RTS.S/AS01 Vaccine in Ghana as a Means of Reducing Malaria Burden

Hena Arif

Health and Pharmaceutical System of Ghana

Ghana is a low- and middle-income country situated in West Africa on the coast of the Gulf of Guinea and has a population of about 32,256, 713 people (Worldometer, 2022). Approximately 56.7% of the population is urban and the median age in Ghana is 21.5 years (Worldometer, 2022).

In terms of the demographics in Ghana, as of 2020, the average life expectancy in Ghana is 64.94 years at birth in both sexes, 66.1 years in females, and 63.8 years in males (Worldometer, 2022). The infant mortality rate is 30.8 infant deaths per 1,000 live births and deaths under age 5 is 44.7 per 1,000 live births (Worldometer, 2022). The total fertility rate (TFR) in Ghana is 3.9 live births per woman. Generally, a value of 2.1 may cause the population to decline and Ghana is much above that threshold (Worldometer, 2022).

The major diseases causing the most disability adjusted life years (DALYs) in all age groups and both sexes are shown in Appendix 1. Neonatal disorders cause the greatest amount of DALYs which is 12.4% of total DALYs in all age groups, decreased by 2.07% from the year before (IHME, 2022). This is followed by malaria, responsible for 11.68% of total DALYs which has also decreased by 1.63% from the year prior (IHME, 2022). Other prominent diseases are lower respiratory infections causing 5.5% of total DALYs and HIV causing 6.24% of total DALYs, both of which are communicable diseases (IHME, 2022). One thing to note is while many of the diseases have decreased in their annual percent of change in DALYs, HIV has actually increased by 2.51% in causing DALYs (IHME, 2022). For children under the age of 5, neonatal disorders are the most prominent cause of total DALYs and are responsible for 35.24% of total DALYs (IHME, 2022). Malaria is the second highest cause of DALYs in children under

5 and is responsible for 21.85% of total DALYs (IHME, 2022). This has decreased by 1.27% from the year before (IHME, 2022).

The top disease states causing the most deaths in all age groups and both sexes in Ghana are somewhat similar to the disease states causing the most DALYs in all ages. The disease states causing the most deaths in Ghana can be seen in Appendix 2. Malaria trumps the list in causing the most deaths in all age groups in Ghana. It causes 10.38% of total deaths in Ghana which has decreased by 1.01% from the previous year (IHME, 2022). The second highest cause of total deaths in Ghana is stroke, causing 8.27% of total deaths (IHME, 2022). This is followed by lower respiratory infections, neonatal disorders, ischemic heart diseases, HIV, all causing around 7-8% of total deaths in all ages and both sexes (IHME, 2022). With respect to children under 5, the major cause of total deaths is neonatal disorders, as expected, which is responsible for 36.07% of total deaths (IHME, 2022). The second highest cause of total deaths in children under 5 is malaria which comprises 22.83% of total deaths (IHME, 2022). This makes sense as children and pregnant women are the most vulnerable groups to get malaria.

A comparison of the top causes of death in all ages in Ghana from 1990 to 2019 is shown in Appendix 3. The top 3 causes of death in 1990 have either decreased in rank or stayed the same in 2020 (IHME, 2022). Cardiovascular diseases and NTDs & Malaria have increased in rank to make their place in the top 3 causes of death in 2019, with cardiovascular diseases being at the top position and NTDs & Malaria being at the third position.

The health care structure in Ghana is comprised of a three-tier deliver system (Dresser, 2022). There is a primary care system that includes the local health center. Their job is to mainly provide curative and preventative medicines as well as reproductive health centers (Dresser, 2022). Secondary care is provided in district hospitals (Dresser, 2022). These districts are

subdivided into subdistricts and then also divided into Community Health Planning and Services zones which provide decentralized health service from the district level (Dresser, 2022). Tertiary care is specialized care provided in specialist and teaching hospitals (Dresser, 2022).

Health care in Ghana can be categorized as variable (ITA, 2022). Ghana spends an average of 6% of its GDP on health infrastructure (ITA, 2022). Most of the hospitals, clinics, and pharmacies are found in the urban centers whereas rural areas have no developed healthcare facilities. These patients often depend on traditional African medicine. Other patients travel great distances to access medical care. Ghana's medical system mainly centers around its two largest cities, Accra and Kumasi (Drislane, 2022). This is a disadvantage to smaller towns where most of the population resides. It requires physicians and medical facilities there, but most physicians do not want to be in rural areas.

