Effect of 3 years of biannual mass drug administration with albendazole on lymphatic filariasis and soil-transmitted helminth infections: a community-based study in Republic of the Congo

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Summary

Background The standard treatment strategy of mass drug administration with ivermectin plus albendazole for lymphatic filariasis cannot be applied in central Africa, because of the risk of serious adverse events in people with high *Loa loa* microfilaraemia. Thus, alternative strategies are needed. We investigated one such alternative strategy for mass drug administration for elimination of lymphatic filariasis and soil-transmitted helminth infections in Republic of the Congo.

Methods In 2012, we started a 3 year community trial of biannual mass administration of albendazole in a village in Republic of the Congo. All volunteering inhabitants aged 2 years or older were offered albendazole (400 mg) every 6 months. Infection with *Wuchereria bancrofti* was diagnosed with a rapid card immunochromatographic test for antigenaemia. People with antigenaemia were tested for microfilaraemia by night blood smears. Individuals were also tested for soil-transmitted helminth infections (ie, hookworm, *Ascaris lumbricoides, Trichuris trichiura*) with the Kato-Katz method. Assessment surveys were done at 12, 24, and 36 months. The main outcome measure was change in infection rates from baseline to year 3.

Findings Therapeutic coverage was more than 80% in all six rounds of mass administration of albendazole. Between 2012 and 2015, *W bancrofti* antigenaemia and microfilaraemia rates in the community fell significantly, from 17·3% (95% CI 14·7–20·0) to 4·7% (3·3–6·6; p<0·0001) and from 5·3% (3·9–7·1) to 0·3% (0·1–1·2; p<0·0001), respectively. The geometric mean microfilaria count in microfilaraemic people fell from 199·4 (120·4–330·5) per mL in 2012 to 39·1 (95% CIs not computed) per mL in 2015 (p=0·0095). Hookworm infection was undetectable after 1 year. Between 2012 and 2015, the number of *A lumbricoides* eggs expelled per g of faeces fell from 9844·6 (8209·0–11 480·0) to 724·4 (340·7–1114·2; p<0·0001), and of *T trichiura* eggs from 1107·4 (878·5–1336·3) to 366·0 (255·7–476·2; p<0·0001).

Interpretation Our findings strongly support WHO's provisional strategy of biannual mass administration of albendazole to eliminate lymphatic filariasis in areas where loiasis is co-endemic and ivermectin cannot be safely mass administered.

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See Comment page 683

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Introduction

The strategy for elimination of lymphatic filariasis caused by *Wuchereria bancrofti* in Africa is annual mass drug administration of ivermectin plus albendazole for 5–7 years, supported, when possible, by vector control.[1] However, ivermectin can cause serious adverse events in people with *Loa loa* microfilaria densities of greater than 30 000 per mL of blood.[2] The risk of serious adverse events induced by ivermectin precludes the launch of standard lymphatic filariasis elimination programmes in areas where loiasis is endemic—ie, in forest and forest–savannah transition zones in central Africa.[3] The distribution of lymphatic filariasis in central Africa is still unclear, and thus millions of people could live in areas that are ivermectin naive, endemic for *Loa loa*, and potential targets for elimination activities for lymphatic filariasis.

In several previous clinical trials,[4–10] various treatment regimens for *W bancrofti* infection have been investigated. The findings showed that one dose of albendazole can reduce microfilaria counts, but this reduction was less substantial than that associated with one dose of albendazole plus ivermectin.[9,10] These results, and the fact that drug-related and loa-related serious adverse events have never been reported after treatment of patients with high loa microfilaraemia with albendazole,[11–13] led WHO to propose a provisional strategy for interruption of transmission of lymphatic filariasis in areas where loiasis is endemic and onchocerciasis is not meso-hyperendemic. The strategy included mass administration of albendazole (400 mg every 6 months) along with insecticide-treated bednets to reduce exposure to vectors of lymphatic filariasis.[14]

Before the WHO provisional policy was announced in 2012, we had independently started a 3 year community trial of biannual mass administration of albendazole for lymphatic filariasis in a village in Republic of the Congo.

Research in context

Evidence before this study

In 2012, WHO proposed a provisional strategy for controlling lymphatic filariasis in areas with co-endemic loiasis where onchocerciasis is absent. This strategy includes mass drug administration with albendazole (preferably biannually), together with integrated vector management. However, the evidence for this policy was scant, and more information was needed about the efficacy of mass administration of albendazole for control or elimination of lymphatic filariasis in community settings. We searched PubMed and Web of Science with the terms "(albendazole OR zentel) AND (LF OR *Wuchereria bancrofti* OR filari$) AND community" for articles published in any language on or before Dec 1, 2016 (the date of our final search) to identify previous studies on the effect of community treatments with different drug regimens on lymphatic filariasis and soil-transmitted helminth infections. We also searched the reference lists of any identified studies. We found no evidence of previous studies of mass administration of albendazole alone for lymphatic filariasis.

