Effect of two different house screening interventions on exposure to malaria vectors and on anaemia in children in The Gambia: a randomised controlled trial

Matthew J Kirby, David Ameh, Christian Bottomley, Clare Green, Musa Jawara, Paul J Milligan, Paul C Snell, David J Conway, Steve W Lindsay

Summary
Background House screening should protect people against malaria. We assessed whether two types of house screening—full screening of windows, doors, and closing eaves, or installation of screened ceilings—could reduce house entry of malaria vectors and frequency of anaemia in children in an area of seasonal malaria transmission.

Methods During 2006 and 2007, 500 occupied houses in and near Farafenni town in The Gambia, an area with low use of insecticide-treated bednets, were randomly assigned to receive full screening, screened ceilings, or no screening (control). Randomisation was done by computer-generated list, in permuted blocks of five houses in the ratio 2:2:1. Screening was not treated with insecticide. Exposure to mosquitoes indoors was assessed by fortnightly light trap collections during the transmission season. Primary endpoints included the number of female Anopheles gambiae sensu lato mosquitoes collected per trap per night. Secondary endpoints included frequency of anaemia (haemoglobin concentration <80 g/L) and parasitaemia at the end of the transmission season in children (aged 6 months to 10 years) who were living in the study houses. Analysis was by modified intention to treat (ITT), including all randomised houses for which there were some outcome data and all children from those houses who were sampled for haemoglobin and parasitaemia. This study is registered as an International Standard Randomised Controlled Trial, number ISRCTN51184253.

Findings 462 houses were included in the modified ITT analysis (full screening, n=188; screened ceilings, n=178; control, n=96). The mean number of A gambiae caught in houses without screening was 37.5 per trap per night (95% CI 31.6–43.3), compared with 15.2 (12.9–17.4) in houses with full screening (ratio of means 0.41, 95% CI 0.31–0.54; p<0.0001) and 19.1 (16.1–22.1) in houses with screened ceilings (ratio 0.53, 0.40–0.70; p=0.04). 755 children completed the study, of whom 731 had complete clinical and covariate data and were used in the analysis of clinical outcomes. 30 (19%) of 158 children from control houses had anaemia, compared with 38 (12%) of 309 from houses with full screening (adjusted odds ratio [OR] 0.53, 95% CI 0.29–0.97; p=0.04), and 31 (12%) of 264 from houses with screened ceilings (OR 0.51, 0.27–0.96; p=0.04). Frequency of parasitaemia did not differ between intervention and control groups.

Interpretation House screening substantially reduced the number of mosquitoes inside houses and could contribute to prevention of anaemia in children.

Funding Medical Research Council.

Introduction Since 2001, malaria incidence has been declining in many parts of tropical Africa,1,2 which has led to renewed calls for elimination of the disease. The reduction has mainly been caused by the extensive use of longlasting insecticide-treated bednets and artemisinin-based combination therapy. However, the emergence of vectors resistant to insecticides used for net impregnation1 and parasites resistant to artemisinin derivatives2 will ultimately compromise these hard-won gains and impede efforts to eliminate the disease. Malaria remains one of the world’s greatest childhood killers,3 and accounts for about 40% of public health spending in Africa.4 It is therefore of great strategic importance to focus on sustainable, environmentally friendly, and easily integrated methods of control that can be added to the existing arsenal. Environmental management provides several methods for malaria control that have been effective in the tropics in the past,5,6 and could be useful again if incorporated into integrated vector management programmes.6,7

Making homes mosquito-proof is a key aspect of environmental management that has been associated with protection against malaria,8,9 yet it has been ignored during long-term antimalarial drug and insecticide-driven campaigns. House screening works by reducing exposure to malaria-transmitting mosquitoes and has the added benefit of protecting everyone in the house, therefore avoiding issues of inequity within the household. We anticipated that house screening might be particularly effective in The Gambia, since the primary vector, Anopheles gambiae sensu lato, bites predominantly at night and indoors. Our intervention study was thus designed to show whether house screening is effective against malaria in an African setting. We tested two types of screening:
full screening of doors, windows, and closed eaves, on the basis of established WHO criteria, and screened ceilings, which have proved effective in experimental hut trials, since mosquitoes that enter the house through open eaves are denied access to the room space by the screened ceiling. The efficacy of the screening interventions was measured by monitoring house entry by *A gambiae* and by assessing whether the interventions were durable and acceptable to local communities. We also assessed the frequency of anaemia and parasitaemia in children sleeping in study houses. Anaemia is a particularly useful marker of malaria morbidity since it is a major cause of death in young children.