Ghana has limited production of pharmaceuticals. They have minimal manufacturing of medical supplies and devices as well. They depend on imports for around 85% of its total health care consumption (Drislane, 2022). Ghana used to have a "pay as you go" system which meant health costs were paid upfront before treatment and covered solely by patients (Drislane, 2022). Now the National Health Insurance scheme has coverage for a limited number of diseases. This mainly includes the most prevalent diseases, malaria being one of them (Drislane, 2022).

Ghana has definitely made some improvements in its healthcare system (Drislane & Akpalu & Wegdam, 2022). It has become a leader in West Africa. The majority of its health burden is due to infections and its main problem is extending medical care and facilities to rural areas. It has begun to focus a bit more on rural areas, but there needs to be more progress made especially for common diseases such as infections.

Management of Malaria in Ghana

As noted, malaria is a non-communicable disease that carries a significant health burden in Ghana, causing significant DALYs and deaths in the population. Malaria is caused by *Plasmodium* parasites transmitted to humans via infected mosquitoes. There are five species of the *Plasmodium* parasites of which *Plasmodium falciparum* is the most common and most deadly in the Ghana region. Appendix 4 outlines the prevalence of malaria in children which are a major group of malaria victims. It can be seen that the majority of these causes in children are from rural areas and ages 2-5 are most affected as per the 2019 Ghana Malaria Indicator Survey (GMIS). Other key findings include the effect of socioeconomic conditions on incidences of Malaria. This is outlined in Appendix 5 as per the 2019 GMIS. The data shows 93% of households have an improved source of drinking water which is important in preventing malaria (GSS, 2020). What is less known is that breaking this up further, 99% of urban households have improved drinking water compared to 87% of rural households and about 46% of those households that do have improved drinking water travel about 30 minutes roundtrip to obtain that water (GSS, 2020).

The increase in safe drinking water has definitely helped combat malaria. Another milestone reached by Ghana is that malaria treatment is now covered under the newly created National Health Insurance Scheme (NHIS). About 73% of women aged 15-49 were aware about this coverage with 71% of urban women population knowing and 75% of the rural population being aware (GSS, 2020). This means rural women were more aware of the coverage which is a good indicator since rural areas tend to be more affected.

One key malaria control intervention in Ghana is using insecticide treated nets (ITNs). These ITNs protect against mosquito bites, reducing transmission of possible malaria. ITNs help

to repel the mosquitos away and kill them. This helps to decrease the vector population and thus reduces malaria at the individual level and collectively, at the population level if high enough coverage is achieved. About 74% of households in Ghana have at least one ITN and 52% of households have one ITN for every two people (GSS, 2020). Approximately 67% of these ITNS were acquired due to mass distribution campaigns which is a majority of the ITNs (GSS, 2020). Appendix 6 shows the trends in ownership of ITNs. This emphasizes how crucial these campaigns and governmental help is in combatting malaria. One interesting thing to note is that the lowest-income households have the most ITNs as shown in Appendix 6. ITNs are continuously distributed through antenatal clinics, child welfare clinics, and child welfare visits and continue to help protect against malaria but they don't have the best efficacy and not everyone is using them.

Another common methodology to reduce malaria infection in Ghana is by using indoor residual spraying (IRS). This is significantly much lower than ITNs with an average of 6% using them (GSS, 2020). This is because it is done by a governmental agency or an NGO which are not always continuously doing it. This is different from the distribution of ITNs which households continue to use themselves. A more effective way could be to distribute the sprays, but they will likely not last for long and are not a cost-effective strategy.

A priority area in malaria control is malaria in pregnancy. This poses risks for the mother and child. The WHO has recommended many interventions to reduce the negative effects of malaria in this population. This includes prompt diagnosis and treatment, use of ITNs, and antimalarial medicine (GSS, 2020). Ghana has adopted the use of intermittent preventative treatment in pregnancy using sulfadoxine and pyrimethamine (IPTp-SP) since 2003 (GSS, 2020). This approach is used in antenatal visits. IPTs-SP was given to women from the 16th week

onwards at monthly intervals as directly observed. In 2013 and 2017 to three or more doses of IPTp-SP until delivery (GSS, 2020). This intervention has successfully integrated in Ghana with 91% of women receiving one or more doses of IPTp-SP as of 2019 (GSS, 2020).

