


RESEARCH ARTICLE

Open Access



# Collateral benefits of ivermectin mass drug administration designed for malaria against headlice in Mopeia, Mozambique: a cluster randomised controlled trial

Joanna Furnival-Adams<sup>1,2\*</sup> , Amelia Houana<sup>3</sup>, Patricia Nicolas<sup>1,2,3</sup>, Julia Montaña<sup>1,2,3</sup>, Samuel Martinho<sup>3</sup>, Aina Casellas<sup>1</sup>, Hansel Mundaca<sup>1</sup>, Jenisse Mbanze<sup>3</sup>, Arlindo Soares<sup>3</sup>, Saimado Imputua<sup>3</sup>, Paula Ruiz-Castillo<sup>1</sup>, Marta Ribes<sup>1,2</sup>, Almudena Sanz<sup>1</sup>, Mussa Mamudo Salé<sup>3</sup>, Antonio Macucha<sup>3</sup>, Eldo Elobolobo<sup>3</sup>, Vegovito Vegove<sup>3</sup>, Victor Mutepa<sup>3</sup>, Humberto Munguambe<sup>3</sup>, Aida Xerinda<sup>3</sup>, Felisbela Materula<sup>3</sup>, Regina Rabinovich<sup>1,4</sup>, Francisco Saute<sup>3</sup> and Carlos Chaccour<sup>1,5,6</sup>

## Abstract

**Background** Headlice are prevalent worldwide, with a higher burden in rural, lower-middle income settings. They can cause intense itchiness, discomfort, and secondary bacterial infections with potentially serious consequences. Ivermectin is efficacious against headlice, and is also being evaluated as a malaria vector control tool. In this study, we explored risk factors for headlice, and assessed the efficacy of ivermectin mass drug administration (MDA) designed for malaria against headlice.

**Methods** We conducted an open-label, assessor-blind, cluster-randomized controlled trial in Mopeia, Mozambique. A single dose of ivermectin was given monthly to eligible humans or humans and livestock (humans: 400 µg/kg, livestock: 1% injectable 200 µg/kg) in 3 consecutive months during the rainy season. The control group received albendazole (humans only). Thirty-nine clusters (13 per arm) were randomly selected for the nested assessment of headlice prevalence. 1341 treated participants were followed up at least once, 1, 2 and 3 months and 382 untreated (ineligible) participants at 3 and 6 months after the first MDA round. Headlice diagnosis was determined by scalp examination. Logistic regression was used to identify risk factors for headlice at baseline, and to estimate the treatment effect at each time point.

**Results** A total of 1309 participants were included in the main analysis assessing ivermectin MDA efficacy, and 1332 in the risk factor analysis. The baseline headlice prevalence was 11%. Risk factors included living with a household member with head itch [adjusted odds ratio (aOR) = 48.63, 95% confidence interval (CI): 28.7–82.3, *P*-value < 0.0001], being female (aOR = 2.25, 95% CI: 1.33–3.80, *P*-value < 0.01), and using surface water as the main water (aOR = 2.37, 95% CI: 1.12–5.33, *P*-value = 0.04). The treated population receiving ivermectin had significantly lower odds of having headlice at 3 months compared to those receiving albendazole (aOR = 0.19, 95% CI: 0.04–0.91, *P*-value = 0.04). There was no indirect effect on headlice among children ineligible for treatment.

\*Correspondence:

Joanna Furnival-Adams  
joannafa28@gmail.com

Full list of author information is available at the end of the article



© The Author(s) 2025. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated in a credit line to the data.

**Conclusions** In a highly endemic setting, mass drug administration with ivermectin significantly reduces headlice infestation prevalence among those who receive the drug for three sequential months. The lack of effect among untreated, ineligible children implies that additional interventions would be needed to interrupt local transmission.

**Trial registration** This study is registered with ClinicalTrials.gov (NCT04966702).

**Keywords** Headlice, Ectoparasites, Mass drug administration, Ivermectin, Malaria

## Background

When malaria vector control tools such as indoor residual spraying (IRS) and insecticide treated nets (ITNs) were first being developed, their impact on nuisance parasites such as headlice and bedbugs contributed greatly to their acceptability and uptake [1–3]. Similarly, the early development of resistance in these ectoparasites during dichlorodiphenyltrichloroethane (DDT)-based IRS campaigns led to declines in acceptability and coverage [4, 5]. More recent studies have suggested that resistance in non-target ectoparasites continue to affect acceptability and usage of vector control tools [6–8]. However, the secondary effects on these ectoparasites and off-target diseases are rarely monitored in malaria vector control studies and campaigns.

Headlice infestations are estimated to affect 19% of schoolchildren worldwide, causing stigma and shame among affected individuals, as well as school and work absenteeism [9, 10]. The intense itchiness and discomfort caused by headlice infestations can lead to potentially serious secondary bacterial infections at the lesion sites. Although it has never been incriminated as a vector, some studies have suggested that, like body lice, they may have role in the transmission of *Borrelia* spp., the causal agent of Lyme disease, and relapsing fever [11, 12]. Data on the prevalence and economic burden of headlice is sparse, and the problem of headlice is likely neglected in rural, impoverished areas of the global South, where reporting systems are weak, and other health issues are prioritized [13–15].

A range of topical pediculicidal treatment methods exists including benzyl benzoate, permethrin, lindane, malathion, dimeticone, 1,2-octanediol, and ivermectin [16]. However, many of these are not widely accessible or used to treat headlice in lower-middle income countries. Alternatively, traditional medicines or non-insecticidal treatments can be used. Non-insecticidal treatments include mechanical removal of headlice using a comb, or hands, and head shaving. Resistance to pediculicides has been reported globally, however, most data on this comes from high income countries [17].

