Efficacy of non-pyrethroid indoor residual spraying or intensive behaviour change communication in combination with long-lasting insecticidal nets for malaria control in west Africa: a pragmatic, cluster-randomised, controlled trial

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Summary

Background Since 2015, progress in the control of malaria has stalled owing to multiple factors, including the probable reduced efficacy of long-lasting insecticidal nets (LLINs) caused by insecticide resistance and plateauing LLIN use rates. This study aimed to assess the additional effect of non-pyrethroid indoor residual spraying (IRS) and intensive behaviour change communication (BCC) when combined with LLINs on malaria in rural west Africa.

Methods This pragmatic, parallel-group, cluster-randomised, controlled trial took place in community settings in Burkina Faso and Côte d'Ivoire. Villages (clusters) with an average population of 300 inhabitants, a minimum distance between villages of 2 km, and year-round accessibility by a four-wheel drive vehicle were eligible for inclusion. A simple randomisation approach with a computer-generated random number sequence was used to assign 39 villages with a total population of 10 750 inhabitants to three groups: LLIN alone (16 villages; the control group), LLIN plus IRS (11 villages), and LLIN plus BCC (12 villages). Field teams that collected epidemiological data and laboratory staff were masked to intervention allocation; it was not possible to mask participants, field teams that implemented the interventions, or study investigators to intervention allocation. The IRS intervention consisted of pirimiphos-methyl treatment of the dwellings and the BCC intervention focused on promoting LLIN use, environmental sanitation, and early health-seeking behaviour through home visits, interpersonal talks, and group talks. The primary outcome was malaria incidence rate in the whole population as measured by passive case detection at health centres. Data were collected for 10 months before (the pre-intervention period) and 10 months after (the post-intervention period) randomisation. All outcome data were analysed by intention to treat and using constrained baseline analyses. The trial is registered with ClinicalTrials.gov, NCT03074435, and is completed.

Findings Between November, 2016, and August, 2018, 215 000 theoretical person-months of follow-up resulted in 3612 malaria cases recorded by passive case detection during both pre-intervention and post-intervention periods. During the post-intervention period, passive case detection showed a 23% reduction in malaria incidence rate (rate ratio 0·77 [95% CI 0·64–0·93], p=0·0073) in the LLIN plus IRS group and a 22% reduction (0·78 [0·63–0·96], p=0·020) in the LLIN plus BCC group compared with the LLIN-alone (control) group. No IRS-related adverse effects were recorded.

Interpretation Results show that the addition of non-pyrethroid IRS or intensive BCC to LLINs can effectively reduce the number of malaria cases. The effect of IRS observed in our trial was intermediate compared with that reported in previous trials conducted in Africa. Notably, this study provides the first trial-based evidence supporting the effectiveness of an intensive BCC intervention, which is a promising result but requires confirmation through additional studies.

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For the French translation of the abstract see **Online** for appendix 1

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Introduction

Since the launch of the Roll Back Malaria initiative by WHO and its partners at the end of the last millennium, the mortality rate for malaria, the deadliest vector-borne disease, dropped by 50% from 2000 to 2015 globally.[1] This progress can be credited in large part to vector control: 68% of the estimated 663 million averted cases before 2015 can be attributed to long-lasting insecticidal nets (LLINs),[2] which are still the cornerstone of malaria control. However, since 2015, the decreasing trend in malaria burden has stalled, with the burden either plateauing or worsening on most indicators.[1] Among the multifactorial

Research in context

Evidence before this study

The most recent Cochrane review (2022) of non-pyrethroid indoor residual spraying (IRS) for the prevention of malaria in communities using insecticide-treated nets included four randomised controlled trials (RCTs) in a meta-analysis of incidence rates and concluded that evidence of an effect was low. Among the selected studies, those evaluating pirimiphos-methyl IRS found a reduction in both incidence and prevalence in a trial in Mozambique and a reduction in prevalence in a trial in Tanzania. Until now, the efficacy of pirimiphos-methyl IRS has not been investigated in west Africa. To identify studies of behaviour change communication (BCC) approaches to malaria prevention, we searched PubMed for RCTs containing the terms "communication" and "malaria" in their titles or abstracts using English-language search terms from database inception to April 1, 2025. This search returned 17 results; among these RCTs, only six evaluated BCC strategies. Three of these studies showed an increase in long-lasting insecticidal net (LLIN) use rates. However, none of them included epidemiological outcomes.

Added value of this study

This study is the first evaluation of pirimiphos-methyl IRS in combination with LLINs for malaria control in west Africa. The combined IRS plus LLIN intervention resulted in a 23% reduction in malaria incidence rate compared with LLINs alone, as recorded in health centres. The addition of the present results to the 2022 Cochrane meta-analysis of incidence rates for non-pyrethroid IRS confirmed the effect size and increased its precision (rate ratio 0·83 [95% CI 0·66–1·06]), still indicating a weak effect with low evidence. This study is also the first RCT to evaluate intensive BCC in communities that use LLINs with epidemiological and entomological outcomes. We showed that intensive BCC in combination with LLINs compared with LLINs alone reduced the number of malaria cases recorded in health centres by an average of 22% and reduced the case prevalence among individuals aged 0–18 years recorded during cross-sectional surveys by an average of 40%.

Implications of all the available evidence

There is low-certainty evidence that non-pyrethroid IRS reduces malaria incidence rate. Given the potential negative interactions with LLINs (ie, decreased LLIN use in response to IRS implementation), high costs, toxicity risks, and changing vector behaviours, IRS use should be considered carefully. Although BCC programmes have previously been shown to have significant effects on malaria prevention behaviours, this study is the first to provide epidemiological evidence of their effectiveness. Although further confirmatory trials are warranted, we advocate for BCC, especially interpersonal communication in rural areas, to be considered as a stand-alone strategy rather than only as a supplementary measure.

causes of this stall in progress, resistant phenotypes—both behavioural and physiological—to pyrethroid insecticides in mosquito vectors are known to hinder LLIN efficacy.[1,3] LLINs are designed to kill mosquito vectors that are nocturnal, anthropophilic (ie, human biting), endophagic (ie, indoor feeding), and susceptible to pyrethroid insecticides, and are therefore ineffective against vectors that exhibit alternative phenotypes. Moreover, LLIN coverage and use in populations have plateaued at moderate levels since 2015.[1] Together, these factors contribute to residual transmission. Stakeholders are therefore challenged to propose responsive and flexible strategies to tackle residual transmission and resume progress in reducing the malaria burden. Accordingly, any intervention targeting malaria vectors not adequately controlled by current LLINs, whether due to vector resistance or gaps in population coverage and use, is a relevant candidate. For example, in recent years, new classes of LLINs combining insecticides with different modes of action have shown efficacy.[4]

Indoor residual spraying (IRS) refers to the spraying of the inner walls of human dwellings with insecticides. It targets endophilic vectors—ie, those that rest indoors after blood feeding. In 2012, WHO recognised non-pyrethroid IRS as the only available option to complement LLINs in a management strategy to counter pyrethroid resistance across Africa.[5] However, issues with non-pyrethroid IRS include its short residual efficacy (mostly less than 4 months at that time), which would necessitate multiple spray rounds per year in numerous settings, leading to increased economic costs. In 2013, the WHO Pesticide Evaluation Scheme recommended a new, long-lasting pirimiphos-methyl formulation (Actellic 300CS), which quickly became the most popular formulation for IRS owing to its longer residual efficacy (>6 months in most settings) and the low resistance of African *Anopheles* spp to organophosphates.[6,7] To date, only one randomised controlled trial (RCT) in west Africa has evaluated the epidemiological effect of non-pyrethroid interventions against pyrethroid-resistant malaria vectors: carbamate IRS or carbamate-treated plastic sheeting in combination with LLINs showed no evidence of benefit over LLINs alone.[8] However, in southeast Africa, trials of pirimiphos-methyl IRS have shown an average reduction in malaria incidence risk of 35% in Mozambique and a reduction in prevalence of 45% and 64% in Mozambique[9] and Tanzania,[10] respectively.

