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Estimating the potential impact of surveillance test-and-treat posts to reduce malaria in border regions in sub-Saharan Africa: a modelling study

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Abstract

Background The last malaria cases in near-elimination settings are often found in international border regions due to the presence of hard-to-reach populations, conflict, uneven intervention coverage, and human migration. Test-and-treat border posts are an under-researched form of active case detection used to interrupt transmission chains between countries.

Methods An individual-based, mathematical metapopulation model of *Plasmodium falciparum* was used to estimate the effectiveness of border screening posts on total cases in malaria-endemic sub-Saharan Africa.

Results The implementation of international border posts across 401 sub-national administrative units would avert a median of 7173 (IQR 1075 to 23,550) cases per unit over a 10 year period and reduce $PfPR_{2-10}$ by a median of 0.21% (IQR 0.04 to 0.44%).

Conclusions Border posts were most effective in low-transmission settings with high-transmission neighbours. Border posts alone in sub-Saharan Africa will not allow a country to reach elimination, particularly when considering feasibility and acceptability, but could contribute to broader control packages to targeted populations.

Keywords Malaria, *Plasmodium falciparum*, Border posts, Border malaria, Test-and-treat, Mathematical modelling, Malaria modelling

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Background

The World Health Organization (WHO) has selected 25 countries on the fringes of the malaria map to take part in the E-2025 initiative, with the goal of eliminating malaria in these settings by 2025 [1]. However, due to variations in vector habitats, human behaviour patterns, intervention coverages, and medical capacities to treat and prevent infection, malaria infection patterns often differ within and between sub-national areas and their nearest neighbours. The result is that countries that have recently eliminated malaria or are on the pathway to elimination often share a land border with mid- to high-transmission areas [1, 2]. Within near-elimination countries, land border areas often contain the last malaria cases, due to the presence of remote populations, mobile workers, and/or political complexities limiting the reachability of malaria prevention, diagnosis, and treatment [3]. Borders also artificially divide transmission foci; malaria intervention coverage may be unequal on either side of a border leading to insufficient resources to reduce transmission in a border area.

A key driver of malaria transmission in near-elimination countries is human migration (and to a lesser extent mosquito movement). For example, in South Africa, a large proportion of cases are imported (64.8% in 2019 and 49.1% in 2021) following reductions in indigenous transmission due to malaria control efforts [4]. Human movement patterns have been characterized using survey data and parasite genetic lineage data have confirmed established transmission chains across international borders, both to adjacent border area villages and across long distances to cities further inland [5]. Mobile and migrant groups, and even non-travellers who live in communities of individuals with high travel frequencies, may be at an increased risk for infection compared to the general population [6]. In some instances, such as in Mauritius and Armenia, human migration can lead to re-establishment of endemic transmission in an area which has previously eliminated malaria, such as through workers coming in to rebuild after natural disasters, refugees fleeing conflict zones, and military movements [7].

Two main strategies exist to limit the introduction of new infections from one country to another caused by human movement: (A) targeting the “source” population where most infections originate, and (B) intervening during migration or shortly after entry to interrupt transmission chains before local onward transmission can occur. Several approaches have been deployed to counteract importation using these two strategies, including forming regional initiatives to fund interventions in source areas [8], stationing village malaria workers in hard-to-reach zones to provide better access

to diagnosis and treatment, deploying mobile malaria clinics for active case detection, employing test-and-treat to distinct migrant worker populations returning from overseas, and installing screening posts along transport routes to intercept migrants, seasonal workers, and travellers [9–11].

Setting up border screening posts (“border posts” hereafter) is one such strategy for intercepting infections before individuals cross from one country into another. Border posts are a form of active case detection involving parasitological testing and treatment of cases [12]. Historically, border posts have been added to malaria elimination intervention packages on the China-Myanmar border, the Cambodia-Thailand-Laos borders, Bhutan-India border, and in the Elimination 8 region of southern Africa [3, 13]. Although border post use has been described in these areas, little research exists to quantify the intervention’s effectiveness [14]. The lack of evidence combined with uncertainty around the feasibility of implementation has led the WHO to make a conditional recommendation against routine test-and-treat at points of entry [12]. More research is needed to determine if border posts can be an effective tool in an elimination setting, and if so, which areas are most suitable for implementation. Mathematical modelling is particularly useful in this instance as measuring the benefits of border posts is nearly impossible to disentangle from the effects of other interventions often packaged alongside.

Here an individual-based, mathematical model of *Plasmodium falciparum* was extended to include a metapopulation framework, with the goal of exploring the potential utility of border posts along international borders within sub-Saharan Africa. The research objectives were to (1) estimate the potential impact of border posts in reducing cases of malaria among populations living in border areas, (2) identify characteristics of the sites where the implementation of border posts could be most effective, and (3) determine how their impact depends on intervention coverage and population mixing indicators. Because countries’ last malaria cases are usually identified in border areas, the WHO recommends addressing border malaria early in the elimination agenda, identifying drivers of transmission and defining appropriate interventions [3]. Quantifying the effects of border posts and characterizing priority areas for implementation could provide additional evidence for an under-studied malaria control tool, inform the agenda of regional malaria elimination collaborations, and stimulate empirical research.

Methods

Study design

In this study, an existing individual-based, mathematical model of *P. falciparum* was extended to include a metapopulation framework. Using this metapopulation model, the study aimed to (1) estimate the potential impact of border posts in reducing cases of malaria among populations living in border areas, (2) identify characteristics of the sites where the implementation of border posts could be most effective, and (3) determine how their impact depends on intervention coverage and population mixing indicators.

