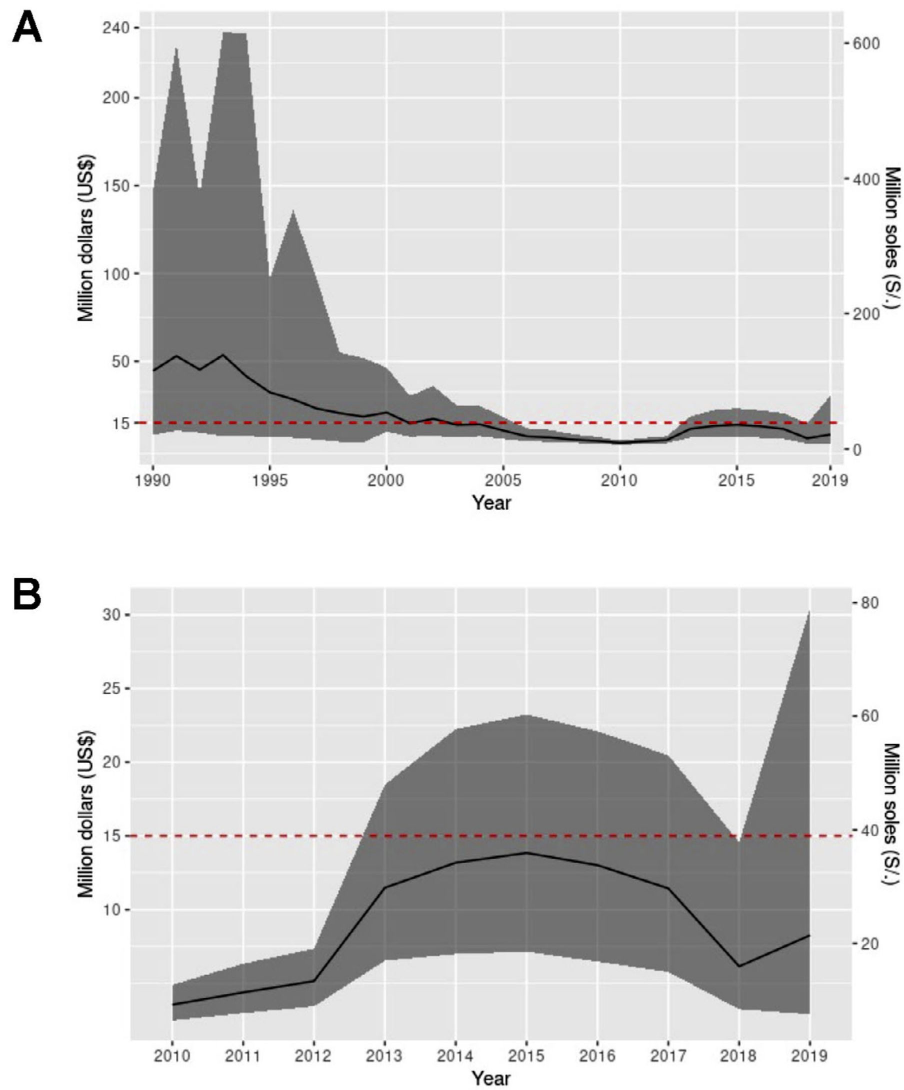

Figure 4. Economic burden of productivity loss due to malaria using the human capital approach considering the entire GDP of Peru in million dollars and million soles. (A) Data for all years covered by the study, Peru, 1990–2019; **(B)** Data corresponding to a zoom of the data for the last decade shown in panel A, which makes it easier to visualize by changing the scale, Peru, 2010–2019. The Shadow area shows 95% uncertainty intervals (UI). The dashed red line marks 15 million dollars of economic burden.