Added value of this study

Ours is the first study to assess the provisional strategy issued by WHO. Our results suggest that six biannual rounds of mass administration of albendazole could have eliminated lymphatic filariasis in a community in central Africa that had a moderate endemicity level at baseline. Mass drug administration had important additional benefits on soil-transmitted helminth infections, with possible elimination of hookworm and significant reductions in prevalence and infection intensities of *Ascaris lumbricoides* and *Trichuris trichiura*.

Implications of all the available evidence

Our findings strongly support the WHO strategy and strategies in central Africa for elimination of lymphatic filariasis in areas where ivermectin cannot be mass administered because of the risk of severe adverse events in people with heavy loiasis infections.

An assessment 6 months after the second mass drug administration showed moderate effects on infection rates.[15] Here we report the effect of six rounds of biannual mass administration of albendazole on lymphatic filariasis and on soil-transmitted helminths in the same village.

Methods

Study site and participants

We did our community trial of biannual mass administration of albendazole in Seke Pembe, a village located in Mabombo Health District (Bouenza division) in Republic of the Congo, which has been described in detail elsewhere.[16] Briefly, Seke Pembe is located in a well drained savannah area. All inhabitants and older children do farm work. Some residents also hunt or fish regularly. Socioeconomic status seems very even in the community. Preliminary surveys done to identify an appropriate site for our study showed that the Mabombo Health District was endemic for loiasis, with microfilaria prevalence ranging from 2·2% to 25·5%. *L loa* microfilaria prevalence was less than 5% in Seke Pembe.

Eligible participants were aged 2 years or older. The purposes of the study were presented during meetings with village leaders, and then explained in French and in the local language, Kituba, to all participants both orally and in a written document that was given to each individual. This study was approved by the Ethics Committee for Research in Health Sciences of Republic of the Congo and done in conjunction with personnel from the Ministry of Health and Population of Republic of the Congo. Adult participants signed an informed consent form. Participants younger than 18 years of age were enrolled only if they expressed verbal assent to participate in the study and if at least one parent signed a consent form.

Procedures

Between October, 2012 (baseline), and October, 2015 (initial endpoint), albendazole was mass administered every 6 months. Serological and parasitological assessments for lymphatic filariasis and soil-transmitted helminths were done annually. All volunteering inhabitants aged 2 years or older were targeted for treatment. However, we assumed that the levels of lymphatic filariasis infection in children aged 2–4 years would be minimal, and so only participants aged 5 years or older were invited to participate in examinations. Mass drug administration was also done in October, 2015, and April, 2016, and an additional examination round restricted to people with positive filarial antigen tests in October, 2015, was held in October, 2016.

We did a population census before the trial, and updated it before each mass drug administration. During assessment periods, roughly ten households (up to 100 individuals) were visited by a member of the study team and a translator (in case the residents did not speak French) per day until all households were covered. During this visit, all household members aged 5 years or older were asked to collect a sample of their stool in a 50 mL plastic container during the early hours of the following morning, and then to report for testing at a central point in the village. All participants were registered with a simple standardised questionnaire to assess the use of bednets during the previous night as a proxy for regular use.

Detection of infections

MB and CBC measured circulating filarial antigen with the BinaxNOW Filariasis card immunochromatographic test (ICT; Alere, Scarborough, ME, USA). The results were scored semi-quantitatively.[17] All individuals with a

positive test result were asked to return for a second blood collection between 2200 h and 0100 h for quantitation of *W bancrofti* microfilaraemia. Two blood smears (70 µL each) were prepared for each person and stained with Giemsa. The microfilaria count for each individual was calculated as the arithmetic mean of the counts of the two slides and expressed as microfilariae per mL.

To detect soil-transmitted helminth infections, stool samples were analysed by SDSP at the laboratory at Madingou Hospital (Madingou, Republic of the Congo). Samples were transported within 6 h, kept in cooling boxes en route, and stored at 6°C. From each sample, two thick smears were prepared within 24 h of collection according to the Kato-Katz method.[18] Slides were examined within 1 h of preparation. The arithmetic mean egg count from the two slides was calculated, and results were expressed for each species as eggs per g of stool.

