

Can head louse repellents really work? Field studies of piperonal 2% spray

Background: Many families find regular checking of children's heads for head louse infestation too onerous and would prefer to be able to prevent infestation by use of a topical application that deters lice from infesting the head. Identification in the laboratory of a repellent activity for piperonal provided the basis for developing a spray product to repel lice.

Methods: A proof of principle field study in Dhaka, Bangladesh, compared the effect of using 2% piperonal spray with that of a placebo in 105 children and adults from three communities with infestation levels close to 100%. All participants were treated for infestation and subsequent incidence of reinfestation monitored daily by investigators. A second randomised, controlled, double blind, study in North London, UK, evaluated the effect of the product in normal use. One hundred and sixty-three children from schools with a high level (20-25%) of infestation were treated and confirmed louse free and randomly divided between 2% piperonal, a placebo spray, and a control group for up to 22 weeks. Parents applied the spray and monitored for infestation. Regular investigator visits confirmed the parental monitoring and replenished supplies of spray.

Results: In Dhaka, over 18 days there were only 4 infestations in the piperonal group and 8 in the placebo group. This difference was not significant ($p = 0.312$). In North London, there were 41 cases of infestation over the course of the study. Although there were fewer infestations in the piperonal group, analysis of time to first infestation showed a no significant ($p = 0.4368$) difference between groups.

Conclusion: Routine use of 2% piperonal spray in communities with a high prevalence of head louse infestation may provide some protection from infestation. However, the difference between use of the product and no active intervention was sufficiently small that regular

checking for presence of lice is likely to be a more practical and cost effective approach to prevention of infestation.

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15 Introduction

16 Most human management of head lice involves treatment post-infestation, either by
 17 combing or other physical removal or using various types of insecticidal chemicals.
 18 Successful interventions often depend upon timely diagnosis of infestation before it
 19 becomes established. Over the years, health educators have encouraged regular and
 20 frequent checking of children's hair for signs of infestation but with limited success
 21 because people are either too busy or not concerned enough about lice. They would
 22 rather deal with the problem if and when it arises.

23 Most parents would like a way to prevent lice from infesting the hair. The majority
 24 ideal is a product that stops lice transferring from one host to another. Of course,
 25 materials can be applied to make the hair unacceptable as a habitat but they are
 26 also mostly unacceptable for cosmetic reasons, such as heavy vegetable oils like
 27 coconut, neem, olive, and sassafras oils, that attract dirt, render hair lank and
 28 greasy, and develop distasteful odours after a short time on the head.

29 The idea of a louse repellent was quite novel when this investigation started in 1989
 30 (Burgess, 1993a), although suggestions that some essential oils had repellent
 31 properties had circulated for years before (Spencer, 1941). At the time the idea was
 32 sufficiently novel that the concept needed careful explanation to health care
 33 professionals. Previously only residual insecticides were thought to confer some
 34 measure of protection against reinfestation (Burgess, 1993b; Peock & Maunder,
 35 1993). While investigating discontinued pediculicides we found that 1,3-
 36 benzodioxole-5-carbaldehyde (piperonal or heliotropin), a fragrance and flavouring
 37 agent with an odour similar to vanilla, deterred lice from walking onto surfaces
 38 treated with the it (Burgess, 1993a). An extensive investigation of this and related
 39 chemicals led to development of a repellent product (Irwin, 1992; Irwin 1993; Oliver,
 40 1992; Peock & Maunder, 1993).

A 2% piperonal spray was marketed in Britain from late 1992 but, as a head louse control product its status was questioned because it did not have a Marketing Authorisation from the Medicines Control Agency (MCA), even though no claims of pediculicidal activity were being made. The MCA initially stated that as a repellent the product was not licensable (no mosquito repellents were licensed at the time) but they reserved the right to change this viewpoint so the manufacturer prepared a pharmaceutical dossier should it be required, which necessitated preparation of a clinical evaluation report.

This report describes two studies, one in Bangladesh, and the other in the UK. The main objective for both studies was to determine whether 2% piperonal spray could protect against contracting head louse infestation, with the expectation that regular use could reduce the risk of becoming infested. An additional aspect for the UK study was to determine whether use of the repellent on a regular basis was a practical proposition for parents and guardians when they were busy preparing their children for school each day.

Materials and Methods

We conducted two field studies. The first was in Dhaka, Bangladesh, where reinfestation risk was high. The second in North London, UK, enabled us to evaluate effectiveness over time. Anyone wishing to take part that was found to be infested at the start of the study was treated so that all participants started louse free.