4·1 million dollars (95% UI 1·4 – 15·1) or 10.6 million soles (95% UI 3·7 – 39·1) (Figure 6) corresponding to only 0·1136% of Loreto's GDP, less than the half of the percentage in 2004 (Figure 5). The EBPL due to malaria in Loreto was less than 7·5 million dollars (Figure 6) and less than 0·25% of Loreto's GDP during the period 2004 – 2019 (Figure 5).

Between 2001 – 2019, the EBPL due to malaria for Loreto was several times higher than Peru's in terms of GDP percentage. For 2019, Loreto's economic burden was almost 30 times the Peruvian's estimation (Figure 5), indicating the disproportionate incidence of malaria in this department.

Discussion

To the best of our knowledge, this is the first analysis of the burden of malaria in Peru comprising a period of 30 years (from 1990 to 2019) using data from the GBD 2019. This is also the first study of the EBPL due to malaria in Peru using the human capital approach, comprising the same period of 3 decades. The studied indicators (death incidence, DALYs, YLLs, and YLDs) and the calculated economic burden allow the estimation of the malaria impact on the health status of the Peruvian population as well as the economic pressure that it exerts, constituting remarkable tools for policy-making aimed at reducing the burden of this disease.[5,6]

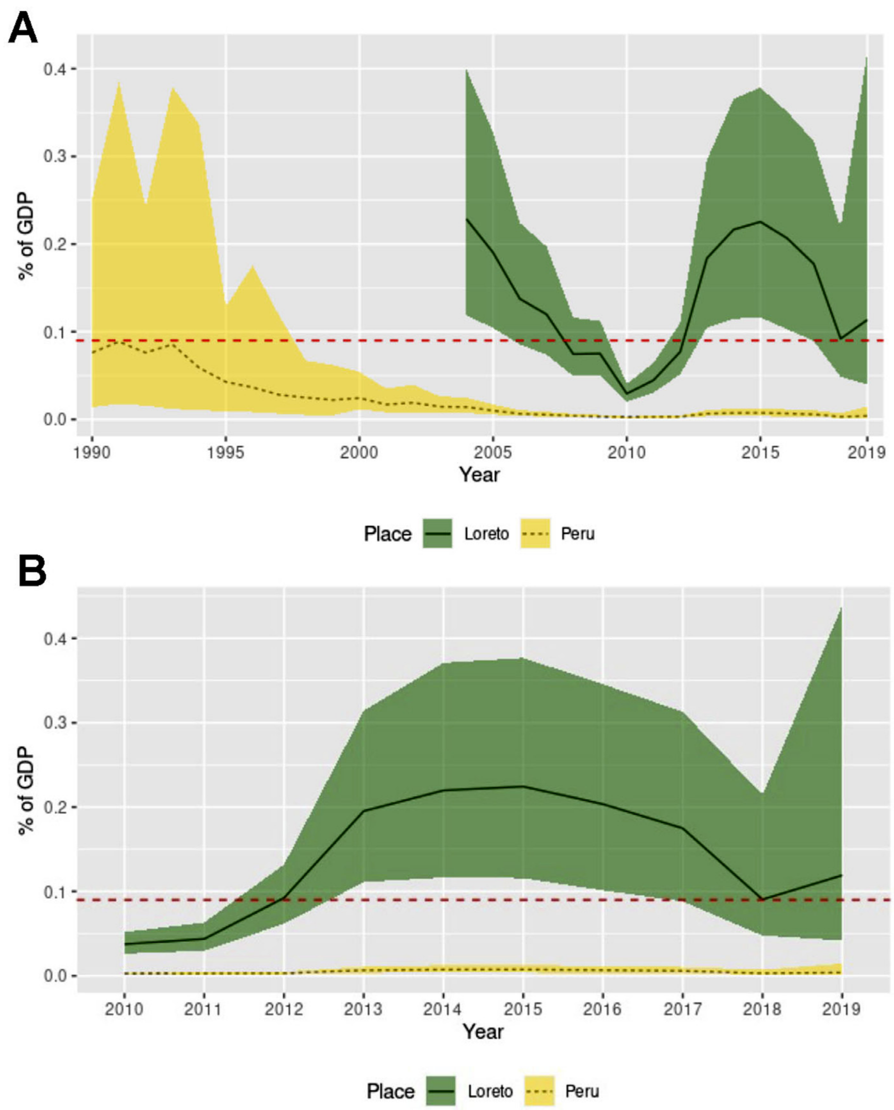

Figure 5. Economic burden of productivity loss due to malaria in Peru and Loreto as a percentage of their respective GDP. GDP data available for Loreto since 2001. Epidemiologic data available from the Peruvian Ministry of Health to estimate the proportion of DALYs corresponding to Loreto since 2004. **(A)** Data for all years covered by the study, Peru, 1990−2019; **(B)** Data corresponding to a zoom of the data for the last decade shown in panel A, which makes it easier to visualize by changing the scale, Peru, 2010-2019. The Shadow area shows 95% uncertainty intervals (UI). The dashed red line marks 0·09% of GDP.