Methods

Study households and participants

The trial was based at the Medical Research Council (MRC) laboratories at Farafenni field station in The Gambia, and carried out in 2006 and 2007. The characteristics of the area have been described in detail elsewhere. Briefly, the study area was situated approximately 170 km from the mouth of the Gambia River and covered 70 km² of the north bank, an area of open Sudan savanna. The climate consists of a single rainy season from June to October followed by a long dry season. There was 808 mm of rain in 2006, and 751 mm in 2007. Malaria cases are almost entirely attributable to *Plasmodium falciparum*. Members of the *A gambiae* complex are the main vectors and the entomological inoculation rate varies from 0 to 166 infective bites per person per rainy season. Combination therapy based on chloroquine and sulfadoxine-pyrimethamine was the first-line treatment for uncomplicated malaria throughout the trial. An effectiveness study that tested artesunate combined with lumefantrine, at the Armed Forces Provisional Ruling Council (AFPRC) General Hospital in Farafenni and at other health centres in the north bank region, started at the end of the trial, in December, 2007. The study area population was composed of 7852 people, with roughly equal numbers of men (n=4162, 53%) and women, and dominated by three ethnic groups: Wolof (n=2984, 38%), Mandinka (n=2199, 28%), and Fula (n=2120, 27%).

MRC Farafenni ran a demographic surveillance system in the study area throughout the study, which included 46 residential blocks in Farafenni town and 23 surrounding villages. Lists of potentially eligible houses, and children sleeping in those houses, were generated from this census and visited to check criteria for recruitment. Houses had to be single-storey buildings, have open eaves, less than five rooms, no existing ceilings, no existing screening, and at least one child aged between 6 months and 10 years sleeping there at night. There were no other exclusion criteria for children. Village and urban block sensitisation meetings were held to explain to the residents the purpose of the study and the benefits from participation in the trial. Subsequently, information sheets were read to individual house owners and to parents or guardians of children. Comprehension was checked before written consent was sought. Participants were invited to sign (or thumbprint if not literate) the consent documents, which were countersigned by the fieldworker present. Separate consent forms were filled in if the house owner was not the parent or guardian of the resident eligible children. Houses were enrolled between December and February before the intervention. Eligible children were enrolled at the same time, and a second round of enrolment of children was done in September of each year to include all children born during the screening installation phase (February to April) who would be eligible for the survey in November. In September, every enrolled child was given a unique study number and individual photographic identification card.

The protocol was approved by the Health Services and Public Health Research Board of the MRC UK and The Gambia Government and MRC Laboratories Joint Ethics Committee, and the Ethics Advisory Committee of Durham University. Two independent panels—a trial steering committee and a data monitoring and ethics committee—reviewed the conduct and results of the trial. The only incentives given to households that participated in the trial were provision of screening, treatment of study children during the clinical survey at the end of the transmission season, and a longlasting insecticide-treated bednet at the end of the trial.
Randomisation and masking

The study was a three-armed randomised controlled trial. Eligible houses were sorted by: (1) rural (village) or urban (Farafenni) location; (2) residential block; and (3) the number of children in each house, to achieve implicit stratification before assigning to the treatment group. The randomisation list was generated by use of Stata version 7 in permuted blocks of five (two houses with full screening, two with screened ceilings, and one control house without screening). PJM generated the allocation sequence and MJK enrolled participants and assigned them to trial groups. Clinical assessments were undertaken by a team that was not involved in any other study procedures and that was masked to the intervention status of each child. Investigators who analysed the mosquito trap data were also masked to treatment assignment.

Procedures

Figure 1 shows the trial design. In each year of the study we aimed to install full screening in 100 houses, and screened ceilings in a further 100 houses. 50 different houses each year served as a control group. A detailed description of the intervention arms is published in the trial protocol.18 In homes with full screening, timber framed doors (figure 2A) and windows were constructed and covered with PVC-coated fibreglass netting (1·2 m wide for doors, 2·4 m wide for ceilings, and 1·0 m wide for windows), with a mesh size of 42 holes per cm² (Vestergaard-Frandsen group, Kolding, Denmark). The gap between the top of the wall and roof (eaves) was filled with a mixture of sand, rubble, cement, and water, in accordance with normal local practice (figure 2B). In homes with screened ceilings, netting was stretched across the room below the eaves, fixed to the walls with wooden battens, and any small holes were filled with mortar (figure 3). Screening was not treated with insecticide.

The primary objectives were to estimate the efficacy of the house screening interventions against *A gambiae* house entry, and to assess whether these interventions were comfortable, durable, and acceptable to local communities. The primary endpoints were number of female *A gambiae* caught per light trap per night, proportion of residents willing to continue use of the intervention, and number of screens showing damage at 6 months and 12 months after installation. Secondary endpoints were sporozoite rate estimations in trapped mosquitoes and estimated entomological inoculation rate (ie, mean number of infective mosquitoes per person per season). The trial was also designed to examine the efficacy of house screening in preventing anaemia and reducing malaria infection at the end of the transmission season in November each year. The clinical endpoints were haemoglobin concentration, frequency of anaemia (defined as haemoglobin <80 g/L) and severe anaemia (haemoglobin <50 g/L), presence of malaria parasites, parasite density, and frequency of high parasitaemia (≥5000 parasites per μL). Children were selected for investigation because they are most at risk from anaemia in this population.23

Guidelines for recommending either type of intervention were established before the trial began. Full screening or screened ceilings would be recommended if they reduced house entry by malaria mosquitoes by 50% and were considered acceptable by more than 67% of householders. If both interventions satisfied those criteria, the intervention that was statistically more protective, or, if there was no difference, the cheapest, would be recommended.