Settings and Participant flow

Study 1: In Dhaka, between 4th February and 10th of March 1993 we recruited 107 participants from three communities where, from previous experience, we knew

infestation was close to 100% prevalence. These were two religious-based orphanages at Farmgate and Mohammeপুর in Dhaka city and a 7000 population bostee (slum) community at Gandaria, between Dhaka and Naryanganj. An information leaflet was translated into Bengali by one of us (NAB) and distributed through the institution administrators and the community chairmen. Verbal explanation of the study requirements was provided for anyone unable to read.

Pre-enrolment screening used a plastic detection comb method that has since been shown to be 3.84 times more effective than visual inspection (Balcioglu, et al., 2008). Of the 92 residents in the Farmgate orphanage we screened 70 children and found 68 to be infested. The remainder declined examination. From these we recruited 6 males and 38 females. In Mohammedpur, 160 children were registered. We examined 80 using the same method, all had lice, and 21 agreed to enrol in the study. Those not screened were not in the building at the time. Here we recruited 9 males and 10 females, with ages ranging from 7 to 16 years, with one adult participant. Hair length was long for 41/48 females (85.4%), with three having medium and the remainder short hair. All males had short hair.

Participants were allocated to receive either the 2% piperonal spray or the placebo using the anonymously labelled, randomised bottles supplied by the sponsor. Because fewer than half the residents at each site agreed to participate in the study no more than 50% of children sharing a dormitory were participants, which we considered to adequate to allow opportunities for reinfestation.

Because administrative problems had delayed regulatory release of the study materials, it became necessary to shorten the time allocated to each treatment phase from the planned 14 days to nine. At day 10, during the cross-over, we found minimal louse transmission had occurred in the children's homes so the Gandaria site was initiated to provide additional data. Everybody examined at this site was

found to be infested. To increase the risk of reinfestation we recruited only one person from each household. This site operated for 9 days, in parallel with the second half of the cross-over in the orphanages. At Gandaria, all 42 participants were female aged from 7 upwards, with 14 adult participants

At all three sites continuity was disrupted by participants ending participation or visiting their extended families for the month of Ramadan. Even Christian children took time off to visit family members. Consequently, analyses were conducted on the ITT population only.

Study 2: We had previously worked with the Orthodox Jewish community in the Golders Green, Hendon, and Edgware districts of North London, such as in the first identification in the UK of acquired resistance to pyrethroid insecticides in head lice (Burgess, et al, 1995). Prevalence of infestation in one school averaged 20% to 25% and many families in the community expressed the belief at public meetings that treating children was pointless because reinfestation occurred within days.

Most participants attended a primary school that distributed an invitation letter, study information, and a Consent form, which had previously been discussed with members of the community. Others heard about the study from friends and neighbours. All were pre-assessed for suitability by their general practitioner.

At this site recruitment was based around the family, with 163 children from 48 families taking part. Households ranged in size from three to 17 members, the most common being 8 people (11 households), followed by five households each for 7, 9, 11, and 12 members, four households with 6 people, three each for 5 and 10 people, two each for 4 and 13 members, and one household each for 3, 15, and 17 members. Numbers of participants per household ranged from one to seven with 13 households

115 having 3 participants and 11 having 4, there were eight families each with 2 and 5
116 participants, five with 1, 2 with 6, and only one with 7 taking part.

117 The population comprised 112 (68.7%) females and 51 males. All participating boys
118 had short hair and among the girls 34 (30.4%) had long hair, 70 (62.5%) had medium
119 length, and just eight (4.9%) had short hair.

120 At this site we planned the study for between 6 and 13 weeks, although the protocol
121 allowed this period to be extended. It actually ran over 22 weeks, between 29th May
122 and 11th November 1994. Using a rolling enrolment, the initial distribution of
123 participants was 53 allocated 2% piperonal spray, 48 allocated placebo spray, and 43
124 in the control group. Over the full study period we recorded 41 infestations for the
125 time-to-first-infestation analysis. Some of the participants who caught lice opted to
126 continue in the study in a different randomisation group but not all volunteers
127 actively participated for the whole time and the intention to treat population
128 included families who dropped out for various reasons during the summer months.
129 Some procedures were disrupted by religious festivals during the study period. We
130 did not analyse the outcomes in those reallocated to the alternative study groups
131 because too few people chose to remain in the study to permit meaningful analyses
132 to be carried out, especially since the majority of them were in the no intervention
133 monitoring group.

134 All participants gave baseline data on age, gender, hair characteristics. In Dhaka,
135 participants were photographed and also gave their father's or husband's name (a
136 local cultural practice) for later confirmation of their identity in the large
137 communities where family names are rarely used.

