Scientific Research Publishing

Advances in Infectious Diseases, 2024, 14, 74-86
https://www.scirp.org/journal/aid
ISSN Online: 2164-2656
ISSN Print: 2164-2648

Extension of Chemoprevention of Seasonal Malaria to Five Cycles and to Children from the Age of 6 to 9 Years in Africa: Analysis of Its Acceptability, Feasibility, Cost and Impact A Systematic Review

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How to cite this paper: Nadakou, N.T., Paraïso, M.N., Tapha, O., Lamine, M.M., Yobo, J.B., Alkassoum, S.I., Tossou, F., Lazoumar, H.R. and Adehossi, E.O. (2024) Extension of Chemoprevention of Seasonal Malaria to Five Cycles and to Children from the Age of 6 to 9 Years in Africa: Analysis of Its Acceptability, Feasibility, Cost and Impact A Systematic Review. *Advances in Infectious Diseases*, **14**, 74-86.
https://doi.org/10.4236/aid.2024.141007

Received: October 26, 2023
Accepted: January 23, 2024
Published: January 26, 2024

Abstract

Introduction: Seasonal Malaria Chemoprevention (SMC) aims at preventing malaria in children during the high transmission season. It has been recommended by the WHO since 2013 for children from the age of 3 - 59 months. However, despite the impact of this intervention, a peak in the prevalence and incidence of malaria is observed in children from the age of 5 - 9 years. The aim of this study is to determine from the current literature the feasibility, impact and cost-effectiveness of extending SMC to five cycles and to older children. **Methods:** A litterature search of PubMed/Medline, NCBI and Google scholar identified 1333 articles. After reading the titles and abstracts by two authors, 24 articles were selected and submitted for full reading. Random control studies on the extension of SMC, malaria, feasibility of SMC, impact of SMC and cost-effectiveness of SMC were selected. A total of 16 articles were included for the qualitative synthesis after excluding 8 studies. **Results:** Following the summary of the evidence, we conclude that the extension is feasible but will be confronted with the unavailability of older children. The intervention period coincides with field work. SMC is effective in reducing the prevalence and incidence of malaria and the parasite density in children. The financial cost of administering SMC is lower than that of treat-

ing a child suffering from malaria. **Conclusion:** After analysing the information, it was found that the majority of the African population supports the extension of the SMC to the number of cycles and the age group in order to alleviate the high mortality and morbidity rates among children due to malaria.

Keywords

SMC, Feasibility, Impact, Profitability and Africa

1. Introduction

Malaria is a parasitic disease transmitted by Anopheles mosquitoes resulting from the development of protozoan parasites [1]. It is one of the major public health and development problems faced by tropical countries. The disease has disappeared from Europe, North America and Australia [1].

Africa remains the continent where almost all cases of malaria occur worldwide [2]. According to the WHO Malaria Report 2022, 95% of cases worldwide come from Africa, compared with 2.5% in the Eastern Mediterranean, 2% in South-East Asia, 0.6% in the Western Pacific and 0.2% in the Americas [2]. Nigeria is the African country most affected by malaria in 2021, followed by the Democratic Republic of Congo, Uganda and Mozambique. These 4 countries account for almost half of all malaria cases worldwide [3]. Niger is ranked 7th as the most endemic country in Africa,

Malaria is endemic throughout Niger, which is one of the 11 countries bearing 70% of the global burden of malaria; the country has adopted the "High Burden to High Impact" (HBHI) approach. In 2020, Niger accounted for 3.3% of global malaria cases, 2.8% of global malaria deaths and 6.7% of deaths in West Africa [4].

As malaria is a global health problem, effective control is needed to reduce and eventually eradicate the disease. Malaria control measures are preventive, curative and promotional. SMC, one of the preventive measures, was the subject of this study.

Recommended in March 2012 by the WHO, SMC is a prevention method involving the intermittent administration of a full course of Sulfadoxine Pyrimethamine + Amodiaquine during the high transmission season. This intervention aims to prevent malaria infection by maintaining therapeutic blood levels during the period when the risk of transmission is highest.

In Niger, the National Malaria Control Program (PNLP) has been implementing the SMC at national level since 2016. It takes place from July to October each year, coinciding with the rainy season.

Studies on SMC in the Sahel and Niger have shown its impact on the prevalence and incidence of the disease in children from 0 - 5 years. For example, the study by Issa Salissou *et al.* carried out in Niger in 2017 showed that SMC re-

duced the incidence of uncomplicated malaria by 73% [5]. In addition to this study, the results of an ACCESS-SMC partnership consortium in several African countries support this view and conclude that SMC is a promising intervention in efforts to eliminate malaria in areas where it is rife.