Ivermectin mass drug administration (MDA) has been used for decades in the control of endo- and

ectoparasites, and it is now under evaluation for use against malaria vectors [18]. If it demonstrates success, it will likely be scaled-up, covering a larger population than currently targeted by the Mectizan Donation Program, which targets onchocerciasis and lymphatic filariasis. Ivermectin is known to be efficacious against headlice when used either topically or orally [19–21]. However, to our knowledge, only one study has assessed the effect of ivermectin MDA (two doses 7 days apart of 200 µg/kg) on headlice [22]. This study reported a significant reduction in headlice prevalence of around 90%. In addition to this, a household-randomized study in Brazil assessed the impact of treating household contacts of headlice cases on their risk of re-infestation, and found that those living in households that received oral ivermectin were significantly more likely to be headlice free after 60 days [23]. Finally, a pilot study in Australia assessed the effect of headlice screening and treating cases and siblings within a school with oral ivermectin versus topical treatment, and the findings suggest that oral ivermectin is more effective than topical treatment [24]. The results from these studies suggest that similar effects may be observed in the context of ivermectin MDA for malaria in areas where headlice are prevalent.

Within a cluster-randomised trial that took place in Mopeia, Mozambique, assessing ivermectin MDA for malaria control, we assessed its impact on headlice prevalence, at both individual and community level, as well as the risk factors for having headlice, and compared the effects of the different treatment arms on headlice.

## Methods

### Study setting and design

The study took place between March and October 2022, in Mopeia, a rural district in Zambezia Province, central Mozambique, which remains highly endemic for malaria despite dual coverage with IRS and ITNs [25]. It has a population of approximately 131,000, and covers an area of 7671 km<sup>2</sup> [26].

The study was nested within a three-arm cluster-randomised controlled trial, aiming to assess the effect of ivermectin MDA on malaria transmission [27]. Each cluster consisted of a core area in which at least 35

children under 5 lived, and a buffer area with a radius of 400 m around the core. Written consent was obtained from all participants or their legal guardian. The following interventions were given once per month for three consecutive months: (a) ivermectin in humans: a single dose of 400 µg/kg in eligible humans; (b) ivermectin in humans and livestock: a single dose of 400 µg/kg in eligible humans plus 1% injectable ivermectin at a dose of 200 µg/kg to all pigs/cattle in the cluster; (c) control: albendazole was given to humans only at a single dose of 400 mg.

Ivermectin was purchased from Merck Sharp & Dohme (Haarlem, the Netherlands) as Stromectrol® and supplied in 3 mg tablets. Albendazole was purchased from Cipla (Mumbai, India) as 400 mg chewable tablets. All study drugs were delivered door-to-door and drug administration was directly observed by the responsible fieldworker. Within the main Broad One Health Endectocide-based Malaria Intervention in Africa (BOHEMIA) trial, two cohorts were followed up; the safety cohort, and the efficacy cohort. The safety cohort consisted of individuals who met the following criteria: weighing over 15 kg, ability to consent, and a negative pregnancy test for women aged between 13 and 49; and exclusion: known hypersensitivity to ivermectin or albendazole, risk of *Loa loa* as assessed by travel history, pregnancy, lactating in the first week postpartum, currently participating in another clinical trial, unwilling to consent or adhere to study procedures, severely ill, currently under treatment with inhibitors of cytochrome P450 3A or P-glycoprotein (see Supplementary File 1 for the full list of excluded drugs). The purpose of the safety cohort was to serve as delivery vehicle for the insecticidal intervention and to monitor the safety of the treatment regime. These participants were followed up at 1, 2 and 3 months after the first round of MDA.

The efficacy cohort consisted of children under 5 (the primary age group affected by malaria in the region). The purpose of this cohort was to assess the impact of the intervention on malaria. Participants in this cohort were followed up at 3 and 6 months after the first round of MDA.

This headlice sub-study included randomly selected participants from both cohorts. In the analysis, the safety cohort and any participants from the efficacy cohort who had taken ivermectin at least once were categorised as “treated”, and participants from the efficacy cohort who had not taken ivermectin were categorised as “untreated” regardless of their assignment arm.

#### Randomisation and sampling

During October 2020 to November 2021, a local demography survey took place under a separate protocol,

where all households were mapped and the population was enumerated [26]. Using this data, clusters were created, and randomized 1:1:1 to each intervention using a computer-generated random sequence. Study investigators were masked from the treatment allocation during the study, however, the study participants were aware of which intervention they received. Following treatment allocation, 13 clusters per arm (39 clusters in total) were randomly selected for follow-up of headlice. Within these clusters, all children enrolled into the efficacy cohort of the main study, and 40 participants enrolled into the safety cohort of the main study were randomly selected for inclusion in this study. Participants from the efficacy cohort were followed up at 3 and 6 months after the first round of MDA. Participants from the safety cohort were followed up 1, 2 and 3 months after the first round of MDA.

#### Outcomes

The primary outcome was headlice prevalence at 3 months. Secondary outcomes were headlice prevalence at 3 months in treated participants, and at 3 and 6 months in untreated participants.

As part of the main malaria trial, adverse events, and severe adverse events were monitored to assess the safety of the intervention. A Data Safety Monitoring Board was constituted, approved the protocol, received regular reports and met periodically throughout the study period. The safety data will be reported in a separate manuscript.