Drug administration

People with negative results for circulating filarial antigen (and children aged 2–4 years) were immediately treated with 400 mg oral albendazole. The drug was administered by a local nurse under the direct supervision of FM. People positive for circulating filarial antigen were treated just after collection of night blood samples. Village residents who did not participate in the examinations were visited at home and offered albendazole treatment. Self-identified pregnant women were excluded from mass drug administration, but albendazole was offered to them after delivery. Therapeutic coverage was calculated as the number of individuals who received the drug divided by the target population for treatment (≥2 years old) recorded during the latest census. The primary endpoint was the change in infection rates with *W bancrofti* (circulating filarial antigen and microfilaraemia).

Statistical analysis

Changes in infection rates from baseline to year 3 were analysed by comparison of cross-sectional data (all individuals tested at each timepoint) to determine the actual situation in the community. Indicators of lymphatic filariasis infection were also analysed for individuals examined both in 2012 and 2015 to assess the effect of repeated doses of albendazole at an individual level. In cross-sectional analyses, infection rates were compared with the χ^2 test, and infection intensities (ie, microfilariae per mL or eggs per g of stool) were compared with the Mann-Whitney test. Prevalence and infection intensities in individuals examined in 2012 and 2015 were calculated with McNemar and Wilcoxon signed ranks tests for matched samples, respectively. All people with negative circulating filarial antigen tests were assumed to be amicrofilaraemic. Although this method slightly underestimates the true microfilaria prevalence, our small study team could not feasibly collect night blood samples for the entire village population. For each soil-transmitted helminth species, infection intensities were classified as heavy, moderate, or light according to WHO guidelines.[19]

Role of the funding source

The sponsor had no role in study design; data collection, analysis, or interpretation; or writing of the Article. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

	October, 2012	April, 2013	October, 2013	April, 2014	October, 2014	April, 2015	October, 2015
Total community population	1055	1032	1010	921	888	939	907
Population aged ≥2 years	985	967	963	896	839	885	854
Population aged ≥2 years treated with albendazole	871 (88%)	825 (85%)	804 (83%)	800 (89%)	725 (86%)	796 (90%)	732 (86%)
Population aged ≥5 years	876	..	853	..	867	..	837
Population aged ≥5 years treated with albendazole	715 (82%)	..	712 (83%)	..	665 (77%)	..	648 (77%)
Age, years*	23 (10–40)	..	24 (10–41)	..	23 (10–43)	..	23 (11–43)
Sex ratio*	0·8	..	0·8	..	0·9	..	0·9
Tested with ICT	773 (88%)	..	741 (87%)	..	697 (80%)	..	661 (79%)
ICT positive	134	..	123	..	44	..	31
ICT positive with night blood smears	133	..	121	..	43	..	26
Tested for soil-transmitted helminths	462	..	335	..	237	..	350
Age, years†	22 (10–40)	..	28 (10–44)	..	37 (12–50)	..	28 (10–48)
Sex ratio†	0·8	..	0·8	..	0·7	..	0·8
Bednet usage	553 (75%)	..	553 (75%)	..	515 (74%)	..	76%

Data are n, n (%), or median (IQR), unless otherwise specified. ICT=immunochromatographic test. *In patients tested with ICT. †In patients tested for soil-transmitted helminths.

Table 1: **People treated with albendazole and tested during each round of mass drug administration**

Results

Table 1 shows the number of participants included in parasitological assessments, therapeutic coverage, and bednet use. Therapeutic coverage was above 83% in all treatment rounds. At the time of the last community-wide parasitological survey in October, 2015, 313 (47%) of the 661 participants tested with ICT received all six albendazole doses, 108 (16%) had received five doses, 87 (13%) had received four doses, 37 (6%) had received three doses, 38 (6%) had received two doses, and 47 (7%) had received one dose. 31 individuals (5%) who had moved into the village between April and October, 2015, did not receive any albendazole.

See Online for appendix

Prevalence of lymphatic filariasis fell significantly between 2012 and 2015 (table 2). Prevalence of circulating filiarial antigenaemia fell from 17·3% (95% CI 14·7–20·0) to 4·7% (3·3–6·6; p<0·0001; table 2), with only weak ICT scores detected in 2015 (appendix). In 2015, circulating filiarial antigenaemia rates were negligible in children and young adults (appendix). The prevalence of microfilaraemia in the village also fell, from 5·3% (95% CI 3·9–7·1) to 0·3% (0·1–1·2), between 2012 and 2015 (p<0·0001; table 2). Of the 31 participants with circulating filiarial antigenaemia in 2015, five refused to be resampled by night, and their microfilaraemia status is thus unknown. Four were amicrofilaraemic at previous examination rounds (two in 2012, and two in 2013), and the other individual (who took all six albendazole doses) had 7 microfilariae per mL in 2014. The geometric mean microfilarafemia in microfilaria-positive subjects fell by 80·4% (p=0·0095; table 2).