Individual-based model

Modelling was performed using *malariasimulation* (v1.6.0; Charles G, et al. 2023), an open-source individual-based mathematical model of *P. falciparum* in R 4.3.2 (R Core Team, 2023). The model has been previously parameterized by fitting to age-stratified severe disease, clinical disease, and parasite prevalence data across sub-Saharan Africa [15, 16]. *Malariasimulation* incorporates variations in vector species-specific biting rates, population age-structures, adaptive immunity, seasonality, and intervention usage. In the model, individuals enter at birth and become susceptible to *P. falciparum* infection over time as maternally acquired immunity fades. Individuals become infected with *P. falciparum* with an age-based probability, developing either asymptomatic infection or clinical disease, with a proportion of clinically diseased individuals developing severe disease. Mosquito vectors are modelled compartmentally, and mosquitoes become infectious through biting an infected human. Individual human immunity includes maternal antibodies at birth, pre-erythrocytic (anti-infection) immunity, blood stage (anti-parasitic) immunity, and infection detection immunity which are functions of age and previous exposure to infection. Individual level biting rates are assumed to be heterogeneous in the population.

Anti-malarial interventions incorporated in the model include treatment, insecticide-treated nets (ITNs), indoor residual spraying (IRS), seasonal malaria chemoprevention (SMC), and malaria vaccines, allowing for modelling of historical intervention coverages in specific settings. Treatment clears infection from individuals experiencing clinical disease and provides a drug-dependent partial protection from repeat infection which wanes following a Weibull survival curve. ITNs are implemented by reducing female mosquito attempts to feed and by increasing the probabilities of these mosquitoes being repelled or killed. ITN efficacy is dependent on the type of insecticide used, the level of insecticide-resistance specified, and the age of the net [17]. Administration of SMC clears existing infection with a drug-dependent probability

and provides a period of temporary prophylaxis against re-infection. Malaria vaccine efficacy reduces the probability of infection following administration of the primary doses and follows a biphasic model with short and long lived anti-circumsporozoite protein antibody decay dynamics. RTS, S vaccine parameters were previously fit to data from a multi-site Phase III randomized controlled trial [18].

Additional details can be found in the Supplementary Information under Technical Methods. Functions and documentation for *malariasimulation* are open source and can be found at: <https://github.com/mrc-ide/malariasimulation>.

Metapopulation model

The metapopulation component of *malariasimulation* allows for multiple, simultaneous, interconnected model runs, with each run or “unit” uniquely parameterized for a given setting. Rather than model the movement of individual humans between units, *malariasimulation* simulates movement and spatial interconnectedness by allowing the malaria transmission levels of one unit to influence the malaria transmission levels of neighbouring units with a user-specified probability. Malaria transmission levels are captured via the entomological inoculation rate (EIR), the number of infectious mosquito bites per person per day, and the force of infection on mosquitoes (FOIM), the rate of infection acquired by mosquitoes from infectious humans. The probability of influence that one unit exerts on a neighbouring unit is drawn from a user-specified mixing matrix, where each row indicates the primary unit, and each column indicates the secondary connected units that may influence transmission within the primary unit. Each element of the matrix can vary between 0 (no mixing) and 1 (fully random mixing between two units). An illustrative example of mixing patterns and the resulting effects on malaria outcomes is shown in Figure S1.

The probability of human movement between primary and secondary units was calculated using a previously established gravity movement model fit to data from travel surveys in Burkina Faso, Mali, Tanzania, and Zambia [19]. The model estimates the probability of travel based on destination population size and the travel time between origin and destination population-weighted centroids, with larger destination populations and shorter travel times corresponding to higher probabilities. To translate these into connectivity between primary and secondary units, gravity model estimates were used to calculate the bi-directional interactions between all cells of a 0.1×0.1 degree grid overlaid on top of the administrative units with these then aggregated by administrative unit. The trip duration estimates were

fit using commune- and ward-level data from the same surveys mentioned previously [20]. The overall mixing matrices were calculated by combining information from male and female respondents on (a) the estimated bi-directional travel between administrative units; (b) the trip duration; and (c) the probability of travel, estimated from Demographic and Health Survey (DHS) data on the number of trips away from home for one or more nights in the last year [21]. It was assumed that between-country and within-country movement patterns were the same for the primary analysis (i.e. that borders did not affect movement).

Additional details can be found in the Supplementary Information under Technical Methods.

Site selection and parameterization

The primary analysis consists of 33 year model runs (representing years 2000–2032) for 636 sites, representing all first sub-national administrative level (also referred to as admin1) units in malaria-endemic sub-Saharan Africa. 401 of these units include an international border and

were the main focus of the analysis (Fig. 1A, B). Islands were excluded as these units did not include an international land border.

Each unit was parameterized using GADM (v4.0) administrative boundaries [24], and site-specific files from the *foresite* (v.0.1.0; Winskill P, 2023) and *site* (v.0.2.2; Winskill P, 2023) packages. Units were characterized from years 2000 to 2022 using data from WorldPop population counts [23], World Malaria Report cases and deaths [4], Malaria Atlas Project *PfPR*_{2–10} estimates [25], Malaria Atlas Project vector species abundance and distribution [26], and Malaria Atlas Project [27] and the DHS StatCompiler [28] estimates of historical intervention coverage from ITNs, IRS, and treatment. SMC coverage estimates were taken from ACCESS-SMC [29] and the SMC Alliance [30], and RTS, S coverage was drawn from the Malaria Vaccine Implementation Programme [31]. Treatment was categorized as artemether-lumefantrine (an artemisinin combination therapy currently recommended as a first-line treatment) [4] or sulfadoxine-pyrimethamine (used historically). ITNs