Fieldworkers were trained in headlice detection over a 2-day period by Joanna Furnival-Adams and Amelia Houana through power point presentations, exercises using a tablet, and written assessments. In the field, participant scalps were inspected visually in daylight or under a torchlight, and signs of headlice (live lice or eggs) were recorded. In the main analysis, only participants with live headlice were categorized as having headlice. Those found infested were offered a referral to the health facility.

#### Risk factor analysis variables

Baseline data on headlice, and data from a demographic survey that took place prior to the start of the trial were used to conduct the risk factor analysis. Household wealth index was calculated using a formula detailed in Xie et al. [28]. All variables were determined through a pre-designed questionnaire. Bed net use was a binary variable, assessed by asking the participant or their parent/guardian whether they slept under a bed net the previous night. Details of how water sources were categorised are provided in Supplementary File 2 [29]. Open

defecation refers to those whose household does not have a sanitation facility available to them.

### Statistical analysis

The sample size of this nested study was calculated to detect a significant difference between the control and the treatment arms in scabies prevalence, which was another outcome that will be reported in a separate publication (Furnival-Adams et al., *submitted*). Assuming a 7% baseline scabies prevalence in the control group, a cluster size of 40 participants with 13 clusters per arm was required to detect a 60% effect size with 80% power at 5% significance and a kappa of 0.25.

For the risk factor analysis, logistic regression using the lme4 R package (v1.1–26) was used to conduct bivariate and multivariate analyses in the R programming language, version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria). In all analyses, odds ratios or adjusted odds ratios (aORs) with 95% confidence interval (CI) were calculated. All variables associated with headlice in bivariate analysis ( $P < 0.10$ ) were assessed for inclusion in multivariate analysis. Variables that were statistically significantly associated with headlice ( $P < 0.05$ ) were included in the multivariate model.

To assess the treatment effect, we compared headlice prevalence in the control versus the treatment arms at each time point, using logistic regression model. To account for correlation between clusters, we used generalised estimating equations to fit each logistic model of prevalence to the available data. Known risk factors of headlice, age, sex and wealth, were included as covariates in the adjusted models. These data were collected during the census survey that took place prior to the start of the trial. Intervention effects were expressed as adjusted odds ratios. After analysing the data, we found no statistically significant difference between the two treatment arms (human and human + livestock) existed, and therefore pooled the two intervention arms. Statistical significance was considered when the  $P$ -value was  $< 0.05$  using to the Wald test.

This study was conducted in accordance with the CONSORT guidelines for reporting randomized controlled trials (Supplementary File 3) [30].

## Results

### Enrolment and baseline characteristics of the study population

Between March 2022 and October 2022, 102 clusters were enrolled into the main malaria trial, and of these, 39 clusters were randomly selected for this nested headlice study. 1500 participants were randomly selected to be included in this nested study from the participants enrolled into the main trial, and 1309 were included in

the final analysis. The estimated treatment coverage ranged from 50% to 67% per round in eligible participants, and 43% to 52% in the overall population (eligible and ineligible to take ivermectin) (Supplementary File 4). The coverage was similar across arms and across all visits. Further information on the cluster and participant selection process is detailed in a separate publication [31].

At baseline, characteristics of the households and participants were similar across all three intervention arms (Table 1). The median age of participants who took the study drug was 19 years old, and it was 3 years old in the ineligible population. The sex distribution was balanced across all arms in both cohorts. The majority of participants were categorised as being in Rank 2 or 3 according to the wealth rank index in both cohorts. The overall baseline prevalence of headlice was 9.8% in the treated cohort and 9.1% in the untreated cohort.

### Headlice risk factors

The risk factors identified for headlice infestation at baseline are shown in Table 2.

Of the covariates assessed, four were significantly associated with headlice. Having another household member with an itchy head, female sex, practising open defecation, and using surface water as the principal water source were each associated with having headlice.

In the multivariate regression analysis, having another household member with an itchy head (aOR = 48.63, 95% CI: 28.7–82.3,  $P$ -value  $< 0.0001$ ), being female (aOR = 2.25, 95% CI: 1.33–3.80,  $P$ -value  $< 0.01$ ) and using surface water as the main water source (aOR = 2.37, 95% CI: 1.12–5.33,  $P$ -value = 0.04) were the strongest predictors of headlice. Practising open defecation was considered for inclusion in the model, however, it was no longer statistically significant in the multivariate model.

### Treatment seeking behaviour in participants with headlice

Regarding treatment-seeking, 13.3% (95% CI: 11.5–15.2,  $n = 1345$ ) of participants reported having headlice in the previous month. Of these participants, 3.9% (95% CI: 1.6–7.9,  $n = 179$ ) sought treatment, and 71.4% (95% CI: 29.0–96.3,  $n = 7$ ) of those who sought treatment reported it to be effective.

### The efficacy of ivermectin MDA against headlice

There were lower odds of having headlice in the overall populations of the ivermectin arms compared to the control arm 3 months after the first dosing (aOR = 0.27, 95% CI: 0.06–1.15) (Table 3). Whilst there was a strong tendency towards a reduction in headlice in the ivermectin arms, this difference was not statistically significant.