During the study period, malaria incidence, deaths, and burden indicators (YLLs, YLDs, and DALYs) showed considerable reductions in Peru (Table 1), reaching reductions of more than 95% in deaths YLLs, and DALYs rates, reaching only 5.8 DALYs per 100 000 inhabitants in 2019. Interestingly, the DALYs rates of the other Latin American countries with the highest numbers of malaria cases in 2019 show a similar burden of 5.4 and 8.5 for Brazil and Colombia, respectively; except for Venezuela with a notably higher burden of 147.6 DALYs per 100 000 inhabitants (*Supplementary Figure* S1). The fact that there is not a direct correlation between the number of malaria cases and DALYs is due to the proportion of severe and mortal cases and the size of the population living in transmission areas, indicating that it would be more informative to compare rates from transmission areas only, which is not an option due to data limitation. Additionally, the reduction of the burden over time did not perfectly match with a constant reduction of cases over time, having some years with a higher number of cases but still smaller DALYs. This remarkable decreasing DALYs trend is due to several policies implemented over the years by local, regional, and national governments to

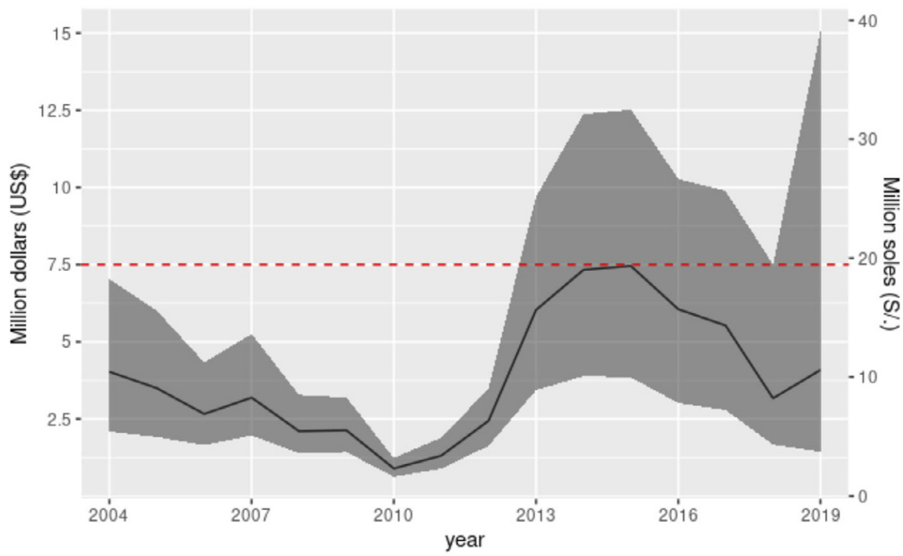

Figure 6. Economic burden of productivity loss due to malaria using the human capital approach considering the GDP of Loreto-Peru in million dollars and million soles. The Shadow area shows 95% uncertainty intervals (UI). The dashed red line marks 7·5 million dollars of economic burden.