138 The lower age limit was 4 years, with an upper limit of 14 years in London but there
139 was no upper limit in Dhaka. All treatments and assessments were domiciliary,

140 except at Gandaria where we used a community clinic to examine and treat
141 participants.

142 Inclusion criteria were fitting the age profile; normal physical health; willingness to
143 participate and to be treated for lice. Exclusion criteria were a history of allergy,
144 asthma, eczema, contact dermatitis or psoriasis; or concomitant steroid use.
145 Participation in North London was subject to GP approval.

146 *Ethics*

147 Ethical approval in Dhaka was granted by the ad hoc ethics committee of the
148 Metropolitan Medical Centre, Mohakhali, Dhaka; Protocol RAP001. Study
149 medications were granted access to the country by the Directorate of Drug
150 Administration of the Ministry of Health and Family Welfare, Bangladesh.

151 Consent to treat and participate was provided en bloc in the two orphanages by
152 administrators, acting *in loco parentis*. Also each volunteer was counselled and gave
153 a witnessed signed assent to participate. In Gandaria, participants provided a
154 signed/marked assent prior to enrolment.

155 Ethics approval in North London was granted by Barnet Research Ethics
156 Committee; Protocol RAP002. A Clinical Trial Exemption Certificate (CTX) was
157 granted by the MCA. Parents provided written consent for all children of their
158 household. Anyone unwilling to participate and ineligible household members could
159 join a monitoring group to provide information on the background infestation risk in
160 the community.

161 The studies were conducted in conformity with the principles of the Declaration of
162 Helsinki and the OECD Guidelines for Good Clinical Practice (GCP) prevailing at
163 the time, which are no longer available but which were embodied in the

164 International Conference on Harmonization guideline on Good Clinical Practice
165 E6(R1) (ICH-GCP, 1996).

166 *Study medications*

167 The investigational spray was a marketed general sales list (GSL) product
168 containing 2% piperonal in an aqueous alcohol base (Rappell®, Charwell
169 Pharmaceuticals Ltd, UK). It was supplied in 90mL pump spray plastic bottles
170 delivering metered 130µL doses. The recommended application rate stated by the
171 manufacturer on the product label was 5-25 sprays daily, according to the length and
172 thickness of hair, before school or other activities. So for a boy with a 5mm long
173 cropped hair the minimal dose would be applied whereas for a girl with thick hair
174 that hung below the shoulders the maximum application would be necessary. The
175 product could be reapplied if the hair was wetted during the day, e.g. after
176 swimming.

177 The placebo comparator was a superficially identical spray containing 1% vanillin to
178 mimic the odour. Previous laboratory tests had found vanillin was not repellent
179 (Irwin, 1992; Irwin 1993; Oliver, 1992).

180 We used carbaril 1% aqueous emulsion (Derbac-C liquid, Charwell Pharmaceuticals
181 Ltd), which was found in a series of comparative tests to be effective with a single
182 application and left no insecticide residue (Burgess, 1990), to eliminate lice before
183 using the investigation products or if lice were caught during the study.

184 In Bangladesh all medications were applied by investigators. After treatment,
185 participants were checked to confirm efficacy and the allocated spray applied daily
186 by an investigator. Assessments were made on alternate days using visual
187 inspection and detection combing.

In North London the sprays were applied by a parent. A louse detection comb was supplied so they could check for lice, at least three times weekly. The parent noted on a diary card when spray was applied and when they checked for lice. If lice were found our pharmacist investigator (JK) supplied insecticide treatment. An investigator visited every family once each month to make an independent check for lice, collect diary cards, and replenish the spray.

Outcomes

The primary outcome measure was the time to first infestation with head lice, confirmed by detection combing. Secondary endpoints were whether infestations occurred at any time while using the product, and the safety of the spray in use.

Sample size

There were no precedents for estimating sample size. No studies at that time had ever been conducted of incidence of head louse infestation in any community, and assumptions of risk had never been quantified. Consequently, we assumed that in populations with a high prevalence of infestation there would be sufficient reinfestation risk that protective activity would be detectable in a relatively small population. That assumption has since been partially confirmed by a recent study conducted in Brazil showing that, in a high prevalence population, reinfestation is likely to occur in around 14-24 days (Pilger, et al., 2010).

The Dhaka study was a proof of concept comparing the active spray with placebo, with underlying prevalence close to 100% in participating communities, as determined by scalp examination and detection combing. We estimated that recruiting up to half the children in the orphanages would provide a reasonable risk of reinfestation from other residents. In Gandaria, we recruited a cohort equal to the larger orphanage group.

