

Evaluation of onchocerciasis control in the Upper Denkyira East municipal in the forest area of Ghana: Responses of participants and distributors to the CDTI programme

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ARTICLE INFO

Keywords:

Onchocerciasis
CTDI
Ivermectin
Compliance
Coverage
Ghana

ABSTRACT

The African Programme for Onchocerciasis Control (APOC), which focused on annual mass treatment with ivermectin, was launched in 1995 and was replaced by the Expanded Special Project for Neglected Tropical Diseases (ESPEN) by the end of 2015. In Ghana, the Community Directed Treatment with Ivermectin (CDTI) was introduced in 1999. After a decade, biannual reinforcement was introduced during which the Ghana Health Service (GHS) recorded coverage rates through routine data collection. Transmission studies conducted in the Upper Denkyira East Municipal (UDEM) of the forest zone of Ghana in 2002 and 2006 had shown that annual treatments with ivermectin had hardly any effect on the transmission of *Onchocerca volvulus* by the vector *Simulium sanctipauli*. In order to establish whether or not this was due to an insufficient compliance to the CDTI programme, an additional questionnaire survey was carried out in 2013 following those conducted in 2002 and 2006. The repeat transmission survey conducted in 2013 in the same area revealed that the vector *S. sanctipauli* had apparently disappeared from the rivers Ofin and Pra due to gold mining activities. In 2006 and 2013, we conducted surveys using structured questionnaires to address issues related to compliance and to compare results on the effectiveness of CDTI. A total of 692 individuals from 7 villages and 447 individuals from 9 villages were interviewed in 2006 and 2013 respectively. Questions asked included whether or not they had taken the ivermectin and reasons for not doing so when that was the case. Results were compared with the previous investigations conducted in 2002. Whereas official reported coverage rates ranged from 59 to 85% in 2006 and from 88 to 97% in 2013, compliance rates decreased from 36% in 2006 to 21% in 2013. Factors affecting compliance included fear of unpleasant side effects (pruritus and oedema), which decreased from 36% to 21% for the same period. Lack of awareness of CDTI sharply increased from 12% to 46% for the same period. Participants believed that treatments were no longer necessary due to the absence of vectors observed in 2013. There seems to be a considerable difference between coverage and compliance rates in the study communities. The difference can be attributed to the performance of the Community-Directed Distributors (CDDs) and the absence of the vector population observed in 2013. Discussions with CDDs suggested that factors that led to non-compliance were mostly side effects, unawareness of the disease by immigrants and lack of financial motivation for the CDDs. Also included was the fact that they needed to complete distribution of the drugs in the entire village, covering all households within just one week irrespective of the size of the catchment area. This, they thought was too much work for a short period of time. We propose to intensify the training of CDDs by the national Neglected Tropical Diseases Programme (NTDP) and to include the Community-based Health and Planning Services (CHPS) concept into onchocerciasis control efforts for awareness creation while the vector population and the transmission should be further monitored. The population should be made aware that the side effects they experienced from previous treatments or had heard about had reduced significantly. They also should be in the known that vector flies may return and so the risk of transmission remains.

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1. Introduction

The WHO Onchocerciasis Control Programme (OCP) in West Africa started in 1974 to interrupt transmission of onchocerciasis and was extended in 1977 to the savannah areas of 7 countries including Ghana. OCP was mainly based on the weekly aerial spraying of rivers, where vector species of the *Simulium damnosum* complex were breeding, with the insecticide temephos. The programme was finally extended to 11 West African countries by 1989. Due to invasion of vector flies from southern forest areas, the programme extended further south in 1998 with Ghana being included (Fig. 1). The OCP closed its operations in 2002. In 1987, the microfilaricide drug ivermectin (Mectizan®), donated by Merck & Co Inc., became available and was freely distributed (Crump and Omura, 2011). Onchocerciasis control then successively switched from vector control to mass drug administration of the human population in meso- and hyperendemic areas. The African Programme for Onchocerciasis Control (APOC) was launched in 1995 and ultimately included all endemic areas of sub-Saharan African countries by using long-term distribution of ivermectin with the goal of elimination.