Exposure to mosquitoes was measured by routine surveillance with US Centers for Disease Control and Prevention (CDC) light traps (one per house; model 512; John Hock Company, Gainsville, FL, USA) positioned 1 m above the ground, 1–2 m from the foot end of a bed protected with an untreated net used on that night only. Each study house was sampled every 2 weeks during this surveillance period (June 26–Nov 2, 2006, or July 16–Nov 5, 2007). Sub-samples of *A gambiae* mosquitoes from each trial group and each month of the surveillance period were taken for species identification by PCR.20 To identify infective mosquitoes, heads and thoraces of mosquitoes were homogenised in pools of ten individuals and the presence of sporozoites identified by ELISA.21

A clinical cross-sectional survey of children was done at the end of each transmission season, at least 6 months after the screening was installed. Axillary temperature was measured and a rapid diagnostic test (ICT malaria Pf
Cassette Test, ICT Diagnostics, South Africa) undertaken in children with temperature 37.5°C or more or history of fever in the preceding 48 h, to allow on-the-spot treatment of unwell children with detectable malaria. A finger-prick blood sample was taken from each child to measure haemoglobin concentration by use of a portable haemoglobin photometer (Hemocue, Ängelholm, Sweden), and to make thin and thick films for detection and quantification of malaria parasites. To establish parasite presence and density (asexual stages per μL, assuming a blood volume of 0.002 μL per high-power field), Giemsa-stained blood slides were examined (magnification ×1000). 200 fields were examined before a slide was declared negative.

Children with haemoglobin concentration less than 80 g/L were classified as anaemic and given iron supplementation. Chloroquine and sulfadoxine-pyrimethamine (Fansidar, Roche, Basel, Switzerland) were given to any child who had a positive ICT test result, and to children who had a negative ICT result or who were not tested but found to be positive on subsequent blood-slide examination. The parents of any child treated for malaria were asked to take their child to the nearest maternal and child health clinic if he or she did not recover from the symptoms of malaria within 48 h. Children with haemoglobin concentration less than 50 g/L were taken to the AFPRC General Hospital at Farafenni for blood transfusion and treatment of any underlying illnesses. They were followed up at MRC Farafenni for repeat haemoglobin measurement and general clinical review 2 weeks after discharge from hospital. Socioeconomic status was based on nine household characteristics, including household commodities, livestock, and house structure.22

After the end of the survey, house owners were given the choice of keeping the screening they had been given or having it removed, with the option of having the other screening type installed. Those in the control group were given the choice of having either screening type installed. The relative acceptability of each intervention was measured as the proportion of residents that continued the use of each intervention after they had been given the choice of the alternative or of having no screening. Two durability surveys, carried out at 6 months and 12 months after the screening was installed, recorded data specific to each type of screening.

Two costings incorporating materials and labour were calculated for both interventions on a per-person basis: the cost incurred during the trial, and a cost incorporating locally available netting. Each costing was based on the average study house of 22.2 m², with 2.6 doors and 0.3 windows, with four residents.

Statistical analysis

The trial had in excess of 90% power to detect a 50% reduction or more in the number of mosquitoes collected per trap per night in either intervention group compared with the control group. We also designed the trial to compare the two types of screening. We based our sample size calculations on discriminating between a mean of 7.5 (50% reduction) and 5.0 (67% reduction) mosquitoes per trap per night in the two intervention groups. On the assumption of an SD of log(e) catch of 1.2, 181 houses per intervention group would be needed for a two-group one-sided t test to have 90% power to reject the null hypothesis that the difference between the group means is 2.5 or more, with an alpha level of 0.025 and assuming the expected difference between the means is zero. We considered that a smaller difference would make little, if any, appreciable change to the clinical pattern of malaria in the study area. Thus, in a three-armed trial we needed 200 houses in each intervention group and 100 in the control arm, allowing for 10% of houses to be excluded from the analysis because of withdrawal or non-adherence to protocol. The study was designed to have 90% power to detect a difference of 5 g/L or more in the mean haemoglobin concentration of children in the intervention groups compared with the control group, assuming a standard deviation of 17 g/L, an average of 2.5 children per house, and an intraclass correlation of between 0.04 to 0.08 from earlier studies (Milligan PJ, unpublished data and Figure 3: Screened ceilings fixed, below open eaves, with wooden battens and mortar

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Cisse B, London School of Hygiene and Tropical Medicine, London, UK, personal communication).