In North London the protocol provided for recruitment of up to 100 participants per treatment or control group (i.e. up to 300 participants in total). It was not clear whether a sample size estimation was conducted on behalf of the sponsor because no details were included in the protocol and no specific information was conveyed either formally or informally to investigators.

Randomisation – Allocation concealment

The proof of concept employed a randomisation sequence in which treatment allocation was predetermined and concealed, with bottles anonymously labelled “A” or “B”. In the orphanages, each participant acted as their own control using a cross-over to the other spray half-way through the allotted period.

We planned each treatment phase for 14 days, which was reduced to nine days for logistical reasons. In Gandaria a cross-over was not practicable so treatments were allocated by pairs of individuals. As everyone lived in similar circumstances we considered that risk factors for infestation were essentially similar for all participants, thereby “matching” the individuals in the pairs.

Randomisation in North London was by family, using a computer generated allocation sequence composed of balanced blocks of eight, i.e. each household constituted one block. Treatments were labelled with coded identification numbers, so investigators and participants were both blind to the allocation.

This study operated a form of cross-over design but at this site each participant used the same preparation until they became infested or reached the end of the study period. Participants in either spray group who became infested could cross-over to the non-intervention group (Fig. 1). Participants in the non-intervention group who became infested could cross-over to a randomised spray group provided they were eligible.

238 Product codes were not broken until after completion of data collection, entry into
239 the study database, and database lock.

240 *Statistical analysis*

241 The protocol stated that BIOS (Consultancy & Contract Research) Ltd were to
242 analyse data and prepare a report on behalf of the sponsor, Charwell
243 Pharmaceuticals Ltd. However, as far as we are aware, no formal statistical report
244 was produced by that consultant and no report of any kind was made available to
245 the investigators by the sponsor.

246 We conducted a post hoc analysis for the primary outcome in which Kaplan-Meier
247 curves have been used to illustrate the time pattern of participants remaining free
248 from infestation when using either 2% piperonal or placebo sprays, or where no
249 intervention was used.

250 We conducted analyses based on both the intention-to-treat (ITT) and the per-
251 protocol (PP) populations (Altman, 1991; Kirkwood & Sterne, 2003). Analysis of
252 data from Dhaka took into account the majority cross-over design so we tested
253 binary outcomes using the McNemar test and, due to the low number of events,
254 essentially evaluated whether an infestation occurred at all (Klingenberg & Agresti,
255 2006; Klingenberg, et al., 2009). Analyses of counts or ranked data used the
256 Wilcoxon signed rank test for paired data. However, because the three curves from
257 North London data were independent, being based on different participants, it was
258 possible to use the log-rank test to test differences between treatments for
259 significance (Bland & Altman, 1998). There were insufficient data available to
260 conduct demographic analyses.

261 **Results**

262 *Outcomes*

263 *Dhaka*

264 One reason these communities were selected for the study was that, given the high
 265 prevalence of head louse infestation in each community, we anticipated that those
 266 we treated ran a high risk of catching lice from their untreated peer group.
 267 Consequently, we expected an incidence of several cases each day, especially in the
 268 placebo treated group. However, the rate of reinfestation observed at all three sites
 269 was surprisingly low compared with expectation, particularly in the orphanages
 270 where nobody slept in individual beds and children routinely gathered to watch us
 271 with their heads together. We saw similar clusters of curious onlookers at Gandaria,
 272 where family members slept in close proximity in each household.

273 Only 12 reinfestation events occurred. One boy caught lice on both phases of the
 274 cross-over and one pair (one active and one placebo) of the parallel group
 275 participants also caught lice. Four participants were infested using placebo but not
 276 using piperonal and two from the parallel group were infested using placebo. Two
 277 were infested using piperonal but not using placebo. This gave 8 infestations using
 278 placebo and 4 using active. Comparison of the Kaplan-Meier curves (Fig. 1) for
 279 protection against infestation using a log-rank test showed a non-significant
 280 difference (chi-squared = 1.577, $p = 0.2091$) between the piperonal and placebo
 281 sprays, although in part these data were not strictly independent. If compared by
 282 Wilcoxon signed rank analysis the outcome was also non-significant ($z = -1.0097$, $p =$
 283 0.312). The application rate for the spray averaged 2.37g daily per participant.