Community Directed Treatment with Ivermectin (CDTI) was introduced in Ghana in 1998 in onchocerciasis-only areas (Personal Communication with Program Manager, NTP, Ghana). Annual mass treatments with ivermectin began in 1999 in selected communities within the Upper Denkyira East Municipal (UEM) (Kutin et al., 2004). To improve the effect of mass ivermectin treatment APOC introduced biannual treatments. Within the period 2002 to 2007, Special Intervention Zones (SIZ) were created to serve as the focus of CDTI implementation after the devolution of OCP to APOC. With CDTI, the communities themselves were given the responsibility to appoint a Community Directed Distributor (CDD) and to decide on date and mode of distribution. Cases of severe adverse reactions were reported and transferred to appropriate institutions for treatment and

documentation. The CDD mobilizes the communities, distributes the ivermectin and reports coverage rates to the Disease Control Officer (DCO) of the district health facilities, which in turn are passed to the Neglected Tropical Diseases Programme (NTDP) of the Ministry of Health. The coverage rate is the proportion of the total population to whom the drugs were delivered at their households. The national coverage is defined as the proportion of people requiring ivermectin and who receive ivermectin in the country. The national coverage reported for Ghana for 2016 was 83.8% of the 5,169,058 total population requiring Mass Drug Administration (MDA) (WHO, 2017). The reported coverage rate is different from the compliance rate, which is the proportion of eligible people who actually took the antifilarial drug. This is also called the surveyed or estimated coverage (UNICEF, 1996). The same report mentioned differences between reported and surveyed coverage the latter, to be lower in 36 villages investigated in Ghana. Turner et al. (2014) discussed models on the influence of coverage and compliance over several years on the expected duration of treatment to reach elimination. A coverage rate of at least 65% in endemic communities over a period of 15 years is projected to limit the transmission of onchocerciasis by reducing the parasite reservoir in the humans and to control the disease (Sékétéli, 2002). It was found later that a partial temporary interruption of transmission is not sufficient and will allow the parasite reservoir to remain at a viable level (Brieger et al., 2012).

A study observed suboptimal treatment results and discussed the possibility that *O. volvulus* had developed sub-optimal response to ivermectin in Ghana (Awadzi et al., 2004). In 2009 therefore, Ghana changed to biannual treatment, which was extended to the Upper Denkyira East Municipal (UEM), an area hyperendemic for onchocerciasis, to achieve effective control and prevent recrudescence of onchocerciasis leading to elimination. Early CDTI coverage rates were made available for 4 villages for 1999 and 2000: Nyaduom 42.2 and 9.4%, Akwanhyiamu 73.4 and 33.8%, Asaman 64.9 and 48.8% and