Analysis of this trial adhered, as far as possible, to a detailed analytical plan established before the investigators had access to the finalised data. We used a modified intention-to-treat (ITT) approach to compare each intervention group with the control group. The modified ITT population for the analysis of the entomological endpoint included all randomised houses for which there were some outcome data (excluding collections when the light trap was not working, houses that were vacated by residents or destroyed, and houses for which the occupier withdrew consent). When comparing the two intervention groups, it was also useful to make a comparison by use of a per-protocol analysis, which excluded all houses from either intervention group with screening that had scored as badly damaged in the durability study done 6 months after installation. The definition of badly damaged screens differed between treatment groups. In houses with full screening, badly damaged screening was defined as doors not closing tightly or five or more holes in the netting. This number of holes was selected because in a study of untreated bednets in The Gambia, more than five small holes reduced greatly the protective efficacy of untreated bednets against parasite infection. In houses with screened ceilings, screening was defined as badly damaged if there were five or more holes in the netting or if netting had come away from the battens that secured it to the walls.

We estimated the relative reduction in mean mosquito count for each intervention group compared with the control group by use of Poisson regression models. Additionally, we incorporated a variable for household in these models as a gamma-distributed random effect; this incorporation provided a means of accounting for dependence among counts made at the same house, and

### Figure 4: Trial profile for study houses

ITT=intention-to-treat.
1085 children from 500 houses recruited; randomisation at house unit level

- 439 sleeping in 200 houses with full screening
- 421 sleeping in 200 houses with screened ceilings
- 225 sleeping in 100 houses with no screening

Figure 5: Trial profile for study children

ITT=intention-to-treat. “Children moved to non-study houses within the same village (n=42); to non-study houses in Farafenni (n=7), outside the study area (n=33), or to an unestablished destination (n=68).†Child date of birth was recorded from parent/guardian recollection at consent stage, but more accurately from health card records, where available, at the time of identification card issue before fingerpricking.

100 did not enter cohort for fingerpricking
71 moved away
26 over age†
2 died
1 withdrew consent

- 43 did not enter cohort for fingerpricking
29 moved away
12 over age†
2 died

74 did not enter cohort for fingerpricking
50 moved away
23 over age†
1 died

- 52 not fingerpricked
16 travelled on day
19 withdrew consent
18 did not attend
1 in hospital

- 43 not fingerpricked
18 travelled on day
12 withdrew consent
13 did not attend

- 18 not fingerpricked
5 travelled on day
3 withdrew consent
9 did not attend
1 died

365 entered cohort for fingerpricking
321 entered cohort for fingerpricking
182 entered cohort for fingerpricking

- 313 included in modified ITT population
- 278 included in modified ITT population
- 164 included in modified ITT population

was also a way of modelling overdispersion in the distribution of mosquito counts. To estimate the effect of the screened ceilings intervention, data from this intervention group and the control group were selected and the outcome was regressed on an indicator for the ceiling intervention. We report the exponentiated coefficient, which is interpreted as the ratio of the mean mosquito count for the group receiving the ceiling intervention relative to the mean count of the control group. The statistical significance of the effect was tested with the p value obtained from this regression. To adjust for multiple comparisons, a significance level of α=0·025 was used. Poisson regression was also used to determine the efficacy of full screening, and to compare the relative efficacies of screened ceilings versus full screening. For the latter comparison, a non-inferiority analysis was undertaken in which we considered the two treatments to be equivalent if the lower bound of the CI for the ratio of full screening/screened ceilings exceeded 2/3.

In a further analysis of the entomological data, efficacy was estimated by use of negative binomial regression models for the number of A gambiae and number of culicine mosquitoes caught per house. Multiple imputation was used to reduce bias due to missing mosquito counts and missing covariate data. Ratios of the mean mosquito count (screened ceiling/control and full screening/control) were adjusted for covariates specified in the analysis plan that were shown to be associated with mosquito catch size in this area: (1) presence of horse(s) tethered near the house at night; (2) number of people sleeping in the trapping room; (3) household socioeconomic status. Where variables were recorded at each visit (ie, covariates 1–2), the mean value was used. Socioeconomic status scores were computed with the first component of a principal components analysis of nine household characteristics (wall material, roof material, radio, iron or carved wooden bed, cart, bicycle, car or motorbike, livestock, literacy of mother).21

The modified ITT population for the analysis of clinical data included all children (from the houses included in the modified ITT analysis) recruited before the clinical survey who were sampled for haemoglobin and parasitaemia at that survey. We report mean haemoglobin concentration for each of the trial groups. Differences between trial groups were estimated from a regression model that included household as a random effect.