Although suboptimal population coverage with LLINs is an important and obvious limiting factor for their use and efficacy, LLIN use rates remain well below coverage rates.[1] There is, therefore, room for improvement, and changes in human behaviours represent an opportunity to reduce residual transmission. Population surveys in Côte d'Ivoire and Burkina Faso have shown that the most frequently cited source of information about malaria is mass media (television and radio).[11,12] However, these surveys also

showed that people with low incomes and people living in rural areas (ie, those most at risk of malaria) have lower access to mass media and are less informed than are wealthier and urban populations, and therefore have weaker knowledge about malaria and its prevention. Other means of communication, such as interpersonal or small group communication, have been shown to be effective in various domains[13] and sometimes superior[14] or synergistic with mass-media campaigns.[15] In rural Burkina Faso and Côte d'Ivoire, less than 5% of people report having heard messages on malaria from a health worker in the last 6 months.[11,12] We therefore hypothesised that a community-based intensive behaviour change communication (BCC) approach, involving interpersonal and group talks about malaria prevention, might fill the knowledge gap and contribute to reducing malaria burden in areas where there is limited access to television and radio. Until now, there have been no studies assessing the epidemiological efficacy of BCC as a malaria prevention strategy per se.

In the present study, in collaboration with the National Malaria Control Programs (NMCPs) of Burkina Faso and Côte d'Ivoire, we aimed to compare the efficacy of non-pyrethroid IRS or intensive BCC in combination with LLINs on malaria, using passive case detection, cross-sectional epidemiological surveys, and entomological surveys. Hence, this was a pragmatic trial that evaluated available strategies that could be used in the near future to complement LLIN universal coverage—the standard malaria control strategy implemented by NMCPs in both countries.

Methods

Study design and participants

This study is part of the REACT project, which was a pragmatic, five-arm, parallel-group, cluster-RCT that aimed to evaluate the effects of additional malaria control strategies in combination with LLINs in Burkina Faso and Côte d'Ivoire. Results from three arms (LLIN alone, LLIN plus IRS, and LLIN plus BCC), which were implemented in both countries, are presented here. The other two arms assessed the use of a larvicide-based intervention (LLIN plus BTI) in Côte d'Ivoire and ivermectin treatment of domestic animals (LLIN plus IVM) in Burkina Faso, and will be reported elsewhere. The trial is registered with ClinicalTrials.gov, NCT03074435.

The study was carried out in communities of the Diébougou health district in southwestern Burkina Faso and the Korhogo health district in northern Côte d'Ivoire (appendix 2 pp 2–3, 6). Villages (clusters) with an average population of 300 inhabitants, a minimum distance between villages of 2 km, and year-round accessibility by a four-wheel drive vehicle were eligible for inclusion. Identification and selection of villages was based on health district databases, census data collected in 2016 in both countries, geographical coordinates of villages recorded in institutional databases (the Base Nationale de Données Topographiques and the Base de Données de la Direction Générale de l'Eau), and georeferencing.

The target population for passive case detection was the total population of all participating villages in the two health districts included in the study. The target population for the cross-sectional surveys was the youngest 50% of the population of all participating villages (ie, individuals aged 0–18 years in Burkina Faso and 0–21 years in Côte d'Ivoire, according to 2016 census data). Survey participants (accompanied by their parents or legal guardians if <18 years) were enrolled during the 2016 population census; during the cross-sectional surveys, individuals who were missed in the census or in previous surveys were also enrolled.

The trial was approved by the Comité National d'Ethique de la Recherche in Côte d'Ivoire (063/MSHP/CNER-kp) and the Comité d'Ethique Institutionnel pour la Recherche en Santé of the Institut de Recherche en Sciences de la Santé in Burkina Faso (A06-2016/CEIRES). The project included an independent external scientific advisory board composed of medical entomologists, public health specialists, and epidemiologists from France, Benin, Côte d'Ivoire, and Burkina Faso, which was responsible for validating the study protocols, analysis plans, and randomisation procedures. Community chiefs, parents or guardians of survey participants, survey participants aged 18 years and older, mosquito collectors, owners of collection houses, and owners of sprayed houses gave written informed consent.

Randomisation and masking

Randomisation was performed during a workshop on June 13, 2017, in the presence of the REACT project's steering committee and the external advisory board. Intervention allocation was done using a simple randomisation approach with a computer-generated random number sequence that was generated by an external data manager and applied independently in each country. Villages were randomly assigned with an allocation ratio of 8:6:5:8 in Burkina Faso to LLIN alone (control), LLIN plus BCC, LLIN plus IRS, or LLIN plus IVM, and with an allocation ratio of 8:6:6:8 in Côte d'Ivoire to LLIN alone, LLIN plus BCC, LLIN plus IRS, or LLIN plus BTI (appendix 2 p 4). Field teams that collected epidemiological data and laboratory staff were masked to intervention allocation; it was not possible to mask participants, field teams that implemented the interventions, or study investigators to intervention allocation.

See Online for appendix 2

Procedures

The baseline and control intervention (LLIN alone) corresponded to the standard intervention for malaria control implemented in each country by their respective NMCPs. In Burkina Faso, the villages received a universal distribution of LLINs (Permanet 2.0; Vestergaard, Lausanne, Switzerland) in July, 2016. In Côte d'Ivoire, the

research team distributed new LLINs (Permanet 2.0; one for every two people) to the inhabitants of the study villages in June, 2017. The LLIN plus IRS intervention consisted of the application of IRS with Actellic 300CS (Syngenta, Basel, Switzerland) at a target dose of 1 g of active ingredient (pirimiphos-methyl) per m² in all houses in the selected villages in September and October, 2017. Spray quality control was conducted, and any potentially related adverse effects were documented by staff at participating health centres during the study period (appendix 2 pp 3–4). The intensive BCC intervention (LLIN plus BCC) was designed to promote the following behaviours: (1) all household members sleep under an LLIN every night; (2) all household and community members clean their environment to limit mosquito proliferation; (3) all pregnant women seek and take intermittent preventive treatment; and (4) caregivers of children younger than 5 years seek health care within 24 h of fever onset. Existing health workers designated by their communities to work on this project were employed by the research programme and additional health workers were designated and recruited when needed to achieve a ratio of one health worker for every 35 households; a total of 25 community health workers were involved in the project. The objectives of each health worker included performing 15 home visits (15–20 min), 20 interpersonal talks (15–20 min), and four group talks (15–30 min) per month (appendix 2 p 4). The BCC intervention was implemented from September, 2017, to August, 2018, in both countries.

Data were collected for the passive case detection, cross-sectional survey, and entomological survey components of the study at differing timepoints, as detailed below, during the year (from September, 2016, to August, 2017) before the interventions were introduced (the pre-intervention period) and 10 months (from November, 2017, to August, 2018) during (BCC) or after (IRS) implementation of the interventions (the post-intervention period; appendix 2 pp 5–6).

Passive case detection was carried out in collaboration with the health centres (12 in Burkina Faso, seven in Côte d'Ivoire) to which the villages were affiliated. Nurses from our team retrieved consultation data from the health centre registries using digital forms. Consultation records of all residents of the study villages were retrieved and those with a diagnosis of either simple or severe malaria were considered for further analyses. Passive case detection data were collected in both countries for 10 months (November, 2016, to August, 2017) during the pre-intervention period and for the 10-month post-intervention period (November, 2017, to August, 2018; appendix 2 p 6).

Three cross-sectional surveys took place during the pre-intervention period and four took place during the post-intervention period, according to the schedule outlined in appendix 2 (pp 5–6). Field staff conducted interviews with participants (or their parents or legal guardians if they were too young to respond themselves), before performing clinical evaluations and thick and thin blood smears. Participants were asked whether they used an LLIN the preceding night. Participants with a temperature above 37·5°C or with a recent history of fever (within 48 h) were tested for *Plasmodium falciparum* infection using a rapid diagnostic test to enable prompt medical care (either artemisinin-based combination therapy prescription or referral to the nearest hospital).