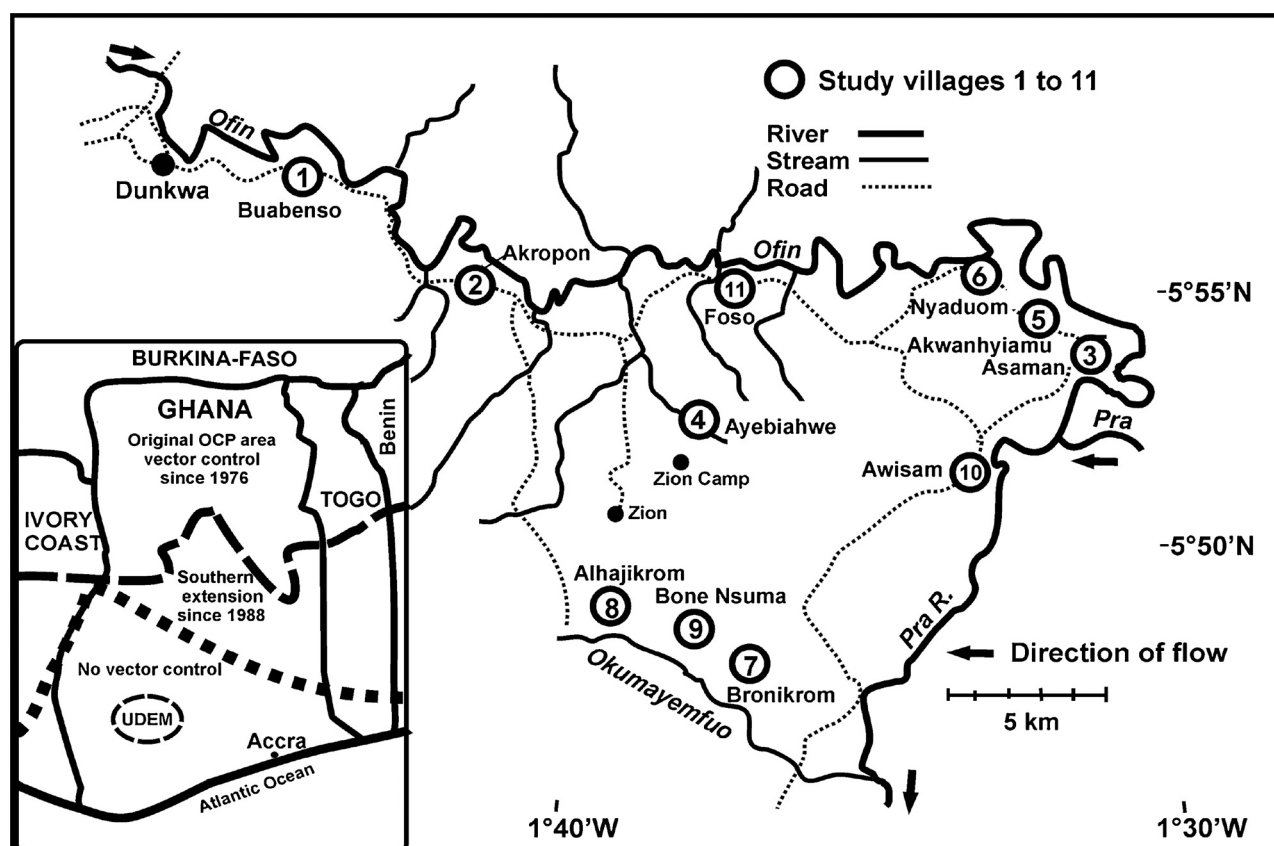


Fig. 1. Map of study area UDEM with villages 1–11 investigated at the rivers Ofin, Pra and the tributary Okumayemfuo in Upper Denkyira East Municipal where questionnaires were conducted in 2002, 2006 and 2013. Inset with original OCP area and its southern extension in Ghana and UDEM.

Awisam 56.4 and 13.8% respectively. Coverage rates declined from the first to second year and no further information for the reason of the decline is available (Neglected Tropical Diseases Programme, Ghana Health Service unpublished data, 2001).

Productive breeding sites and transmission of onchocerciasis by *S. sanctipauli* Pra form, the main vector of *O. volvulus* in the forest zone of Ghana, were studied along the rivers Ofin and Pra in 2001, 2002, 2006 and 2013 (Garms et al., 2015; Kutin et al., 2004). In the latter year, they found out that the *S. sanctipauli* breeding sites in the rivers Ofin and Pra had apparently disappeared, in part due to gold mining activities. However, in 2014 people from villages along the rivers Ofin and Pra claimed that after several years of absence, biting blackflies were noticed after heavy rains in June, July, and August, but again no flies were caught in 5 villages in October 2014. A corresponding observation was made by Lambertson et al. (2014) when no blackflies were caught on the lower Pra river in the dry season in 2011 due to gold mining activities. We know that the rivers have been highly polluted due to the gold mining activities with accompanying high levels of suspended solids and turbidity (Garms et al., 2015). Thus the disappearances of the vectors are directly linked with pollution of the river, unlike the Okumayemfu tributaries that have no gold mining activity on it. Another onchocerciasis vector, *S. yahense*, was found in two short rapids of this river (Garms et al., 2015). The disappearance of onchocerciasis was reported in a localised area in Uganda as a result of the elimination of the vector and continued annual ivermectin treatments (Lakwo et al., 2013). We envisage a similar situation in the UDEM where, due to gold mining, the vector might not be readily found.

Transmission of onchocerciasis by the efficient vector *S. sanctipauli* Pra form remained high in 2002 and 2006 despite annual CDTI. Therefore, the objective of this study was to assess the compliance to CDTI in selected communities in UDEM in 2006 and 2013 and to compare results with those obtained in 2002 (Garms et al., 2015; Kutin et al., 2004). We further wanted to provide information on the quality of the distribution of ivermectin to the population in an area of plausibly low compliance due to various factors like side effects caused by ivermectin, gold mining and immigrating work force, the presence or absence of *Simulium spp* vectors and the performance of CDDs. Transmission of onchocerciasis evaluated in UDEM in 2002 and 2006 was high and obviously not affected after 7 years of ivermectin distribution.