A further analysis of clinical data was based on a complete case analysis (ie, only individuals with complete outcome and covariate data were included). Differences in mean haemoglobin densities between trial groups were estimated by use of a normal model in which household was included as a random effect. Adjusted estimates of mean difference were based on a model that incorporated the full set of covariates used for the analysis of the entomological outcome, plus age of study participant. Unadjusted and adjusted odds ratios (ORs) were estimated for anaemia, severe anaemia, the presence of malaria parasites, and high parasitaemia. In each case, a logistic regression was used in which the household was modelled as a random effect. Adjusted ORs were obtained by including the covariates used in the model for haemoglobin concentration previously described.

For all adjusted analyses, we explored the effect on estimates of the inclusion of variables that represented other methods of mosquito control that might be affected by the intervention—namely, churai (local incense) burnt at night, bednet use, and bednet condition. By including these mediator variables in the regression models, the direct effect of the intervention could be estimated—ie, the effect in households where these characteristics were the same.

Contingency tables were used to compare the durability between years, sporozoite rates between years and trial groups, and the relative acceptability of each type of screening. Analyses were done with SPSS version 15.0, EpInfo version 6, and Stata version 10.1. This study is registered as an International Standard Randomised Controlled Trial, number ISRCTN51184253.

Role of the funding source
The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. MJF and SWL had full access to all the data in the study and had final responsibility for the decision to submit for publication.
Results

Figure 4 and figure 5 show the trial profiles for study houses and study children, respectively. 500 houses were recruited and randomised to the intervention and control groups. Two teams, each consisting of one leader and three assistants, installed full screening into two to three houses, or screened ceilings into four to five houses per day. Outcome data were available for 462 houses; these houses were included in the modified ITT analysis. 1085 children aged 6 months to 10 years old lived in the 500 houses; 755 of these children were included in the clinical survey at the end of the transmission season. Table 1 shows the characteristics of the houses and children in the trial. At the end of the transmission season, use of bednets was slightly lower in the two intervention groups than in the control group. Use of untreated bednets (irrespective of quality) was lowest for children in houses with full screening (20% [64/313] vs control 31% [50/162], χ²=6·35, p=0·012), whereas use of insecticide-treated bednets was lowest in houses with screened ceilings (26% [70/272] vs control 35% [57/162], χ²=4·4, p=0·04).

Table 2 shows the entomological, clinical, and acceptability outcomes by treatment allocation. During the two trapping periods, 180472 mosquitoes were caught. Of these, 86627 (48%) were anophelines and the rest were culicines. 75365 (87%) of all anophelines caught were *A gambiae*. A sub-sample of 2079 (3%) *A gambiae* were identified to species by PCR. 1048 (50%) were *Anopheles gambiae sensu stricto*, 947 (46%) *Anopheles melas*, and 84 (4%) *Anopheles arabiensis*. Overall levels of malaria transmission were lower in 2007 than in 2006 (table 2).

Both screening interventions reduced house entry of mosquitoes (table 2 and table 3). The mean number of mosquitoes collected over all trapping visits in houses with full screening compared with control houses and in houses with screened ceilings compared with controls.

At the end of the trial, 171 (94%) of 182 householders opted to continue using full screening while only 82 (46%) of 179 were willing to continue use of screened ceilings. There was a significant association between the type of screening that participants received and whether or not they would opt to change to the other type (χ²=97·5, df=1, p<0·0001). The odds of changing intervention type were 18·5 times greater for households that received screened ceilings than for those that received full screening. Full screening was also the preferred choice of the participants in the control arm: 79 (82%) of 96 households opted for full screening, 16 (17%) opted for screened ceilings, and 1 (1%) chose not to have either screening type installed.

The extent of damage to houses with full screening varied substantially (data not shown). Screened windows had little or no damage, with 36 (80%) of 45 windows still intact after 12 months. The mortar blocking the eaves was similarly durable, with 220 (90%) of 245 installations remaining intact after 12 months. The screened doors showed the greatest damage: only 105 (29%) of 365 were intact after 12 months. Nonetheless, there were more intact doors in houses included in the second year of the study (68/186 [37%]) than there were in houses included in the first year (37/179 [21%]; χ²=10·5, p=0·001), which suggests that people in the second year might have learnt about the advantages of the screens from neighbours who took part in the first year of the study, and therefore looked after them better. Damage to the doors was minor, with a median number of holes of only four (IQR one to eight) in

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**Table 1: Characteristics of study houses and children**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Full screening</th>
<th>Screened ceilings</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of trapping room occupants†</td>
<td>4·1 (4·0–4·2)</td>
<td>4·1 (3·9–4·2)</td>
<td>4·2 (4·0–4·4)</td>
</tr>
<tr>
<td>Use of churai incense (%)</td>
<td>28% (23–34)</td>
<td>29% (23–34)</td>
<td>28% (21–36)</td>
</tr>
<tr>
<td>Mosquito coil use (%)</td>
<td>1% (0–2)</td>
<td>2% (1–3)</td>
<td>2% (0–3)</td>
</tr>
<tr>
<td>Number of horses tethered near house†</td>
<td>0·9 (0·8–1·0)</td>
<td>0·9 (0·7–1·0)</td>
<td>0·9 (0·7–1·1)</td>
</tr>
<tr>
<td>Child’s time to bed (h)†</td>
<td>2144 (2134–2200)</td>
<td>2149 (2136–2202)</td>
<td>2150 (2134–2206)</td>
</tr>
</tbody>
</table>