Among 451 individuals, circulating filiarial antigenaemia was present in 89 (19·7%) in 2012, and 27 (6·0%) in 2015 (p<0·0001). 62 individuals (70%) with circulating filiarial antigenaemia in 2012 tested negative in 2015. The seven participants who had ICT scores of 3 in 2012 had ICT scores of 1 in 2015. Of 25 individuals with a score of 2 in 2012, 14 had negative antigen tests in 2015, and 11 had a score of 1. 48 (84%) of the 57 people

	2012	2013	2014	2015	% reduction 2012–15	p value 2012–15
Rounds of mass drug administration before assessment, n	0	2	4	6	..	..
CFA, n/N	134/773	123/741	44/697	31/661	..	..
CFA prevalence (95% CI)	17·3% (14·7–20·0)	16·6% (13·9–19·3)	6·3% (4·7–8·4)	4·7% (3·3–6·6)	72·8% (60·6–81·4)	<0·0001
Microfilaraemia, n/N	41/772	31/739	9/696	2/656	..	..
Microfilaraemia prevalence* (95% CI)	5·3% (3·9–7·1)	4·2% (3·0–5·9)	1·3% (0·6–2·4)	0·3% (0·1–1·2)	94·3% (76·4–98·6)	<0·0001
Microfilaraemia in patients with positive ICTs, n/N	41/133	31/121	9/43	2/26	..	..
Microfilaraemia prevalence in patients with positive ICTs (95% CI)	30·8% (23·5–39·2)	25·6% (18·5–34·3)	20·9% (10·0–36·0)	7·7% (1·7–28·1)	75·0% (3·2–93·6)	0·0096
Geometric mean microfilarial density per mL in microfilaraemic individuals (95% CI)	199·4 (120·4–330·5)	79·6 (46·0–137·6)	27·8 (13·4–57·5)	39·1†	80·4%†	0·0095

CFA=circulating filarial antigenaemia. ICT=immunochromatographic tests. *Individuals with negative ICT results were assumed to be amicrofilaraemic. †Calculated on the basis of the two positive values; thus 95% CIs were not computed.

***Table 2*: Effect of biannual mass drug administration with albendazole on *Wuchereria bancrofti* infection**

	2012 (n=462)	2013 (n=335)	2014 (n=237)	2015 (n=350)	% reduction 2012–15	p value 2012–15
Rounds of mass drug administration before assessment	0	2	4	6	..	..
Ascaris lumbricoides						
n	261	122	44	45	..	..
Prevalence (95% CI)	56·5% (52·0–61·0)	36·4% (31·2–41·6)	18·6% (14·1–24·1)	12·9% (9·7–16·8)	77·2% (69·8–82·9)	<0·0001
Arithmetic mean eggs per g (95% CI)	9844·6 (8209·0–11 480·0)	4149·7 (3154·3–5145·1)	1887·7 (1069·8–2705·6)	724·4 (340·7–1114·2)	92·6% (75·5–100)	<0·0001
Trichuris trichiura						
n	363	238	130	208	..	..
Prevalence (95% CI)	78·6% (74·8–82·3)	71·0% (66·2–75·9)	54·9% (48·4–61·1)	59·4% (54·2–64·5)	24·4% (16·5–31·5)	<0·0001
Arithmetic mean eggs per g (95% CI)	1107·4 (878·5–1336·3)	734·8 (439·3–1030·3)	399·5 (50·8–748·3)	366·0 (255·7–476·2)	66·9% (44–89·9)	<0·0001
Hookworm						
n	30	2	0	0	..	..
Prevalence (95% CI)	6·5% (4·2–8·7)	0·6% (0·0–1·4)	0	0	100% (N/A)	<0·0001
Arithmetic mean eggs per g (95% CI)	4·4 (1·8–7·0)	0·1 (0·0–0·3)	0	0	100% (N/A)	<0·0001

N/A=not applicable.

***Table 3*: Effect of biannual mass administration of albendazole on soil-transmitted helminth infections**

with a score of 1 in 2012 were tested negative for circulating filiarial antigenaemia in 2015. Although the sample size was small, the evolution of ICT scores in relation to the number of albendazole doses received suggests that compliance to treatment affected the rate of antigen clearance (appendix).