In participants who took ivermectin, there was a significant difference in the odds of having headlice prevalence

**Table 1** Baseline sociodemographic characteristics of the study population in the treated and untreated population in each study arm

| Variable                      | Humans                   | Humans and livestock     | Control                  |
|-------------------------------|--------------------------|--------------------------|--------------------------|
| Treated                       |                          |                          |                          |
| Number of clusters            | 13                       | 13                       | 13                       |
| Number of participants        | 307                      | 347                      | 348                      |
| Household wealth index rank   |                          |                          |                          |
| Rank 1 <sup>a</sup>           | 56/307 (18.2%)           | 27/344 (7.8%)            | 42/346 (12.1%)           |
| Rank 2                        | 62/307 (20.2%)           | 101/344 (29.4%)          | 97/346 (28.0%)           |
| Rank 3                        | 78/307 (50.6%)           | 79/344 (23.0%)           | 81/346 (23.4%)           |
| Rank 4                        | 46/307 (15.0%)           | 65/344 (18.6%)           | 82/346 (23.7%)           |
| Rank 5                        | 65/307 (21.2%)           | 72/344 (20.9%)           | 44/346 (12.7%)           |
| Median age in years (IQR) [n] | 20.81 (9.31–39.40) [307] | 18.90 (7.92–34.47) [347] | 18.90 (7.92–34.47) [347] |
| Sex: female                   | 155/307 (50.5%)          | 167/347 (48.1%)          | 166/348 (47.7%)          |
| Median weight (SD) [n]        | 40 (25) [307]            | 40 (30) [347]            | 40 (28) [348]            |
| Headlice prevalence           | 23/304 (7.6%)            | 35/347 (10.1%)           | 39/344 (11.3%)           |
| Untreated, ineligible under 5 |                          |                          |                          |
| Number of clusters            | 13                       | 13                       | 13                       |
| Number of participants        | 111                      | 106                      | 125                      |
| Household wealth index rank   |                          |                          |                          |
| Rank 1 <sup>a</sup>           | 13/108 (12.0%)           | 5/104 (4.8%)             | 13/123 (10.6%)           |
| Rank 2                        | 23/108 (21.3%)           | 23/104 (22.1%)           | 27/123 (22.0%)           |
| Rank 3                        | 19/108 (17.6%)           | 27/104 (26.0%)           | 40/123 (32.5%)           |
| Rank 4                        | 17/108 (15.7%)           | 25/104 (24.0)            | 28/123 (22.8%)           |
| Rank 5                        | 36/108 (33.3)            | 24/104 (23.1)            | 15/123 (12.2%)           |
| Median age in years (IQR) [n] | 2.8 (1.7–3.9) [111]      | 2.8 (1.8–4.0) [106]      | 2.8 (2.0–3.8) [125]      |
| Sex: female                   | 61/111 (55.0%)           | 52/106 (49.0%)           | 59/125 (47.2%)           |
| Median weight (kg) (SD) [n]   | 11 (3) [111]             | 11 (3) [106]             | 11 (4) [125]             |
| Headlice prevalence           | 13/111 (11.7%)           | 10/106 (9.4%)            | 8/125 (6.4%)             |

<sup>a</sup> Wealthiest

SD standard deviation, IQR interquartile range

between arms, with significantly lower odds of having headlice in the intervention arms after 3 months in participants who took the drug (aOR=0.19, 95% CI: 0.04–0.91) (Table 4) (Fig. 1). The effect on headlice was statistically significant after 2 months, and the effect size gradually increased after each consecutive month. There was no significant difference when comparing the two ivermectin arms, therefore we pooled the data from these arms. We found no evidence of an indirect impact of ivermectin MDA on headlice in the ineligible, untreated population who did not take the study drug at any time point (Supplementary File 5).

## Discussion

In this study, we described headlice epidemiology in Mopeia, Mozambique, and assessed the effect of ivermectin MDA on headlice prevalence within a cluster-randomised controlled trial. We found that the baseline prevalence of headlice was approximately 10% in the

study area, and having headlice was significantly associated with having another household member with an itchy head; being female; and having surface water as the main water source. We also found that only a small proportion of those who believed they have headlice sought treatment. Finally, ivermectin MDA designed for malaria (with a higher dosage and frequency of dosages compared to those used for MDA programmes for onchocerciasis and lymphatic filariasis), significantly reduced the odds of having headlice by around 78% after 3 months in the population who took the study drug. However, in participants who were ineligible to take ivermectin, no effect was observed. Within the main trial, there was no statistically significant difference in the rate of severe adverse events between the ivermectin and albendazole arms.

The findings show that headlice are common in the district of Mopeia, and that infestations are clustered within households. Regions with inadequate access to safe water and sanitation facilities, such as Mopeia,

**Table 2** Sociodemographic and water and sanitation-related risk factors for headlice infestation (bivariate analysis) at baseline