Data are arithmetic mean (95% CI), n (%), or % frequency (IQR). *Number of houses: full screening, n=188; screened ceilings, n=178; control, n=96. †Missing houses: full screening, n=1; screened ceilings, n=2; Full screening, n=94; screened ceilings, n=89; control, n=69. ††Incomplete cases: full screening, n=315; screened ceilings, n=277; control, n=163. †|Missing cases: full screening, n=2; screened ceilings, n=5; control, n=1. ‡Missing cases: full screening, n=2; screened ceilings, n=5; control, n=2. ‡‡Socioeconomic score scale 0–9. ††Incomplete cases: full screening, n=9; screened ceilings, n=12; control, n=1. †Net intact or with no more than five ≤2 cm diameter holes, which was long enough to tuck under mattress.
Table 2: Outcomes by treatment allocation

<table>
<thead>
<tr>
<th>Entomological outcomes</th>
<th>Full screening</th>
<th>Screened ceilings</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean number of Anopheles gambiae sensu lato per trap per night</td>
<td>15.2 (12.9–17.4)</td>
<td>19.1 (16.1–22.3)</td>
<td>17.5 (16.6–43.3)</td>
</tr>
<tr>
<td>Entomological inoculation rate*</td>
<td>0.77 (0.52–0.96)</td>
<td>1.14 (0.85–1.42)</td>
<td>2.27 (1.38–3.16)</td>
</tr>
</tbody>
</table>

Acceptability and durability outcomes

| Number of screens with damage at 12 months | 260/365 (71%) | 133/156 (85%) | N/a |
| Number of screens with damage at 6 months | 248/426 (58%) | 110/169 (65%) | N/a |
| Residents willing to continue use of intervention | 171/182 (94%) | 82/179 (46%) | 1/96 (1%) |

Residents willing to continue use of intervention was compared between groups (Fisher’s exact test). The corresponding differences between the screened ceilings group versus the control group were 3·6 g/L (–0.6 to 7.8; p=0.09) and 4·2 g/L (0.6–7.7; p=0.02; table 4). A greater proportion of children from houses without screening had anaemia than did children from houses with full screening or with screened ceilings (table 5). Seven children had severe anaemia: four (3%) children from houses without screening, two (0·6%) from houses with full screening, and one (0·4%) from houses with screened ceilings (full screening vs control p=0.186; screened ceilings vs control p=0.068; comparison of intervention groups combined vs control p=0.043 [Fisher’s exact test two-tailed value]).

Mortality 1/389 (0.3%) 2/350 (0.6%) 3/196 (1.5%)

Clinical outcomes

<table>
<thead>
<tr>
<th>Haemoglobin concentration (g/L)</th>
<th>Full screening</th>
<th>Screened ceilings</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006</td>
<td>103 (100–106)</td>
<td>103 (99–106)</td>
<td>98 (93–102)</td>
</tr>
<tr>
<td>Moderate anaemia (haemoglobin &lt;80 g/L)</td>
<td>Full screening</td>
<td>Screened ceilings</td>
<td>Control</td>
</tr>
<tr>
<td>2006</td>
<td>18/164 (11%)</td>
<td>16/140 (11%)</td>
<td>17/89 (19%)</td>
</tr>
<tr>
<td>2007</td>
<td>22/151 (15%)</td>
<td>17/137 (12%)</td>
<td>13/74 (18%)</td>
</tr>
<tr>
<td>Severe anaemia (haemoglobin &lt;50 g/L)</td>
<td>Full screening</td>
<td>Screened ceilings</td>
<td>Control</td>
</tr>
<tr>
<td>2006</td>
<td>1/164 (0.6%)</td>
<td>1/140 (0.7%)</td>
<td>2/89 (2%)</td>
</tr>
<tr>
<td>2007</td>
<td>1/151 (0.7%)</td>
<td>0/137 (0%)</td>
<td>2/74 (3%)</td>
</tr>
<tr>
<td>Presence of parasites (all parasitaemias)</td>
<td>Full screening</td>
<td>Screened ceilings</td>
<td>Control</td>
</tr>
<tr>
<td>2006</td>
<td>47/154 (29%)</td>
<td>45/140 (32%)</td>
<td>29/89 (33%)</td>
</tr>
<tr>
<td>2007</td>
<td>13/151 (9%)</td>
<td>13/137 (8%)</td>
<td>7/74 (9%)</td>
</tr>
<tr>
<td>Presence of high parasitaemia (≥5000 parasites per μL)</td>
<td>Full screening</td>
<td>Screened ceilings</td>
<td>Control</td>
</tr>
<tr>
<td>2006</td>
<td>6/164 (4%)</td>
<td>7/140 (5%)</td>
<td>9/89 (10%)</td>
</tr>
<tr>
<td>2007</td>
<td>7/151 (5%)</td>
<td>4/137 (3%)</td>
<td>1/74 (1%)</td>
</tr>
<tr>
<td>Mortality</td>
<td>1/389 (0.3%)</td>
<td>2/350 (0.6%)</td>
<td>3/196 (1.5%)</td>
</tr>
</tbody>
</table>