Among the 451 individuals tested in 2012 and 2015, prevalence of microfilaraemia decreased from 6·0% to 0·5% (p<0·0001). 25 (93%) of the 27 people who were microfilaria positive at baseline were microfilaria negative in 2015. Similar results were noted in 366 individuals who took part in all four examination rounds (appendix). Microfilarial intensity in the 41 individuals who were microfilaria positive at baseline fell substantially after they started taking albendazole (appendix), but there were exceptions.

Four (0·8%) of 472 individuals negative for circulating filarial antigenaemia in 2012 became ICT positive (score 1) in 2013, but all were microfilaria negative. The incidence of circulating filarial antigenaemia was 8·5 per 1000 person-years between 2012 and 2013, and undetectable thereafter. Therapeutic coverage was 83% during the mass drug administration that took place in April, 2016. 29 (94%) of the 31 individuals who were ICT positive in October, 2015 (all with a score of 1) were retested in October, 2016. 17 were still ICT positive in 2016, including two people with a score of 2. All 17 individuals provided a night blood smear and all were microfilaria negative.

The prevalence of *Ascaris lumbricoides* decreased from 56·5% (95% CI 52·0–61·0) in 2012, to 12·9% (9·7–16·8) in 2015 (p<0·0001; table 3; appendix). Infection intensities also decreased significantly, with the arithmetic mean egg counts dropping by 92·6% (table 3). A clear shift of distribution towards lower intensity infections was noted, and no participants were in the highest intensity class after the second round of mass drug administration (appendix). Decreases in both prevalence and intensity of *A lumbricoides* infection were particularly impressive in adults (figure).

The prevalence of *Trichuris trichiura* was substantial at baseline (78·6%, 95% CI 74·8–82·3); despite a significant decrease (p<0·0001), prevalence remained high (59·4%, 95% CI 54·2–64·5) in 2015 (table 3). Mean *T trichiura* infection intensity decreased by 66·9%, from 1107 eggs per g to 366 eggs per g (p<0·0001), with a clear shift towards lower infection classes with time (appendix). Decreases in prevalence and intensity of *T trichiura* infection were more impressive in adults than in children (figure).The baseline prevalence of hookworm infection and infection intensity were low at baseline, and decreased significantly throughout the trial. No hookworm eggs were detected in stools in 2014 or 2015 (table 3).

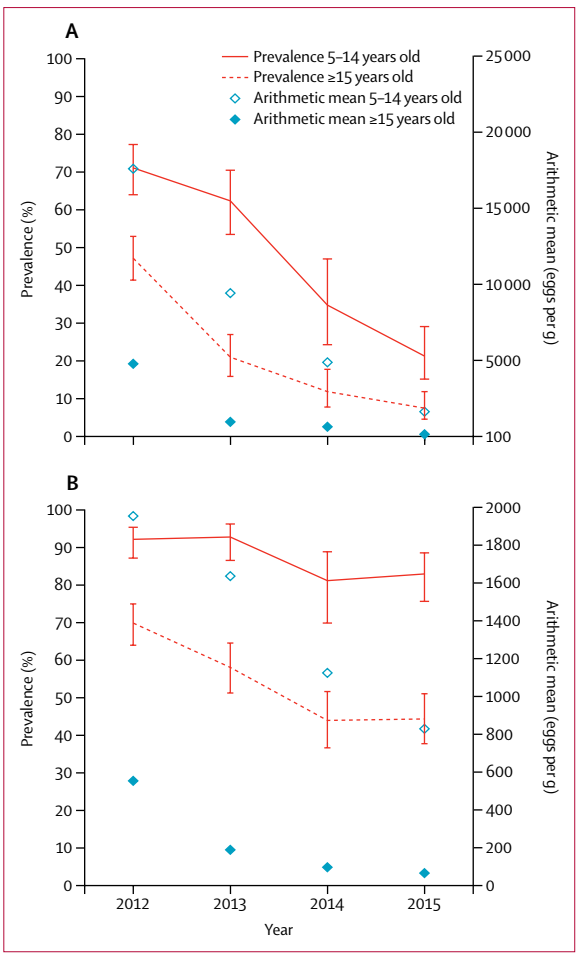

Figure: ***Ascaris lumbricoides*** **(A) and** ***Trichuris trichiura*** **(B) infections in children and adults before and after biannual mass administration of albendazole**
Error bars represent 95% CIs.