| Variable  | n/N      | Prevalence          | OR (95% CI)      | P-value            |
|---|----------|---------------------|------------------|--------------------|
| Sex   |          |                     |                  |                    |
| Male  | 47/678   | 6.93 (5.14–9.11)    | REF              |                    |
| Female  | 81/654   | 12.38 (9.96–15.16)  | 1.90 (1.3–2.8)   | <b>0.0009</b>      |
| Age, years  |          |                     |                  |                    |
| 0–4   | 26/310   | 6.93 (5.14–9.11)    | REF              |                    |
| 4–11  | 39/355   | 12.38 (9.96–15.16)  | 1.90 (1.3–2.8)   | 0.261              |
| 11–29   | 34/343   | 6.93 (5.14–9.11)    | REF              | 0.500              |
| > 29  | 29/324   | 12.38 (9.96–15.16)  | 1.90 (1.3–2.8)   | 0.801              |
| Another member of the household has an itchy head |          |                     |                  |                    |
| Yes   | 101/181  | 55.8 (48.2–63.2)    | 52.6 (32.5–85.0) | <b>&lt; 0.0001</b> |
| No  | 27/1,151 | 2.3 (1.6–3.4)       | REF              |                    |
| Household size (members)                          |          |                     |                  |                    |
| < 5   | 76/699   | 10.87 (8.66–13.42)  | REF              |                    |
| > 5   | 52/633   | 8.21 (6.20–10.63)   | 0.73 (0.51–1.06) | 0.10               |
| Wealth index rank                                 |          |                     |                  |                    |
| Rank 1 <sup>c</sup>                               | 17/154   | 11.04 (6.56–17.09)  | REF              |                    |
| Rank 2  | 27/335   | 8.06 (5.38–11.51)   | 0.75 (0.38–1.51) | 0.42               |
| Rank 3  | 26/325   | 8.00 (5.29–11.50)   | 0.69 (0.34–1.40) | 0.31               |
| Rank 4  | 29/261   | 11.11 (7.57–15.57)  | 1.15 (0.58–2.28) | 0.69               |
| Rank 5  | 29/252   | 11.51 (7.84–16.11)  | 1.04 (0.52–2.08) | 0.91               |
| Animal ownership <sup>a</sup>                     |          |                     |                  |                    |
| Yes   | 42/454   | 9.25 (6.75–12.30)   | 0.94 (0.63–1.39) | 0.76               |
| No  | 79/808   | 9.78 (7.82–12.04)   | REF              |                    |
| Open defecation <sup>b</sup>                      |          |                     |                  |                    |
| Yes   | 81/675   | 12.00 (9.64–14.69)  | 1.86 (1.26–2.78) | 0.002              |
| No  | 40/588   | 6.80 (4.90–9.15)    | REF              |                    |
| Water source                                      |          |                     |                  |                    |
| Safely managed                                    | 12/97    | 12.37 (6.56–20.61)  | 1.99 (0.99–3.98) | 0.053              |
| Basic   | 35/528   | 6.63 (4.66–9.10)    | REF              |                    |
| Limited   | 18/194   | 9.28 (5.59–14.27)   | 1.44 (0.80–2.61) | 0.228              |
| Unimproved  | 25/233   | 10.73 (7.07–15.43)  | 1.69 (0.99–2.90) | 0.055              |
| Surface   | 20/99    | 20.20 (12.80–29.46) | 3.57 (1.96–6.49) | <b>&lt; 0.0001</b> |
| Bed net use                                       |          |                     |                  |                    |
| Yes   | 89/871   | 10.22 (8.29–12.42)  | 1.45 (0.90–2.35) | 0.124              |
| No  | 23/317   | 7.26 (4.65–10.69)   | REF              |                    |

<sup>a</sup> Any of the following animals: cats, dogs, chickens, cattle, pigs, goats or sheep <sup>b</sup>we planned to classify sanitation according to the DHS/WHO as Safely Managed, Basic, Limited, Unimproved, or Open Defecation, however, only 12 participants were classified in the former 3 categories. We therefore chose to classify participants according to whether they practised open defecation. <sup>c</sup>Wealthiest, OR odds ratio, CI confidence interval, REF reference

**Table 3** Effect of ivermectin MDA on headlice prevalence at 3 months in the overall population (both treated and untreated)

| Population             | n/N    | Headlice prevalence, % (95% CI) | Unadjusted OR (95% CI) | P-value | Adjusted OR* (95% CI) | P-value |
|------------------------|--------|---------------------------------|------------------------|---------|-----------------------|---------|
| Control                |        |                                 |                        |         |                       |         |
| 3 months               | 50/452 | 11.06 (8.32–14.32)              | –                      | –       | –                     | –       |
| Ivermectin arms pooled |        |                                 |                        |         |                       |         |
| 3 months               | 47/857 | 5.48 (4.06–7.22)                | 0.59 (0.16–2.16)       | 0.43    | 0.27 (0.06–1.15)      | 0.08    |

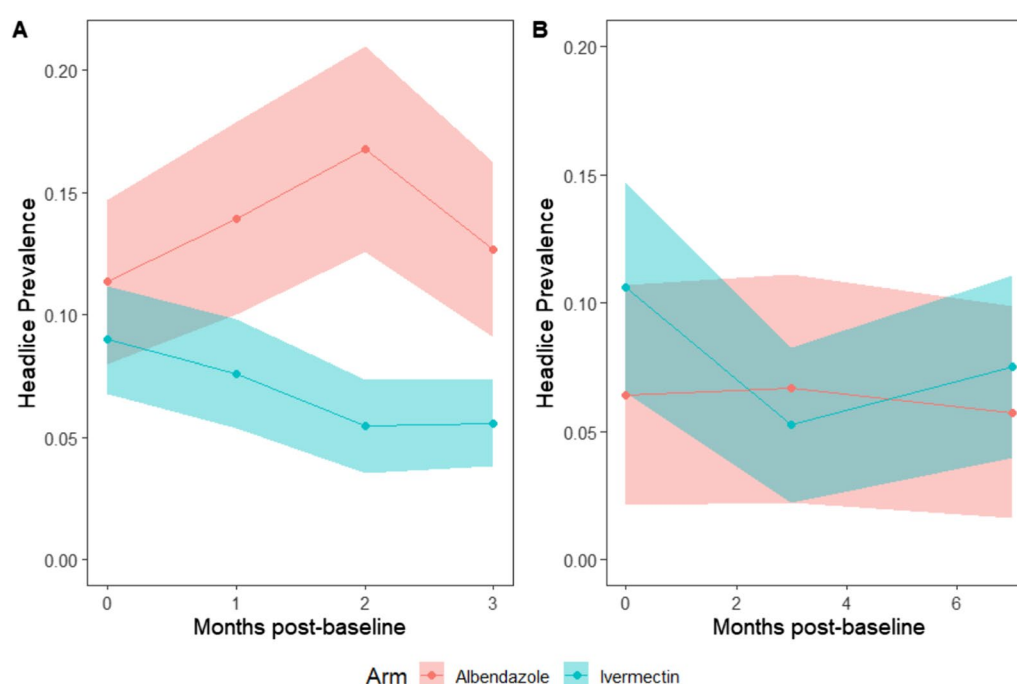
\* Adjusted for baseline headlice prevalence, age, sex and wealth. – means not applicable, OR odds ratio, MDA mass drug administration