2. Materials and methods

The study was conducted in 2006 and 2013 within 10 communities: Buabenso, Akropon, Asaman, Ayebiahwe, Akwanhyiamu, Nyaduom, Bronikrom, Alhajikrom, Bone Nsuma and Awisam in the UDEM (Central Region) of the forest zone of Ghana (Fig. 1), where onchocerciasis is hyperendemic (Garms et al., 2015). UDEM is bound to the east by the Pra river, which flows south towards the Atlantic Ocean, and to the north by the Ofin, a major tributary of the Pra. The area is extensively drained by small tributaries of these two rivers. Our study area is situated south of the southern extension of the former Onchocerciasis Control Programme (OCP) of the World Health Organisation operated from 1974 to 2002. Vector control has never been carried out in UDEM although clinical research programmes have been carried out in the area since 1997. These included treatment trials with doxycycline and other antibiotics (Hoerauf et al., 2008). Residents of UDEM are generally aware of CDTI.

Participants gave their voluntary consent after the study was explained to them and face-to-face interviews were conducted in their local language using structured questionnaires. We took a representative random sample of household members and recruited them into the study after written informed consent had been obtained, using the agreed population based data from the district health directorate and were followed for both 2006 and 2013. Results were compared with those of 2002 (Garms et al., 2015; Kutin et al., 2004). In 2006, we interviewed 692 individuals from 7 villages and in 2013, 447

individuals from 9 villages, all more than 17 years old. All participants were mobilized by the chiefs of the town in advance. The 2013 investigation included three additional villages at the Okumayemfu, a tributary of the Pra River (Fig. 1). In this area the population size fluctuates, peaking during the cocoa harvesting season from November to February. Questions asked comprised whether medication had been given and actually swallowed, years of receipt and source of medication. Other questions included reasons for non-compliance with the treatment programme, profession, exposure to biting flies and knowledge of the blackfly vector.

In 2017, we conducted interviews at intervals with former vector collectors, villagers and opinion leaders and liaised with the UDEM district health directorate to perform focus group discussions with 28 CDDs and DCO. This was done to obtain information on the presence or absence of *Simulium* vectors, the month when CDTI takes place, the main reason why drugs are not taken and what could be done to enhance the compliance.

A house-to-house distribution of ivermectin was administered by the CDDs supplied by the District Health Directorate to persons above the height of 90 cm. Further inclusion criteria were health and lack of any other medication being taken. Pregnant and breastfeeding women with a child less than one week old were excluded. A projected census was conducted by the district and the names and gender of people in the household were also recorded by the CDDs.

The Committee of Human Research, Publication and Ethics (KNUST) granted permission for the work to be carried out (CHRPE/AP/426/13). Data were entered into Microsoft Excel, cleaned and then imported to STATISTICA, Windows 1993 (StatSoft Inc., Tulsa, OK, USA) for statistical analysis of the results.

Villages were selected on the basis of the previous intervention that had taken place, for the purpose of comparison. The total sample size of the study participants interviewed was estimated to be 384; this was based on the anticipated yield and response rate of 50%. Sample size was determined using the binomial model to estimate the confidence interval (CI).

$$N = Z^2(pq)/d^2$$

Sample size was calculated with a 95% CI and precision level of 5%. In the equation above, N is the sample size, Z is the critical value of the standard normal distribution at the 5% level (1.96), p anticipated response rate (0.50), q = 1 – p, and d is the precision level. The minimum sample size obtained was 384. A random sample was interviewed from each community within the households that had previously participated in the CDTI. Probability proportional to size method was later applied to distribute the sizes according to the population of the villages and anticipated previous participation rates and yield. A total of 692 were interviewed in 2006 and 447 interviewed in 2013.