Despite these encouraging results, other recent studies show that a significant peak in malaria infection is observed in older children [5]. Also, among children who received SMC, a rebound in malaria incidence was observed after four cycles of SMC [6].

In the light of these observations, those involved in the fight against malaria have decided to extend the SMC to five cycles and to children aged between 5 to 9 years old. However, this policy is still in the pilot phase in the countries concerned, and the results of this phase will serve as a basis for national implementation.

For the moment, to our knowledge, there have been no systematic reviews that have attempted to cross-reference the results of studies on the extension of SMC. It would therefore be useful to look further into the matter by cross-referencing previous results and carrying out an updated literature search.

Thus, the aim of this systematic review was to determine from the current literature the feasibility, cost and impact of extending SMC to five cycles and to older children.

2. Method

The methodology of this study was guided by the PRISMA guidelines and checklist [7]. Specific information on how to extract, code and analyse qualitative themes was taken from Butler *et al.* *[8]*. The extracted data were summarised in an analytical narrative. The choice of this method was justified by the qualitative nature of the data collected and the heterogeneity of the methods used in the literature.

2.1. Research Strategy

To carry out this work, we followed the PRISMA recommendations. We searched PubMed/Medline, Embase, Google Scholar, published and unpublished documents up to the 10 of March 2023. In order to respect the reproducible nature of any systematic review, we defined key words using the PICOTS method (Patients, Intervention, Comparison, Outcome, Time, Study).

2.1.1. Selection of Studies

After searching for articles in the various engines, we eliminated duplicates using the reference management software (Zotero).

Following the PRISMA recommendations, the authors of this work read the titles and abstracts of all the articles retained after eliminating duplicates in order to exclude articles that were not consistent with the objectives of our research.

Finally, a complete reading of the articles selected at the previous stage enabled us to select articles that have been included in the statistical analysis in this

document.

Throughout the article selection process, plenary sessions are held at each stage to pool the results.

2.1.2. Inclusion Criteria

Our work took into account published randomised studies of the extension of seasonal chemoprevention (SMC) to children from the age of 3 - 59 months from 6 - 9 years, which addressed feasibility, impact or cost-effectiveness.

With regard to interventions, only studies dealing with the extension of SMC in the fight against malaria were included.

In terms of outcome, the studies included had to deal with the feasibility, impact or cost of extending the SMC. All other studies that did not address at least one of these aspects were excluded.

Other criteria such as editorial language or articles that are not open access were used.

2.1.3. Non-Inclusion Criteria

Systematic reviews, studies not involving children and the extension of the SMC are not included in this study.

2.1.4. Data Extraction

The quality of the full papers was reviewed and the data extracted independently by the authors using forms designed for this purpose and listing the relevant variables. Any disagreements were resolved by discussing the articles and reaching a consensus.

2.1.5. Data Analysis

For the purposes of this work, the data extracted was the subject of an analytical narrative synthesis. The choice of this method is justified primarily by the more qualitative nature of the data collected in the articles.

3. Results

To arrive at the studies that served as the basis for our analysis (see **Figure 1**), 1333 studies were identified in the databases and sorted according to predefined criteria. After initial screening, 24 articles were retained, 8 of which were excluded on the basis of specificity criteria

Of the sixteen (16) articles included in this systematic review, eight (08) dealt with the perception or acceptability of extending the SMC, the number of cycles and/or the age of eligibility of the target population.

Of the eight (8) studies, three (03) studied the extension of SMC to children from the age of 5 - 14 years; three (03) studies were carried out on children from 5 - 10 years; one (01) study only studied the extension of SMC to 5 cycles and one (01) study studied the extension to 5 cycles and to children from 5 - 10 years.