**Table 4** Direct protection in treated participants

| Population             | n/N    | Headlice prevalence, % (95% CI) | Unadjusted OR (95% CI) | P-value | Adjusted OR <sup>a</sup> (95% CI) | P-value |
|------------------------|--------|---------------------------------|------------------------|---------|-----------------------------------|---------|
| Control                |        |                                 |                        |         |                                   |         |
| 1 month                | 41/294 | 13.95 (10.20–18.44)             | –                      | –       | 1 (REF)                           | –       |
| 2 months               | 51/304 | 16.78 (12.75–21.46)             | –                      | –       | 1 (REF)                           | –       |
| 3 months               | 42/332 | 12.65 (9.27–16.71)              | –                      | –       | 1 (REF)                           | –       |
| Ivermectin arms pooled |        |                                 |                        |         |                                   |         |
| 1 month                | 41/541 | 7.58 (5.49–10.14)               | 0.59 (0.21–1.62)       | 0.303   | 0.41 (0.13–1.25)                  | 0.116   |
| 2 months               | 30/551 | 5.44 (3.70–7.68)                | 0.37 (0.12–1.11)       | 0.077   | 0.29 (0.10–0.81)                  | 0.018   |
| 3 months               | 36/647 | 5.56 (3.93–7.62)                | 0.51 (0.15–1.74)       | 0.285   | 0.19 (0.04–0.91)                  | 0.038   |

<sup>a</sup> Adjusted for baseline headlice prevalence, age, sex and wealth. – means not applicable. OR odds ratio

**Fig. 1** Headlice prevalence in albendazole and ivermectin arms in **A**) treated participants, and **B**) ineligible, untreated participants

may be at higher risk of headlice. Whilst headlice are primarily spread through person-to-person contact, access to clean water, sanitation and hygiene, and regular washing likely reduces transmission through mechanical removal of headlice [32]. Poor water and sanitation conditions may therefore indirectly propagate the spread of headlice. These risk factors have also been identified in previous studies [9, 32, 33]. Being female is a risk factor for headlice in many settings, most likely due to the tendency for females to have longer hair [34, 35]. The low levels of treatment-seeking behaviour may suggest that treatments are not available or affordable, or that headlice are not perceived as a

health issue amongst the community. Further research would be needed to understand this better.

The significant impact that we observed on headlice for those who took ivermectin may have an important role in improving the quality of life of participants, as well as the acceptability of the malaria intervention, and its perceived efficacy. The effect we observed in the treated cohort is consistent with a previous before–after study that took place in the Solomon Islands that indicated a relative reduction of 70% [22]. However, the lack of an effect in those not taking ivermectin reduces its potential, as a stand-alone intervention, to control headlice at a community level. Ivermectin is not ovicidal, therefore a second dose of ivermectin is typically

recommended 7 days after the first dose to target eggs that are not targeted with the first dose. However, in this study, only a single dose was given per month, which suggests that a single dose can effectively treat headlice. Further research on the pharmacokinetics of 400 µg/kg ivermectin for headlice would be needed to understand this effect.

Our study has some limitations. The fieldworkers examining participants' scalps were not able to use a comb, so it is possible that we underestimated the prevalence of headlice. The follow-up period of 3 months is relatively short; it is not clear whether the reduction in headlice would be sustained beyond the follow-up points in our study.

## Conclusions

In this study, we identified some risk factors of headlice, namely having another household member with an itchy head; being female; and having surface water as the main water source. We also found that ivermectin MDA designed for malaria offers an opportunity to target headlice infestations in the eligible population. This implies that there are secondary benefits to implementing ivermectin MDA for malaria in co-endemic areas, which has implications for the quality of life amongst the community, as well as the acceptability of the intervention.

## Abbreviations

|       |                                 |
|-------|---------------------------------|
| MDA   | Mass drug administration        |
| IRS   | Indoor residual spraying        |
| ITN   | Insecticide-treated net         |
| DDT   | Dichlorodiphenyltrichloroethane |
| CYP3A | Cytochrome P450A                |
| CI    | Confidence interval             |
| OR    | Odds ratio                      |
| P-gp  | P-glycoprotein                  |
| GEE   | Generalized estimating equation |

## Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s40249-025-01290-z>.

Supplementary Material 1  
Supplementary Material 2  
Supplementary Material 3  
Supplementary Material 4  
Supplementary Material 5  
Supplementary Material 6  
Supplementary Material 7

## Acknowledgements

We acknowledge the support from staff at CISM, and are very grateful for the involvement of all participants. We acknowledge that data from this study were presented at ASTMH, Chicago, October 2023.