Even with these interventions in place, malaria continues to cause a significant health care burden. Better malaria control comes with better knowledge and an informed public. The increase in ITNs is a great step in this direction. In a recent study as per 2019 GMIS, women ages 15-49 were asked about malaria prevention techniques and 79% stated using ITNs, 54% said keeping there are clean, 24% said filling in stagnant waters, and 20% mentioned spraying house with insecticide. This shows the knowledge in Ghana is increasing and ITNs are the most popular prevention strategy. One thing to note is that all this data is provided via the recent 2019 Ghana Malaria Indicator Survey and as with all surveys, there could be possible survey bias. The most important thing to acknowledge is that malaria still continues to be a significant health burden despite the improvements made as specified earlier.

Ghana was also invited to trial out the world's first malaria vaccine, RTS,S/AS01 along with Kenya and Malawi with the support of the WHO and other global partner (Dimala, 2022). This intervention was at first welcomed by the country, but then misinformation quickly spread, and uptake decreased (Dresser, 2022). The WHO has a goal to decrease incidence and mortality due to malaria by 90% (Dresser, 2022). They hope to achieve this by 2030 (Dresser, 2022). One other goal is also to eliminate malaria in 35 endemic countries (Dresser, 2022). Some interventions have already been well integrated in Ghana and other countries in hopes of meeting that goal. Other possible efforts include mass drug administration and genetically modified mosquitoes. They are also working hard to implement malaria vaccines and maximize the

benefits out of the RTS,S/AS01, which is the most advanced malaria vaccine till this date (CDC, 2021).

The use of RTS,S/AS01 Vaccine in Ghana

The burden of malaria is quite significant in sub-Saharan Africa and to combat this disease, malaria vaccines have been in development since the 1960s. Just recently, on October 6th, 2021, WHO recommended the use of the novel RTS,S/AS01 malaria vaccine created by GSK in children living in sub-Saharan Africa with moderate to high *Plasmodium falciparum* malaria transmission. This vaccine was created years ago, in the GSK labs with help from PATH and support from the Bill and Melinda Gates foundation (PATH, 2022). After the promising results of the phase III trials of the RTS,S/AS01 vaccine, large pilot studies were run and are scheduled to continue on till 2023, but the preliminary results were promising which is why the WHO is in favour of the vaccine (CDC, 2021). The RTS,S vaccine decreased severe cases of malaria by approximately one third in 5-17 month old children over four years in children who received the three dose vaccination series plus a booster dose (CDC, 2021). It is generally less effective in older children. Another study concluded that the vaccine successfully prevented about 36% of malaria cases in children who received 4 doses of the vaccine in a trial (Hogan, 2022). It also shows about a 30% reduction in deadly malaria even when used in areas that have high uptake of ITNs and good access to diagnosis and treatment (CDC, 2021). A table of the phase 3 efficacy results can be found in Appendix 7. These studies show that the RTS, S vaccine has promising effects and can be used to help prevent malaria in children who are a highly susceptible group to malaria. A routine administration of four doses of the RTS, S/AS01 malaria vaccine with the first dose at 5 months of age and the third dose done by 9 months as well as a booster dose at 15-18

months should be employed in Ghana, being a sub-Saharan African country endemic to malaria (Laurens, 2019).

The vaccine pilot studies have shown many preliminary results to support its use. The first thing is that the vaccines are feasible to deliver. They have good enough coverage of RTS,S and help save lives. The vaccine also helps increase equity in malaria prevention. The pilot data shows that more than two thirds of children who do not sleep under an ITN are benefiting from the vaccine (CDC, 2021). With the vaccine intervention and ITN usage combined, over 90% of children are benefiting from a malaria preventative intervention (CDC, 2021).

Along with efficacy, the vaccine also has a strong safety profile. More than 2.3 million doses of the vaccine have been administered during the pilot studies with negligible safety concerns (CDC, 2021). Another good indication is that in areas where the vaccine has been introduced, there has been no decrease in ITN usage, other vaccinations, and health seeking for fever (CDC, 2021). This means it is not having a negative impact in other dimensions of health care. To add on, it is also shown to be a cost-effective strategy in regions with moderate to high malaria transmission (CDC, 2021).