3. Results

CDTI compliance determined in 2002 in 6 villages (Kutin et al., 2004), in 2006 in 7 villages and in 2013 in 9 villages are summarized in Table 1. The proportion that had some knowledge of onchocerciasis was high (88%) in 2006 and relatively lower in 2013 (64%). Inquiries in Buabenso, Akropon, Ayebiahwe, Akwanhyiamu, Nyaduom and Asaman in 2006 and 2013 revealed a decline in mean compliance rate from 39% to 26% within the 7 years. The compliance in 7 villages in 2006 was highest in Akwanhyiamu (61%) and lowest in Buabenso (18%). In 2013 compliance was highest in Ayebiahwe (51%) followed by Akwanhyiamu (36%) and lowest in Akropon (7%). Respondents of Bone Nsuma did not take part in CDTI at all. A slight increase of mean rates of compliance within 11 years was observed in 4 villages: Buabenso, Akropon, Ayebiahwe and Asaman which were 22% in 2002, 30% in 2006 and 23% in 2013. The compliance in Buabenso dropped from 18% in 2006 to 11% in 2013 and in Akropon from 25% to 7% (Table 1).

Table 1

Results of compliance studies conducted in 2002, 2006, and 2013 in 6, 7 and 9 communities respectively of the Upper Denkyira East Municipal in the forest zone of Ghana.

Village Name	Registered population			Study 2002		Study 2006		Study 2013		p-value	
	2002	2006	2013	N	Cpl (%)	N	Cpl (%)	N	Cpl (%)	2002/06	2006/13
Buabenso (1)	1297	1007	1243	100	0 (0)	125	22 (18)	100	11 (11)	0.0000	0.7210
Akropon (2)	942	807	899	98	36(37)	100	25 (25)	100	7 (7)	0.0347	0.0003
Asaman (3)	521	402		116	24 (21)	75	29 (39)	40	9 (23)	0.0037	0.4300
Ayebiahwe (4)	987	242	127	100	32 (32)	102	40 (39)	35	18 (51)	0.1500	0.1084
Akwanyiamu (5)	736	990		ND		100	61 (61)	69	25 (36)		0.0008
Nyaduom (6)				ND		100	51 (51)	50	13 (28)		0.0041
Bronikrom (7)			201	ND		ND		21	6 (29)		
Alhajikrom (8)				ND		ND		21	4 (19)		
Bone Nsuma (9)				ND		ND		11	0		
Awisam (10)	2427	1024		101	30 (30)	90	22 (24)	ND		0.1767	
Foso (11)				99	28 (28)	ND	ND	ND			
Totals				614	150 (24)	692	250 (36)	447	93 (21)		

Ayebiahwe, a cocoa farming village situated further away from the Ofin and Pra rivers, had a higher compliance rate of 39% in 2006 and 51% in 2013. Three east villages Nyaduom, Akwanhyiamu and Asaman had a significantly higher mean compliance rate of 50% in 2006 than the remaining UDEM villages with a compliance rate of 26% ($p = 0.0000$). The same pattern was observed in 2013 with 29% and 23% respectively ($p = 0.0005$).

Our data contrasted with the CDDs reported coverage rates of 2006 and 2013 for the communities Buabenso (85% and 97%), and Alhadjikrom (61% and 88%) respectively (Table 2). The majority of communities investigated are situated alongside the rivers Ofin and Pra where small-scale gold mining in the rivers and at the riverbanks is common and people and goods are transported across the rivers in canoes. According to our findings, fishing activities have been reduced to the barest minimum if any at all, probably as a result of the high turbidity in the Ofin and Pra (Garms et al., 2015). In 2006, 46% respondents reported farming as their main source of income which increased to 52% in 2013. Over the same period the percentage of people engaged in small-scale gold mining increased significantly from 7 to 14% whilst factors like trading, tailoring, school (teacher, students) remained similar. The number of people not aware of CDTI significantly increased from 2006 (12) to 2013 (46). Twenty one percent (21%) in 2013 did not get the ivermectin treatment which is actually a decrease over that in 2006 (36%). Reasons for not taking ivermectin were fear of unpleasant side effects (pruritus and oedema), lack of awareness and absence through travelling. Nevertheless fear of unpleasant side effects decreased significantly from 76% in 2002 to 16% in 2013 (Table 3).

