at the household level with an agent-based mathematical model and investigated the effects of various case management rates, maintenance of vector control, features of reactive case detection programs, and larger-scale drug- and insecticide-based responses on outbreak management and prevention of resurgence in three representative communities in southern Zambia. We find that excellent surveillance is a necessary condition for preventing reestablishment, and we predict that many areas of sub-Saharan Africa will require continued refreshing of vector control until elimination is achieved on a broader regional scale and importation becomes unlikely. The intensity of reactive activities needed to maintain elimination varies with both local receptivity and local configuration of households, with densely populated areas requiring larger radius of follow-up activities. Since asymptomatic infections remain likely when infections are imported into areas with substantial lingering immunity, adaptive responses where mass drug campaigns are triggered when clinical case counts surpass a pre-determined threshold can be a powerful tool for managing outbreaks. These results suggest a general set of guidelines for programs seeking to maintain elimination in areas that remain vulnerable to importation pressure.

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DEVELOPING A NATIONAL MALARIA ELIMINATION INVESTMENT CASE: A FRAMEWORK AND APPLICATION

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The World Health Organization's *Global Technical Strategy for Malaria 2016-2030* calls for malaria elimination in at least 35 countries by 2030. To achieve this ambitious target, national malaria programs will require adequate financial resources to interrupt local transmission and prevent reintroduction. Donor funding for malaria elimination, however, has decreased in recent years, and competing priorities, coupled with a low priority given to malaria as a result of reduced transmission rates, often lead governments to withdraw funding for malaria at a critical juncture. Historical evidence suggests that ill-timed downsizing of malaria programs can lead to deadly and costly resurgences. To sustain political and financial commitment, policymakers responsible for resource allocation must be convinced of the economic returns of eliminating malaria. An investment case can present the rationale for investing in clear and concise terms. Building on existing literature, we developed a framework for national malaria elimination investment cases. The framework has four sections, namely (1) proposed investment, (2) rationale for investing, (3) financial landscape, and (4) issues to consider. The framework, when properly adapted, can help malaria programs gather and generate evidence on the costs, benefits, risks, and financial viability of national malaria elimination. We applied this framework to Papua New Guinea, a malaria endemic country that has aligned itself with the regional goal of making Asia Pacific malaria-free by 2030. Using the outputs of a dynamic transmission model, we estimated the total cost of eliminating malaria to be US$454 million (range: US$282-701 million) in 2016-2030, or $30 million on average per year. This is roughly US$14 million more than what was spent on malaria control in 2015. Elimination by 2030 can save over 14,500 lives and avert over 7.8 million cases. The net economic benefits of elimination compared to a business-as-usual scenario is roughly US$5 billion (range: US$4-7 billion). The median return on investment is 17, indicating that the incremental costs of elimination greatly outweigh its costs.

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HIGH LEVEL EFFICACY IN HUMANS OF A NEXT-GENERATION *PLASMODIUM FALCIPARUM* ANTI-SPOROZOITE VACCINE: R21 IN MATRIX-M™ ADJUVANT

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It remains a global health priority to develop a durable and highly efficacious malaria vaccine. The most advanced malaria vaccine candidate, RTS,S/AS01 has completed Phase III testing in a multicentre study across several African sites and demonstrates low-level (~30%) efficacy against clinical malaria in children aged 5-17 months after a three dose schedule. Efficacy wanes rapidly over time and there remain some safety concerns that require further assessment in the planned pilot deployment trials due to commence in Africa in 2018. There is a need to improve on RTS,S/AS01 to achieve WHO development goals of a durable vaccine with >75% efficacy. RTS,S comprises recombinant particles expressing the central repeat and the C-terminus of the circumsporozoite protein (CSP) fused to Hepatitis B surface antigen (HBsAg). R21 has been developed at the Jenner Institute, University of Oxford. This is an improved HBsAg-CSP-based construct, but without any unfused HBsAg protein which is present at a four-fold molar excess in RTS,S particles. This excess of HBsAg was required for RTS,S to form a particle; however, R21 forms particles without excess HBsAg by utilizing the better expressing yeast, *Pichia pastoris*. Matrix-M (MM) is a promising, novel saponin-based adjuvant that has been tested safely with vaccines for a number of diseases in over 1000 subjects. We previously showed that R21 administered with MM is safe and has comparable immunogenicity at much lower doses compared to RTS,S/AS01: 10µg doses of R21/MM induced the same antibody titres to the CSP repeat as 50µg of RTS,S/AS01B. Durable humoral responses at 6 months were higher for the 10µg than the 50µg dose of R21/MM. We report a Phase IIa efficacy trial using controlled human malaria infection in healthy UK adult volunteers. Three doses of 10µg R21 adjuvanted with MM given 4 weeks apart demonstrated high level sterile efficacy [(81.8%; n=11); p=0.0009]. Furthermore, we observed significantly reduced reactogenicity compared to reported data on the standard RTS,S/AS01 regimen. These data provide strong support for this R21/MM vaccine to be evaluated further in African adults, children and infants.

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SAFETY AND IMMUNOGENICITY OF THE NOVEL *PLASMODIUM FALCIPARUM* BLOOD-STAGE VACCINE RH5.1/AS01B IN A PHASE I/IIA CLINICAL TRIAL

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