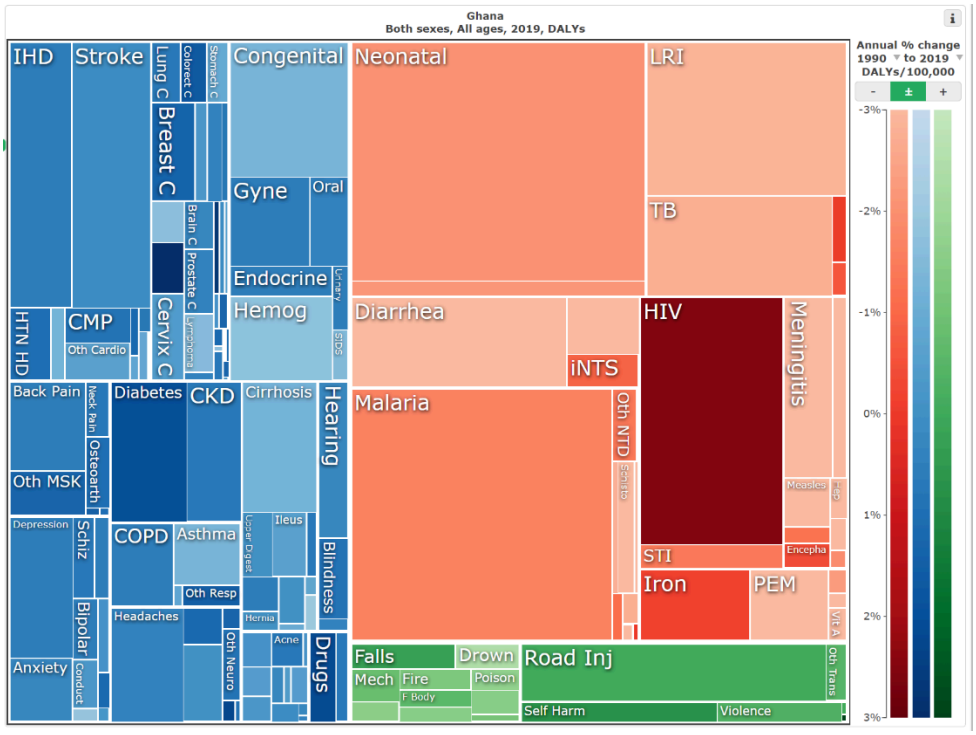
With vaccinations, another strategy that would help would be to empower pharmacists in Ghana to promote these vaccinations and spread correct information. It would be less likely for them to be involved in the vaccinations as the vaccination is for under 2-year-olds and usually occur in clinics, but they can definitely promote it and reduce vaccine hesitancy. Vaccine hesitancy is a barrier which must be addressed to effectively implement this initiative. In 2019, the malaria vaccine was rolled out in Guinea, but people thought they were just being used for testing and mistrusted the vaccines and now uptake of the vaccines is very low (Dresser, 2022). This is similar to other sub-Saharan African countries such as Ghana where mistrust is common.

This misinformation must be prevented, and local pharmacists can play a big role in that by being trusted healthcare professionals. In the future, pharmacists may be trained enough to administer these vaccines as well along with reducing hesitancy which would improve access and increase uptake. There is vaccine training going on currently which is a direction in the right way.