The CDDs ($N = 28$) of UDEM stated at a focus group discussion that the most important factors leading to non-compliance are side effects. Side effects reported were real but the sequence of records looked like a rich store of occasional instances of individual cases. These side effects reported were in the foremost pruritus, different forms of oedema (swollen limbs, face eyes, penis), rashes, joint pains, reduction in body

weight, dizziness, collapsing and the emergence of other diseases that led to the death of some people. One CDD reported that two people from her community developed a stroke after taking the ivermectin drug. Both were then advised to take the drug again; the one that refused the next round of treatment which was after 3 months is still suffering from stroke while the other who took it became well. Another said that in the early stages of drug administration when education was low, an immigrant died after taking a dosage greater than that appropriate for his height. Another CDD also said that a woman developed swollen legs for which she was hospitalized and he had to cater for her and support her financially. CDDs reported further that the farming population fear days lost for work due to side effects and are of the view that there was a general apathy towards the ivermectin campaign. CDDs complained about the short duration of one week for the campaign and wished to be better resourced. The massively expanded gold digging activities nearly all year round in rivers Ofin and Pra led to new employments in the area. Individuals are attracted from other parts of Ghana and are difficult to convince to take part in CDTI as repeatedly reported from Buabenso and Akropon. The migrant population living for many years in Buabenso claimed that they never heard of the ivermectin drug being distributed. We also observed that the farming population, active in large-scale cocoa plantations, fluctuates and increases considerably during the harvesting season (from November to February). This work force are not be covered by CDTI. No or low compliance was observed at the cocoa farming communities in Bone Nsuma, a village with individuals arriving mainly for the cocoa farming activities

Some of our former vector collectors informed us that in 2013 blackflies had apparently disappeared from six sentinel villages along the rivers Ofin and Pra. Inhabitants were therefore less exposed and obviously reluctant to accept CDTI. Farmers in villages distant from the rivers assume that the decline of the vector population is due to the increased use of insecticides (imidacloprid and thiamethoxam) to secure higher yields in the cocoa plantations. In some of the villages individuals claimed that no ivermectin drugs arrived, others said that they prefer to go to a clinic to receive the treatment.

A higher proportion of males (26%) than females (16%) were found to comply with CDTI. The majority of the participants that had the highest compliance were found in the 39–59 age group with significant more males (11%) than females (8%). Results of compliance for males and females and age groups are compiled in Table 4. There existed difference in compliance with regards to gender, with the male being more compliant than the female.

Shown are the registered populations for some of the villages, where available, numbers of participants (N), numbers and percentages who had complied (Cpl) with the CDTI. ND = not done. Numbers (in brackets) of villages refer to their locations as shown in map (Fig. 1).

Table 2

Registered populations and coverage rates of four villages in Upper Denkyira East Municipal for the years 2006 and 2010–2015 reported by the CDDs.

Year	Buabenso N (%)	Akropon N (%)	Ayebiahwe N (%)	Alhajikrom N (%)
2006	1007 (85)	807 (61)	242 (59)	165 (61)
2010	1243 (81)	899 (69)	127 (80)	201 (82)
2011	1243 (91)	899 (84)	127 (73)	201 (92)
2013	1537 (97)			112 (88)
2014	1585 (90)			116 (61)
2015	1164 (92)			119 (87)

Populations are shown as N, coverage rates in %. Data were provided by the NTDCP, MoH Ghana.

Table 3

Reasons for not participating in community-directed treatment with ivermectin (CDTI) and profession of local people in 11 communities of Upper Denkyira East Municipal in 2002, 2006 and 2013.

Year	2002 N (%)	2006 N (%)	2013 N (%)	p-value 2002 < > 2006	p-value 2006 < > 2013
Number responded	614	692	447	0.0064	0.0042
Not treated (%)	150 (24)	250 (36)	93 (21)		
Fear of side effects	468 (76)	161 (23)	72 (16)	0.0000	0.0021
Not aware of CDTI	65 (11)	83 (12)	205 (46)	0.2826	0.0000
Travelled	24 (4)	77 (11)	30 (7)	0.0000	0.0343
Not important	36 (6)	21 (5)	25 (6)	0.2139	0.2327
Trading	18 (3)	35 (8)	30 (7)	0.0001	0.2670
Farming	ND	317 (46)	232 (52)		0.0240
Gold mining	ND	47 (7)	64 (14)		0.0001
School	ND	125 (18)	70 (16)		0.3614
Tailoring	ND	19 (3)	7 (2)		0.4454

Numbers of participants are shown as N and their percentages as %.