## Author contributions

Conceptualisation: JFA, CCh, RR. Data curation: EE, VV. Formal analysis: JFA, CCh. Investigation: JFA, AH, FS, PN, JM, SM, HM, JM, AS, SI, PRC, MR, AS, MS, AM, VM, HM, AX, FM. Methodology: JFA, RR, CCh. Supervision: CCh, FS. Writing—original draft: JFA, CCh. Writing—review & editing: all authors contributed, reviewed and approved the last draft.

## Funding

This study was funded and supported by Unitaid under the BOHEMIA grant. The funder had no role in the decision to submit this manuscript for publication. ISGlobal acknowledges support from the Spanish Ministry of Science and Innovation through the “Centro de Excelencia Severo Ochoa 2019–2023” Program (CEX2018-000806-S), and support from the Generalitat de Catalunya through the CERCA program.

## Availability of data and materials

Anonymized individual data relevant to this article is available in Supplementary File 6, and the corresponding code is in Supplementary File 7.

## Declarations

### Ethics approval and consent to participate

The study protocol was approved by the Internal Scientific Committee and Institutional Review board from the Centro de Investigação em Saúde de Manhiça (Ref: CIBS-CISM/004/2021), Hospital Clinic of Barcelona Clinical Research Ethics Committee (ISGlobal's Internal Review Board) (Ref: HCB/2019/0938) and The Ethics Research Committee of the WHO (Protocol ID: ERC.0003265). Written consent was obtained from all adult participants, and assent was obtained from parent/guardian's of children aged between 12–17. For children under 12, consent was obtained from their parent/guardian. All records that contained names or other personal identifiers, such as locator forms, participant identification code list and informed consent forms, were stored separately from study records identified by code number.

### Consent for publication

Not applicable.

### Competing interests

The authors declare that they have no competing interests.

### Author details

<sup>1</sup>ISGlobal, Barcelona Institute for Global Health, Barcelona, Spain. <sup>2</sup>Facultat de Medicina i Ciències de La Salut (Faculty of Medicine and Health Sciences), Universitat de Barcelona (University of Barcelona), Barcelona, Spain. <sup>3</sup>Centro de Investigação em Saúde de Manhiça (Manhiça Health Research Centre), Mopeia, Mozambique. <sup>4</sup>Harvard T.H. Chan School of Public Health, Boston, USA. <sup>5</sup>CIBERINFEC, Madrid, Spain. <sup>6</sup>Navarra Center for International Development, Universidad de Navarra, Pamplona, Spain.

Received: 7 October 2024 Accepted: 2 March 2025

Published online: 27 March 2025

## References

1. Lindsay SW, Snow RW, Armstrong JRM, Greenwood BM. Permethrin-impregnated bednets reduce nuisance arthropods in Gambian houses. *Med Vet Entomol*. 1989;3:377–83.
2. Temu EA, Minjas JN, Shiff CJ, Majala A. Bedbug control by permethrin-impregnated bednets in Tanzania. *Med Vet Entomol*. 1999;13:457–9.
3. Sharma SK, Upadhyay AK, Haque MA, Padhan K, Tyagi PK, Ansari MA, et al. Wash resistance and bioefficacy of Olyset net—a long-lasting insecticide-treated mosquito net against malaria vectors and nontarget household pests. *J Med Entomol*. 2006;43(5):884–8.
4. Gunasekaran K, Sahu SS, Jambulingam P, Das PK. DDT indoor residual spray, still an effective tool to control *Anopheles fluviatilis*-transmitted *Plasmodium falciparum* malaria in India. *Trop Med Int Heal*. 2005;10(2):160–8.