We performed human landing collections of mosquitoes at approximately 2-month intervals: four surveys in Côte d'Ivoire and three in Burkina Faso in the pre-intervention period and four surveys in the post-intervention period in both countries, according to the schedule outlined in appendix 2 (pp 5–6). Collections took place for one night per survey, both indoors and outdoors, at four houses in each village to assess mosquito biting rates, biting behaviours, and parity rates, and for molecular analyses. Molecular analyses of individual *Anopheles* consisted of species identification, detection of *P falciparum* DNA, and detection of insecticide resistance target-site mutations (kdr-west [Leu1014Phe], kdr-east [Leu1014Ser], and ace-1 [Gly119Ser] in *Anopheles gambiae* sensu lato). The entomological survey design and mosquito processing have been described extensively elsewhere.[16]

Owing to updates in the study design (appendix 2 p 2), deviations from these procedures occurred before implementation of the interventions in Côte d'Ivoire, where blood smears, molecular analysis of mosquitoes, and parity rate measurements were performed only in a subsample of study villages.

Outcomes

The primary outcome was the malaria incidence rate in the whole population (ie, the number of cases per person-time recorded by passive case detection in health centres). Secondary outcomes ascertained from cross-sectional survey data focused on individuals aged 0–18 years (data from those aged 19–21 years in Côte d'Ivoire were not analysed to ensure consistency between countries), and included the prevalence of malaria cases in young people (proportion that tested positive on rapid diagnostic testing), the prevalence of *P falciparum* infection (proportion with positive blood smears), parasite density of *P falciparum* in asymptomatic participants (per µL), and LLIN use rate (proportion that reported using a net the night before the cross-sectional survey).

Secondary outcomes determined from mosquito collections included human biting rate by *Anopheles* (bites per human-night), mosquito nuisance biting by mosquitoes of all genera (bites per human-night), sporozoite rate (proportion of collected *Anopheles* infected with *P falciparum*), entomological inoculation rate (nightly number of infectious bites received per person), parity rate (proportion of parous *Anopheles* females), exophagy rate (proportion of *Anopheles* collected outdoors), median hour

of biting (time of night when 50% of *Anopheles* vectors were collected), and allelic frequencies of the kdr-west (Leu1014Phe), kdr-east (Leu1014Ser; Burkina Faso only), and ace-1 (Gly119Ser) insecticide-resistance target-site mutations. No active surveillance for adverse events was conducted but, as noted above, local health district medical teams monitored and reported any medical complaints potentially related to the IRS intervention during the study period.

Statistical analysis

We calculated the number of clusters and individuals required to detect 33% protective efficacy against malaria incidence rate conferred by combinations of interventions compared with the control intervention, with a power of 80%, a significance level of 5%, a coefficient of variation of 0·25, and an average of one clinical malaria episode per person-year in the study areas.[17,18] The estimated minimum number of clusters for each intervention was eight with an average of 300 individuals per cluster. Simulations based on pre-intervention data and the actual study design predicted that both BCC and IRS interventions would have a power of more than 90% to detect a 30% reduction in incidence rate and case prevalence (appendix 2 pp 7–8).

Binary, discrete, and continuous outcomes were analysed using binomial, negative-binomial, or Gaussian mixed-effect models, respectively. We performed intention-to-treat analyses of all outcomes using a constrained baseline analysis approach.[19,20] Unlike conditional approaches, constrained baseline analysis explicitly incorporates baseline data into the model. This approach avoids potential misspecification issues, allows for the inclusion of individuals with missing outcomes, and offers a more efficient estimation of treatment effects. In constrained baseline analysis, baseline means are constrained to be equal across randomised groups, based on the assumption that any baseline differences arose by chance, as expected in a randomised trial.

The incidence rate model was fitted to weekly incidences in each age group (≤5 years, 6–18 years, and ≥19 years). A first-order autoregressive covariance structure and random intercepts for clusters (villages) nested in health centres were introduced to account for both temporal and spatial autocorrelation (appendix 2 p 7). The case prevalence model was fitted to individual participant data from cross-sectional surveys. This model included crossed random intercepts for surveys and participants, with the latter nested in clusters. The pre-intervention and post-intervention periods were included in the epidemiological outcome models, and these models were fitted without adjustment or with adjustment for the country (ie, the single areas in each of Burkina Faso and Côte d'Ivoire, as defined above) and age group of participants (≤5 years, 6–18 years, and ≥19 years for the incidence rate model; ≤5 years and 6–18 years for the case prevalence model). We tested for interactions between intervention groups and country or age group for epidemiological outcomes. Sensitivity analyses examining the effect of baseline constraints and missing observations were performed. The result from the incidence rate model was combined with data from the 2022 Cochrane meta-analysis of non-pyrethroid-like IRS plus insecticide-treated nets versus insecticide-treated nets alone by Pryce and colleagues[21] to provide an updated incidence rate estimate.

Other secondary outcomes were analysed using the same approach unless pre-intervention data were unavailable (eg, for human and *Anopheles* infection outcomes, *Anopheles* parity, and resistance in Côte d'Ivoire). In such cases, data were analysed separately by country and, for Côte d'Ivoire, analyses included post-intervention data only, potentially reducing statistical power. Post-intervention median hours of biting were compared between groups using Dunn's tests. Data from entomological survey four (post-intervention) in Burkina Faso were excluded from analyses of molecular data owing to suspected DNA contamination among samples. Although the BCC and IRS effects were tested against the same control condition, they can be considered unrelated and p values were therefore not corrected (ie, controlling the family-wise error rate was not necessary). All analyses were performed using R (version 4.2).

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Data collection took place from September, 2016, to August, 2018. Of 74 villages assessed for eligibility, 57 were identified as eligible and were enrolled into the REACT trial in July, 2016. Four villages in Côte d'Ivoire that did not meet the criteria for minimum distance between villages were erroneously included in the study; they were excluded and replaced by two eligible villages in June, 2017, before randomisation. Of the 55 randomised villages, 39 (19 in Burkina Faso, 20 in Côte d'Ivoire, with a total population of 10 750 inhabitants) were assigned to the control (LLIN alone) group (16 villages), the LLIN plus IRS group (11 villages), or the LLIN plus BCC group (12 villages). The remaining 16 villages received either LLIN plus BTI or LLIN plus IVM; the results of these interventions are not presented here (figure). The 39 study villages had an average population size of 276 inhabitants (SD 94), with an average of 5·82 (SD 1·23) individuals per household. The mean age was 23·2 years (SD 2·8) and the male:female ratio was 0·82. There were no notable differences in baseline characteristics between the intervention groups (table 1; appendix 2 p 9).