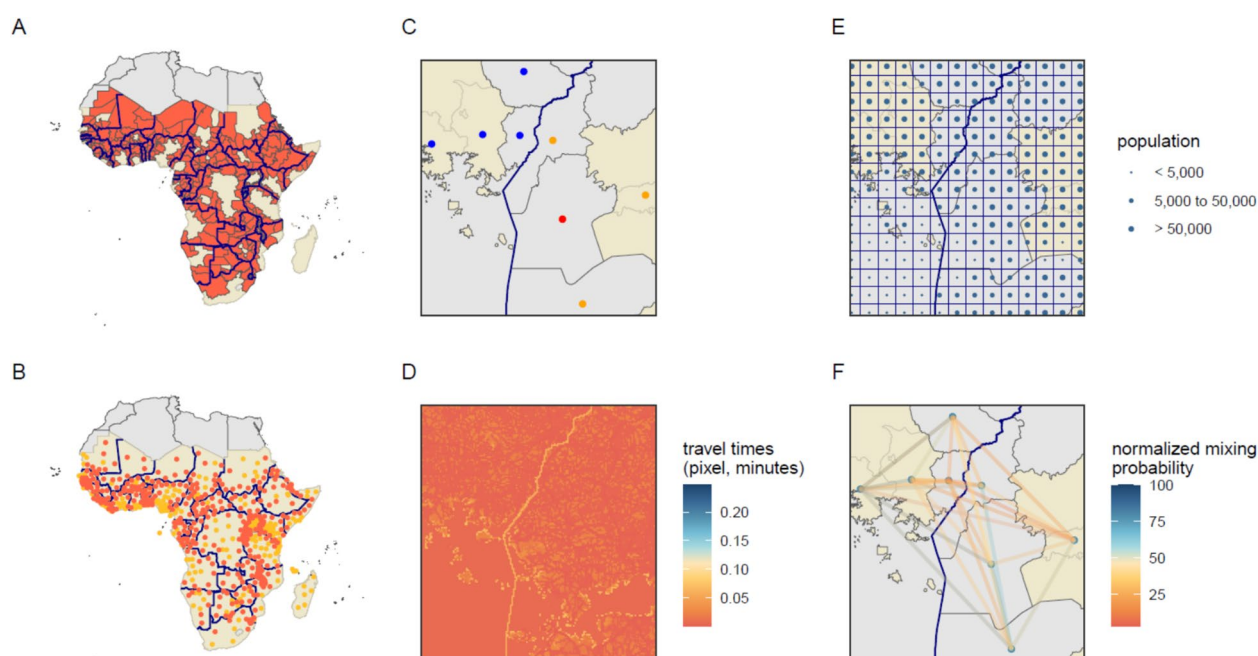


Fig. 1 Illustration of approach. Beginning with malaria-endemic countries in sub-Saharan Africa, the study first (A) identified all administrative units with an international border (red) and (B) the administrative unit centroids of border areas (red) and non-border areas (orange). From there, mixing matrices were created for each cluster of 8 administrative units. Panels (C–F) show an example cluster with the international border indicated with a bolded line. Grey polygons indicate border administrative units, yellow polygons indicate non-border units. For each cluster the following were identified: (C) a seed point (red), the seed point's three nearest neighbours within the same country (orange), and four nearest neighbours outside of the country (blue). Panel (D) shows the travel time raster developed by the Malaria Atlas Project [22] overlaid on the example cluster area. Each pixel (1 km x 1 km) represents the travel time to cross the pixel in minutes according to the fastest mode of transportation, with an additional one-hour time penalty added at the border. Panel (E) shows the 0.1 x 0.1 degree grid surface used in partnership with travel times and trip durations to calculate the mixing matrix. Dots represent the population sizes taken from the centroids of the grid and were obtained from WorldPop [23]. Finally, panel (F) displays the normalized mixing probabilities between units using the gravity model based on population sizes and travel times, aggregated from the grid to the administrative unit level

were classified as pyrethroid, pyrethroid + piperonyl butoxide, or pyrethroid + pyrrole with setting-specific estimated pyrethroid insecticide resistance levels. IRS was classified using a variety of insecticide options, with the assumption that a DDT-type insecticide was used prior to 2017 and an actellic-like insecticide was used post 2017. All SMC interventions are assigned the drug sulfadoxine-pyrimethamine + amodiaquine. A standard demography profile corresponding to the population age structure in sub-Saharan Africa in 2021 was used across all model runs [32]. Seasonality profiles for each unit, which remained static across years, were created using *umbrella* (v0.1.4; Winskill P, 2021) which constructs a Fourier series model using CHIRPS daily rainfall data from the year 2020 [33]. If one unit was parameterized for both urban and rural settings, the two were combined proportional to the populations living in each setting so that there was only one distinct parameter set assigned to each site. Since models were run into the future through year 2032, years 2023–2032 were parameterized with 2022 intervention coverage levels assumed to be kept constant over the remainder of the simulation period.

Each metapopulation model run began with the selection of a single seed site, defined as the centroid of an administrative unit with an international border. The three closest neighbouring units within the same country as the seed site were also selected, as well as the four nearest neighbouring sites across an international border from the seed site; the eight total selected sites represented one model run or “cluster” (Fig. 1C). The distance between sites was calculated via Euclidean distance between unit centroids. 401 clusters were formed with seed sites representing each of the 401 administrative units touching an international border. Clusters allow for interpretation of trends in malaria in border regions, but do not account for importation of infection from a border area to population centres further inland.