N/a=not applicable. Data are arithmetic mean (95% CI) or n/N (%). Clinical data were recorded at the end of the transmission season. *Mean number of sporozoite-infected A gambiae per person per transmission season. †Number of doors, not houses. ‡There are complete clinical data on 755 children.

Four households (2%) from each intervention group withdrew consent during the study because of problems relating to the screening. The most common concern expressed by participants was that the netting was hard to keep clean (86 [48%] of 181 respondents from houses with full screening vs 103 [60%] of 172 from houses with screened ceilings). However, this concern was outweighed by advantages common to both screening types, including reducing dust (180 [99%] vs 169 [98%]) and improving the appearance of the house (181 [100%] vs 161 [94%]). Occupants of houses with full screening reported that their screening improved privacy (181 [100%] vs 125 [73%]) and prevented mosquitos (174 [96%] vs 137 [80%]) and other pests from entering the house (181 [100%] vs 96 [56%]) more often than did those from houses with screened ceilings.

With a mean house occupancy of four individuals, the cost of full screening per person protected in the trial (netting donated free of charge) was US$9·98, compared with $8·69 for screened ceilings per person protected. If locally available netting was used, the mean cost per person would be $11·11 for full screening and $21·17 for screened ceilings.
importance of screening. Perhaps for this reason the studies failed to quantify the degree of protection offered by screening per se. From these studies, it is therefore difficult to find a barrier against malaria is not a novel idea, but there was no random allocation of the interventions. Additionally, although other investigations have shown an association between house architecture and malaria transmission, infection, and morbidity, many of them have been done during observational studies, and the focus has often been on the quality of walls, ceilings, and floorboards rather than on screening per se. From these studies, it is therefore difficult to quantify the degree of protection offered by screening alone; perhaps for this reason the studies failed to convince those implementing public health policy of the importance of screening.

House screening proved an effective barrier against both anopheline and culicine mosquitoes. Although both interventions worked well, full screening was more protective than screened ceilings, suggesting that doors and windows were important routes of entry for many mosquitoes. It is perhaps surprising that even in fully screened houses we caught an unadjusted mean of 30 mosquitoes (all species) per trap per night. This finding probably occurred because screened doors were often propped open during daylight hours, only being closed at 1900–2000 h. Mosquitoes that were active...
earlier in the day could enter homes before the doors were closed; therefore, even greater reductions in transmission might be achieved by persuading home owners to shut doors earlier in the evening. At best, house screening should protect people from 80% of bites that occur indoors.37

In this trial, children living in houses with screening had substantially higher haemoglobin concentrations and were less likely to have anaemia than children from houses without screening. These findings are important because anaemia is a clinically relevant measure of malaria in children in this setting. Many intervention trials have only examined anaemia in children aged up to 24–36 months because its prevalence, and thus the effect of malaria control, is often greatest in children from this age-group.38 For this reason it was crucial to adjust the house screening efficacy estimates by age.

The reduction in anaemia associated with house screening compares favourably with the RTS,S/AS02A vaccine, which failed to reduce anaemia prevalence.39 The adjusted increase in haemoglobin concentration of 3.7 g/L in the group with full screening and 4.2 g/L in the group with screened ceilings is similar to the weighted mean increase of 1.7% packed cell volume (the equivalent of approximately 5.7 g/L) across six randomised controlled trials of insecticide-treated bednets compared with controls,40 and to the 7.2 g/L increase after indoor residual spraying with lambda cyhalothrin in Tanzania.41 The reduction is also similar to the percentage increase in packed cell volume associated with chemoprophylaxis with pyrimethamine-dapsone (1.5%) or chlorproguanil (1.0%) compared with control found in the same study area in The Gambia.42 Although there was no statistical difference in severe anaemia between groups, its frequency was lower in the screening groups compared with the control, suggesting that a larger study might show that screening is also protective against severe anaemia. Nevertheless, the proportion of children with severe anaemia was significantly lower in the combined intervention groups than in the control group.