The IRS coverage rate in villages assigned to this intervention was 94% (1328 of 1408 structures). The mean

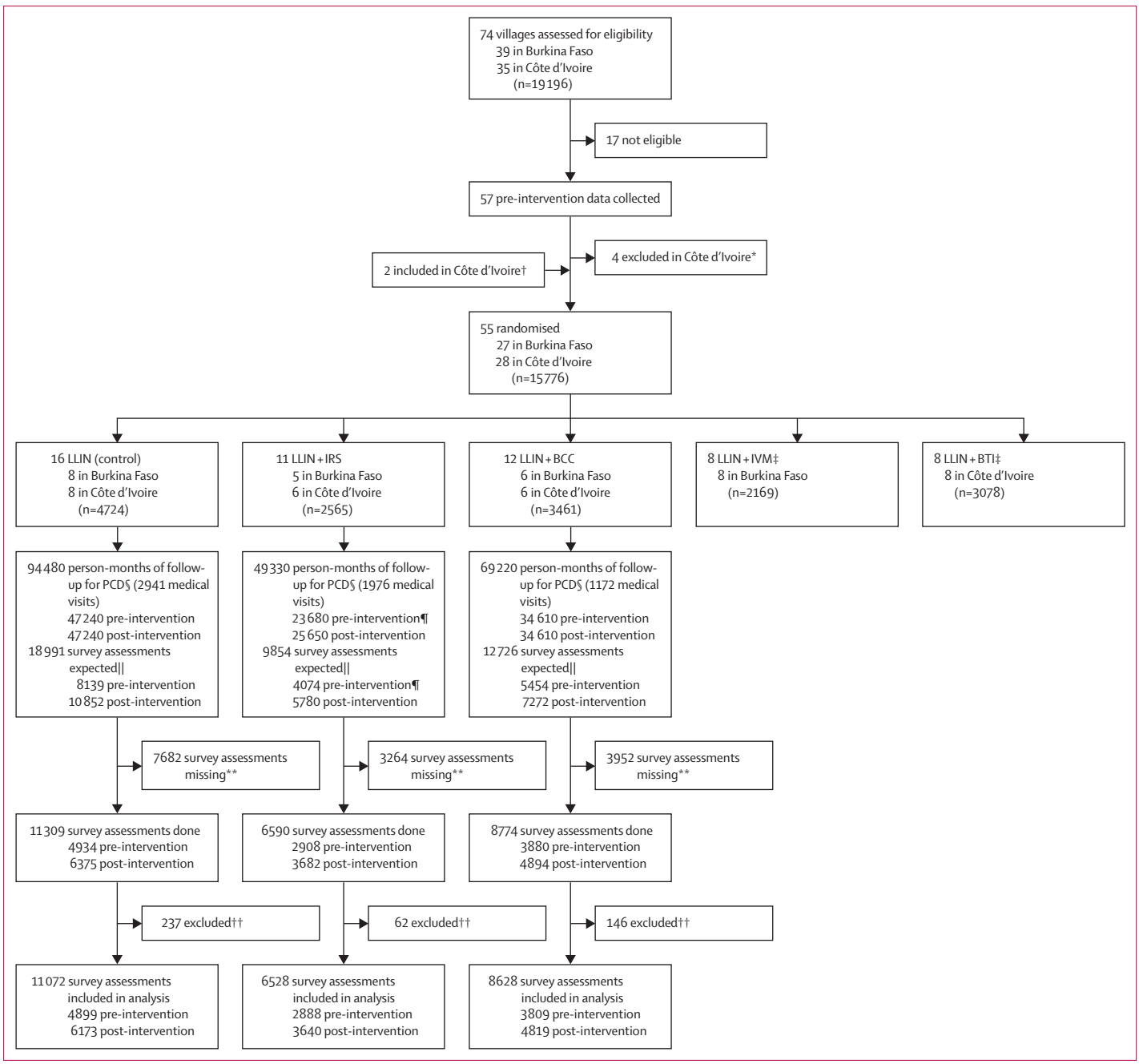

Figure: **Trial profile**
LLIN=long-lasting insecticidal net. IRS=indoor residual spraying. BCC=behaviour change communication. IVM=ivermectin-based intervention. BTI=larvicide-based intervention. PCD=passive case detection. *Did not meet the criteria for minimum distance between villages. †One village received IRS, one received BTI at randomisation. ‡Results for LLIN plus IVM and LLIN plus BTI arms not reported here. §Theoretical person-time of follow-up, in person-months (population × 20 months [November, 2016, to August, 2017, and November, 2017, to August, 2018]). ¶Data from one cluster were missing from the pre-intervention phase for the LLIN plus IRS arm (see †). ||The expected number of cross-sectional surveys if the target population of all registered individuals aged 0–18 years took part in all seven surveys. **Participants missed assessments for one or more of the seven cross-sectional surveys. ††Participants attended the assessments but refused rapid diagnostic testing or axillary temperature testing (see appendix 2 pp 13–15 for further details on missing survey data).

applied dose of insecticide, as measured using filter papers, was 1·34 g/m² higher than the recommended target dose of 1 g/m². No IRS-related adverse effects were recorded. In the villages that received BCC, 25 health workers conducted a total of 9460 communications (including home visits, interpersonal talks, and group talks) between September, 2017, and August, 2018, achieving 92% of the initial target of 10 257 communications.

During 20 months of pre-intervention and post-intervention follow-up (215 000 person-months; figure),

passive case detection in primary health centre registries identified 6089 medical visits, with age information available for 5739, of which 3612 resulted in a malaria case diagnosis among people of all ages. During the pre-intervention period, the crude incidence rates were 2·35, 1·36, and 3·34 cases per 100 person-months in the LLIN-alone control, LLIN plus BCC, and LLIN plus IRS groups, respectively (table 2). During the post-intervention period, the crude incidence rates were 1·38, 0·64, and 1·41 cases per 100 person-months in the LLIN-alone control, LLIN plus BCC, and LLIN plus IRS groups, respectively. Taking into account autocorrelation sources and assuming that pre-intervention differences occurred by chance, constrained baseline analysis indicated an average 22% reduction in incidence rate in the LLIN plus BCC group compared with the LLIN-alone group, when adjusted for country and age of cases (adjusted rate ratio [RR] 0·78 [95% CI 0·63–0·96], p=0·020; table 2). Although the post-intervention crude incidence rate estimate in the IRS group was close to that of the control group, constrained baseline analysis indicated an average 23% reduction in adjusted incidence rate (0·77 [0·64–0·93], p=0·0073; table 2). The effect size was not significantly different between countries (appendix 2 pp 9–10). The addition of our estimate to the Cochrane meta-analysis of non-pyrethroid-like IRS plus insecticide-treated nets versus insecticide-treated nets alone[21] resulted in an average effect size (RR) of 0·83 (0·66–1·06; appendix 2 pp 11–12).

A total of 5889 individuals aged 0–18 years (56·1% of the overall population) were registered in the 2016 census. After randomisation (and inclusion of an additional cluster in Côte d'Ivoire), the number of registered individuals aged 0–18 years was 5976 (55·6% of the overall population of 10750 inhabitants) for the post-intervention period, which was expected to yield 41 571 assessments (comprising interviews and clinical evaluations) over the course of the seven cross-sectional surveys (appendix 2 pp 13–14). A total of 26 673 assessments (64% participation) were performed during the cross-sectional surveys, of which 26 228 were kept for analysis (445 were excluded owing to absence of outcome data because participants refused rapid diagnostic testing or axillary temperature testing; figure). 3080 (12%) of the assessments resulted in diagnosis of a malaria episode. During the pre-intervention phase, the prevalence of cases among participants aged 0–18 years was 14%, 18%, and 11% in the LLIN-alone control, LLIN plus BCC, and LLIN plus IRS groups, respectively (table 2). During the post-intervention phase, case prevalence was 11%, 9%, and 9% in the LLIN-alone control, LLIN plus BCC, and LLIN plus IRS groups, respectively (table 2). Constrained baseline analysis indicated that the odds of diagnosing a malaria case among children and adolescents aged 0–18 years during the cross-sectional surveys, when adjusted for country and age group, were reduced in villages that received the BCC intervention by 40% on average (adjusted odds ratio [OR] 0·60 [95% CI 0·50–0·71], p<0·0001; table 2), but not in villages that received IRS (1·01 [0·82–1·25], p=0·94), compared with the LLIN-alone group. The effect of LLIN plus BCC was stronger in the group aged 6–18 years than in the group aged ≤5 years (OR ratio [ORR] 0·65 [95% CI 0·48–0·89], p=0·0063), and probably stronger in Côte d'Ivoire than in Burkina Faso (0·68 [0·45–1·01], p=0·058; appendix 2 pp 12–13). Results were not sensitive to constraint on baseline or missing data (appendix 2 pp 13–16).