Mixing matrices were formed for each cluster of eight sites using the gravity model process described above, using a grid comprised of 0.1×0.1 degree cells and summarizing at the first administrative unit level. Origin and destination points were assigned to geo-spatial grid centroids and the travel times between grid centroids were set using an algorithm to calculate the path-of-least-resistance from origin to destination across a pixelated friction surface [22] at a $1 \text{ km} \times 1 \text{ km}$ resolution, created by the Malaria Atlas Project which accounts for land type, and presence of roads or water (Fig. 1D). A one-hour travel time penalty has already been incorporated into the friction surface [22] at international borders, extending the time needed for cross-border movement and reducing the likelihood of journeys relative to those of a similar distance made without a border crossing. The

resulting travel times and administrative unit WorldPop population sizes (2023) [23] (Fig. 1E) were used to create a mixing matrix for the metapopulation model (Fig. 1F). Data were not available to incorporate market centres and road conditions, which may also drive movement in certain areas. Groupings of eight administrative units allowed for capture of malaria trends in border areas, but this analysis did not account for importation of malaria cases from border areas to population centres further inland. Each of the 401 site metapopulation models were run with equal population sizes (100,000 people per unit) and 50 random draws from the main model parameter distributions to generate uncertainty estimates.

Border intervention

Border posts were implemented in the model by modifying the influence of EIR and FOIM between sites by a coefficient ranging between 0 and 1. Coefficients are functions of the estimated percent of travellers captured by border posts (as opposed to travel through unsurveyed routes), the non-linear relationship between population-level rapid diagnostic test (RDT) prevalence and true prevalence, and treatment efficacy (Figure S2). A value of 0 means that the border post stops all transmission, and a value of 1 indicates that the border post has no effect. A value of 0.2 representing 80% coverage (80% of travellers “screened” at a border post) was used for all site runs. This value represents an optimistic best-case scenario. A sensitivity analysis was performed to vary coverage, but the feasibility of implementing border posts along international borders is likely to be challenging and country specific. The relationship between population RDT prevalence and population true prevalence is non-linear, meaning that a higher proportion of true positives will be positive by RDT in high $PfPR_{2-10}$ settings than in low $PfPR_{2-10}$ settings, due to a greater proportion of infections with higher parasitaemia levels. RDT to polymerase chain reaction (PCR) positivity curves were obtained from previously published parameters (Figure S3) [34, 35], with the assumption that the sum of subpatent, infected, and clinically diseased individuals in the model at each time point represented the true PCR prevalence. Treatment was assumed to be effective in 95% of treated individuals [36]. Border posts represent real world interventions such as static border posts at border entry points, or mobile malaria posts along border crossing areas and community focal points frequented by target populations [14, 37]. Border posts were only implemented between sites across an international border; no posts were implemented between sites falling within the same country. All border posts were assumed to capture bi-directional movement across international borders.

Statistical analysis

The primary outcome of interest was the number of cases per year averted in each unit (accounting for unit population size) after the implementation of border posts. Secondary outcomes included the change in $PfPR_{2-10}$ after the intervention and identification of areas where border posts could have the greatest effect on malaria elimination goals. The period of analysis was ten years following border post implementation (the last 10 years of the simulation).

Sensitivity analyses

Three scenarios were run to examine the influence of (1) site $PfPR_{2-10}$, (2) border post coverage, and (3) level of international mixing on the effectiveness of border post interventions over 10 years. In the first scenario 2-unit models were run with every combination of $PfPR_{2-10}$ ranging from 10 to 80% in 5% step intervals, and 80% intervention coverage. In the second case study, 2-unit models were run with $PfPR_{2-10}$ values of 10, 20, 40, 60 and 80%, and border post coverage assumptions ranging from 0 to 100% in 20% step intervals. Both scenarios were set-up in the metapopulation model framework assuming equal population sizes (100,000 people per unit per run), a 20 year warm-up period, and 5% mixing between units. The third scenario explored variation in international-cross border mixing vs. national mixing using a 2-unit model with $PfPR_{2-10}$ values ranging from 0.2 to 0.8 and cross-border mixing values assigned to the median, 25 th percentile, and 75 th percentile of international mixing values in clusters across sub-Saharan Africa. Each 2-unit model was run using 50 unique random draws from the

main model parameter distributions to generate uncertainty estimates.

Results

Modelling border areas in sub-Saharan Africa

An individual-based, mathematical metapopulation model of *P. falciparum* was used to estimate the potential impact of border posts in malaria-endemic sub-Saharan Africa and to identify characteristics of sites most amenable to the intervention. Here, the WHO definition of border malaria was used, represented as “malaria transmission or potential for transmission that takes place across or along borders between countries sharing a land border” [3]. Border areas were defined as first sub-national administrative level units which share a land border with a malaria endemic country.

A total of 44 countries were represented in the analysis, consisting of 636 first sub-national administrative level units in malaria-endemic sub-Saharan Africa. The median administrative unit population size [23] was 989,582 (range: 295 to 48 million) (Figure S4) and the median travel time between units was 9 h (range: 15 min to 246 h) (Figure S5). Each unit was represented in a median of 5 unique clusters (range: 1 to 24).

