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**Prevention of Pediatric Mortality Associated with Malaria:
An Exhaustive Literature Review**

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Prevention of Pediatric Mortality Associated with Malaria: An Exhaustive Literature Review

Elimination and eradication of malaria, a deadly yet preventable disease most often caused by the bite of female *Anopheles* mosquitos that harbor *Plasmodium* parasites, have been goals of the World Health Organization (WHO) since 1955 (Centers for Disease Control and Prevention [CDC], 2017). While complete eradication is unlikely in the coming years, significant progress has been made to reduce morbidity and mortality associated with malaria, including 99 countries that have since been designated as malaria-free. Between 2000 and 2015, the WHO showed a global reduction in the rates of incidence and mortality by 37% and 60% respectively. Africa, the country with the largest disease burden, experienced 943 million less cases in the same timeframe, and it is estimated that 70% of this can be attributed to the implementation of prevention and treatment interventions (Korenromp et al., 2017, p. 30; WHO, 2019).

In spite of the these interventions and the resulting progress that was made within 15 years, malaria remains a significant public health threat as it “is still one of the most infectious diseases that cause far more deaths than all patristic diseases together,” and these deaths are disproportionately seen among pediatric African patients (Talapko et al., 2019, p. 8). In 2017, there were 219 million cases recorded worldwide, an increase by 2 million from 2016, and more than 90% of these occurred in Sub-Saharan Africa. Of the 219 million total cases, there were approximately 435,000 resulting deaths with more than 60% of these being children below the age of 5-years old. This translates to a child under the age of 5 dying every two minutes from a disease that is both preventable and treatable (United Nations Children’s Fund [UNICEF], 2019). Many studies fail to address this plateau and regression in the fight against malaria, specifically in countries such as Nigeria and the Democratic Republic of Congo that have seen a marked

increase in cases over the last 5 years. The purpose of this literature review is to assess what factors have contributed to this stagnation, and what interventions can best mitigate the effects of malaria in vulnerable pediatric African populations.

Methods

Information Source and Search Strategy

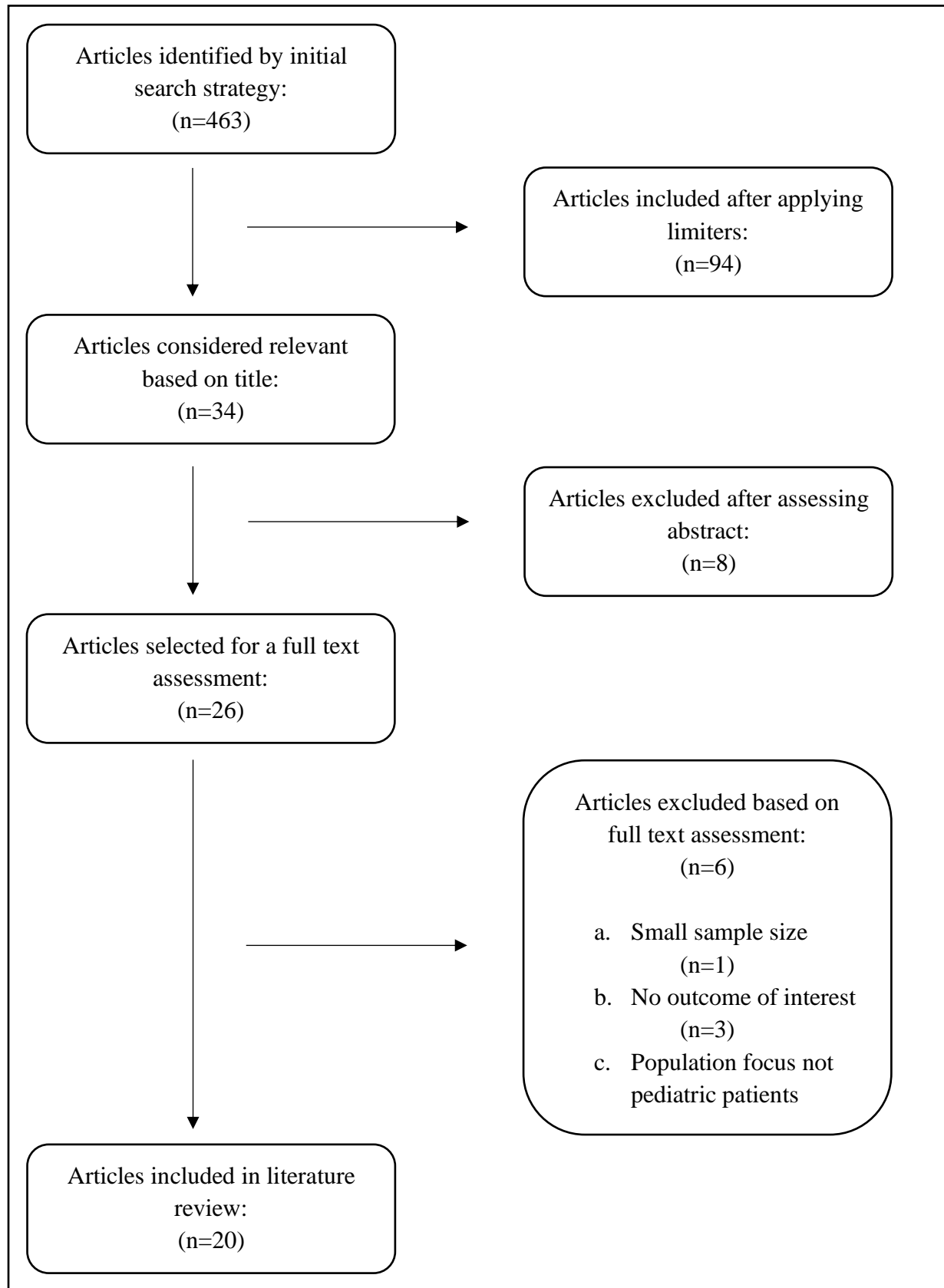
A Boolean search was conducted in August 2020 using the CINAHL Complete database. The single search consisted of multiple phrases including: (a) pediatric OR child OR children OR infant; (b) malaria; (c) prevention OR intervention OR treatment OR program; and (d) Africa OR African countries. This search yielded 565 results, but many were focused on anemia or sickle cell anemia due to its high prevalence in Africa, so an additional Boolean phrase (e) NOT sickle cell anemia OR anemia OR anaemia was added which resulted in a total of 463 articles.