Unsurprisingly, neither screening intervention was associated with a reduction in the frequency of parasitaemia, since such a decline can only be achieved if the infection level in the intervention groups is substantially suppressed.43–46 Thus, the introduction of major interventions such as insecticide-treated bednets,47 indoor residual spraying,47 and intermittent preventive treatment of infants,48 have all had limited effect on parasite prevalence within 6 months of introduction. Our interpretation of the results is that although house screening did not reduce parasitaemia, it reduced malaria superinfection of children, a condition that leads to anaemia. We also expect that screening might lower clinical episodes of malaria, since reductions in entomological inoculation rate, in areas of moderate transmission, are associated with declines in malaria incidence.39 Malaria transmission was much lower in the second year of the study than in the first, as suggested by the decline in parasite prevalence in the second year of the study. This finding is unlikely to be the result of an increase in use of insecticide-treated bednets between years (35% coverage in cohort participants in 2006, 24% in cohort participants in 2007) or of the use of artemisinin-based combination therapy, because this was introduced after the 2007 transmission season. No reduction in parasite density was seen in either of the intervention groups; again, this finding is not uncommon for otherwise effective prophylactic interventions49 and can be hard to detect because of large variations between slide readers in the estimates of parasite density by microscopy.50

Both screening interventions were well tolerated and safe to use. Since a higher proportion of participants in the full screening group reported that their screening improved privacy, improved the appearance of the house, and stopped the entry of mosquitoes and other pests, these are likely to be the reasons that full screening was the more acceptable intervention.

One possible concern is that installation of screening might have reduced the use of bednets in those houses. Children in both intervention groups were less likely to sleep under any sort of bednet than those in houses without screening, which might reflect a belief among some participants that the screening operated as a replacement for bednets. Therefore, the introduction of screened ceilings to areas where coverage of insecticide-treated bednets is high might increase transmission risk to individuals. We advocate house screening to augment, rather than replace, insecticide-treated bednet use. However, we note that estimates of the direct effect of the intervention (obtained by including bednet use and bednet condition in models for clinical and entomological outcomes) were almost identical to estimates of the combined effect (direct and indirect effects), suggesting that indirect effects mediated through bednet use are of limited significance.

Our results show the feasibility of developing an effective house screening design against malaria. Both techniques offered satisfactory protection against *A gambiae* and anaemia, but only the full screening intervention met the acceptability criteria for recommendation, and offered added protection against culicine mosquitoes, including some species that are vectors of arbovirus infection. This finding is important because vector control activities that do not reduce nuisance biting will not encourage community support. Full screening can be a sustainable control method: the interventions were largely made with use of locally available materials and installed by local carpenters to a standard screening blueprint, at a reasonable cost—especially if one considers that the screening can be protective for several years. Although most screening...
on the doors and ceilings was damaged after 12 months, faults were minor. As with many new technologies, it is likely that durability can be improved by changes in materials and design. Insecticide-impregnated screening might provide an even more effective barrier, especially when the screening is damaged. At a cost of around $10 per person, full screening has a similar cost to insecticide-treated bednets and indoor residual spraying, providing it can remain effective for 3–4 years. Where the resources are available, there is also the opportunity to improve the durability of the interventions by the use of longer-lasting materials such as metal frames for doors.

Although screening should be tailored to local house designs, the general principles involved in this trial should help to inform approaches to screening for malaria control in other African settings and elsewhere in the tropics. Screening is most likely to be successful in areas of low transmission where a large reduction in indoor biting could substantially reduce malaria morbidity, especially in households where people prefer not to use bednets, or have stopped using them because nuisance biting occurs infrequently. House screening could be easily incorporated into integrated vector management programmes, and because it does not rely on insecticides, it could be particularly beneficial in areas where insecticide resistance develops. The results of this trial contribute to the evidence base from which malaria control programmes, local administrations, and non-governmental organisations throughout sub-Saharan Africa can make an informed decision about house screening. We would encourage the initiation of a larger trial to assess whether this intervention reduces clinical episodes of malaria in diverse settings, including areas where use of insecticide-treated bednets is high. We also hope that the results of our trial will stimulate the development of additional sustainable methods that, in combination with improved health care and access to treatment, can help to strengthen efforts to eliminate malaria.

Contributors
MJK designed the interventions, coordinated the fieldwork, drafted the analytical plan, and analysed the data. DA led the clinical survey team at Farafenni. CG and MJ performed the sporozoite ELISAs. PJM contributed to study design and drafting of the analysis plan and CB analysed the data. PCS was responsible for data management. SWL conceived the study, its design and coordination, and drafted the analytical plan. MJK and SWL wrote the manuscript, and all authors contributed to study design and drafting of the analysis plan and CB analysed the data. PCS was responsible for data management. SWL conceived the study, its design and coordination, and drafted the analytical plan. MJK and SWL wrote the manuscript, and all authors contributed to the drafts and read and approved the final draft. MJK and SWL had full access to the data and made the final decision to submit for publication.

Conflicts of interest
We declare that we have no conflicts of interest.

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References