improve malaria surveillance, treatment, control, and elimination strategies, as well as multisectoral actions and citizen participation during the fight against malaria in Peru.[18,19]

Remarkably, the contribution of YLLs to the DALYs rate changed from 89·8% in 1990 to 46·6% in 2019, evidencing that the current burden of malaria in Peru is mainly composed of the years lived with malaria rather than the years lost due to the disease, reaffirming the substantial reduction in the related mortality (Figure 1a). Despite the important reduction of the burden of malaria between 1990 and 2019, during the last decade an increment of DALYs rates was observed from 2010 to 2015, even more pronounced in the period 2012–2013; however, a reductive trend is observed from 2016 onwards, especially in the period 2017–2018 (Figure 1b). These phenomena coincide with the end of the program "Malaria Control in the Border Zones of the Andean Region: A Community Approach" (PAMAFRO) in 2010 and the beginning of the elimination plan "Malaria Cero" in 2017,[20,21] which highlights the importance of continuous control and elimination programs by the government and international collaborators.

From 1990 to 2019, DALYs rates were markedly reduced for both sexes, with slightly higher values for females than males in general (Figure 2). This observation is probably not related to a higher incidence of malaria in women than in men but mainly to a higher burden of the disease in pregnant women who are more vulnerable than other adults to malaria.[22] Thus, developing efficient preventive and control policies focused on pregnant women to reduce this gap is highly recommended. However, the role of gender must be considered in every health intervention, since men and women have different risks from their different types of jobs, access to information, or cultural and social pressures.[23]

Drastic reductions of DALY were also evidenced in all age groups (Figure 3). All over the 1990–2019 period, higher values were found in the youngest group of "<1 year old" as it is reported that the heaviest burden of malaria is shouldered by children less than 5 years of age.[24] On the other hand, changes in the distribution of the burden of malaria in Peru were observed from the initial pattern (1990 and 1999) (Figure 3a and b) to the recent one (2009 and 2019) (Figure 3c and d), where the burden of children younger than 5 years old is still higher than the average, but less pronounced. This redistribution is similar to the Brazilian case, where the youngest groups had the highest DALYs values in 1990 as well, but no peak values were observed in the youngest groups in 2017, with the highest DALYs values observed among young adults instead.[25] This current pattern of malaria's burden means that, proportionally, more of the economically active population is being affected by the disease so greater investments are recommended to control the disease, not only to reduce its impacts on individuals' health but also to minimize the economic pressure that it exerts on the population.[26]

For the EBPL analysis, we choose the human capital approach that values the lives and quality of life lost according to the not generated income. This method presents limitations such as that it tends to overestimate the total cost burden because lost work time can sometimes be compensated when the individual returns and replacement workers can also be taken from the pool of unemployed labour to replace those who were absent.[27] Moreover, since this approach is evaluating the economic burden of lost productivity, it does not consider the healthcare cost. However, it has been applied in the valuation of health benefits in cases of both avoidable morbidity and mortality,[28] such is the case of malaria, giving a clear quantification of the economic loss due to the disease. Here, we have calculated that the EBPL due to malaria in Peru was 8·3 million dollars or 21·4 million soles in 2019, even after a drastic reduction of more than 80% from 1990 (Figure 4). It is noteworthy that the total economic burden due to malaria would be much higher if it included all the direct and indirect costs related to the disease, as it was calculated up to 119·5 million soles in 1998.[29] Also, among the affected people in the Peruvian Amazon, many of them are not users of any type of currency, depending on bartering, which is also interfering with our perception of how malaria is affecting the quality of life of them.