Eligibility Criteria

To narrow down the search further, it was limited by inclusion criteria of research articles that were peer reviewed, had the full text and abstract available, written in the English language, and published in academic journals between 2015-2020. This resulted in a total of 94 articles, 60 of which were excluded based on their title focusing on information or populations irrelevant to this review such as reproductive health, nutrition programs, community health workers, reporting systems, pneumonia, and HIV or AIDS. Of these 34 articles, an additional 8 were excluded after evaluating their abstract. A full text assessment excluded 6 more articles that had a small sample size, lacked an outcome of interest, or focused on a population other than pediatric patients. This resulted in a final outcome of 20 articles being selected for the literature review as illustrated in Figure 1.

FIGURE 1

Inclusion and Exclusion Criteria Diagram



Results

Of the 20 articles selected by the search strategy, common themes regarding both protective and risk factors associated with pediatric mortality secondary to malaria were identified including prevention interventions, socioeconomic factors, improved diagnostics and treatment, and the necessity of adequate funding. Four primary studies—Akoakwah et al. (2018), Jakubowski et al. (2017), Bikundi & Coppieteres (2017), and Ndong et al. (2019)—highlighted these and were evaluated at greater depth. The characteristics of these studies are summarized in Table 1.

Prevention Interventions

The multifaceted interventions that have been implemented to combat malaria are primarily focused on vector control to reduce exposure to the *Plasmodium* parasite and prevent infection in the first place. One of the cheapest and most common methods is the use of a bed net as a physical barrier while sleeping, especially for vulnerable populations such as children and pregnant women. Insecticide-treated bed nets (ITNs) offer additional protection serving as a physical barrier along with insecticidal effects; however, retreatment is necessary over time as the insecticide wears off. Even if most households have received ITNs, studies have shown the added barriers of increased cost and lack of understanding regarding retreatment can negatively impact proper adherence, thereby decreasing the effectiveness of the ITN. This has been partially mitigated through the development of long-lasting insecticide-treated nets (LLINs) that have the insecticide interwoven in its fibers. Retreatment is not necessary, and they remain effective for 3-5 years (CDC, 2019).