Comparing a year to another year are shown as < > .

Table 4

Compliance per age and sex distribution in 2013 of 9 communities in UDEM.

Sex	Total investigated	Male N (%)	Female N (%)	p-value
17–39	245	23 (9)	12 (5)	0.0453
40–59	148	25 (17)	18 (12)	0.0109
60–79	49	8 (16)	6 (12)	0.2930
80–101	5	1 (20)	0 (0)	
Total number of complied people	447	57 (13)	36 (8)	0.0102

Numbers of complied participants are shown as N and their percentages as % per each age group.

4. Discussion

The aim of onchocerciasis control changed from reducing disease burden to the elimination of infection. Low therapeutic coverage due to a weak programme implementation will be detrimental to reaching the morbidity elimination goal (Turner et al., 2014). It was shown that in a hyperendemic area of Sierra Leone treatment with repeated doses of ivermectin distributed to 30% of the population could reduce transmission (Chavasse et al., 1995). Six years of annual ivermectin mass treatment in the savannah region of Ghana reduced the community microfilarial load (CMFL) by at least 50% which reduced > 36% further after three years of biannual treatment (Frempong et al., 2016). This study was done in the savannah region of Ghana. The epidemiology of onchocerciasis is different in the forest region of Ghana where our studies were carried out. Our study area (UDEM) was never included into OCP vector control activities.

The study attempts to clarify the compliance of the population with ivermectin mass treatments. We found that the compliance fluctuates in the communities investigated. One outcome of this study is the overall low compliance rate of only 7–51% in 2013 in contrast to a reported coverage rate of 69–97%. One of the strongest predictors of compliance with mass drug treatment schemes is the perception of how well the CDDs are doing their work (Nuwaha et al., 2005). We could demonstrate that despite many obstacles higher compliance can be achieved. The significantly higher compliance rates at the three east UDEM villages Nyaduom, Akwanhyiamu and Asaman depend on one highly motivated and well-accepted CDD. In addition, these villages belong to the Health Directorate of the neighbouring Assin North Municipal District. CDDs receive the drugs, training and instructions at Assin Fosu. The higher compliance rate at Ayebiahwe is linked to its association with a farming community 4 km off the river Ofin with a specifically marked strong leadership guiding the community including the CDD. We identified local conditions contributing to the majority of villages with low compliance of less than 40% in 2002, 2006 and 2013. The

gold mining activity in southern Ghana contributed to an influx of workers from all over the country prospecting for gold in the rivers. It has proved difficult to convince this highly exposed mostly young working group to participate in CDTI. The gold mining activity is shifting presently from the riverbed to the riverbank. This may further contribute to a higher turbidity of rivers and an unstable transmission pattern (Garms et al., 2015). The majority of villagers interviewed near the rivers Ofin and Pra reported not to have seen blackflies for years. Individuals are increasingly reluctant to understand that after years of not noticing blackflies at UDEM, transmission may still occur by change of weather conditions such as abnormally high rainfall. The low awareness of the programme to control onchocerciasis in rural communities in the UDEM was aggravated when a biannual indoor residual insecticide spraying program (IRS) to control malaria started in 2002. Individuals in villages along the river Ofin from Buabenso to Foso and Ayebiahwe confirmed in 2003 and 2004 that their houses were sprayed accordingly. People may misunderstand the participation in one or the other programme. The factors influencing non-compliance include CDDs insufficient knowledge or training on the disease during the early years of drug administration, low performance of CDDs due to lack of motivating factors, the low prevalence of the vector, possible side effects, fear of developing diseases that may lead to death, unawareness of the onchocerciasis by immigrants, migrating workers at cocoa plantations and the absence of individuals during drug administration. Lack of awareness of CDTI is attributed to the lack of health education of the community, immigrant gold miners and individuals in the community not taking note of announcements all best described by one CDD as apathy towards participation in the programme.