Simulations of border posts assuming that 80% of people who cross borders undergo testing by RDT and that treatment of positive cases with artemether-lumefantrine is 95% effective, averted a median of 7173 (IQR 1075 to 23,550) cases per administrative unit in all border seed points over a 10-year period (Fig. 2A, Figure S6). When looking at relative impact, border posts resulted in a median 0.21% decrease (IQR 0.04 to 0.44%) in *P. falciparum* prevalence among 2–10-year-olds ($PfPR_{2-10}$) from

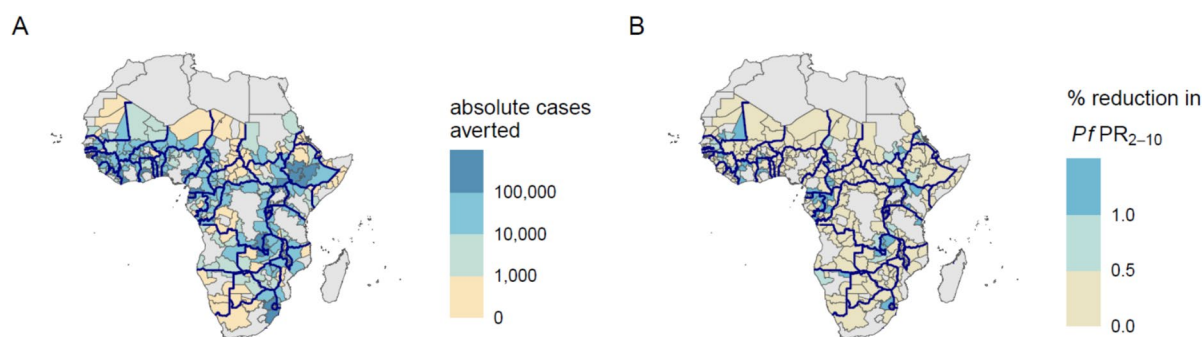


Fig. 2 Effects of border post simulations with 80% coverage of rapid diagnostic testing over the 10-year intervention period relative to no intervention. Administrative units are parameterized with unit-specific epidemiological and historical intervention data. Colours represent median values out of 50 unique model parameter draws. Panel (A) represents the absolute number of cases averted in each unit when it was the seed point for the cluster. Panel (B) represents the percent reduction in $PfPR_{2-10}$ in each unit when it was the seed point for the cluster, from before to after the border post intervention. Bold lines indicate boundaries between countries included in the analysis. All units with outcomes slightly less than 0 due to model stochasticity at extremely low values of $PfPR_{2-10}$ were set at 0. Results should not be interpreted as recommendations for specific countries or sub-national areas. Larger versions of these plots are available as Figure S6 and S7

baseline to post-intervention period (Fig. 2B, Figure S7). Accounting for the non-linear relationship between population-level RDT prevalence and true parasite prevalence, particularly in low-transmission settings, a median of 14 (IQR 5 to 82) people would need to be screened at a border post to prevent one case, across all border seed points (Fig. 3A). Border posts appeared to be most effective in low transmission areas with high transmission neighbours, similar to areas along the Kenya-Ethiopia-South Sudan borders, Rwanda, and western Côte d'Ivoire regions of sub-Saharan Africa. Due to a lack of sub-national and temporal data on human movement patterns, and an optimistic, universally applied border post coverage value of 80%, results should not be interpreted as specific recommendations for individual countries or sub-national areas, but as supporting identification of patterns and characteristics of areas where border post interventions could be most effective.

Sensitivity of findings to site and intervention characteristics

To further investigate the drivers behind border post effectiveness, three sensitivity analyses using 2-unit models were performed to assess the effects of $PfPR_{2-10}$, intervention coverage, and level of international mixing on cases averted. The first scenario, examining the effectiveness of border posts by $PfPR_{2-10}$, showed that border posts reduced the highest percentage of cases in scenarios where a high transmission unit bordered a low-transmission unit (Fig. 4A). $PfPR_{2-10}$ units in low-transmission settings of 10%, paired with high-transmission $PfPR_{2-10}$ units of 50 to 80% resulted in 4.0 to 13.5%

of cases averted in low-transmission units in the total population over 10 years. These scenarios are similar to the above-mentioned regions in sub-Saharan Africa, although border neighbours tend to have smaller transmission differences (Fig. 3B). Border posts had little effect when $PfPR_{2-10}$ combinations of low-transmission units were paired with other low-transmission units, due to the low number of infections mixing and the imperfect ability of RDTs to capture all infections. When border posts were added to the model with testing through PCR instead of RDT (representing complete capture of all infections), results showed similar trends, with a higher proportion of cases averted, ranging from 9.5 to 22.0% when low-transmission units of $PfPR_{2-10}$ 10% were paired with high-transmission units of 50 to 80% (Figure S8). A higher proportion of cases were detected by RDT when examining movement from high-transmission areas vs. low-transmission areas, ranging from a median of 32.3% (IQR 31.4 to 33.1%) across 2-units of $PfPR_{2-10}$ 10% to a median of 96.2% (IQR 95.3 to 97.4%) across two-units of $PfPR_{2-10}$ 80% (Fig. 4B).

The second scenario, examining the effectiveness of border posts by the percentage of transmission captured by the test-and-treat structure using a 2-unit model, demonstrated that higher border post coverage led to a higher percentage of cases averted, but only when a low transmission setting ($PfPR_{2-10}$ 10%) was paired with a medium to high $PfPR_{2-10}$ (60 or 80%) (Fig. 4C). Values ranged from <1% cases averted when border post coverage was 60% or less when a $PfPR_{2-10}$ 10% unit was bordering a $PfPR_{2-10}$ 20% unit, to a maximum of 16.5% when