Insecticidal vector control in high burden regions has also depended on the use of indoor residual spraying (IRS) which involves long-lasting insecticides being sprayed on the internal

walls and ceilings of buildings. IRS is known to be effective as most vectors that carry malaria are endophilic meaning when they enter a dwelling in search of a source of nourishment, they consume blood and proceed to rest on walls or other surfaces nearby for a period of time. If this surface has been treated with IRS, a fatal dose of insecticides will be absorbed by the vector. This particularly helps minimize malaria transmission within a neighborhood or community if a majority of the buildings and houses have been treated, with a minimum treatment goal of 80% and ideal treatment goal of 100% (WHO, 2015, pp. 4-5 & 41).

Many studies have suggested that IRS may offer more protection than ITNs or LLINs as seen with Afoakwah et al (2018). This cross-sectional study assessed malaria infection and accompanying prevention interventions in 2,449 children under the age of 5-years old in Ghana, Africa using the Ghana Demographic and Health Surveys of 2014. Of the children included in the study, approximately 40% had tested positive for malaria when a rapid diagnostic test (RDT) was performed. The prevalence of malaria among the study participants that were protected with IRS was only 36%, while the prevalence of malaria among the participants that solely relied on an ITN was increased at 45% (pp 4-6). This finding was supported by Katureebe et al. (2016) as their study showed LLINs had a slight but varying effect on the human biting rate of vectors, malaria test positivity rate, and incidence of malaria in Uganda while IRS resulted in a significant decline of all three indicators (p. 2). Selvaraj et al. (2018) also found that IRS can greatly reduce the prevalence of malaria as spraying insecticides at the end of August during the peak of the wet season can result in as much as an 80% reduction of cases the following year (p. 8).

Socioeconomic Factors

In addition to the benefits of IRS, Afoakwa et al (2018) found evidence that maternal education status can impact the incidence of malaria in children. The prevalence in children under the age of 5-years old was 26% if the mother had a secondary education or higher but was 54% in children whose mothers lacked any formal education (p. 6). Socioeconomic factors associated with malaria infection were also assessed in a cross-sectional study by Bikundi & Coppeters (2017). This study involved 61,292 children under the age of 5-years old in 16 sub-Saharan African countries using data collected from the Demographic and Health Surveys and Malaria Indicator Surveys between 2010 and 2015. Of the 29.1% of subjects that had malaria as identified using RDTs, there was a significant association with the maternal education level. More than 91% of these children had a mother that was illiterate or only had a primary level of education. Wealth status was also shown to impact the risk a child faces as 29% of those that tested positive belonged to the poorest households, while only 6% belonged to the richest (pp. 398-399).

Numerous other studies have had similar results. Bisi-Onyemaechi et al. (2017) conducted a study in Nigeria and while 85% of the subjects owned an ITN, only 53% of them reported using it. Educational status was the most significant factor as those with a secondary or tertiary level of education accounted for 89% of those that used their ITN (p. 1038). In rural areas of Ethiopia, Muchie et al. (2017) found that a household was 60% more likely to own a net if they had a secondary education or higher (pp. 3-5). Fokam et al. (2017) found that 63% of the 384 households assessed in Cameroon owned a bed net while only 69% of them used it (p. 8). As with the previous studies, those with a lower educational level had lower odds of utilizing the net. Tusting et al. (2017) assessed 284,532 children from 21 countries in sub-Saharan Africa and determined wealth and housing can impact the risk of malaria infection. Regardless of ITN

ownership or IRS use, living in modern housing had a 9-14% reduction in the odds of infection (p. 6). Similarly, another study found that factors not commonly associated with modern housing contributed to higher rates of infection. Those diagnosed with malaria had 75% lower odds of having waste collection devices in the home and were 4 times more likely to have slept outdoors (Tesfahunegn et al., 2017, pp. 3-4).

Improved Diagnostics and Treatment

Because prevention interventions are not infallible and proper adherence can be impacted by numerous factors, another method to prevent pediatric mortality associated with malaria is to improve early diagnostics and treatment of the disease. The campaigns associated with this are primarily referred to as mass testing, treatment, and tracking (MTTT) and mass drug administration (MDA) (Hayes et al., 2017, p. 2). Ndong et al. (2019) completed a longitudinal study in Ghana involving 5000 subjects, 597 of which were under the age of 5-years old. The study utilized MTTT to diagnose and treat asymptomatic carriers of malaria as they can help perpetuate outbreaks within a community. The researchers performed RDTs every 4 months between 2017 and 2018 with coverage ranging between 78-99%. 96 participants were determined to have symptomatic malaria infection, but MTTT increased access to artemisinin-based combination therapy (ACT) and decreased symptomatic cases by 4.2% during the year it was implemented (pp. 4-6). Asymptomatic parasitemia was decreased by 24% (p. 1).

