Institution: Queen Mary University of London		
Unit of Assessment: 10		
Title of case study: **Advanced modelling for strategic decision-making in the fight against malaria**		
Period when the underpinning research was undertaken: 2016–2018		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s): Jamie Griffin	**Role(s) (e.g. job title):** Lecturer in Applied Probability	**Period(s) employed by submitting HEI:** Sep 2015–present
Period when the claimed impact occurred: 2017–2019		
Is this case study continued from a case study submitted in 2014? N		

1. Summary of the impact (indicative maximum 100 words)

By revealing the most cost-effective interventions to combat malaria, advanced modelling by Dr. Griffin and collaborators has informed leading international investment in antimalarial intervention – and protected millions of lives as a result. Griffin assessed the costs and benefits of four leading malaria intervention strategies to form recommendations that were subsequently used by the Global Fund – an international funding partnership that provides 65% of all international funding to anti-malaria programmes in 41 countries in sub-Saharan Africa – to strategically allocate USD4,000,000,000 of funding in 2017–2019. Typically, the Fund allocates its funding according to World Health Organization (WHO) guidelines, but in 2017, no such guidelines existed. By following the advice of Griffin and colleagues, the Fund's activities saved as many as 87,000 lives and reduced the number of new malaria cases by up to 27,000,000.

2. Underpinning research (indicative maximum 500 words)

Malaria is one of the leading global causes of death and morbidity, infecting 230,000,000 and killing over 440,000 people per year. Over 80% of fatalities occur in Africa, making this continent a priority for research and policy efforts. Griffin is part of an influential network of scientists guiding international policy on malaria interventions, and has applied his modelling expertise to researching malaria control in collaboration with staff members at the WHO: a) estimating the progress of funding in relation to the 2020 milestone of USD6,500,000,000 [3.1]; b) mapping malaria in human and parasite populations [3.2] and c) assessing the efficacy of malaria interventions [3.3]. In recognition of his expertise, Griffin also holds an honorary position at Imperial College's MRC Centre for Outbreak Analysis and Modelling. Griffin's work covers two key areas of malaria research: the mechanism of transmission, and the effectiveness of different interventions.

Modelling the transmission of malaria and the likelihood of local eradication

Many simple modelling studies suggest that malaria transmission demonstrates bistable equilibrium behaviour. This means that the disease can persist indefinitely even if its basic reproduction number (R0), the average number of secondary infections caused by a single malaria case within a susceptible population, is below one. Griffin used two published mathematical models, which had both been fitted to detailed, age-stratified data on multiple outcomes, to demonstrate that this is not the case. Instead, he found that immunity reduces onward infectiousness. This implies that if interventions can reduce R0 to below one for long enough, then malaria can be locally eradicated [3.4].

Modelling the efficacy of malaria control interventions

Griffin and collaborators addressed a knowledge gap by evaluating the costs and benefits of introducing new anti-malaria interventions versus scaling up existing interventions [3.5]. Previous studies had proved the effectiveness of measures such as 'long-lasting insecticide-treated bed nets' ('bed nets') in reducing malaria deaths, but the relative cost-effectiveness of these measures remained unknown – particularly in light of new and emerging interventions such as the RTS,S malaria vaccine. In this research, which was carried out as part of his honorary position at the MRC Centre for Outbreak Analysis and Modelling, Griffin and colleagues developed a model that accounted for parasite prevalence in the absence of interventions other than treatment, the annual seasonal pattern of transmission and the mosquito vector species present and their associated biology. They considered two approaches for costing increasing coverage of four interventions (bed nets, house spraying, seasonal drugs and the vaccine). The first approach assumed increases in coverage were associated with linear increases in cost, while the second approach derived non-linear relationships between coverage and unit costs [3.5]. The analysis would not have been possible without Griffin's contribution, which was to combine data on the effect of these interventions from experimental studies and clinical trials covering 42 countries in sub-Saharan Africa with the developed disease transmission model, enabling this comprehensive and comparative simulation of multiple epidemiological outcomes for malaria.

The research in [3.5] revealed that the vaccine should only be implemented after high coverage has been achieved with the three other interventions, which should remain of higher priority across sub-Saharan Africa than rollout of the vaccine. Specifically, bed nets are the most cost-effective intervention to prevent malaria infection; once 60% coverage of bed nets has been achieved (Figure 1), the next most cost-effective measures are to a) prioritise seasonal drug treatment in settings where transmission is seasonal or b) otherwise focus on spraying houses with insecticide. The vaccine only becomes cost-effective once high coverage of other interventions has been achieved. The recommended schedule for the RTS,S vaccine only covers a small subset of the exposed population (children aged 5–27 months), and offers partial protection to this group for a duration of roughly 4 years. As a result, it does not induce herd immunity in the population and, at a cost of USD5 per dose, is considerably more expensive per person than other interventions – lowering its relative cost-effectiveness. However, there were two exceptions to these recommendations: where malaria transmission is very low, the cost-effectiveness of the vaccine is comparable to that of bed nets; and where malaria transmission is high, the vaccine is the best secondary intervention after bed nets.