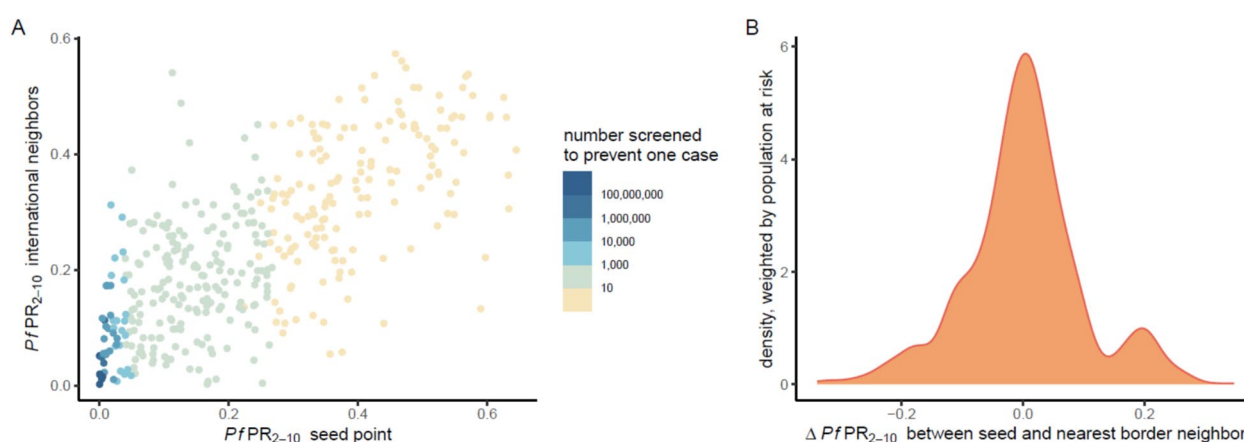


Fig. 3 Model outcomes by prevalence differences between neighbours. Panel (A) shows the number of people who need to be screened to prevent one case per cluster via rapid diagnostic test. The location of each point on the plot represents the $PfPR_{2-10}$ of the seed point (x-axis) vs. the mean $PfPR_{2-10}$ of the four international neighbours in the cluster (y-axis). The colour of each point on the plot represents the number of individuals who must be screened to prevent one case of malaria when travelling from the international neighbours to the seed point. Each point represents the median cluster value of 50 parameter draws. Panel (B) is a density plot showing the distribution of the population at risk of *P. falciparum*. The x-axis represents the difference in $PfPR_{2-10}$ between each seed point and its nearest border neighbour

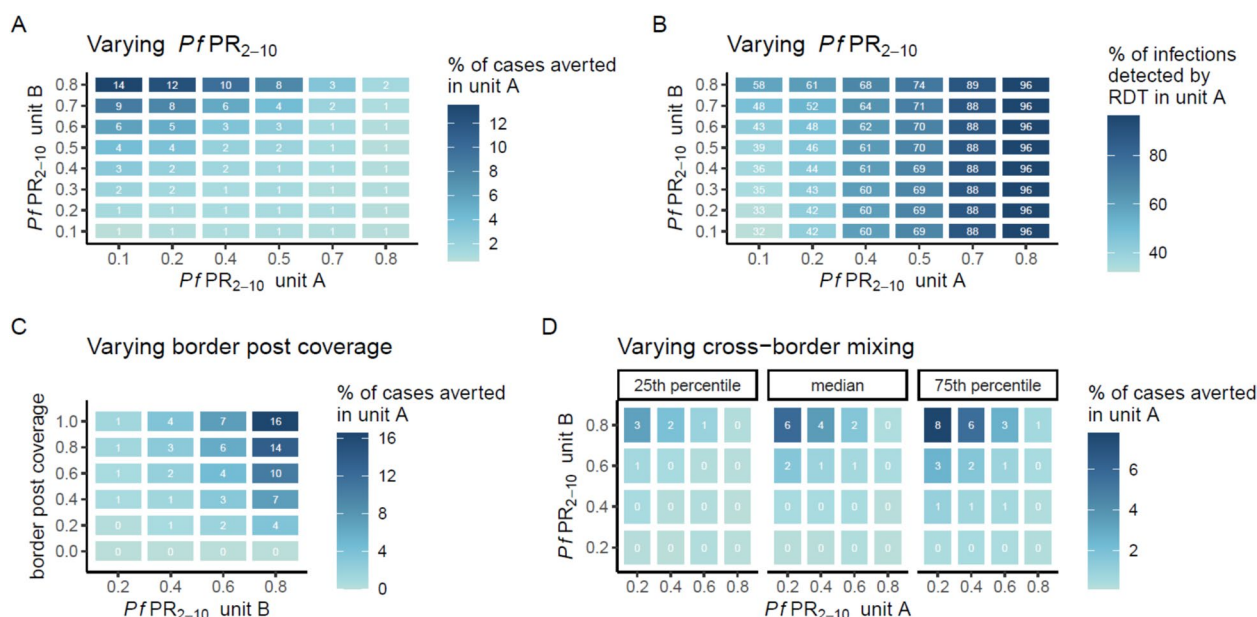


Fig. 4 Measuring the sensitivity of outcomes to $PfPR_{2-10}$, border post coverage, and cross-border mixing. The scenarios represented used a 2-unit metapopulation model which varies the value of each unit's $PfPR_{2-10}$ from 0.1 to 0.8 and is run over a 10-year period. The first scenario examines the effects of (A) the $PfPR_{2-10}$ of unit B on the percent of cases averted in unit A and (B) the $PfPR_{2-10}$ of unit A on the percent of infections detected by RDT in unit A. The second scenario examines the effects of (C) border post coverage on the percentage of cases averted in unit A. These first two scenarios assume that 95% of mixing occurs within a unit and 5% of mixing occurs between units. The third scenario examines the effects of (D) varying cross-border mixing (vs. national mixing) on the percentage of cases averted in unit A. Colours represent median values out of 50 unique parameter draws. Note: RDT = rapid diagnostic test

a $PfPR_{2-10}$ 10% unit was bordering a $PfPR_{2-10}$ 80% unit with 100% border post coverage.