Discussion

To our knowledge, ours is the first community trial to assess the effect of repeated rounds of mass administration of albendazole on *W bancrofti*. Our results show that, in a region of moderate endemicity with bednet use of around 75%, biannual mass drug administration with high therapeutic coverage had a substantial effect on filarial infection rates and intensities. Our results cannot be explained by migration within the area (appendix), and strongly support WHO's provisional strategy for elimination of lymphatic filariasis in areas with co-endemic loiasis.[14]

The low prevalence of microfilaraemia recorded in Seke Pembe in 2015 (0·3%) is below the median of breakpoint values (0·73%) estimated by modelling for sites where *W bancrofti* is transmitted by anopheles mosquitoes.[20] However, we believe that biannual mass administration of albendazole should probably be continued in this village and in the surrounding district pending a broader survey of microfilaraemia and the results of a transmission-assessment survey. That none of the 29 people with filarial antigenaemia in 2015 were microfilaria positive when they were retested in 2016

suggests that any persistent adult worms are permanently sterilised and unlikely to contribute to transmission in the future.

The risk of recrudescence of transmission in case of interruption of mass drug administration depends not only on the proportion of the population remaining infected and on vector density, but also on the types and duration of effects that albendazole has on different stages of the parasite. Changes in *W bancrofti* microfilarial densities after a single dose suggest that albendazole has little or no direct microfilaricidal effect.[21–23] The decrease in microfilarial densities is due to albendazole's embryotoxic effect (destruction of the embryos in the uteri) or to a partial macrofilaricidal effect—previous studies showed that treatment regimens lasting several weeks can have a substantial macrofilaricidal effect on *W bancrofti*.[24] The very few people in whom microfilarial densities were not substantially reduced might not have swallowed the albendazole, or they could have been reinfected during the study. Reductions in antigen numbers and clearance in most people infected at baseline, which was especially noteworthy in younger age groups (appendix), is strong presumptive evidence of the macrofilaricidal activity of repeated rounds of albendazole treatment. Further studies including ultrasonographic examination of the lymphatic system to detect live adult worms (the so-called filaria dance sign) could provide additional information on this point.[25]

The National Malaria Control Programme distributed bednets in Seke Pembe about 2 years before we started this study. We repeatedly visited many households in the village and noted that bednets were often missing or in poor condition. Therefore, although bednets might have protected some individuals from lymphatic filariasis transmission,[16] we believe that reductions in filarial infection rates during this study were primarily a result of mass albendazole administration.

WHO recommends preventive chemotherapy focused on school-aged children to reduce morbidity related to soil-transmitted helminths.[26] The frequency of mass drug administration depends on the prevalence of the three major soil-transmitted helminths—biannual administrations are recommended when the prevalence of any helminth exceeds 50%. However, mathematical modelling suggests that transmission of soil-transmitted helminths cannot be interrupted in most cases if mass drug administration is limited to school-aged children.[27,28] This finding is particularly true for hookworm because of high infection rates and intensities in adults.[29] Thus, there is a rationale to expand mass drug administration for soil-transmitted helminths to all age groups. A cluster-randomised trial[30] has begun in Kenya to investigate the effect of community-wide mass drug administration compared with that of the standard strategy targeting school-aged children.

Although our trial had another objective, it is one of the few studies done that provides data for the effect of community-wide mass administration of albendazole over a period of years on soil-transmitted helminths. Because therapeutic coverage was high, this study provides information on the maximum effect that can be practically achieved with biannual mass administration of albendazole in this timeframe. That no hookworm infections were detected in 2014 or 2015 in Seke Pembe suggests that transmission was interrupted in this village with a low baseline prevalence (6·5%). The effect of mass drug administration was less pronounced for ascariasis, although infection rates and intensities decreased significantly, as predicted by modelling.[28] The lower effect of mass drug administration on trichuriasis is not surprising, because albendazole is less effective against that infection.[31] However, despite a high initial prevalence (78·6%), mass administration of albendazole reduced the proportions of individuals with heavy-intensity and moderate-intensity infections by 66% and 82%, respectively (appendix). Because *T trichiura* has its greatest health effects in children,[32] supplemental school-based treatment for soil-transmitted helminths should be considered. If such a strategy is adopted, a 3 day treatment with albendazole might be appropriate for school-aged children—multiday treatment is more effective than single-dose albendazole for trichuriasis.[33] Our findings suggest that, although community-wide mass drug adminstration can greatly reduce the morbidity caused by soil-transmitted helminths in areas with extensive faecal contamination, elimination of the transmission of these parasites without substantial improvements in sanitation is probably impossible.

One limitation of our study is that the region had only moderate baseline endemicity for lymphatic filariasis and hookworm. Results could be different in areas with higher endemicity. Another limitation is the diagnostic methods that were used: the new Filariasis Test Strip (Alere, Scarborough, ME, USA) is more sensitive than the ICT for detection of circulating filarial antigenaemia,[34] but this test was not available when we started the study. Rates of soil-transmitted helminth infections might have been higher if we had done Kato-Katz tests on 2 or 3 successive days (as recommended for diagnosis of individuals). However, we believe that impact assessments obtained with these slightly more sensitive methods would have been very similar to those reported here.