Other forms of treatment have centered on intermittent preventive treatment (IPT) with sulfadoxine-pyrimethamine during pregnancy to help prevent infant mortality associated with maternal malaria infections due to the increased vulnerability in these populations. Adeoye & Fagbamigbe (2019) found that women that received at least two doses of the medication during pregnancy had 28% lower odds of infant mortality (p. 142). While more recently implemented,

the WHO has also contributed to the development of a vaccine that had been tested in clinical trials through 2014 with a goal of administering the pilot dose to children in Ghana, Kenya, and Malawi in 2018 (2017).

Necessity of Adequate Funding

While the aforementioned prevention techniques and treatment options may be effective, they all require sufficient funding for implementation. Bjorkman et al. (2019) showed that all-cause mortality among children under the age of 5-years old decreased by 72% after implementing ACT and vector control programs in the 2000s, and this coincides with the introduction of substantial international funding programs (p. 2). Jakubowski et al. (2017) assessed the impact the United States President's Malaria Initiative (PMI) had on 2,112,951 children in 32 sub-Saharan African countries in a longitudinal study from 1995 to 2014. PMI has been a leading source of funding in the fight against malaria since 2005, and this study found there was an association between the implementation of PMI and a 16% reduction in the risk of child mortality in countries included in the initiative. Moreover, "each additional dollar disbursed through PMI was associated with a reduction in the annual risk of under-5 mortality" (p. 8). There was also an 8.3% increase in ITN and 6.6% increase in IRS coverage (p. 10).

Funding in recent years has decreased, however, and there are estimates that tens of thousands may die as a result. While the WHO has a current annual goal of US \$5.6 billion for adequate funding, 2019 totals only reached \$3 million (WHO, 2020). Boakye et al. (2018) addressed this shift in funding. Although community case management programs have helped in the delivery of interventions and treatment, their sustainability is decreasing due to plateauing funds. Providers have observed decreased access to necessary commodities such as bed nets, medications, and RDTs (p. 4-6).

Table 1*Data Extraction and Characteristics of Primary Studies*

Study	Study Design	Subjects	Findings
Afoakwah, Deng, & Onur (2018)	Cross-sectional survey	2,449 children aged 6-59 months in Ghana, Africa	Approximately 40% of the subjects tested positive for malaria via a RDT. The prevalence of malaria was 36% for those using IRS, and 45% for those using ITNs. Sole ITN use was only associated with a reduced incidence of malaria if the mother had a secondary education or higher.
Bikundi & Coppieters (2017)	Cross-sectional survey	61,292 children under 5 years of age in 16 countries in sub-Saharan Africa	29.1% of the subjects tested positive for malaria. Approximately 63% of these subjects had mothers that were illiterate, and 28.5% had a mother with only a primary level of education. 55% belonged to economic levels designated as poor or the poorest of the study.
Ndong et al. (2019)	Longitudinal study	5,000 individuals including 597 children under 5 years of age in Ghana, Africa	RDTs were performed every 4 months for a year with each subject receiving a median of 3 tests. Coverage varied between 77.8 to 98.8% at its peak.

			Asymptomatic parasitemia decreased by 24% after the implementation of MTTT.
Jakubowski, Stears, Kruk, Angeles, & Thirumurthy (2017)	Longitudinal study	2,112,951 children in 32 countries in sub-Saharan Africa	The PMI introduced significant funding for sub-Saharan African countries. 9.4% of the subjects died before the age of 5; however, there was a 16% reduction in risk of child mortality, and the coverage of ITNs and IRS increased by 8.3% and 6.6% respectively.