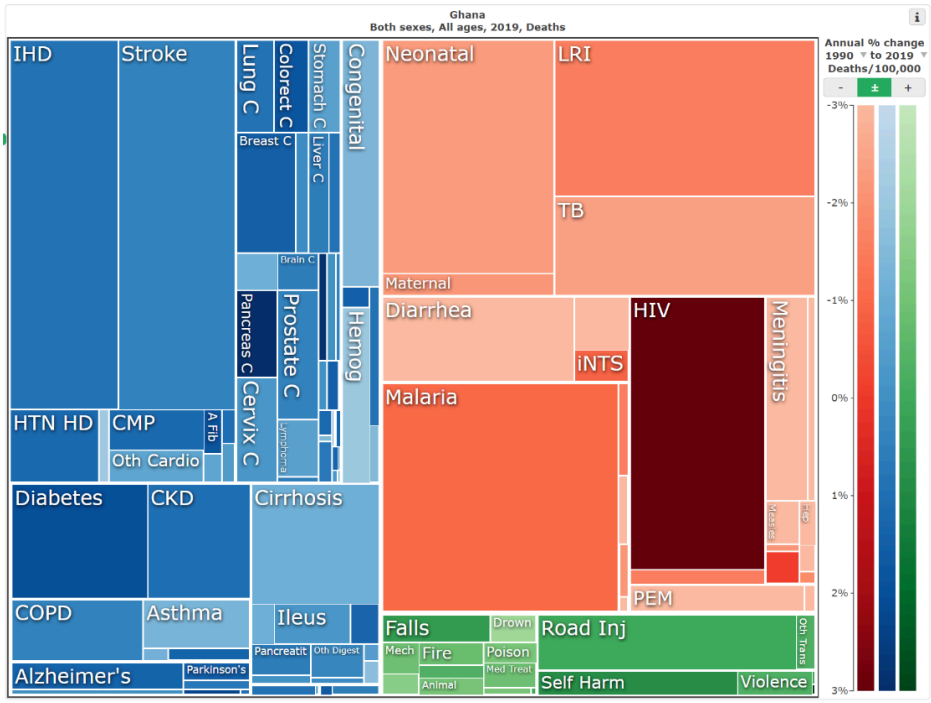
Effective malaria vaccines such as the RTS,S/AS01 are very valuable in combatting the spread of malaria in Ghana. It is a cost-effective strategy in preventing malaria and is recommended by the WHO just by looking at its preliminary results. This vaccine should be administered to all children of countries endemic to malaria in routine doses as specified to help curb the spread of malaria. The RTS,S/AS01 vaccine along with use of ITNs provides a synergistic effect to curb the spread of malaria. To successfully employ the vaccination strategy, vaccine hesitancy must be addressed. The public must be informed about the vaccine and its benefits, and this requires partnering up with local health care workers and leaders of the nation to promote vaccine uptake and correct information. Along with this, adequate funding is also needed to implement this program. Bill and Melinda Gates foundation has helped quite a bit with this venture, but more funding and donations are needed to successfully run this program so that it can improve the health of malaria endemic regions around the globe. Ghana is just one example of a country that will benefit from this intervention; there are many other countries in sub-Saharan Africa and countries where malaria is endemic who will benefit from this intervention. Malaria is a global health issue and the RTS,S/AS01 vaccine will help decrease its burden not only in Ghana, but all around the globe where malaria is endemic. This vaccine should definitely be funded for use in Ghana and other sub-Saharan countries as it can have long lasting benefits in improving the health of children and in turn, the entire nation.

Appendix

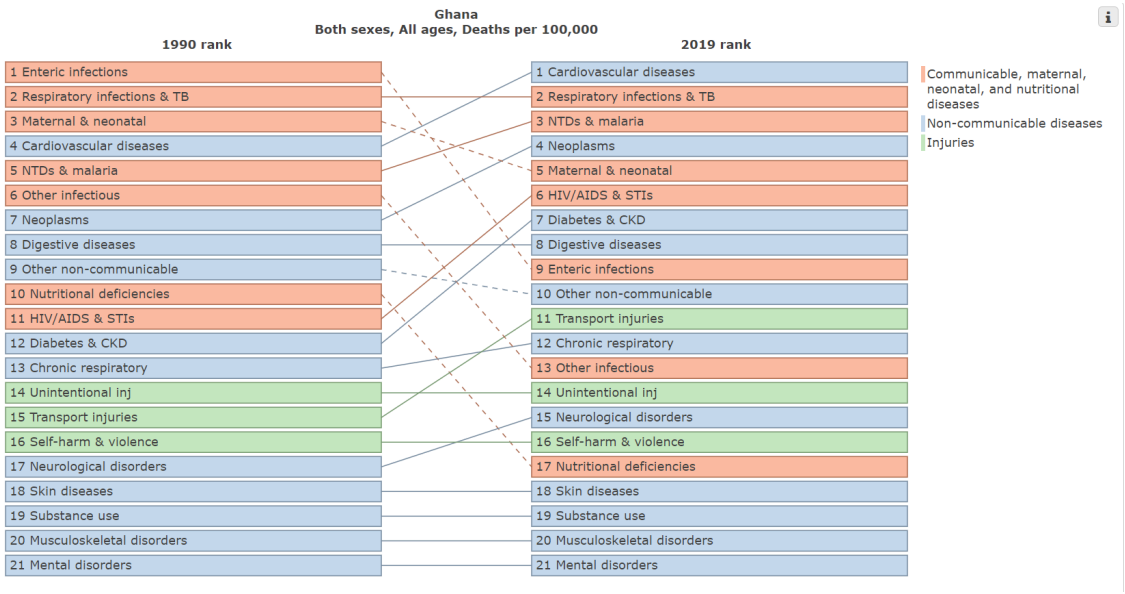
Appendix 1: Top Disease States Causing DALYs (all ages) in Ghana from IHME