Acceptability of the SMC

Out of the 1333 articles analysed, 16 met our eligibility criteria. Amongst

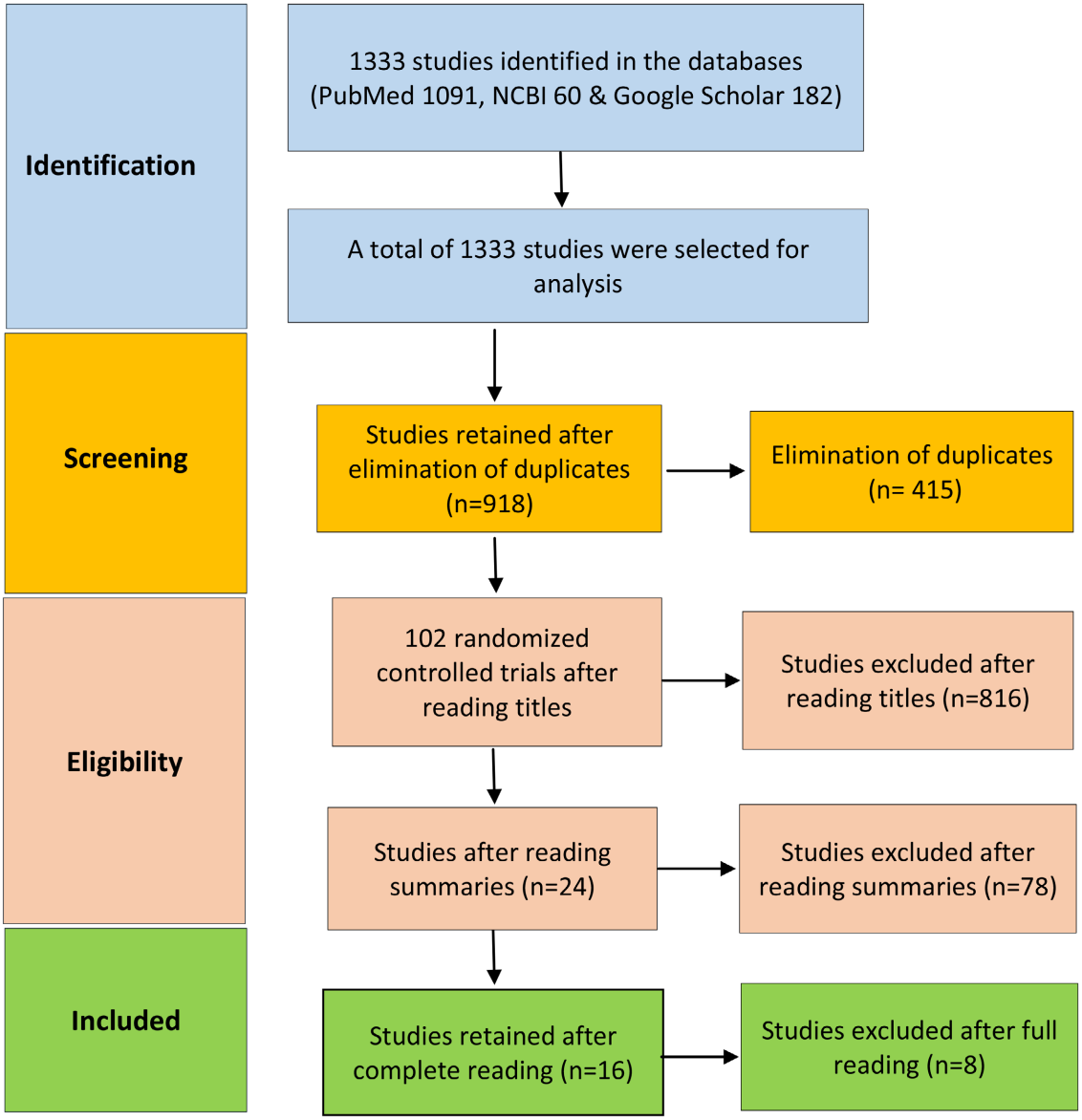

Figure 1. PRISMA flow chart illustrating the selection process for studies found during the literature search.

these, eight (08) studies were carried out among beneficiary parents to gather their perceptions of the extension of the SMC. Three (03) of these studies focused on SMC coverage during the 5th cycle and among older children. Analysis of the data from these studies showed that the extension of the SMC is accepted by the population, as described in the studies presented below.

Traore's work in Burkina Faso in 2022 showed that, during the 5th SMC cycle, the coverage rate was very high (87.67%) [9]. With regard to the extension of the age of eligibility for the SMC, El-Hadj Bâ *et al.* in Senegal showed that the SMC covered 87% of children from 5 - 10 years in 2009 compared with 96% in 2010 [10]. This increase between the two periods could lead us to conclude that the population is in favour of extending the SMC.

Similar results were found by Jean Louis A. Ndiaye *et al.* in their study con-

ducted in Senegal. They showed that parents focused more on the seriousness or otherwise of side-effects when accepting SMC for older children [11].

Work on the feasibility of extending the SMC has produced mixed results both within and outside the studies.