284 *North London*

285 In order to show parents that reinfestation did not occur as rapidly as believed, we
 286 set up a small programme for 22 children from 10 closely associated families to
 287 monitor incidence of infestation. Anyone with lice was treated to eliminate

infestation and then confirmed to be louse free. The parent then checked the children using the detection comb at least once weekly. If lice were found they were treated after which the monitoring continued. All the children were followed over 9 weeks, showing that reinfestation was considerably less likely than anticipated, with no infestations until the third week. Overall there were 13 cases of infestation in nine individuals, with four children from two families being infested twice (Table 1). These data suggested that transmission within households was more common but we were unable to identify links to explain the importation of lice into any of the households.

Intention to treat comparison of the three treatment groups for time to first infestation by log-rank analysis showed fewer participants caught lice when using repellent but this was not significant (chi-squared = 1.6567, $p = 0.4368$). Fig. 2 shows the Kaplan-Meier curves of probability of remaining louse free for the ITT group over the 22 weeks. The PP analysis was essentially similar with no significant difference between the groups (chi-squared = 2.2035, $p = 0.3323$).

Some families applied the spray conscientiously throughout the study period. Others found the need for daily application too burdensome in a busy household with numerous children. Consequently, spray use was inconsistent, although residues of the piperonal could persist for a few days since most children on the study washed their hair just once each week. We observed that fine hair looked greasier than normal, which was resolved by reducing the application rate. We could not estimate the daily application rate due to inconsistencies of use and because some of the bottle weight data were not returned to the investigation site by the sponsor. However, the sponsor reported that most parents applied less spray than they thought they had, and this was apparent from the partial data available to the investigators.

314 *Adverse events*

315 There were no serious adverse events and no adverse events that could be related to
316 use of the sprays. Several parents reported dry flaky skin on their children's scalps.
317 This was not considered treatment related as screening in school showed that most
318 children had flaky scalps and the parents only noticed this while combing to check
319 for lice. One child experienced an unexpected rash on her neck but her mother did
320 not think it was treatment related, stopped spraying for a few days, and then
321 continued with no further incidence. An outbreak of chicken pox occurred in the
322 community during late June and early July 1994, which caused some parents to stop
323 spraying on a temporary basis.

324 **Discussion**

325 We have conducted two field studies evaluating a spray designed to repel head lice.
326 Our proof of concept suggested that 2% piperonal might reduce the incidence of
327 reinfestation for short periods but the study could not run for long enough to
328 properly evaluate its effectiveness in a population with a high prevalence of head
329 louse cases. The double-blind randomised study, with a moderately high
330 reinfestation risk, suggested that regular use of the product may have offered some
331 benefit, although the differences between the groups were not significant ($p < 0.05$)
332 at any level. Our knowledge of the families suggested that any observed benefit was
333 probably mostly related to the diligence of the carer in using the product.

334 Despite most parents wanting a product that helps prevent infestation, no louse
335 repellent product had been developed previously (Peock & Maunder, 1993; Canyon &
336 Speare, 2007). Because nobody knows when children are at risk of infestation it
337 would need to be used more or less continuously when children have contact with
338 others. Increased risk occurs occasionally such as "outbreaks" in schools and when
339 attending parties and sleepovers, meeting new contacts and for children spending

more time in close proximity with their peers than normal (Parison, et al., 2008). We found that many parents are more concerned about the risk of lice from school rather than social contacts so they were less likely to apply repellent before the children went to parties and at weekends when children regularly visited their friends.

Piperonal is a novel, pharmacologically safe repellent, widely used as a fragrance and flavouring agent for cosmetics and foodstuffs, with an acceptable odour. Piperonal melts at 35°-39°C, so when sprayed on hair it is borderline to melting, needing formulation to maintain a fluid state. It is physically and chemically stable and slightly more volatile than the flying insect repellent *N,N*-diethyl-3-methylbenzamide (DEET) but, unlike DEET, piperonal is not absorbed transdermally. During the investigations conducted as part of the development of the 2% piperonal product it was compared *in vitro* with other putative repellents. We tested several apparently identical samples of DEET for repellence against lice but unlike the observations of Canyon & Speare (2007) they were found to exhibit variable levels of activity ranging from similar to piperonal to no effect at all, with the majority in the latter category (Burgess IF, unpublished). The study sponsor checked each of these samples by GCMS for purity and chemical consistency and no differences were detectable by this method. There is also one enigmatic report suggested that 3-(*N*-acetyl-*N*-butyl)aminopropionic acid ethyl ester (IR3535) may be more repellent to lice, but the article omits relevant data (Bohlmann, 2008).

Both our studies involved communities where the prevalence of infestation was high, effectively 100% in Dhaka and around 22%-25% during 1993 in the North London index school. However, at a school examination near the end of the study (October 1994), when we expected high infestation following summer holiday family visits, the prevalence was just 10.6%, suggesting that increased vigilance by parents during the study to deal with any cases of infestation quickly had reduced transmission enough

367 to impact on overall prevalence. It is unlikely that the small observed repellent
368 effect had played a role in this reduction.