Finally, since 2012, people knew that they would be treated every 6 months for free and we therefore do not think that the inhabitants had recourse to take additional anthelmintic drugs during the study, but it is a possibility that cannot be excluded.

Contributors

GJW and PUF designed the study. SDSP, CBC, FM, and MB implemented the study. All authors contributed to the preparation of the Article.

Declaration of interests
We declare no competing interests.

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References

1 WHO. Preparing and implementing a national plan to eliminate lymphatic filariasis. WHO/CDS/CPE/CEE/2000.16. Geneva: World Health Organization, 2001.
2 Gardon J, Gardon-Wendel N, Demanga-Ngangue, Kamgno J, Chippaux J-P, Boussinesq M. Serious reactions after mass treatment of onchocerciasis with ivermectin in an area endemic for *Loa loa* infection. *Lancet* 1997; **350:** 18–22.
3 Zouré HGM, Wanji S, Noma M, et al. The geographic distribution of *Loa loa* in Africa: results of large-scale implementation of the rapid assessment procedure for loiasis (RAPLOA). *PLoS Negl Trop Dis* 2011; **5:** e1210.
4 Ismail MM, Jayakody RL, Weil GJ, et al. Long-term efficacy of single-dose combinations of albendazole, ivermectin and diethylcarbamazine for the treatment of bancroftian filariasis. *Trans R Soc Trop Med Hyg* 2001; **95:** 332–35.
5 Makunde WH, Kamugisha LM, Massaga JJ, et al. Treatment of co-infection with bancroftian filariasis and onchocerciasis: a safety and efficacy study of albendazole with ivermectin compared to treatment of single infection with bancroftian filariasis. *Filaria J* 2003; **2:** 15.
6 Panicker KN, Krishnamoorthy K, Sabesan S, Prathiba J, Abidha. Comparison of effects of mass annual and biannual single dose therapy with diethylcarbamazine for the control of Malayan filariasis. *Southeast Asian J Trop Med Public Health* 1991; **22:** 402–11.
7 Cartel JL, Spiegel A, Nguyen Ngnoc L, et al. Single versus repeated doses of ivermectin and diethylcarbamazine for the treatment of *Wuchereria bancrofti* var pacifica microfilaremia. Results at 12 months of a double-blind study. *Trop Med Parasitol* 1991; **42:** 335–38.
8 Cartel JL, Spiegel A, Nguyen Ngnoc L, et al. Compared efficacy of repeated annual and semi-annual doses of ivermectin and diethylcarbamazine for prevention of *Wuchereria bancrofti* filariasis in French Polynesia. Final evaluation. *Trop Med Parasitol* 1992; **43:** 91–94.
9 Dembele B, Coulibaly YI, Dolo H, et al. Use of high-dose, twice-yearly albendazole and ivermectin to suppress *Wuchereria bancrofti* microfilarial levels. *Clin Infect Dis* 2010; **51:** 1229–35.
10 Kazura JW, 2010. Higher-dose, more frequent treatment of *Wuchereria bancrofti*. *Clin Infect Dis* 2010; **51:** 1236–37.
11 Tsague-Dongmo L, Kamgno J, Pion SDS, Moyou-Somo R, Boussinesq M. Effects of a 3-day regimen of albendazole (800 mg daily) on *Loa loa* microfilaraemia. *Ann Trop Med Parasitol* 2002; **96:** 707–15.
12 Tabi T-E, Befidi-Mengue R, Nutman TB, et al. Human loiasis in a Cameroonian village: a double-blind, placebo-controlled, crossover clinical trial of a three-day albendazole regimen. *Am J Trop Med Hyg* 2004; **71:** 211–15.
13 Kamgno J, Nguipdop-Djomo P, Gounoue R, Téjiokem M, Kuesel AC. Effect of two or six doses 800 mg of albendazole every two months on *Loa loa* microfilaraemia: a double blind, randomized, placebo-controlled trial. *PLoS Negl Trop Dis* 2016; **10:** e0004492.
14 WHO. Provisional strategy for interrupting lymphatic filariasis transmission in loiasis-endemic countries. Report of the meeting on lymphatic filariasis, malaria and integrated vector management. WHO/HTM/NTD/PCT/2012.6. Geneva: World Health Organization, 2012.
15 Pion SDS, Chesnais CB, Bopda J, et al. The impact of two semiannual treatments with albendazole alone on lymphatic filariasis and soil-transmitted helminth infections: a community-based study in the Republic of Congo. *Am J Trop Med Hyg* 2015; **92:** 959–66.