In this study, we evaluated the burden of malaria in Peru and Loreto, the Amazon department with the highest malaria incidence over the period between 1990–2019. We found that while the EBPL due to malaria in Peru in 2019 represents 0·0039% of the national GDP, in Loreto it represents 0·1136% of Loreto's GDP, a percentage almost 30-fold higher in comparison (Figure 5). From this, we can say that the fact that the GBD 2019 does not consider any Peruvian department individually is masking the true impact of malaria in the higher transmission areas. Further analysis of both health and economic burdens of productivity loss due to malaria in each department with active transmission is highly recommended, especially considering that outbreaks in other departments are occurring cyclically.[30] Also, it is relevant to state that even when the absolute monetary value of the economic burden increases from 2004 to 2019 in Loreto (from 4·0 to 4·1 million dollars) (Figure 6), the percentage of the Loreto's GPD decreases to less than a half (from 0·2287% to 0·1136%), which is related to the growing population and higher productivity of Loreto over time (Figure 5). It is important to consider that malaria's not-related factors, such as economic depressions or economic-political crisis, may affect the calculations of the economic burden; however, in general terms, our calculations resulted coherent even to these confounding variables.

Current efforts against malaria in Peru are focused mainly on ensuring diagnosis and treatment, reducing the risk of transmission by implementing preventive measures directly within at-risk communities, promoting a healthier lifestyle, and optimizing the surveillance system.[20] These efforts are aligned with the global strategy based on ensuring universal access to malaria prevention, diagnosis and treatment; accelerating efforts towards elimination and attainment of malaria-free status, and transforming malaria surveillance into a core intervention.[31] Moreover, it is remarkable that the Peruvian government budget for vector-borne and zoonotic diseases has been properly executed by over 90% in most cases. Even so, Peru is the fourth country with the lowest funding per person at risk in the American region (less than one dollar),[2] while the average cost per malaria episode in Loreto is reported to be up to 161 dollars.[32] Increasing the funding per person at risk should be a priority for the government.

Concerning adopted policies in Peru, they are mainly based on distributing long-lasting insecticidal nets (LLINs) for free and recommending indoor residual spraying (IRS) by malaria control programs,[2] not addressing important considerations such as outdoor transmission or insecticide resistance which would threaten the efficacy of such efforts. A recent recommendation to be considered is to start using the RTS,S/AS01 malaria (caused by *P. falciparum*) vaccine for children at risk which has proven to substantially lower the incidence of uncomplicated malaria, severe malaria, and death from malaria when it is used in combination with chemoprevention.[33,34] However, this alternative should be adapted to the Peruvian context where most malaria cases are due to *P. vivax*. Nevertheless, it could be convenient to apply during *P. falciparum* outbreaks or endemic zones with a high prevalence of malaria caused by *P. falciparum*. Here, we have another clear example of the great importance of understanding the spatiotemporal distribution and burden of plasmodial species to implement effective control and elimination planning.[17,35] We suggest GBD consider publishing a free-access disaggregated burden due to malaria caused by each of the 5 plasmodial species to better address these situations. Additionally, the investment in research to improve the quality and delivery of mosquito vector control should be increased to develop novel control strategies.

Finally, we must comment that the COVID-19 pandemic has impacted Peru's malaria situation by apparently reducing the number of cases. It could result from the reduction in human mobility or changes in practices that would decrease malaria exposure. It may also be a sub-diagnosis effect because of postponed detection programs,[30] or reduced governmental malaria control activities.[36] In any case, we hope this study helps establish a point of reference for the health burden and economic burden of loss of productivity due to malaria before COVID-19, helping to better comprehend the extension of its impact on malaria.