Analysis of the prevalence of *P falciparum* infection showed that, in Burkina Faso, both interventions reduced the proportion of children and adolescents with positive blood smears as recorded during cross-sectional surveys,

	LLIN alone	LLIN plus BCC	LLIN plus IRS
Study clusters			
Number of clusters	16	12	11
Burkina Faso	8	6	5
Côte d'Ivoire	8	6	6
Population characteristics			
Population size per cluster	295·3 (106·5)	288·4 (102·0)	233·2 (49·2)
Participants aged 0–18 years (%)	57·5% (5·3)	54·0% (4·5)	57·0% (4·9)
People per household	6·14 (1·14)	5·49 (1·17)	5·73 (1·40)
Age (years)	22·2 (2·8)	24·3 (2·2)	23·5 (3·0)
Sex ratio (male:female)	0·83 (0·11)	0·80 (0·16)	0·82 (0·14)
Household characteristics			
Households with at least one LLIN (%)*	84·2% (18·7)	83·7% (16·9)	72·3% (26·5)
Households with adequate LLIN coverage (%)*	49·2% (24·1)	49·8% (25·3)	45·9% (28·3)

Data are n or mean (SD) calculated at the cluster level. Data are based on the 2016 population census. LLIN=long-lasting insecticidal net. BCC=behaviour change communication. IRS=indoor residual spraying. *Data on LLIN ownership and coverage in Côte d'Ivoire were collected before LLIN distribution.

Table 1: **Baseline characteristics**

	Pre-intervention	Post-intervention	Effect size* (95% CI)	p value	Adjusted† effect size* (95% CI)	p value
Incidence rate per 100 person-months (n cases/person-months of follow-up)						
LLIN	2·35 (1112/47 240)	1·38 (654/47 240)	1 (ref)	..	1 (ref)	..
LLIN plus BCC	1·36 (472/34 610)	0·64 (221/34 610)	0·73 (0·56–0·94)	0·014	0·78 (0·63–0·96)	0·020
LLIN plus IRS	3·34 (791/23 680)	1·41 (362/25 650)	0·73 (0·58–0·93)	0·0095	0·77 (0·64–0·93)	0·0073
Prevalence of cases (n cases/N assessments)						
LLIN	14% (701/4899)	11% (680/6173)	1 (ref)	..	1 (ref)	..
LLIN plus BCC	18% (674/3809)	9% (410/4819)	0·59 (0·50–0·71)	<0·0001	0·60 (0·50–0·71)	<0·0001
LLIN plus IRS	11% (305/2888)	9% (310/3640)	1·03 (0·83–1·28)	0·78	1·01 (0·82–1·25)	0·94

Incidence rates in the whole population based on passive case detection using health centre data (the primary outcome). Prevalence of malaria cases in participants aged 0–18 years based on cross-sectional survey data. LLIN=long-lasting insecticidal net. BCC=behaviour change communication. IRS=indoor residual spraying. *Rate ratios for incidence rates and odds ratios for case prevalence, according to constrained baseline analyses. †Adjusted for country and age group.

Table 2: **Effect of combination of LLINs with BCC or IRS versus LLINs alone on malaria incidence rates in the whole population and case prevalence in participants aged 0–18 years**

	Pre-intervention	Post-intervention	Constrained baseline analysis		Post-intervention-only analysis	
			Effect size* (95% CI)	p value	Effect size* (95% CI)	p value
Prevalence of *P falciparum* infection (n infected/N blood smears)						
Burkina Faso						
LLIN	39% (960/2466)	51% (1513/2950)	1 (ref)	..	..	..
LLIN plus BCC	38% (648/1706)	44% (957/2179)	0·70 (0·57–0·86)	0·0003	..	..
LLIN plus IRS	39% (538/1367)	37% (616/1670)	0·48 (0·38–0·59)	<0·0001	..	..
Côte d'Ivoire						
LLIN	..	87% (2810/3227)	..	..	1 (ref)	..
LLIN plus BCC	..	88% (2112/2401)	..	..	1·24 (0·58–2·65)	0·74
LLIN plus IRS	..	90% (1786/1994)	..	..	1·19 (0·56–2·52)	0·82
Parasite density per µL in asymptomatic participants, geometric mean (95% CI), N						
Burkina Faso						
LLIN	546 (484–615), 876	679 (619–744), 1371	1 (ref)	..	..	..
LLIN plus BCC	682 (589–790), 586	791 (702–890), 872	0·88 (0·69–1·12)	0·40	..	..
LLIN plus IRS	838 (719–977), 511	781 (671–910), 557	0·95 (0·73–1·24)	0·85	..	..
Côte d'Ivoire						
LLIN	..	102 (96–108), 2159	..	..	1 (ref)	..
LLIN plus BCC	..	118 (111–127), 1767	..	..	1·25 (0·83–1·87)	0·38
LLIN plus IRS	..	77 (72–83), 1404	..	..	0·77 (0·51–1·16)	0·28

Based on cross-sectional survey data. LLIN=long-lasting insecticidal net. BCC=behaviour change communication. IRS=indoor residual spraying. *Odds ratios for prevalence of infection and multiplicative coefficients for parasite density, adjusted for age group.

Table 3: **Effect of combination of LLINs with BCC or IRS versus LLINs alone on prevalence of *Plasmodium falciparum* infection and parasite density in participants aged 0–18 years**

when adjusted for age group, by an average of 30% for LLIN plus BCC (adjusted OR 0·70 [95% CI 0·57–0·86], p=0·0003; table 3) and 52% for LLIN plus IRS (0·48 [0·38–0·59], p<0·0001) compared with the LLIN-alone control group. In Côte d'Ivoire, using a post-intervention-only analysis, we did not detect any reduction in prevalence of *P falciparum* infection regardless of intervention type (1·24 [0·58–2·65], p=0·74 for LLIN plus BCC; 1·19 [0·56–2·52], p=0·82 for LLIN plus IRS; table 3).

We did not detect differences in parasite density in asymptomatic participants between either of the BCC or IRS intervention groups and the control group, regardless of country (table 3). During the post-intervention period, reported crude LLIN use was 74% (4732 of 6367 assessments) in villages that received LLIN alone, 72% (3492 of 4882 assessments) in those that received LLIN plus BCC, and 69% (2531 of 3663 assessments) in those that received LLIN plus IRS. Constrained baseline analysis indicated that the odds of reporting LLIN use, when adjusted for age, country, and night-time temperature, increased by 23% in villages in the LLIN plus BCC group (adjusted OR 1·23 [95% CI 1·04–1·47], p=0·015; appendix 2 p 17). For BCC, the odds of reporting LLIN use were greater in Côte d'Ivoire than in Burkina Faso (ORR 2·38 [95% CI 1·73–3·29], p<0·0001) and in the group aged 6–18 years than in the group aged ≤5 years (1·44 [1·16–1·78], p=0·0009; appendix 2 p 18). The odds of reporting LLIN use decreased by 19% in the LLIN plus IRS group (adjusted OR 0·81 [0·67–0·98], p=0·029) compared with the LLIN-alone group. For IRS, the odds were greater in the group aged ≤5 years than in the group aged 6–18 years (ORR 1·36 [1·08–1·70], p=0·0083), but there was no difference in effect size between countries.