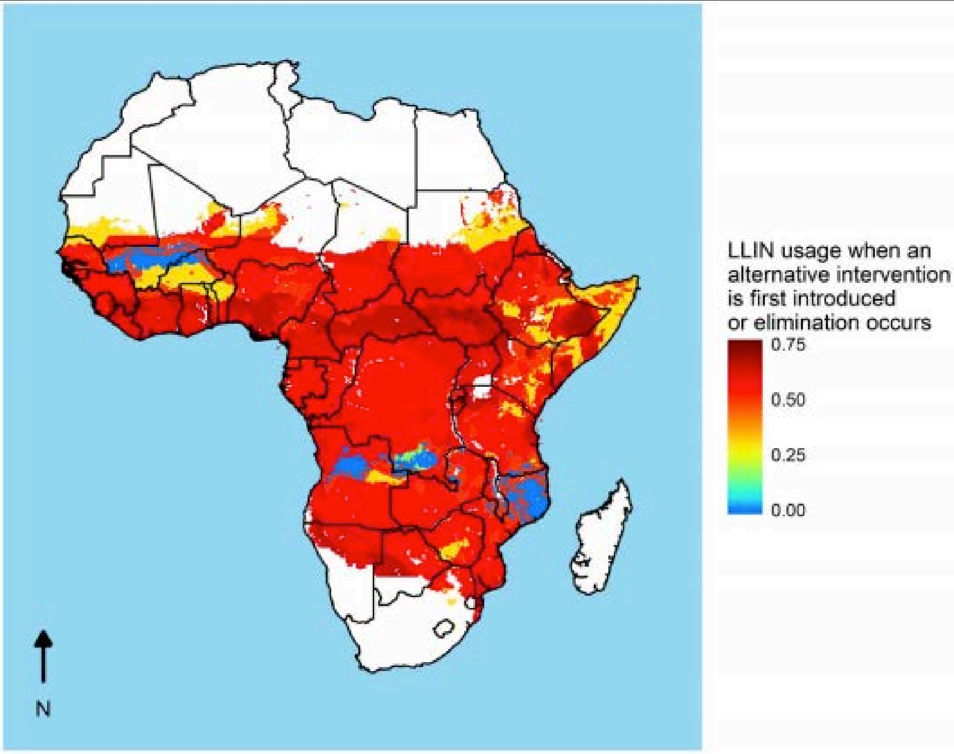

Figure 1. The long-lasting insecticide-treated nets (LLIN) usage rate at which a second intervention is estimated to be more cost-effective than further scale up [3.5].

3. References to the research (indicative maximum of six references)

[3.1] Patouillard, E., Griffin, J. T., Bhatt, S., Ghani, A. C., & Cibulskis, R. (2017). Global investment targets for malaria control and elimination between 2016 and 2030. *BMJ global health, 2(*2*)*, http://dx.doi.org/10.1136/bmjgh-2016-000176

[3.2] Okell, L.C., Griffin, J. T., & Roper, C. (2017). Mapping sulphadoxine-pyrimethamine-resistant Plasmodium falciparum malaria in infected humans and in parasite populations in Africa. *Scientific reports, 7 (*7389*).* https://doi.org/10.1038/s41598-017-06708-9

[3.3] Sherrard-Smith, E., Griffin, J. T., Winskill, P. et al. (2018). Systematic review of indoor residual spray efficacy and effectiveness against Plasmodium falciparum in Africa. *Nature communications, 9 (*4982*).* https://doi.org/10.1038/s41467-018-07357-w

[3.4] Griffin, J. T. (2016). Is a reproduction number of one a threshold for Plasmodium falciparum malaria elimination? *Malaria journal 15 (*389*).* https://doi.org/10.1186/s12936-016-1437-9

[3.5] Winskill, P., Walker, P. G., Griffin, J. T., & Ghani, A. C. (2017). Modelling the cost-effectiveness of introducing the RTS, S malaria vaccine relative to scaling up other malaria interventions in sub-Saharan Africa. *BMJ global health, 2(*1*).* http://dx.doi.org/10.1136/bmjgh-2016-000090

4. Details of the impact (indicative maximum 750 words)

As a result of his advanced modelling on malaria transmission and intervention, Griffin has:

Advised on international investment in antimalarial intervention – in the absence of WHO guidelines

By identifying the most cost-effective combinations of malaria interventions – those that will achieve the greatest reductions in cases and deaths while being less logistically and financially demanding – Griffin's work directly informed, advised, and optimised funding allocation for the Global Fund. The Global Fund is a leading global partnership that works to combat the malaria epidemic, provides 65% of all international funding, and distributed around USD4,000,000,000 to malaria control programmes in the 2017–2019 period [5.1]. Griffin and co-workers' cost-benefit analysis of four malaria interventions (bed nets, house spraying, seasonal drug treatment or vaccine) enabled the Global Fund to strategically allocate its funding in 41 sub-Saharan African countries to specific interventions in 2017–2019. This filled a vital knowledge gap; the Global Fund is typically guided by WHO recommendations, but guidance on whether to fund new interventions (eg a vaccine) or scale up existing measures did not exist in 2017.