Appendix 2: Top Disease States Causing Deaths (all ages) in Ghana from IHME



Appendix 3: Top Disease States (all ages) in Ghana in 1990 and 2019 from IHME



Appendix 4: Prevalence of Malaria as per 2019 GMIS

Example 1: Prevalence of Malaria
A Biomarker Measure Taken from All Eligible Respondents

Table 4.6 Prevalence of malaria in children (1)

Percentage of children age 6-59 months classified in two tests as having malaria, according to background characteristics, Ghana MIS 2019

(3) Background characteristic	Malaria prevalence according to RDT: RDT positive	Malaria prevalence according to RDT: Number of children	Malaria prevalence according to microscopy: Microscopy positive (2)	Malaria prevalence according to microscopy: Number of children
Age in months				
6-8	8.7	167	6.2	167
9-11	13.7	108	7.8	108
12-17	18.2	286	13.3	286
18-23	21.6	286	13.2	287
24-35	22.8	612	13.9	615
36-47	25.3	576	13.7	578
48-59	29.7	577	19.1	577
Sex				
Male	24.3	1,321	13.9	1,329
Female	21.6	1,292	14.3	1,290
Mother's interview status				
Interviewed	22.3	2,243	13.7	2,250
Not interviewed	26.6	369	16.5	369
Residence				
Urban	9.8	1,057	6.1	1,062
Rural	31.9	1,556	19.6	1,556
Region				
Western	31.2	283	27.0 (5)	283
Central	29.9	187	17.6	186
Greater Accra	1.0	304	2.4	307
Volta	33.3	301	20.4	301
Eastern	26.4	267	12.3	270
Ashanti	15.8	413	10.4	413
Brong Ahafo	35.4	228	17.3	230
Northern	18.7	421	13.0	421
Upper East	30.6	124	9.8	124
Upper West	22.6	83	10.5	83
Mother's education[1]				
No education	29.4	511	17.9	510
Primary	26.6	488	16.3	493
Middle/JSS/JHS	20.8	848	12.9	849
Secondary/SSS/SHS or higher	11.2	396	7.0	397
Wealth quintile				
Lowest	35.1	630	22.4	629
Second	33.5	576	18.3	579
Middle	22.1	550	15.0	550
Fourth	10.9	468	6.8	468
Highest	3.2	389	2.1	393
Total (4)	23.0	2,612	14.1	2,619

RDT = Rapid diagnostic test (SD BIOLINE Malaria Ag P.f)
[1] Excludes children whose mothers were not interviewed

Appendix 5: Key Socioeconomic Findings from the 2019 GMIS

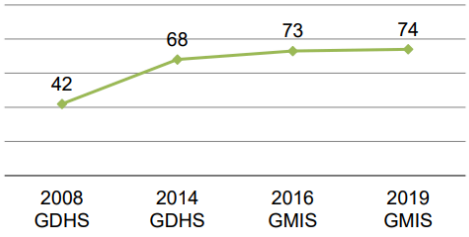
Key Findings

- ***Drinking water:*** 9 in 10 households (93%) have an improved source of drinking water.
- ***Sanitation:*** 75% of households use an improved sanitation facility, 11% use an unimproved sanitation facility, and 15% do not use a facility.
- ***Electricity:*** 84% of households in Ghana have electricity (94% in urban areas and 73% in rural areas).
- ***Education:*** 17% of women age 15-49 have no education.
- ***Literacy:*** 6 in 10 women (59%) age 15-49 are literate.