5. Myamba J, Maxwell CA, Asidi A, Curtis CF. Pyrethroid resistance in tropical bedbugs, *Cimex hemipterus*, associated with use of treated bednets. *Med Vet Entomol*. 2002;16:448–51.
6. Malede A, Aemero M, Gari SR, Kloos H, Alemu K. Barriers of persistent long-lasting insecticidal nets utilization in villages around Lake Tana, Northwest Ethiopia: a qualitative study. *BMC Public Health*. 2019;19(1):1–11.
7. Liheluka EA, Massawe IS, Chiduo MG, Mandara CI, Chacky F, Ndekuka L, et al. Community knowledge, attitude, practices and beliefs associated with persistence of malaria transmission in North-western and Southern regions of Tanzania. *Malar J*. 2023;22(1):1–16.
8. Parker W, Pennas T, Kommwa I. Community health priorities: lessons for malaria prevention from Balaka district. *Malawi Med J*. 2018;30(2):99–102.
9. Jamani S, Rodríguez C, Rueda MM, Matamoros G, Canales M, Bearman G, et al. Head lice infestations in rural Honduras: the need for an integrated approach to control neglected tropical diseases. *Int J Dermatol*. 2019;58(5):548–56.
10. Hatam-Nahavandi K, Ahmadpour E, Pashazadeh F, Dezhkam A, Zarean M, Rafiei-Sefiddashti R, et al. Pediculosis capitis among school-age students worldwide as an emerging public health concern: a systematic review and meta-analysis of past five decades. *Parasitol Res*. 2020;119(10):3125–43.
11. Amanzougaghene N, Akiana J, Mongo Ndombe G, Davoust B, Nsana NS, Parra HJ, et al. Head lice of pygmies reveal the presence of relapsing fever borreliae in the Republic of Congo. *PLoS Negl Trop Dis*. 2016;10(12):e0005142.
12. Feldmeier H. Head lice as vectors of pathogenic microorganisms. *Trop Med Health*. 2023;51(1):53.
13. Coscione S, Kositz C, Marks M. Head lice: an under-recognized tropical problem. *Am J Trop Med Hyg*. 2017;97(6):1636–7.
14. Dagne H, Biya AA, Tirfie A, Yallew WW, Dagnew B. Prevalence of pediculosis capitis and associated factors among schoolchildren in Woreta town, northwest Ethiopia. *BMC Res Notes*. 2019;12(1):1–6.
15. Manrique-Saide P, Pavia-Ruz N, Rodríguez-Buenfil JC, Herrera Herrera R, Gómez-Ruiz P, Pilger D. Prevalence of pediculosis capitis in children from a rural school in Yucatan, Mexico. *Rev Inst Med Trop Sao Paulo*. 2011;53(6):325–7.
16. Sangaré AK, Doumbo OK, Raoult D. Management and treatment of human lice. *Biomed Res Int*. 2016;2016:8962685.
17. Durand R, Bouvresse S, Berdjane Z, Izri A, Chosidow O, Clark JM. Insecticide resistance in head lice: clinical, parasitological and genetic aspects. *Clin Microbiol Infect*. 2012;18(4):338–44.
18. Billingsley P, Binka F, Chaccour C, Foy BD, Gold S, Gonzalez-Silva M, et al. A roadmap for the development of ivermectin as a complementary malaria vector control tool. *Am J Trop Med Hyg*. 2020;102(2\_suppl):3–24.
19. Deeks LS, Naunton M, Currie MJ, Bowden FJ. Topical ivermectin 0.5% lotion for treatment of head lice. *Ann Pharmacother*. 2013;47(9):1161–7.
20. Chosidow O, Giraudeau B, Cottrell J, Izri A, Hofmann R, Mann SG, et al. Oral ivermectin versus malathion lotion for difficult-to-treat head lice. *N Engl J Med*. 2010;362(10):896–905.
21. Nofal A. Oral ivermectin for head lice: a comparison with 0.5 % topical malathion lotion. *J Dtsch Dermatol Ges*. 2010;8(12):985–8.
22. Coscione S, Esau T, Kekeubata E, Diau J, Asugeni R, MacLaren D, et al. Impact of ivermectin administered for scabies treatment on the prevalence of head lice in Atoifi, Solomon Islands. *PLoS Negl Trop Dis*. 2018;12(9):e0006825.
23. Pilger D, Heukelbach J, Khakban A, Oliveira FA, Fengler G, Feldmeier H. Household-wide ivermectin treatment for head lice in an impoverished community: randomized observer-blinded controlled trial. *Bull World Health Organ*. 2010;88(2):90–6.
24. Currie MJ, Reynolds GJ, Glasgow NJ, Bowden FJ. A pilot study of the use of oral ivermectin to treat head lice in primary school students in Australia. *Pediatr Dermatol*. 2010;27(6):595–9.
25. Chaccour C, Zulliger R, Wagman J, Casellas A, Nacima A, Elobolobo E, 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(1):1–15.
26. Ruiz-Castillo P, Imputiua S, Xie K, Elobolobo E, Nicolas P, Montaña J, et al. BOHEMIA a cluster randomized trial to assess the impact of an endectocide-based one health approach to malaria in Mozambique: baseline demographics and key malaria indicators. *Malar J*. 2023;22(1):1–12.
27. Chaccour C, Casellas A, Hammann F, Ruiz-Castillo P, Nicolas P, Montaña J, et al. BOHEMIA: Broad One Health Endectocide-based Malaria Intervention in Africa—a phase III cluster-randomized, open-label, clinical trial to study the safety and efficacy of ivermectin mass drug administration to reduce malaria transmission in two African set. *Trials*. 2023;24(1):1–16.
28. Xie K, Marathe A, Deng X, Ruiz-Castillo P, Imputiua S, Elobolobo E, et al. Alternative approaches for creating a wealth index: the case of Mozambique. *BMJ Glob Heal*. 2023;8:12639.
29. UNICEF and WHO. Progress on drinking water and sanitation. UNICEF and WHO; 2012. p. 1–58.
30. Moher D, Hopewell S, Schulz KF, Montori V, Gøtzsche PC, Devereaux PJ, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. *BMJ*. 2010;340:869.
31. Furnival-Adams J, Houana A, Saute F, Rudd M, Nicolas P, Montaña J, et al. Direct and indirect protection against scabies through ivermectin mass drug administration designed for malaria in Mozambique: a cluster randomised controlled trial; 2024. <https://doi.org/10.2139/ssrn.4952002>
32. Mahmud S, Pappas G, Hadden WC. Prevalence of head lice and hygiene practices among women over twelve years of age in Sindh, Balochistan, and North West Frontier Province: National Health Survey of Pakistan, 1990–1994. *Parasit Vectors*. 2011;4(1):1–10.
33. Munusamy H, Elsa E, Murhandarwati H, Rahmah S. The relationship between the prevalence of head lice infestation with hygiene and knowledge among the rural school children in Yogyakarta. *Trop Med J*. 2014;01(02):102–9.
34. Suleman M, Jabeen N. Head lice infestation in some urban localities of NWFP, Pakistan. *Ann Trop Med Parasitol*. 1989;83(5):539–47.
35. Counahan M, Andrews R, Büttner P, Byrnes G, Speare R. Head lice prevalence in primary schools in Victoria, Australia. *J Paediatr Child Heal*. 2004;40:616–9.