We observed a reduction in *Anopheles* human biting rate, when adjusted for country, for the LLIN plus IRS group (adjusted RR 0·49 [95% CI 0·33–0.72], p<0·0001; table 4), but not for the LLIN plus BCC group (1·16 [0·82–1·64], p=0·53), compared with the control group. The IRS effect size for *Anopheles* human biting rate was not significantly different between countries (RR ratio [RRR] 1·76 [95% CI 0·83–3·72], p=0·14; appendix 2 pp 18–19). A similar trend was observed for nuisance biting, with a 60% average reduction in the LLIN plus IRS group (adjusted RR 0·40 [0·28–0·56], p<0·0001) compared with the control group, with no difference in effect size between countries for this intervention (RRR 0·93 [0·50–1·74], p=0·82; appendix 2 p 19), and no evidence of an effect of the LLIN plus BCC intervention (adjusted RR 1·12 [0·82–1·52], p=0·64). We also observed a strong reduction in the sporozoite infection rate (OR 0·21 [95% CI 0·05–0·83], p=0·023) and the entomological inoculation rate (RR 0·13 [0·03–0·67], p=0·011) in villages that received the BCC intervention in Côte d'Ivoire, but not in Burkina Faso, and not in the IRS group in either country (table 5). We did not find evidence of any effect of the interventions on parity rates (appendix 2 pp 19–20).

In Burkina Faso, median time of biting for *Anopheles* in villages in the LLIN plus IRS group was 3 h later than for those in control villages (p<0·0001), whereas biting time

	Pre-intervention	Post-intervention	Effect size* (95% CI)	p value
***Anopheles* nightly human biting rate (bootstrap 95% CI), bites/human-night**				
LLIN	31·60 (24·96–38·29), 14158/448	10·91 (8·86–13·23), 5588/512	1 (ref)	..
LLIN plus BCC	22·65 (17·62–28·10), 7609/336	8·94 (6·91–11·23), 3432/384	1·16 (0·82–1·64)	0·53
LLIN plus IRS	24·39 (19·07–30·07), 6828/280	7·21 (5·24–9·39), 2537/352	0·49 (0·33–0·72)	<0·0001
All mosquitoes nightly human nuisance biting rate (bootstrap 95% CI), bites/human-night				
LLIN	39·02 (32·95–45·32), 22478/576	12·22 (9·94–14·48), 6255/512	1 (ref)	..
LLIN plus BCC	24·30 (18·88–30·12), 8166/336	10·70 (8·41–13·15), 4109/384	1·12 (0·82–1·52)	0·64
LLIN plus IRS	26·79 (21·20–32·43), 7502/280	8·85 (6·37–11·35), 3115/352	0·40 (0·28–0·56)	<0·0001

Based on mosquito collections. LLIN=long-lasting insecticidal net. BCC=behaviour change communication. IRS=indoor residual spraying. *Rate ratios, adjusted for country, according to constrained baseline analyses.

Table 4: **Effect of combination of LLINs with BCC or IRS versus LLINs alone on *Anopheles* biting rates and mosquito nuisance biting in participants aged 0–18 years**

	Pre-intervention	Post-intervention	Constrained baseline analysis		Post-intervention-only analysis	
			Effect size* (95% CI)	p value	Effect size* (95% CI)	p value
Sporozoite infection prevalence (bootstrap 95% CI), n infected/N tested						
Burkina Faso						
LLIN	0·74% (0·18–1·48), 4/542	8·75% (2·53–15·00), 7/80	1 (ref)	..	..	..
LLIN plus BCC	3·05% (0·61–6·10), 5/164	10·81% (5·41–16·36), 12/111	1·43 (0·24–8·34)	0·85	..	..
LLIN plus IRS	0·92% (0·00–2·75), 1/109	13·33% (0·00–33·33), 2/15	1·28 (0·12–14·17)	0·95	..	..
Côte d'Ivoire						
LLIN	..	1·79% (1·09–2·57), 23/1283	..	..	1 (ref)	..
LLIN plus BCC	..	0·41% (0·00–0·95), 3/735	..	..	0·21 (0·05–0·83)	0·023
LLIN plus IRS	..	1·27% (0·57–2·12), 9/707	..	..	0·68 (0·27–1·73)	0·55
Nightly entomological inoculation rate (bootstrap 95% CI), infectious bites/human-night						
Burkina Faso						
LLIN	0·02 (0·00–0·05), 4/192	0·04 (0·01–0·07), 7/192	1 (ref)	..	..	..
LLIN plus BCC	0·03 (0·01–0·07), 5/144	0·08 (0·04–0·13), 12/144	1·63 (0·34–7·77)	0·70	..	..
LLIN plus IRS	0·01 (0·00–0·03), 1/120	0·02 (0·00–0·04), 2/120	0·63 (0·07–5·81)	0·84	..	..
Côte d'Ivoire						
LLIN	..	0·47 (0·23–0·80), 120/256	..	..	1 (ref)	..
LLIN plus BCC	..	0·08 (0·00–0·20), 14/183	..	..	0·13 (0·03–0·67)	0·011
LLIN plus IRS	..	0·11 (0·04–0·20), 21/189	..	..	0·42 (0·09–1·89)	0·34

Based on mosquito collections. LLIN=long-lasting insecticidal net. BCC=behaviour change communication. IRS=indoor residual spraying. *Odds ratios for sporozoite infection and rate ratios for entomological inoculation rate.

Table 5: **Effect of combination of LLINs with BCC or IRS versus LLINs alone on *Anopheles* sporozoite infection prevalence and entomological inoculation rate**

was not affected by the LLIN plus BCC intervention in this location (appendix 2 p 21). In Côte d'Ivoire, we observed a significant but marginal shift (<1 h; p<0·0001) in both LLIN plus IRS and LLIN plus BCC groups. Exophagy rates, adjusted for country, were higher in both the LLIN plus BCC group (adjusted OR 1·41 [95% CI 1·25–1·59], p<0·0001) and the LLIN plus IRS group (1·24 [1·08–1·43], p=0·0013) compared with the control group, with no differences in effect size between countries (ORR 1·31 [95% CI 0·79–2·19] for LLIN plus BCC; 0·76 [0·37–1·57] for LLIN plus IRS; appendix 2 pp 21–22).

In Côte d'Ivoire, mutation frequencies in villages that received the LLIN plus BCC intervention were higher for the Leu1014Phe mutation (OR 3·90 [95% CI 2·17–7·00], p<0·0001) and lower for the Gly119Ser mutation (0·74 [0·56–1·00], p=0·050) than in the control villages. There was no effect of the LLIN plus IRS intervention on mutation frequencies in Côte d'Ivoire or of either intervention on mutation frequencies in Burkina Faso (appendix 2 pp 20–21).

Discussion

This study reports the results of the REACT trial of LLIN plus BCC and LLIN plus IRS interventions compared with an LLIN-alone control in rural settings in west Africa. Both interventions reduced malaria incidence rate recorded in health centres, whereas only LLIN plus BCC reduced case prevalence recorded during cross-sectional

surveys. According to the case prevalence outcome, LLIN plus BCC was potentially more effective in Côte d'Ivoire. The two study areas (one in Côte d'Ivoire, one in Burkina Faso) differed in several characteristics, with higher vector density, higher levels of pirimiphos-methyl resistance,[22,23] higher endemicity (as indicated by infection prevalence), and higher immunity (as indicated by asymptomatic parasitaemia) in Côte d'Ivoire. This ecological and epidemiological variability could have contributed to differences in efficacy between countries. In addition, LLINs in Côte d'Ivoire were 1 year newer, meaning that they had higher efficacy and physical integrity compared with those in Burkina Faso. Furthermore, the additional effect of BCC might be diminished with older, damaged LLINs, as people might be less motivated to continue to use them.[24]

This trial showed that pirimiphos-methyl IRS, in addition to LLINs, reduced the malaria incidence rate, recorded by passive case detection, by an average of 23% compared with LLINs alone. This effect was weaker than that observed in Mozambique in an RCT evaluating the same IRS formulation.[9] However, we did not detect any significant effect of the additional IRS intervention on malaria case prevalence, as measured by cross-sectional surveys, in young people aged 0–18 years. Since passive case detection primarily detects symptomatic cases with high-grade fever,[18] younger children (aged ≤5 years) were, due to lower immunity, overrepresented in passive case detection data relative to true age distribution (appendix 2 pp 22–23); by contrast, the cross-sectional surveys included cases that were less severe and occurred more frequently in individuals with immunity (aged 6–18 years). A plausible explanation is that IRS did not provide sufficient protection for the 6–18-year age group because they spent more time away from home (eg, for schooling), reducing their exposure to IRS-treated environments.