Discussion

All of the studies referenced in this literature review highlight how prevalent malaria and subsequent pediatric mortality remain in sub-Saharan Africa despite the implementation of numerous programs to combat this phenomenon. Approximately 198,000 children in the Jakubowski et al. (2017) study died before the age of 5. 40% of children under the age of 5 were found to have malaria in the study conducted by Afoakwah et al. (2018), and 29% were diagnosed with malaria in Bikundi & Coppitiers’ study (2017). Out of all the prevention techniques utilized to reduce these rates including intermittent prophylactic treatment, bed nets, and insecticide spraying, IRS was the most effective and had the unique ability to protect the majority of a community rather than just individuals. Consequently, and unlike the other interventions, the efficacy of IRS was not negatively impacted by socioeconomic factors such as wealth, modern housing, or education status (Afoakwah et al., 2018, p. 6). Still, IRS and other malaria control tools require significant funding to protect African communities, and sources of

funding have been decreasing since 2015. The funding provided in 2019 was \$2.6 billion less than what the WHO estimated was needed to help decrease the rise in cases that has been seen in recent years. Sufficient data has not yet been collected, but experts expect this gap to worsen in 2020 and coming years due to the impact of COVID-19 (WHO, 2020).

Implications for Practice

As funding is so limited and will likely become more scarce, officials should dedicate most resources to increasing coverage of IRS. In addition to studies suggesting it is more effective and protects a greater number of people, considerations of socioeconomic status are not as pertinent. Studies found that many possess ITNs and LLINs but neglect to use them. Therefore, these individual interventions including IPT should be designated to those that are especially vulnerable such as young children and pregnant women. Providers should emphasize education during distribution of these products to help increase understanding and adherence—especially if the recipient lacks an education at or above the secondary level. Finally, intermittent MTTT and MDA should be considered as more than 50% of children in the Ndong et al. (2019) study tested positive for malaria while being asymptomatic. Identifying, treating, and reducing the number of asymptomatic carriers can decrease the disease burden in high endemic areas.

Strengths and Limitations

All 4 of the primary studies included in this review had large sample sizes with a total of 2,177,289 children from 32 different sub-Saharan African countries being assessed. This helps ensure the data and interpretations are more precise with narrow confidence intervals leading to firm, significant conclusions. Moreover, all of the outcomes were supported by other studies with similar findings among different patient populations in Africa. One limitation of this literature review, however, is the varying time frames between the studies. The duration of the study

performed by Ndong et al. was only 12 months long. This is drastically shorter than that of Jakubowski et al. which assessed data over a nearly 20-year period. Obtaining more extensive, long-term data could alter the outcomes observed in the former study. An additional limitation involves the nature of literature reviews relying on published research that analyzes current, accurate data. The purpose of this review is to assess changes that have occurred since 2015, but it is possible thorough data with a broad perspective on the issue may not be available yet. Furthermore, only searching the CINAHL complete database could have neglected the selection of studies that may be accessible in other databases.

Implications for Future Research

While LLINs and IRS are effective current methods to prevent and reduce the prevalence of malaria, *Anopheles* mosquitos have started becoming resistant to the insecticides used including pyrethroids, organochlorines, organophosphates, and carbamates which could render these interventions obsolete (Bird, 2017, A51). In addition to resistance among vectors, these interventions include recurring costs associated with replacement nets and retreatments when the insecticidal sprays wear off. A cost effective and longer-term solution could be found with additional research and implementation of the RTS,S vaccine as data and models following Phase III of trials have demonstrated between 65-80% efficacy in African populations (Penny et al., 2015, p. 13).

Similarly, some species of the *Plasmodium* parasite have become immune to antimalarial medications such as sulfadoxine-pyrimethamine and chloroquine which can negatively impact the efficacy of MTTT and MDA. As seen in the study conducted by Hayes et al. (2017), inaccurate dosing of antimalarial medications can contribute to this drug resistance and

negatively impact the outcomes of patients. Additional research is needed to determine proper age-based dosing that is effective in treating malaria to prevent additional drug resistance.

Conclusion

While malaria is both preventable and treatable, a significant number of people in Africa, particularly children below the age of 5-years old, are still dying from this disease on a daily basis. Progress that was made between 2000 and 2015 has stalled primarily due to financial constraints associated with insufficient funding, but other factors include inadequate education, drug resistance, insecticide resistance, and lack of adherence. While COVID-19 will likely further strain funding in coming years, it is imperative to implement interventions that are the most effective with minimal barriers to proper adherence, namely IRS. When implementing other programs such as ITN and LLIN distribution, emphasizing and including education can positively impact their efficacy and maximize protection for vulnerable populations.

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