In the four (04) studies that examined the feasibility of SMC, data were collected from parents or guardians of children, community health workers (CHWs), distributors and political authorities.

Malaria Consortium in Chad, has shown that extending the SMC is feasible, but will be difficult with a doubling of the population, as administering the treatment will take longer and require more resources to cover the additional costs [12].

The work of El Hadj Ba *et al.* in Senegal, on the other hand, showed that the number of households to be visited does not increase proportionally with the increase in the target population. According to these authors, extending the SMC to children from 5 - 9 years old would double the number of children to be protected and increase the number of households to be visited by only 13%. In their view, extending SMC is feasible and does not significantly increase the costs and time required to administer medicines.

Studies carried out in Ghana in 2016 by Gifty D. Antwi *et al.*, and in Burkina Faso in 2022 by Adama Traore *et al.* found that the extension of SMC is feasible but will have to face obstacles if it is to succeed. According to them, the main barrier is their absence during the household SMC distribution campaign, which would coincide with agricultural activities [13].

Effects or impact of extending SMC: Before recommending the extension of SMC to five (05) cycles and to older children at the national level, pilot studies were conducted to evaluate the effects or impact of SMC on older children in different countries in the African sub-region. Of the sixteen (16) studies selected for this study, nine (09) addressed the effects or impact of extending SMC, five (05) of which were conducted in Mali, three (03) in Senegal and one (01) in Burkina Faso.

Tatiana KOUAKOU's study, carried out in Mali in 2020, looked at SMC in children aged between 3 months and 9 years, divided into two groups: an intervention group and a control group [14].

According to the authors, the incidence of malaria infection among children from 5 - 9 years in the SMC intervention and control sites was higher than in the intervention site from August to September. On the other hand, in November, the incidence of malaria infection among children from 5 - 9 years in the intervention site was higher than in the control site ($p = 0.03$). As for the prevalence of malaria infection in children from 5 - 9 years, it was higher in the control site than in the intervention site from July to October, with a statistically significant difference between the two groups ($p = 0.02$). These results show that SMC administered to children aged 5 - 9 significantly reduces the prevalence and incidence of malaria in this group of children.

The study by MAHAMADOU Fayiçal carried out in Mali in 2020 involved

children from 5 - 14 years divided into two groups to assess the effect of extending the SMC to children aged 5 - 14 [15]. A control group and an intervention group of 175 participants each. The results showed that the intervention reduced the incidence of malaria by 78%. Further analysis showed that in December (the month in which the intervention stopped), the incidence of malaria was 75% compared with 40% in the intervention group. This study proves once again that extending SMC to children from 5 - 14 years significantly reduces the incidence of malaria in this group of children.

The work of Abdourhamane CISSE in (2022) and Drissa Konate *et al.* in (2023), respectively in the Ouélessébougou and Dangassa health districts, still in Mali, focused on the extension of SMC among children from 5 - 14 years and essentially on the number of visits [16] [17].

Abdourhamane CISSE conducted a case control study. Both groups received treatment during the first four (04) visits of the year. At the 5th visit, only the intervention group received SMC [17]. The study showed a significant reduction in the prevalence of malaria infection in the intervention group compared with the control group among children aged 5 - 9 years (8% vs. 29.6%; p = 0.001) and those from 10 - 14 years (15.7% vs. 39.7%; p = 0.002). Drissa Konaté *et al., on the* other hand, I found no difference between the prevalences of malaria infection, fever and gametocyte carriage in the intervention and control groups in children from 5 - 9 years and 10 - 14 years. However, a significant reduction of 51% versus 17% in the incidence of malaria was observed in the intervention group one month after the fifth visit (RR = 0.49; 95% CI [0.26 - 0.94]). The differences between the results of these two studies could be explained by the study settings, albeit in the same country, and the socio-demographic characteristics of the age groups of children concerned. Nevertheless, these studies show that extending the SMC to five cycles will not only contribute to a significant reduction in the prevalence but also in the incidence of malaria after the 5th passage. Jean Louis A. Ndiaye *et al.*, in their study in Senegal in 2019, came to similar results, showing a significant increase in the incidence and prevalence of malaria in children from 5 to 9 years, specifically 121.6 cases per 1000 in the control group compared with 20.2 cases per 1000 in the intervention group. In this study, the average haemoglobin concentration at the end of the transmission season was higher in the intervention villages than in the control villages, thus reducing the rate of anaemia in the intervention villages as a result of the SMC. However, there were 12 deaths in the control group and 14 in the intervention group. This controversial impact result could be explained by the explanatory factors for child deaths not discussed in this section. Mortality rates among children from 5 - 9 years obtained in studies by Badara Cissé, El Hadj Ba *et al.* in Senegal point in the same direction [18]. These authors found a mortality rate of 1.3 per 1000 in the intervention zone compared with 1.2 per 1000 in the control zone. Further studies are needed to determine the factors explaining this high mortality rate in the intervention group compared with the control group.