369 For most potential repellent users, the underlying risk of infestation is lower than in
370 our investigated communities, as European surveys have indicated (Smith, et al.,
371 2003; Harris, Crawshaw & Millership, 2003; Buczek, et al., 2004; Willems, et al.,
372 2005; Jahnke, Bauer & Feldmeier, 2008; Rukke, et al., 2011). Consequently, for
373 consumer satisfaction a repellent could be less effective like, for example, a mosquito
374 repellent. But, are repellents worth the cost and time involved in correct and
375 thorough application, plus continued vigilance to confirm its effectiveness? Perhaps
376 just checking the children's hair regularly and treating any lice found would be
377 better?

378 Dethier defined repellence as “.. *any stimulus that elicits an avoiding reaction may*
379 *be termed a repellent*” (Dethier, 1947). This includes physical and chemical effects
380 but recent public interest in use of natural and plant extracts has resulted in
381 targeting essential oils as repellents, mostly based on folklore and ancient herbals.
382 There is no scientific basis for this because volatile oils from plants are believed to
383 have evolved as feeding deterrents to phytophagous insects or as attractants for
384 pollinators (Dethier, 1947). Consequently, the idea they would repel
385 haematophagous insects is speculative. Volatile oils confuse host seeking flying
386 insects but crawling obligate ectoparasites like lice do not “host seek”. Their
387 migrations are triggered by physical stimuli such as movements of the hair
388 signalling contact of one host with another (Szczesna , 1978; Burgess, 1995). Lice
389 may not detect odours from a potential new host so they would play no role in the
390 transfer process, meaning chemical deterrents must exert potent effects on the
391 sensory physiology of lice to stop them moving onto treated hair. Physically
392 repulsive materials, e.g. heavy oils, may be more deterrent than volatile materials,
393 and some volatile materials may just be chemical irritants rather than true

394 repellents (Canyon & Speare, 2007; Canyon, 2010), although antennectomy indicated
395 that odour plays some role in the louse's response to chemicals like piperonal (Peock
396 & Maunder, 1993).

397 Pre-clinical tests of repellents have difficulty mimicking the natural substrate of
398 hair on a head and lice become acclimated to an odour. An effective repellent must
399 deter head lice within seconds, or at most minutes, of first contact. Therefore,
400 laboratory tests lasting several hours are irrelevant to practical deterrence of head
401 lice, although they could be applied to deterring body/clothing lice (Semmler, et al.,
402 2010; Semmler, et al., 2012). Generally essential oils, single terpenoids, and
403 aliphatic lactones exhibit no more repellence *in vitro* than piperonal (Toloz, et al.,
404 2006a; Toloz, et al., 2006b; Toloz, et al., 2008). However, most of these compounds
405 are also insecticidal (Canyon & Speare, 2007; Canyon, 2010; Semmler, et al., 2010;
406 Semmler, et al., 2012; Toloz, et al., 2006a; Toloz, et al., 2006b; Toloz, et al., 2008;
407 Mumcuoglu, et al., 1996), so some reported repellence may be a misinterpretation of
408 toxicity, e.g. a field study using 3.7% citronella, a concentration that is often
409 insecticidal, may actually have only recorded insecticidal activity against invading
410 lice (Mumcuoglu, et al., 2004).

411 It should be remembered that our first observations were made while investigating
412 the pediculicidal effects of piperonal that had been previously reported decades
413 earlier (Corlette, 1925; Burgess, 1993a). So, if study participants had applied
414 piperonal spray more thoroughly, would the outcome have been improved through
415 accidentally killing lice rather than repelling them? We shall never know. However,
416 as manufacturers and consumers continue to hope for a new preventive product, a
417 piperonal-based spray repellent has recently been launched in Australia
418 (Pharmacare Laboratories Pty Ltd, 2012), which in view of our experience is
419 unfortunately unlikely to prove more effective than the product we tested, unless
420 used rather more thoroughly than we observed.

Acknowledgements

Investigation team members who contributed to the studies but are not named as authors include Ayesha Akhter Ruma, Nasrine Khan, Jafour Iqbal Khan, and the late Dr Nur Islam who was chair of the ethics committee and also acted as medical supervisor (Dhaka); Barbara Shenkin, Susan Peock, and Dr JS Adler who acted as medical supervisor (North London). We wish to thank the various organisations that hosted or facilitated the work in Dhaka including Bottomley Home, Farmgate; Ardasha Islami Mission, Mohammedpur; Gandaria community; and German Doctors for Developing Countries. Also our thanks go to Beis Yaakov Primary School and other schools and institutions in the Golders Green, Colindale, and Edgware areas of North London. The decision to publish the study was that of the authors, with no input from the original sponsor or any of its ex-employees into the content of the writing or the new analyses. Any opinions expressed are those of the authors.