Non-pyrethroid IRS appears to have variable efficacy depending on ecological or epidemiological settings. Indeed, among four trials included in the 2022 Cochrane meta-analysis of non-pyrethroid IRS,[21] two trials, in Mozambique and Sudan, reported a 35% reduction in malaria incidence, whereas two others, in Benin and Ethiopia, did not show any effect. Our study showed intermediate effects compared with these two groups of studies. A better understanding of the settings in which IRS works is therefore needed for spatial targeting of this intervention. The addition of our incidence data to the Cochrane meta-analysis did not change the finding that non-pyrethroid IRS reduces malaria incidence rate, and the level of evidence remained low (appendix 2 pp 11–12).

IRS significantly reduced the human biting rate by *Anopheles* and mosquito nuisance biting in both countries, as commonly observed with non-pyrethroid IRS.[21] This reduction in nuisance biting probably increased people's comfort and possibly reduced exposure to other mosquito-borne diseases. However, reduced nuisance biting might also lead to lower LLIN use rates,[25] as suspected in villages that received IRS. Although predictable, such an interaction between IRS and LLIN use has rarely been tested, and reports of decreased LLIN use rates where IRS has been implemented remain scarce.[10,26]

This trial also evaluated the efficacy of intensive, interpersonal communication-based BCC conducted by community health workers in addition to LLIN use. A large and growing body of evidence supports the effect of BCC programmes on malaria prevention and associated behaviours,[14,15,27] although this is the first evaluation of BCC efficacy in an RCT with epidemiological outcomes. We showed that BCC was associated with a 22% reduction in malaria cases recorded in health centres and a 40% reduction in case prevalence recorded during cross-sectional surveys of individuals aged 0–18 years. Interaction analyses showed that this intervention might have had different effects in Burkina Faso and Côte d'Ivoire. Although these differences might be due to the ages of LLINs varying between countries, we encourage future research to explore how contextual factors might influence BCC. The efficacy of intensive BCC can be explained, at least in part, by an increase in LLIN use (especially among young people aged 6–18 years), a behaviour targeted by the intervention. Our results are supported by those of Nkoka and colleagues,[28] who found, in Malawi, that health workers were the only source of messaging (compared with other forms of messaging such as television, radio, and newspapers) that explained both the increase in LLIN use and the reduction in infection. In our trial, we did not measure the effect of BCC on other targeted behaviours (cleaning environments, seeking and adhering to intermittent preventive treatment, and presenting sick children to health workers), and we therefore could not analyse the different pathways through which the intervention reduced malaria burden.

Another limitation of our study is that we could not prevent the spread of knowledge and healthy behaviour outside the villages that received BCC. Therefore, we cannot exclude the possibility that the BCC intervention had effects in villages in the control or IRS groups (eg, through interpersonal communications among families). If that occurred, it is unlikely that it affected our measurement of IRS efficacy, because both IRS and control groups would have been equally affected. However, if the BCC intervention spread to the control group, this could have resulted in an underestimation of its efficacy. This trial was a pragmatic trial in the sense that we did not interfere with the practices of NMCPs in either study area, with the goal of maintaining a control condition as close as possible to the standard malaria control strategy implemented by NMCPs. A consequence of this approach is that the NMCP in Burkina Faso began implementing seasonal malaria chemoprevention in the Diébougou health district in July, 2018, at the very end of the trial.

Seasonal malaria chemoprevention targeted children aged 3–59 months, representing 18% of the population. This intervention probably reduced the incidence rate recorded by passive case detection and might have decreased the power of analyses of passive case detection data.

A further limitation is that we did not quantify the activities of NMCPs and therefore could not precisely characterise BCC interventions in the control group, against which our intensive BCC programme was tested. Although population surveys in these countries indicated that rural populations had minimal exposure to malaria messages through interpersonal communication with health workers,[11,12] future studies should better characterise the BCC interventions of NMCPs.

Passive case detection has inherent limitations, including the underreporting or misclassification of cases. We implemented several measures to mitigate these issues, including assigning each village to a single designated health centre, regular data verification by dedicated project nurses, statistical adjustments to account for health centre performance and village-level variations, and complementary cross-sectional surveys to capture malaria cases independent of care-seeking behaviour. The cross-sectional surveys were, however, not performed on the entire population, preventing a full assessment of the intervention effects on malaria transmission reservoirs.

We detected differences in behaviours of vectors in terms of biting time and exophagy rates in both the BCC and IRS intervention clusters relative to the control group after intervention implementation. Such temporal and spatial avoidance responses to vector control have been documented in numerous locations across Africa.[29] Because growing evidence suggests that such behavioural shifts are at least moderately heritable,[30] efforts to monitor them should be integrated into all vector control programmes. In Côte d'Ivoire, the allelic frequency of the kdr-west (Leu1014Phe) mutation was increased in villages that received the LLIN plus BCC intervention, which aligns with the expected increased selection pressure due to higher LLIN use in this area. Pirimiphos-methyl IRS did not induce any detectable increase in Gly119Ser mutation frequencies, contrary to expectations.

Evaluation of any public health intervention should consider both its benefits and potential adverse effects.[31] Here, we attempted to anticipate and monitor possible unintended effects, particularly those related to *Anopheles* behavioural and physiological resistance. We also identified a possible negative interaction between IRS and LLIN use rates. However, other potential unintended adverse effects, such as long-term exposure of human populations to non-pyrethroid insecticides, remain unexplored in this trial and elsewhere, and thus warrant further investigation. Although designed to improve health behaviours, BCC strategies—as with any public health intervention—might carry the theoretical risk of unintended or unforeseen consequences, which remain underexplored in this study.

In conclusion, results of this study show that non-pyrethroid IRS can significantly reduce human biting rate by *Anopheles* and mosquito nuisance biting, although evidence for its effect on clinical outcomes is mixed. Therefore, considering this limitation, as well as the possible negative interaction between IRS and LLIN use, its high cost (appendix 2 p 22), and possible adverse effects due to toxicity (for people and the environment), we recommend careful consideration before implementation of non-pyrethroid IRS. This study also provides the first evidence for the epidemiological efficacy of a BCC intervention based on interpersonal communication in rural west African settings, where mass-media awareness campaigns rarely reach people.[11,12] Although further trials are needed, intensive BCC has shown promising results.

Contributors

NM, AAK, RKD, and CP were responsible for study conception. NM, IZ, S-BA, AAK, RKD, and CP were responsible for the study design. AS, NBT, BZ, DDS, DFDSH, and PT collected the data. IZ, S-BA, PT, and LPAA provided instrumentation, computing resources, and analysis tools. NM, BZ, DDS, and PT curated the data. NM did the formal statistical analysis. NM wrote the original draft. IZ, S-BA, AS, NBT, BZ, DDS, DFDSH, PT, LPAA, TL, AC, FF, KM, AAK, RKD, and CP reviewed and edited the manuscript. NM and PT were responsible for the preparation, creation, and presentation of the figure. NM, IZ, S-BA, LPAA, TL, AC, KM, AAK, RKD, and CP supervised the project. NM, FF, AAK, RKD, and CP were responsible for the management and coordination of the project. NM, AAK, RKD, and CP were responsible for funding acquisition. NM and CP have directly accessed and verified the underlying data reported in the manuscript. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests

BZ has been employed by Sumitomo Chemical UK since February, 2021, after completion of his participation in this study. Sumitomo Chemical UK had no role in the study design, data collection, data analysis, data interpretation, or writing of the report. All other authors declare no competing interests.

Data sharing

The study protocol and data collected from this study, including de-identified individual participant data and codes used for analyses, will be made available upon publication on DataSuds (https://doi.org/10.23708/MZ7KZZ) for non-commercial use only.