The third scenario investigated the effects of varying the level of international cross-border mixing (as opposed to national within-border mixing), using values from the median, 25th percentile, and 75th percentile of cross-border mixing in sub-Saharan Africa calculated through the gravity model (Fig. 4D). The results found that a higher level of cross-border mixing led to more cases averted by the border post intervention. Values in low-to-high transmission pairings of a $PfPR_{2-10}$ 20% unit bordering a $PfPR_{2-10}$ 80% unit averted a median of 5.8% of cases in unit A, ranging from 3.3% in the lower quantile of mixing to 7.8% in the upper quantile of mixing.

Discussion

Modelling the effectiveness of border post interventions across 401 uniquely parameterized international border areas in sub-Saharan Africa resulted in a range of outcomes: a median of 7173 (IQR 1075 to 23,550) cases averted per unit and a median 0.21% decrease (IQR: 0.04% to 0.44%) in $PfPR_{2-10}$. Sensitivity analyses using a 2-unit model resulted in two general findings. First, the difference in $PfPR_{2-10}$ values on either side of a border has a large effect on the potential number of cases averted by the intervention. The highest relative cases

averted occurred in near-elimination settings which border a high transmission neighbour, such as $PfPR_{2-10}$ units of 50% to 80% paired with $PfPR_{2-10}$ units of 10%, which averted 4.0 to 13.5% of cases due to the high probability of intercepted travellers carrying infection. Border posts are unlikely to be an effective solution in near-elimination settings which border other low-transmission areas due to the infrequent likelihood of cases, non-linear relationship between RDT prevalence and true population prevalence (since many infected travellers may have undetectable infections due to low-parasitaemia), and screening the large number of people that need to be tested to detect a single infection is difficult to achieve. Second, the proportion of all travellers screened at a border post has the greatest influence on overall cases averted in settings where near-elimination units border high-transmission units. When implementing border posts in appropriate settings, being able to cover highly frequented travel routes or specific populations who are at high risk of transmitting infection will be important to effectively halt cross-border transmission. Third, a higher level of cross border travel leads to more cases averted, due to the higher proportion of the population being screened. Although border posts are unlikely to allow a country to reach elimination in isolation, they can contribute to elimination efforts in border areas as part

of a wider package of regional surveillance, control, and health system strengthening.

Border posts have been used historically in elimination settings in Asia on the China-Myanmar border and the Cambodia-Thailand-Laos borders as part of broader intervention packages [3]. Only one programme implementing border posts has been described in sub-Saharan Africa, which took place in the Elimination 8 region of southern Africa, involving 46 malaria health posts stationed along the five international borders in the region from 2016–2018 [38]. These locations appeared fit for border post implementation at the time, given the presence of a near-elimination country paired with higher transmission neighbours, as seen in this project's case studies. In the Elimination 8 region it was estimated that mobile and static malaria health units contributed to an estimated 30% reduction in malaria incidence in border areas among other activities, although this decrease was not enough to eliminate malaria [38]. Mathematical modelling in the region corroborates these findings, showing that focalized screen-and-treat border interventions could have large but short-lived effects, would need to be continuously implemented to prevent renewed transmission, and would be insufficient to eliminate local infection at less than 100% coverage [39]. Screen and treat methods could also be effective in island situations where there is often a large difference in transmission between the elimination island and the nearest mainland location from which most travellers originate [6, 40].

These findings highlight the importance of regional cooperation to supplement border post activities through initiatives such as regional resource sharing [8], working with private organizations to screen at-risk occupational groups [41], improving health systems in low-resourced areas [8], and coordinating vector control campaigns across borders [42]. Implementing a package of interventions is particularly important as it is unknown what coverage can be feasibly achieved with border posts given the number of informal border crossings in most locations. In places where malaria control decision-makers face national-level political complexities, local collaboration between bordering administrative units could be a more important near-term goal than national-level collaboration [3]. Border posts, while potentially reducing the rate of importation into countries, cannot take the place of ensuring quality implementation and high coverage of malaria interventions by national and subnational malaria programmes.

National malaria control programmes have formed regional consortiums to tackle malaria control across the globe, spanning from the Elimination of Malaria group in Mesoamerica and Hispaniola, to the Malaria-Free Arabian Peninsula Initiative, African Leaders Malaria

Alliance, and the Asia Pacific Malaria Elimination Network, among others [43]. International funders are supportive of these regional partnerships, with the WHO Global Technical Strategy for Malaria 2016–2030 including a goal to “deepen regional collaboration” [44]. However, the success of regional initiatives requires external funding. The Lubombo Spatial Development Initiative, for example, was incredibly successful in reducing malaria along border areas of South Africa, Swaziland, and Mozambique [45], but after the closure of the programme due to a lack of financial resources, malaria rebounded across all three countries [46]. The Global Fund does invest in a few key multicountry priorities, including 20 million allocated for malaria elimination in Southern Africa and 120 million for drug resistance in the Greater Mekong Sub-region [47], but generally the international aid structure currently contains little to accommodate regional proposals in addition to country-specific projects [43].

The feasibility of establishing border posts and acceptance by the target population is also a significant concern. Set-up of cross-border collaboration test-and-treat methods to targeted groups has been feasible in French Guiana, Suriname, and Brazil through distribution of self-test and treatment kits to mobile gold miner populations [48]. However, only a small number of studies have published data on static border post user-acceptance to wider traveller populations with mixed results. In Cambodia, 22% of approached travellers refused to participate in the border post intervention due to a lack of time, a perception of no malaria risk, fear of blood draw, and language or cultural barriers [49]. Alternatively, focus groups regarding a border post in the Solomon Islands indicated high acceptance of test-and-treat, suggesting that in some settings mandatory testing before travel by ship may be feasible if backed up by legislation to empower health workers and reduce noncompliance [50]. Like coverage, the sensitivity of the diagnostic used was found to be a driver of border post effectiveness and the number of cases detected in this study; PCR has a much lower limit of detection compared to RDTs, but processing time can take hours rather than minutes and the technology may not be feasible to implement within a point-of-care design [34, 35, 51]. If it is not feasible to screen a large proportion of individuals crossing a border, targeting high-risk mobile populations may be a better approach. Plantations in Malaysia have worked with the Malaria Control Programme to screen new workers for malaria upon arrival, many of whom are foreign migrants [41], and other countries in Asia have set up programmes to screen returning UN peacekeepers and military members [52].