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Table 1 (on next page)

Outcomes from the preliminary investigation to monitor reinfestation rates in the North London community

Participant		Infestation found									
Family	Child	At start	1	2	3	4	5	6	7	8	9
A	1	No	-	-	-	-	-	-	-	Yes	-
	2	No	-	-	-	-	-	-	-	-	-
B	1	No	-	-	-	-	-	-	Yes	-	-
C	1	No	-	-	-	-	-	-	-	-	-
	2	No	-	-	-	-	-	-	-	-	Yes
D	1	No	-	-	-	-	-	-	-	-	Yes
E	1	No	-	-	-	-	-	-	-	-	-
F	1	No	-	-	Yes	-	-	-	-	Yes	-
	2	No	-	-	-	Yes	-	-	-	Yes	-
	3	No	-	-	Yes	-	-	-	-	Yes	-
G	1	No	-	-	-	-	-	-	-	-	-
	2	No	-	-	-	-	-	-	-	-	-
	3	No	-	-	-	-	-	-	-	-	-
	4	No	-	-	-	-	-	-	-	-	-
H	1	No	-	-	-	-	-	-	-	-	-
	2	No	-	-	-	-	-	-	-	-	-
	3	No	-	-	-	-	-	-	-	-	-
J	1	No	-	-	-	-	-	-	-	-	-
	2	No	-	-	-	-	-	-	-	-	-
	3	No	-	-	Yes	-	Yes	-	-	-	-
K	1	Yes	-	-	-	-	-	-	-	-	Yes
	2	Yes	-	-	-	-	-	-	-	-	-
Weekly incidence %			0	0	13.6	4.5	4.5	0	4.5	13.6	13.6
Cumulative incidence%			0	0	13.6	18.2	22.7	22.7	27.2	45.5	59.1