According to Scott Filler, Leader of the Malaria Team at the Global Fund, Griffin's modelling "helped inform our understanding of the relative cost-effectiveness of different antimalarial interventions, enabling us to understand which activities to approve for front-line delivery to maximise the impact of available funding in preventing malaria" [5.2]. By confirming that bed nets, house spraying, and seasonal drug treatment should remain priorities across sub-Saharan Africa, Griffin's work "enabled the Global Fund to understand how to target funding, in the absence of external guidance, in a way that would otherwise have been impossible."

Cost-effectiveness was a key consideration in this strategic allocation of funding because total malaria funding was short of its target. Citing Griffin and coworkers' findings on the progress of funding towards milestones [5.3, 5.4], the World Malaria Reports states that "overall, malaria funding in 2016 was only 41% of the 2020 milestone of US$ 6.5 billion, putting the 2020 milestones at great risk" [5.3].

Helped prevent up to 87,000 deaths and 27 million symptomatic cases of malaria

In Malawi alone, one of the most affected countries, over 12,000,000 bed nets have been distributed and house spraying targeted a population of 1,000,000 in 2019, resulting in an estimated 62% reduction in the number of cases in Mangochi District according to Alexander Chikonga, Chief of Party – Global Fund Grants from World Vision Malawi [5.3]. More generally, Griffin reapplied the methodology of [3.5] to evaluate what would have happened in 2017–2019 if the Global Fund had instead funded alternative anti-malaria interventions. He found that by following Griffin and colleagues' recommendations and scaling up coverage of bed nets (by 197,000,000 nets) and house spraying (by 12,500,000 structures), the Global Fund saved as many as 87,000 lives and reduced the number of additional malaria cases by up to 27,000,000 (in 2017–2019). Specifically:

- An estimated **23,000,000** more symptomatic cases and **82,000** additional deaths from malaria would have occurred if investment had focused on house spraying alone
- An estimated **27,000,000** more cases and **87,000** more deaths would have occurred if investment had focused on rollout of the RTS,S vaccine

- An estimated **2,500,000** more cases and **7,400** more deaths would have occurred if investment had focused on seasonal drug treatment (in areas deemed suitable by the WHO)

For context, the baseline 2017–2019 projections were 530,000,000 symptomatic cases and 2,200,000 deaths.

Stimulated further essential research on the RTS,S vaccine

Following Griffin and coauthors' findings on the complexities of comparing vaccine efficacy to existing anti-malaria measures, a pilot programme for the RTS,S vaccine has begun in Ghana, Kenya and Malawi to investigate the vaccine's cost-effectiveness and duration of protection [5.1]. The World Malaria Report 2019 states "Through a WHO-coordinated pilot progamme, Ghana, Kenya and Malawi recently introduced the world's first malaria vaccine in selected areas. Evidence and experience from the programme will inform policy decisions on the vaccine's potential wider use in Africa. With support from the Global Fund to Fight AIDS, Tuberculosis and Malaria and from Unitaid, other promising tools are being tested, such as new types of insecticide-treated nets and tools that target outdoor-biting mosquitoes" [5.5], further showing the continued relevance of the work.

5. Sources to corroborate the impact (indicative maximum of 10 references)

[5.1] The Global Fund (2018). *Results Report*. https://www.theglobalfund.org/en/archive/annual-reports/

[5.2] S Filler. Malaria Team Leader. *The Global Fund* (testimonial letter, 8 November 2019).

[5.3] World Health Organization. (2017). *World Malaria Report 2017*. https://apps.who.int/iris/bitstream/handle/10665/259492/9789241565523-eng.pdf?sequence=1

[5.4] World Health Organizath. (2018). *World Malaria Report 2018*. https://apps.who.int/iris/bitstream/handle/10665/275867/9789241565653-eng.pdf?ua=1

[5.5] World Health Organization. (2019). *World Malaria Report 2019*. https://apps.who.int/iris/rest/bitstreams/1262394/retrieve

[5.6] A Chikonga. Chief of Party-Global Funds Grant. *World Vision Malawi*. (testimonial letter, 13 July 2020).