One limitation to this analysis is the inability to capture border post intervention costs, including those related to infrastructure, human resources, and diagnostic and treatment supply chains, all of which are likely to vary between individual settings. Here, a comparison of the number of people needed to test to prevent one case represents a measure of resource effectiveness, but the societal value of setting-up and running border posts, like any intervention, will depend on the cost-effectiveness and affordability of implementation relative to other tools such as targeted vector control, installation of community health workers, or regional resource sharing to reduce incidence in “source” populations. Border posts target a much smaller but higher-risk population than general mass drug administration or vector control of large geographic areas, potentially leading to lower costs, but the expense of set-up and maintenance could vary widely depending on existing infrastructure. Additional sub-national modelling will be necessary to inform country decision making. Sensitivity to the resolution of analysis could also be further explored. In this study, although the gravity model was created using a 0.1×0.1 degree grid, historical intervention use and $PjPR_{2-10}$ was parameterized at the first administrative unit level which is quite broad; country-specific work using smaller geographical units (such as level 2 units) representing heterogeneities in $PjPR_{2-10}$ and intervention use could better inform border malaria outcomes.

This analysis is also limited by a lack of country-specific data and temporal data on human movement, requiring the use of a gravity model and travel time friction surface to build mixing matrices. The friction surface incorporates a static one-hour penalty when crossing an international border due to a lack of country-specific data [22], but future work using country and sub-national models with detailed human movement data will be necessary to draw conclusions on the use of border posts for specific locations. Model results could not be stratified by sex, though it is known that males and females have different travel patterns which vary by location [21], and that the intensity of gender differences in cross-border travel also differ by country [20]. There are also no data available to inform the percentage of travellers across international borders which would be able to be captured by a border post intervention, and this is likely to be country-specific and depend on the route of travel (walking paths through forests, paved roads, boat, air). In sub-Saharan Africa borders are often porous, making it likely that the effectiveness of border interventions will in practice be much lower than the 80% coverage assumed in this study. Information on where travellers cross the border and the estimated proportion of travellers able to be tested and

treated by targeting key routes will be important to generate more accurate, country-specific model runs.

Despite these limitations and a lack of data on costs and feasibility, border posts have the potential to contribute to regional malaria control beyond the treatment of infected individuals, as part of broader malaria control and prevention efforts in near-elimination settings. In the Greater Mekong Subregion, border posts have been used to monitor changes in artemisinin resistant parasites flowing across countries, and to characterize the level of malaria importation stemming from asymptomatic vs. symptomatic individuals [49]. It is possible that border posts can fill gaps where passive case detection of mobile populations through routine health systems is ineffective; in north-eastern Cambodia, mobile malaria workers near the border contributed to 45% of all testing and detected 39% of all cases registered in border areas [37]. Bhutan has integrated malaria screening alongside HIV, tuberculosis, and COVID-19 at border towns for foreign workers entering the country and Timor-Leste has integrated malaria interventions into those already existing for dengue, making border interventions more cost effective by targeting a broader range of infectious diseases, and more sustainable as fewer infections are picked up as malaria transmission declines [13]. Integrating border posts alongside interventions such as screening for other infectious diseases or entomological surveillance could increase the feasibility and cost-effectiveness of this intervention.

Conclusions

Considering the ambitious identification of 25 countries with the potential to eliminate malaria by 2025 and the goal of eliminating malaria in at least 20 countries by 2025 [1], the global community must encourage regional cooperation and the evaluation of strategies targeted towards border malaria. Border posts could be one effective option to utilize alongside existing tools to address cross-border transmission in near-elimination areas with higher transmission neighbours. Although the effectiveness of border posts will ultimately depend on the percentage of travellers captured by the intervention, feasibility, and cost-effectiveness, they can also contribute to wider health benefits for the target population when coupled with other aspects of routine care or screening for additional infectious diseases. Future modelling work should assess the implementation of border posts compared to other forms of regional cooperation, such as resource sharing and synchronizing vector control campaigns, and investigate the role of border posts in settings where a large proportion of

malaria cases in the eliminating country are imported cases from neighbouring districts.

Abbreviations

DHS	Demographic and Health Survey
EIR	Entomological inoculation rate
FOIM	Force of infection on mosquitoes
IRS	Indoor residual spraying
ITN	Insecticide-treated net
PCR	Polymerase chain reaction
RDT	Rapid diagnostic test
SMC	Seasonal malaria chemoprevention
WHO	World Health Organization

Supplementary Information

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Supplementary Material 1

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Author contributions

Conceptualization: HMT, GDC, ACG Methodology: HMT, GDC Data curation: HMT, GDC Formal analysis: HMT, GDC Visualization: HMT Writing – original draft: HMT Writing—reviewing & editing: HMT, GDC, NS, MP, JMM, IK, KH, ACG.

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Availability of data and materials

The data required to fit duration estimates for mixing matrices can be found in Marshall et al. 2016. Unit parameters for epidemiological data, population size, historical intervention coverage, mosquito vectors, and seasonality were obtained from publicly available resources referenced in the methods section. Full analysis code, including model parameterization, unit parameterization, and mixing algorithms are provided at: https://github.com/htopazian/border_elimination.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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