16 Chesnais CB, Missamou F, Pion SD, et al. A case study of risk factors for lymphatic filariasis in the Republic of Congo. *Parasites Vectors* 2014; **7:** 300–12.
17 Chesnais CB, Vlaminck J, Kunyu-Shako B, et al. Measurement of circulating filarial antigen levels in human blood with a point-of-care test strip and a portable spectrodensitometer. *Am J Trop Med Hyg* 2016; **94:** 1324–29.
18 Katz N, Chaves A, Pellegrino J. A simple device for quantitative stool thick-smear technique in *Schistosomiasis mansoni*. *Rev Inst Med trop S Paulo* 1972; **14:** 397–400.
19 Montresor A, Crompton DWT, Hall A, Bundy DA, Savioli L. Guidelines for the evaluation of soil-transmitted helminthiasis and schistosomiasis at community level. WHO/CTD/SIP/98.1. Geneva: World Health Organization, 1998.
20 Gambhir M, Bockarie M, Tisch D, et al. Geographic and ecologic heterogeneity in elimination thresholds for the major vector-borne helminthic disease, lymphatic filariasis. *BMC Biol* 2010; **8:** 22.
21 Dunyo SK, Nkrumah FK, Simonsen PE. A randomized double-blind placebo-controlled field trial of ivermectin and albendazole alone and in combination for the treatment of lymphatic filariasis in Ghana. *Trans R Soc Trop Med Hyg* 2000; **94:** 205–11.
22 Dunyo SK, Simonsen PE. Ivermectin and albendazole alone and in combination for the treatment of lymphatic filariasis in Ghana: follow-up after re-treatment with the combination. *Trans R Soc Trop Med Hyg* 2002; **96:** 189–92.
23 Fox LM, Furness BW, Haser JK, et al. Tolerance and efficacy of combined diethylcarbamazine and albendazole for treatment of *Wuchereria bancrofti* and intestinal helminth infections in Haitian children. *Am J Trop Med Hyg* 2005; **73:** 115–21.
24 Jayakody RL, da Silva C, Weerasinghe W. Treatment of bancroftian filariasis with albendazole: evaluation of efficacy and adverse reactions. *Trop Biomed* 1993; **10:** 19–24.
25 Mand S, Debrah AY, Klarmann U, et al. The role of ultrasonography in the differentiation of the various types of filaricele due to bancroftian filariasis. *Acta Trop* 2011; **120:** S23–32.
26 WHO. Preventive chemotherapy in human helminthiasis. Geneva: World Health Organization, 2006.
27 Anderson RM, Truscott JE, Pullan RL, Brooker SJ, Hollingsworth TD. How effective is school-based deworming for the community-wide control of soil-transmitted helminths? *PLoS Negl Trop Dis* 2013; **7:** e2027.
28 Anderson RM, Turner HC, Truscott JE, Hollingsworth TD, Brooker SJ. Should the goal for the treatment of soil transmitted helminth (STH) infections be changed from morbidity control in children to community-wide transmission elimination? *PLoS Negl Trop Dis* 2015; **9:** e0003897.
29 Turner HC, Truscott JE, Hollingsworth TD, Bettis AA, Brooker SJ, Anderson RM. Cost and cost-effectiveness of soil-transmitted helminth treament programmes: systematic review and research needs. *Parasit Vectors* 2015; **8:** 355.
30 Brooker SJ, Mwandawiro CS, Halliday KE, et al. Interrupting transmission of soil-transmitted helminths: a study protocol for cluster randomised trials evaluating alternative treatment strategies and delivery systems in Kenya. *BMJ Open* 2015; **5:** e008950.
31 Keiser J, Utzinger J. Efficacy of current drugs against soil-transmitted helminth infections: systematic review and meta-analysis. *JAMA* 2008; **299:** 1937–48.
32 Truscott JE, Hollingsworth TDI, Brooker SJ, Anderson RM. Can chemotherapy alone eliminate the transmission of soil transmitted helminths? *Parasites Vectors* 2014; **7:** 1–8.
33 Steinmann P, Utzinger J, Du Z-W, et al. Efficacy of single-dose and triple-dose albendazole and mebendazole against soil-transmitted helminths and *Taenia* spp: a randomized controlled trial. *PLoS One* 2011; **6:** e25003.
34 Weil GJ, Curtis KC, Fakoli L, et al. Laboratory and field evaluation of a new rapid test for detecting *Wuchereria bancrofti* antigen in human blood. *Am J Trop Med Hyg* 2013; **89:** 11–15.