Figure 1

Flowchart of participants in the London study

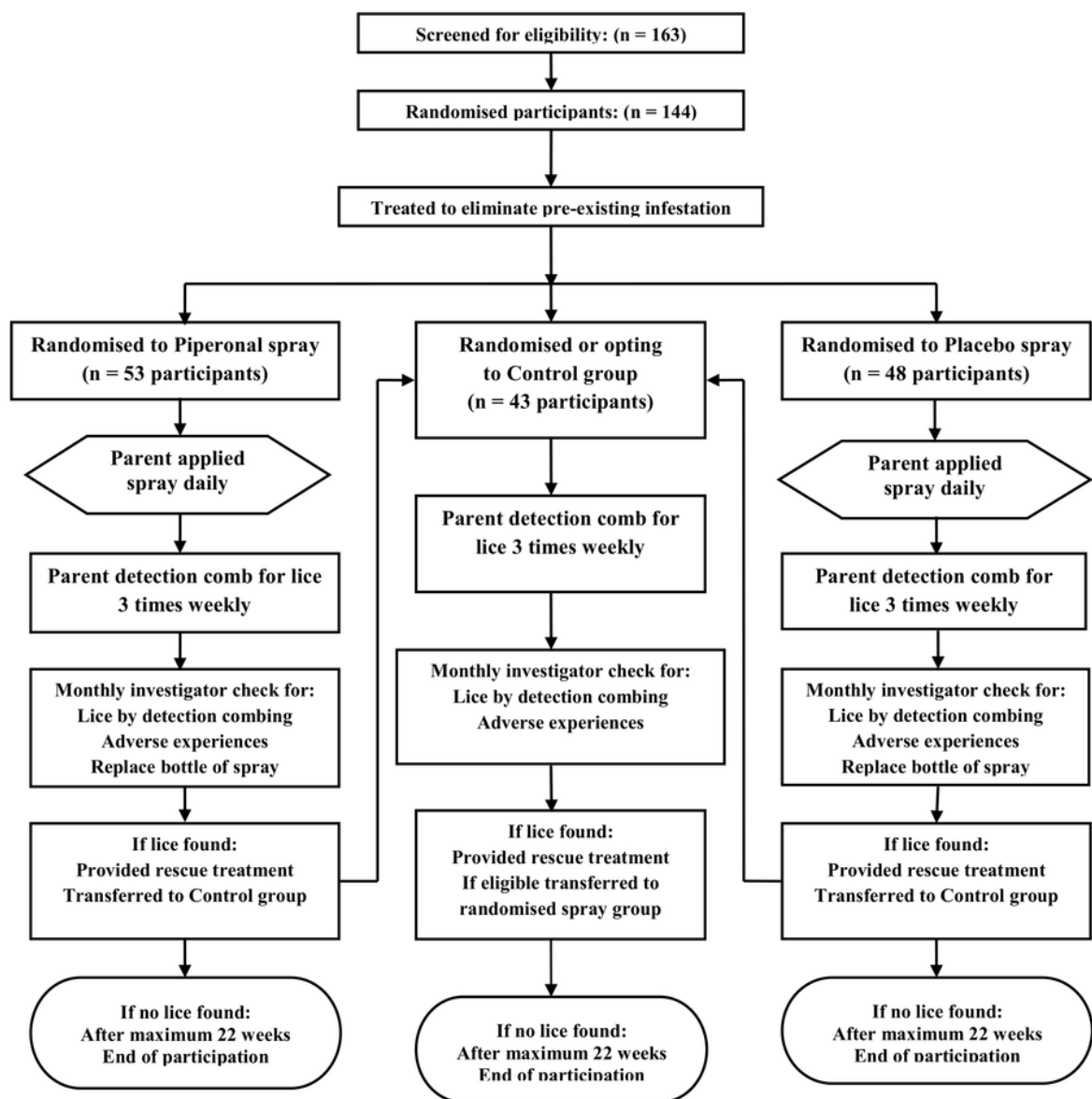


Figure 2

Kaplan-Meyer plot of the proportion of participants louse free in the Dhaka study

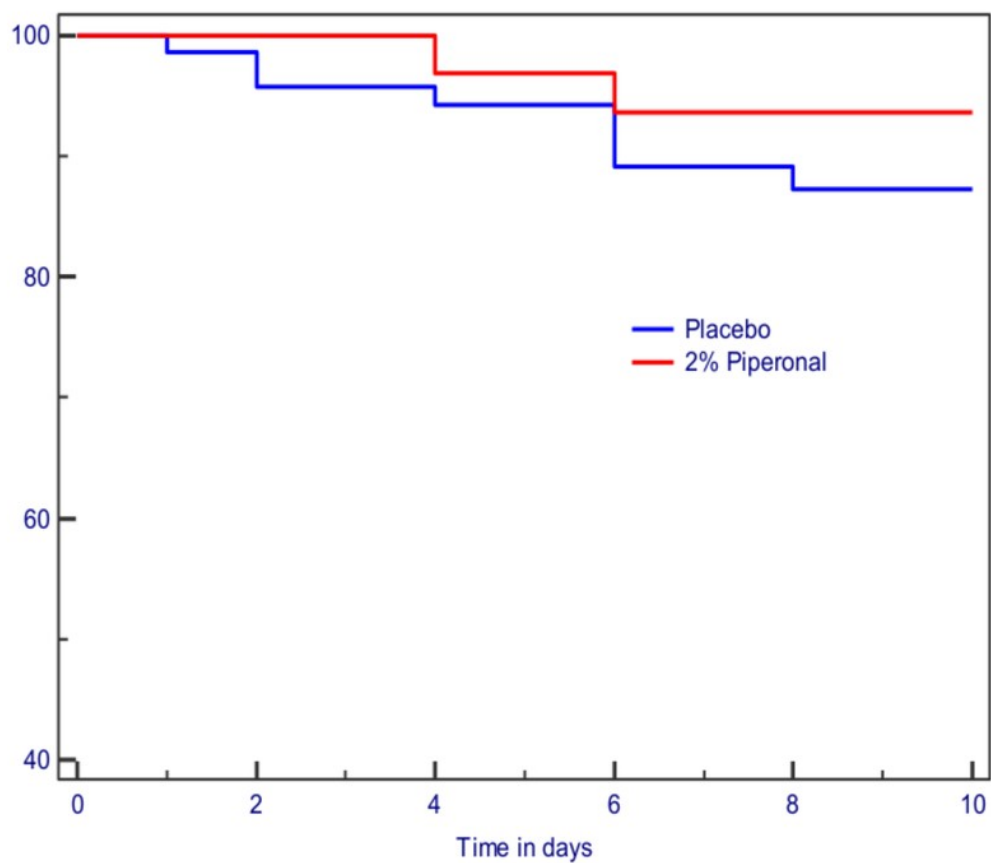


Figure 3

Kaplan-Meyer plot showing the proportion of participants remaining louse free in teh London study