The 2009 study by Badara Cissé *et al.* reported that the extension of SMC re-

duced malaria by 84% in children under 10 in 2009 [18]. It showed a significant difference in the prevalence of anaemia in the intervention zone and the control zone.

Jean Baptiste Y. *et al.* in their study carried out in Burkina Faso in 2022, which concurrently evaluated the extension of the age of eligibility for coverage or the use of impregnated mosquito nets [19], showed that the administration of SMC to children under 10 years of age would reduce the clinical incidence of malaria cases by 9.4% and by 14.6% in children under 15 years of age [19].

Finally, El-Hadj Bâ *et al.*, conducted in Senegal in 2018, showed that extending the SMC to older children increases the SMC coverage rate among children less than 5 years. Thus, SMC coverage in 2009, which was 87% for older children and 82% for children under 5 years old, was 96% for older children and 90% for children below 5 years in 2010.

Estimated cost of SMC extension

Before deciding to extend the SMC to five (05) monthly cycles and to all children, including older children, it is important to know the additional cost that such a decision would have required. To this end, does the current literature make it possible to respond to this essential concern, without which the extension actions could not be carried out? The review of the data from the documents selected gave the results described below.

Out of the sixteen studies included in this review, three addressed the issue of the cost of extending SMC. They were carried out in Senegal. These were the studies by El Hadj Ba *et al.*, 2010; Badara Cissé *et al.*, 2016 and Catherine Pitt *et al.*, 2017 [10] [18] [20].

Catherine Pitt *et al.*, in their study in Senegal, aimed to inform decisions about extending the recommended age range for SMC and to draw relevant conclusions for the implementation of other large-scale health campaigns and for the organisation of the health system. This study looked at the financial and economic costs of the extension. The incremental financial costs reflect the additional funding required to pay for the intervention. The incremental economic costs reflect the total value of the additional resources used to implement SMC, including those that did not result in an incremental financial cost to the health service, such as the time required by the health team. The study took place in 4 health districts, including Bambey, Mbour, Fatick and Niakhar. The targets were Community Health Workers and technical and financial partners. They also found that the peripheral health post had the highest average costs per child per month. The study identified factors associated with variations in costs between health posts. These authors studied variations in costs from one zone to another, from one district to another, and found that there was a considerable variation between health posts [20]. This variation ranged from US$0.38 to US$2.74. Their work showed that the smallest health posts incurred the highest average costs per child/month [21]. The study also showed that costs vary. To administer SMC to 180,000 children, a financial cost of US$234,549 was estimated, compared with an economic cost of US$278,922. Based on this information, these authors

estimated the average monthly cost of administering SMC per child to be US$0.5 per child/month, compared with an economic cost of US$0.59 per child/month [22].

In their study carried out in Senegal, Badara Cissé *et al.* aimed to determine the effectiveness of SMC in Senegalese children under the age of ten. This study focused on the average cost and reasonable cost of extending SMC. The average cost is the unit cost of a SMC treatment. The reasonable cost is the price of malaria treatment. The study was carried out in 3 health districts, including Mbour, Bambey and Fatick in Senegal, which have a total population of around 600,000 and are served by 54 health posts selected at random. The targets were CHWs, local authorities, district health staff and technical and financial partners. These authors found that the inclusion of older children increases the cost of SMC programs, but in their study, which used door-to-door delivery, did not significantly increase the overall time required for delivery, as older children could easily be treated during health worker visits [23].

In their study in Senegal, El Hadj Ba *et al.* aimed to assess the feasibility and cost of implementing SMC in children aged between 3 months and 10 years. The study took place in three health districts: Mbour, Fatick and Bambey. The study involved health facilities involved in smc in order to estimate the marginal costs of its implementation. The marginal cost is the cost of producing an additional unit of SMC extension. The targets were CHWs and technical and financial partners. In their view, extending SMC to older children is feasible and would not significantly increase the costs and time required to administer the drugs. They showed that to administer SMC to 180,000 children, a financial cost of US$234,549 was envisaged, compared with an economic cost of US$278,922. Initially, they found that extending SMC to children from 5 - 9 years would double the number of children to be protected. Based on this information, the total financial cost of administering the SMC was US$0.5 per child per month, compared with a total economic cost of US$0.59 per child per month. As a result, the extension of SMC does not significantly increase the costs and time required to administer medicines.