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References

1 WHO. World malaria report 2023. Geneva: World Health Organization, 2023. https://www.who.int/teams/global-malaria-programme/reports/world-malaria-report-2023 (accessed June 30, 2025).

2 Bhatt S, Weiss DJ, Cameron E, et al. The effect of malaria control on *Plasmodium falciparum* in Africa between 2000 and 2015. *Nature* 2015; **526:** 207–11.

3 Unwin HJT, Sherrard-Smith E, Churcher TS, Ghani AC. Quantifying the direct and indirect protection provided by insecticide treated bed nets against malaria. *Nat Commun* 2023; **14:** 676.

4 Mosha JF, Kulkarni MA, Lukole E, et al. Effectiveness and cost-effectiveness against malaria of three types of dual-active-ingredient long-lasting insecticidal nets (LLINs) compared with pyrethroid-only LLINs in Tanzania: a four-arm, cluster-randomised trial. *Lancet* 2022; **399:** 1227–41.

5 WHO. Global plan for insecticide resistance management in malaria vectors. Geneva: World Health Organization, 2012. https://www.who.int/publications/i/item/WHO-HTM-GMP-2012.5 (accessed June 30, 2025).

6 WHO, WHO Pesticide Evaluation Scheme & Working Group. Report of the sixteenth WHOPES working group meeting: WHO/HQ, Geneva, 22–30 July 2013: review of pirimiphos-methyl 300 CS, chlorfenapyr 240 SC, deltamethrin 62.5 SC-PE, Duranet LN, Netprotect LN, Yahe LN, Spinosad 83.3 monolayer DT, Spinosad 25 extended release GR. Geneva: World Health Organization, 2013. https://iris.who.int/handle/10665/90976 (accessed June 30, 2025).

7 Tangena J-AA, Hendriks CMJ, Devine M, et al. Indoor residual spraying for malaria control in sub-Saharan Africa 1997 to 2017: an adjusted retrospective analysis. *Malar J* 2020; **19:** 150.

8 Corbel V, Akogbeto M, Damien GB, et al. Combination of malaria vector control interventions in pyrethroid resistance area in Benin: a cluster randomised controlled trial. *Lancet Infect Dis* 2012; **12:** 617–26.

9 Chaccour C, Zulliger R, Wagman J, et al. Incremental impact on malaria incidence following indoor residual spraying in a highly endemic area with high standard ITN access in Mozambique: results from a cluster-randomized study. *Malar J* 2021; **20:** 84.

10 Protopopoff N, Mosha JF, Lukole E, et al. Effectiveness of a long-lasting piperonyl butoxide-treated insecticidal net and indoor residual spray interventions, separately and together, against malaria transmitted by pyrethroid-resistant mosquitoes: a cluster, randomised controlled, two-by-two factorial design trial. *Lancet* 2018; **391:** 1577–88.

11 Institut National de la Statistique et de la Démographie/Burkina Faso. Programme National de Lutte contre le Paludisme/Burkina Faso, ICF International. Enquete sur les indicateurs du paludisme (EIPBF) au Burkina Faso 2014. Rockville, Maryland, USA: Institut National de la Statistique et de la Démographie/Burkina Faso, Programme National de Lutte contre le Paludisme/Burkina Faso, and ICF International, 2015. http://dhsprogram.com/pubs/pdf/MIS19/MIS19.pdf (accessed June 30, 2025).

12 Breakthrough ACTION. Survey on the determinants of malaria-related behaviors in Côte d'Ivoire. Malaria behavior survey report. Baltimore, Maryland: Johns Hopkins Center for Communication Programs, 2019. https://malariabehaviorsurvey.org/wp-content/uploads/2020/12/Cote-dIvoire-MBS-Report-2019-En.pdf (accessed June 30, 2025).

13 Snyder LB. Health communication campaigns and their impact on behavior. *J Nutr Educ Behav* 2007; **39** (suppl): S32–40.

14 Ahmed SM, Hossain MS, Kabir M. Conventional or interpersonal communication: which works best in disseminating malaria information in an endemic rural Bangladeshi community? *PLoS One* 2014; **9:** e90711.

15 Orkoh E, Efobi U. Effects of behaviour change communication on knowledge and prevention of malaria among women in Ghana. *Eval Rev* 2024; **48:** 1050–87.

16 Taconet P, Zogo B, Soma DD, et al. *Anopheles* sampling collections in the health districts of Korhogo (Côte d'Ivoire) and Diébougou (Burkina Faso) between 2016 and 2018. *Gigabyte* 2023; **2023:** e83.

17 Henry M-C, Assi S-B, Rogier C, et al. Protective efficacy of lambda-cyhalothrin treated nets in *Anopheles gambiae* pyrethroid resistance areas of Côte d'Ivoire. *Am J Trop Med Hyg* 2005; **73:** 859–64.

18 Tiono AB, Kangoye DT, Rehman AM, et al. Malaria incidence in children in South-West Burkina Faso: comparison of active and passive case detection methods. *PLoS One* 2014; **9:** e86936.

19 Coffman CJ, Edelman D, Woolson RF. To condition or not condition? Analysing 'change' in longitudinal randomised controlled trials. *BMJ Open* 2016; **6:** e013096.

20 Hooper R, Forbes A, Hemming K, Takeda A, Beresford L. Analysis of cluster randomised trials with an assessment of outcome at baseline. *BMJ* 2018; **360:** k1121.

21 Pryce J, Medley N, Choi L. Indoor residual spraying for preventing malaria in communities using insecticide-treated nets. *Cochrane Database Syst Rev* 2022; **1:** CD012688.

22 Zogo B, Soma DD, Tchiekoi BN, et al. *Anopheles* bionomics, insecticide resistance mechanisms, and malaria transmission in the Korhogo area, northern Côte d'Ivoire: a pre-intervention study. *Parasite* 2019; **26:** 40.

23 Soma DD, Zogo BM, Somé A, et al. *Anopheles* bionomics, insecticide resistance and malaria transmission in southwest Burkina Faso: a pre-intervention study. *PLoS One* 2020; **15:** e0236920.

24 Toé LP, Skovmand O, Dabiré KR, et al. Decreased motivation in the use of insecticide-treated nets in a malaria endemic area in Burkina Faso. *Malar J* 2009; **8:** 175.

25 Moiroux N, Boussari O, Djènontin A, et al. Dry season determinants of malaria disease and net use in Benin, West Africa. *PLoS One* 2012; **7:** e30558.

26 Kenea O, Balkew M, Tekie H, et al. Impact of combining indoor residual spraying and long-lasting insecticidal nets on *Anopheles arabiensis* in Ethiopia: results from a cluster randomized controlled trial. *Malar J* 2019; **18:** 182.

27 The Health Communication Capacity Collaborative (HC3). Malaria SBCC evidence literature review. Baltimore, Maryland: Johns Hopkins Center for Communication Programs, 2017. https://behaviorchangeimpact.org/wp-content/uploads/2019/10/Malaria-SBCC-Evidence-Report_Final.pdf (accessed June 30, 2025).

28 Nkoka O, Chuang T-W, Chen Y-H. Influence of maternal exposure to malaria social and behavioral change messages and effectiveness of communication media on bed net use and malaria infection in Malawi. *Health Educ Behav* 2021; **48:** 179–89.

29 Carrasco D, Lefèvre T, Moiroux N, Pennetier C, Chandre F, Cohuet A. Behavioural adaptations of mosquito vectors to insecticide control. *Curr Opin Insect Sci* 2019; **34:** 48–54.

30 Govella NJ, Johnson PCD, Killeen GF, Ferguson HM. Heritability of biting time behaviours in the major African malaria vector *Anopheles arabiensis*. *Malar J* 2023; **22:** 238.

31 Lorenc T, Oliver K. Adverse effects of public health interventions: a conceptual framework. *J Epidemiol Community Health* 2014; **68:** 288–90.