Appendix 6: Key Trends in ITN Ownership from 2019 GMIS

Figure 3.2 **Trends in household ownership of ITNs**

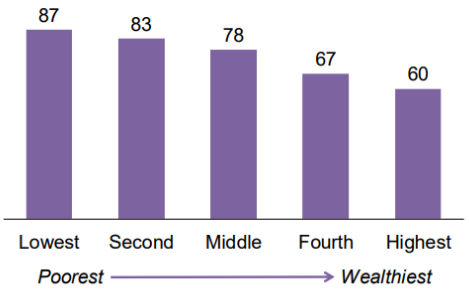
Percentage of households owning at least one insecticide-treated net (ITN)



Note: The definition of an ITN in surveys conducted prior to the 2016 GMIS included nets that had been soaked with insecticides within the past 12 months.

Figure 3.3 **ITN ownership by household wealth**

Percentage of households with at least one ITN



Appendix 7: Phase 3 Efficacy Results of RTS,S/AS01 (Laurens, 2019)

Table 1. RTS,S/AS01 Phase 3 efficacy results

Table 1 of 1

Age Group	6-12 weeks of age (n = 6537)	5-17 months of age (n = 8922)
Vaccine Efficacy against clinical malaria, 3-dose group (95% CI)	18.3% (11.7 to 24.4)	28.3% (23.3 to 32.9)
Vaccine efficacy against clinical malaria, 4-dose group (95% CI)	25.9% (19.9 to 31.5)	36.3% (31.8 to 40.5)
Vaccine Efficacy against severe malaria, 3-dose group (95% CI)	10.3% (−17.9 to 31.8)	1.1% (−23.0 to 20.5)
Vaccine efficacy against severe malaria, 4-dose group (95% CI)	17.3% (−9.4 to 37.5)	32.2% (13.7 to 46.9)

References

Centers for Disease Control and Prevention (CDC). (2021, October 7). *Vaccines*. Malaria. Retrieved April 5, 2022, from https://www.cdc.gov/malaria/malaria_worldwide/reduction/vaccine.html

Dimala, C. A., Kika, B. T., Kadia, B. M., & Blencowe, H. (2018). Current challenges and proposed solutions to the effective implementation of the RTS, S/AS01 Malaria Vaccine Program in sub-Saharan Africa: A systematic review. *PloS one*, *13*(12), e0209744. https://doi.org/10.1371/journal.pone.0209744

Dresser, L. (2022). *Malaria Case Study*. Lecture PDF.

Drislane, F. W., Akpalu, A., & Wegdam, H. H. (2014). The medical system in Ghana. *The Yale journal of biology and medicine*, *87*(3), 321–326.

Ghana Statistical Service (GSS). (2020). Section 3 and Section 5. In *Ghana Malaria Indicator Survey* (pp. 31–61). PDF.

Hogan, A. B., Winskill, P., & Ghani, A. C. (2020). Estimated impact of RTS,S/AS01 malaria vaccine allocation strategies in sub-Saharan africa: A modelling study. *PLOS Medicine*, *17*(11). https://doi.org/10.1371/journal.pmed.1003377

IHME. *GBD compare*. Institute for Health Metrics and Evaluation (IHME). (2022, March 18). Retrieved April 3, 2022, from https://www.healthdata.org/data-visualization/gbd-compare

ITA. (2022, March 24). *Ghana - Healthcare*. Healthcare. Retrieved April 3, 2022, from https://www.trade.gov/country-commercial-guides/ghana-healthcare#:~:text=The%20healthcare%20sector%20in%20Ghana,Healthcare%20is%20variable%20throughout%20Ghana

Laurens, M. B. (2019). RTS,S/AS01 vaccine (Mosquirix™): An overview. *Human Vaccines & Immunotherapeutics*, *16*(3), 480–489. https://doi.org/10.1080/21645515.2019.1669415

PATH. (2022, February 7). *RTS,S*. PATH's Malaria Vaccine Initiative. Retrieved April 5, 2022, from https://www.malariavaccine.org/malaria-and-vaccines/rtss

Worldometer. *Ghana population (live). Worldometer. Retrieved April 3, 2022, from https://www.worldometers.info/world-population/ghana-population/*