These various studies have shown that extending the SMC would not significantly increase the costs and time required to administer medicines. The financial cost of administering SMC is $0.5 per child per month, compared with an economic cost of $0.59 per child per month, varying from $0.38 to $2.74 depending on the size of the health post.

4. Discussion

In the literature, several scientific studies have examined the acceptability, impact and cost of extending SMC according to the number of cycles or age, usually separately. The results of these studies are as likely to converge as they are to diverge, and they use different types of study, population selection criteria, and data analysis methods, which may or may not be similar. These disparities ob-

served in the results of certain studies justify the usefulness of this systematic review with a view to taking a broader critical look at this extension of SMC and more specifically the extension of SMC to five cycles and to older children.

The aim of this study was to review scientific studies on the feasibility, impact and cost-effectiveness of extending SMC to five cycles and to children aged 6 to 9 in Africa. Using the methodology described above, several trends were identified.

Firstly, with regard to the perception (acceptability) of extending the SMC, it emerged from the eight (08) articles studying the perception of parents and key informants that extending the SMC in terms of age or number of cycles is generally accepted, especially if the side effects are less serious.

Secondly, on the feasibility of extending the SMC, from the four (04) studies dealing with the feasibility of extending the SMC, it emerged that the extension is feasible but will be confronted with the unavailability of older children given the coincidence of the distribution period with the period of field work.

Thirdly, on the impact or effect of extending the SMC, it emerged from the nine (09) studies evaluating the impact of extending the SMC that the extension considerably and significantly reduces the prevalence and incidence of malaria, as well as anaemia in older children.

However, a contradictory result has been obtained in some studies. This concerns the number of deaths obtained in each group (intervention and control). In two (02) studies (Jean Louis A. Ndiaye *et al.*, 2019 & Badara Cissé *et al.*, 2016), mortality rates among children aged 5 - 9 years in the intervention group were higher than mortality rates in the control groups that did not receive SMC. The data do not allow us to study the factors explaining this difference in death rates in the two groups.

On the other hand, on the cost of extending the SMC: The three (03) studies on the cost of extending the SMC show that the financial cost of administering the SMC is US$0.5 per child/month compared with an economic cost of US$0.59 per child/month (18.7% higher than the financial cost), with a variation of US$0.38 to US$2.74 depending on the size of the health posts. Extending the SMC doubles the number of children to be protected but only increases the number of households to be visited. Extending the SMC doubles the number of children to be protected but increases the number of households to be visited by only 13%.

Limitations of the study

The strength of this systematic review is the inclusion of sixteen (16) complete research studies on a recent subject studied in the Sahel region. It was carried out using several search engines to ensure that the studies selected on the subject were exhaustive. However, one limitation is the heterogeneity of the methods used in these studies.

5. Conclusions

Extending SMC to five (05) monthly cycles and to older children is acceptable,

feasible, cost-effective and has definite positive effects. It is acceptable to the community, but the side effects will have to be better controlled. It is feasible and would not increase the burden on benefits, and is therefore cost-effective. It would have definite positive effects on the consequences of malaria.

The results of this systematic review show that further studies are needed to better define the contours of this extension in order to better inform decision-making.

Authors' Contributions

Mr NADAKOU N'Kpingou Théodore is the principal author and carried out the literature search, critical appraisal and thematic analysis of the documents in consultation with Dr TAPHA Ounoussa; Dr Jean Blaise YOBO and Dr MOUSTAPHA MAHAMANE Lamine participated in the planning of the study, the literature search and the drafting of the text, while Dr PARAISSO Moussiliou Noel; Mahaman Lamine; Ibrahim Alkassoum; Fidel TOSSOU; Hamidou Ramatoulaye; Jacques SAIZOUNOU; ADEHOSSI Éric provided advice on the qualitative literature review and made substantial changes to the text itself. All authors read and approved the final manuscript.

Availability of Data and Equipment

All the articles included in this study are available in the "References" section. The complete search strategy, as well as the original thematic analysis spreadsheet, can be obtained on request from the corresponding author.

Acknowledgements

Jacques SAIZOUNOU, Bouraima DJIBO and FRI Mercy TAYON, I thank you for the contribution to the translation of my document in English

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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