Limitations

There are methodological challenges and data limitations concerning this study. First, we have no available indicators from the GBD 2019 at the subnational level. Since not all the country is affected by this disease, we estimate the cost specifically for the most affected department, Loreto, according to the proportion of cases occurring there. Second, GBD 2019 consider malaria as one disease, including in this term all the burden of the disease caused by any species of *Plasmodium sp*. This is an issue for Peru where most of the cases have been due to *P. vivax* instead of *P. falciparum* over time, but it is limited to the available data from the GBD 2019. However, since the GBD 2017, they presented the global maps of *P. vivax* clinical burden from 2000 to 2017,[17] so they are internally calculating at least partial differences between species. Third, since we are using data from the GBD 2019, its major limitation, the availability of primary data, is also a limitation of this study, being translated into the uncertainty intervals which are wider at the beginning of 1990 due to a general lack of official informative data. They are implementing several changes to data processing and modelling to improve the accuracy of their estimates, for example, they updated the DisMod-MR, the Bayesian meta-regression tool, based on simulation studies showing that less informative priors helped to improve the coverage of uncertainty intervals. Fourth, there is no data for Peruvian GDP stratified by sex and age, and there is no available information about the socio-economic sector, productivity sector, or other relevant indicators of malaria cases along time, so further economic analyses are not viable. We recommend complementing the results of our study using productivity indicators with appropriate assumptions instead of GDP because it could further support the economic analysis. Fifth, we are working with the macroeconomic indicator GDP, which is good to show the general landscape of economic situations, but it usually fails when we try to understand the costs on a case-by-case basis, especially considering that malaria occurs in places with high levels of labour informality, limited financial inclusion and other socioeconomic gaps, including that some small communities do not even use any currency system at all. It is difficult to correct these situations out of the economic system, usually fixed through assumptions based on surveys and other sources of information that we do not manage; therefore, we state this limitation and consider our results as a perfectible approximation.

Conclusion

The metrics estimated by GBD 2019 allowed for a better understanding of the burden of malaria in Peru. According to this study, the health and EBPL due to malaria have been drastically reduced from 1990 to 2019 in Peru; however, during the last decade, the estimates remained constant or even higher. This persistence of malaria in Peru requires government attention at the national, regional, and local levels for constant evaluation of prevention and control measures. While DALYs rates showed only slight differences in estimates by sex in this study, the highest-burden due to malaria was definitively observed in the youngest age group ("<1 year old"). Interestingly, the pattern of DALYs rates along age groups changed from 1990 and 1999 to 2009 and 2019, with a more equal distribution of the burden recently. From this study, we have identified that the fact that GBD 2019 does not consider any Peruvian department individually is masking the impact of malaria in moderate and high-transmission regions, such as Loreto, and further analysis of both health and EBPL due to malaria in every transmission region is recommended. Also, we hope that this study serves as a point of reference for future studies that will take into consideration the COVID-19 impact on the malaria situation which has affected case numbers as well as control activities. Finally, we state the need for national and international collaboration programs to control and eliminate malaria to reduce both its health burden and economic burden of productivity loss, acknowledging the plan "*Malaria Cero*" and its results in these few years of activity.

Contributors

JRT, SMC and RTL are the principal investigators of this study and secured the necessary funding. EES-C and JRT conceived the study with input from GMC, RTL, SMC, PC, CC-O, and BS. EES-C, JRT, CJG-R, CC-O writing of the paper. EES-C and CJG-R analyzed the data and drafted the first version of the manuscript. JRT, GMC, SMC and RTL validated the results. JRT, GMC, SMC and RTL accessed and verified the data. JRT, CG-D, CC-O, and BS critically revised the manuscript. All authors approved the final version of the manuscript. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Data sharing statement

The burden due to malaria data used in these analyses is available at http://ghdx.healthdata.org/gbd-2019, https://vizhub.healthdata.org/gbd-compare/, and from the authors upon request. The economic data used in these analyses are available at https://data.worldbank.org/indicator/NY.GDP.MKTP.KD?locations=PE, https://data.worldbank.org/indicator/NY.GDP.MKTP.KN?locations=PE, https://www.inei.gob.pe/estadisticas/indice-tematico/pbi-de-los-departamentos-segun-actividades-economicas-9110/, and from the authors upon request.

Declaration of interests

We declare no competing interests.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.lana.2022.100347.

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