To take concerns of CDDs with respect to side effects seriously should be an important component of the training as we could show that those fears lowered from 76% in 2002 to 16% in 2013. We propose to include the results of this study in focus group discussions and training programmes for CDDs and Basic Health workers with the aim of achieving higher compliance. The CDDs at the District Health Directorate should be better equipped to convince the population at UDEM that repeated CDTI will further lower the risk of side effects and that they are still at risk of infection with *O. volvulus*. The distant future of gold mining, presently highly prevalent in Southwest Ghana, is then no longer profitable in the majority of rivers on a large scale. Mining the riverbeds and banks will be also less profitable in the future for smaller companies as the amount of gold is depleting gradually. The government of Ghana is reinforcing laws to prevent illegal mining operations. This combination of factors could change the local ecology and may lead to a resurgence of the *S. sanctipauli* vector in the big rivers and therefore lead to transmission of onchocerciasis resembling the situation demonstrated in 2006 (Garms et al., 2015). There is an urgency to react to this possible ecological change to prevent a significant

resurgence of transmission and clinical cases.

The discrepancies between the high reported coverage rate and lower compliance rate could not be explained by CDDs and DCOs but must be addressed. There is still the possibility that respondents did not recall well after two months CDTI took place or they received the drugs but did not take them. There is also the possibility that CDDs record sheets were incompletely transferred.

5. Implications for future work

We propose to conduct rapid assessments in UDEM to evaluate the prevalence of microfilariae and nodules, and to survey the blackfly population for early stages of *O. volvulus* larvae as an indicator of the contact with the microfilarial reservoir (Garms et al., 2015; Oguttu et al., 2014). An emphasis should be placed on encouraging the non-compliers to understand the risk and to take part in CDTI twice a year to improve the chance of reaching the goal of elimination by 2025 (Turner et al., 2014). There is a good prospect that the WHO goal of elimination of onchocerciasis in the hyperendemic area of UDEM could be achieved, provided that training of CDDs is improved, compliance improved and transmission interrupted. We further propose an O-150-PCR (poolscreen) of blackflies and an Ov-16 sero-surveillance of children under the age of 10 to monitor interruption of transmission to prove absence of recrudescence (WHO, 2017). Local radio stations should be encouraged to inform people in villages spread over a large area and partly difficult to access, to take part in their CDTI campaign with the aim to eradicate onchocerciasis. Ownership of smart phones increased dramatically over the last 10 years especially amongst CDDs, teachers, traders and opinion leaders. Social media should be utilised to communicate short messages about health issues to these key groups in order to create a greater awareness of onchocerciasis. Intensified health education on onchocerciasis should include stages of the disease, its development and manifestation but also its control and elimination.

6. Lessons learnt from long-term observations from 2002–2013

There is still a growing population of miners migrating from the non-endemic areas. These populations should be targeted for education since they are highly exposed. Two-way communication between CDDs, the District Health Directorate and the target population must be strengthened. There should be an integrated approach of CHPS personal and CDDs to achieve the goal of elimination of onchocerciasis. CHPS will play a key role to tackle the fear of side effects by offering free effective treatment for those affected and to prevent days lost at work.

Conflict of interest

The authors declare that they have no competing interests.

Acknowledgements

We thank the chiefs, opinion leaders and residents of the study communities for their cooperation, and we are grateful to the CDDs for

their support. The support of the Kumasi Centre for Collaborative Research in Tropical Medicine is appreciated. The visits of Rolf Garms to Ghana were made possible by the support of the German Senior Expert Service, Bonn, in 2006 and 2013. We are grateful to Dr. Bari Howell for the proof-reading of the manuscript. The work was funded by the Bernhard Nocht Institute for Tropical Medicine. The funders had no role in the study design, data collection and analysis, decision to publish, or preparation of the manuscript.

References

- Awadzi, K., Boakye, D., Edwards, G., Opoku, N., Attah, S., Osei-Atweneboana, M., Lazdins-Helds, J., Ardrey, A., Addy, E., Quartey, B., 2004. An investigation of persistent microfilaridermias despite multiple treatments with ivermectin, in two onchocerciasis-endemic foci in Ghana. *Ann. Trop. Med. Parasitol.* 98, 231–249.
- Brieger, W.R., Okeibunor, J.C., Abiose, A.O., Ndyomugenyi, R., Wanji, S., Elhassan, E., Amazigo, U.V., 2012. Characteristics of persons who complied with and failed to comply with annual ivermectin treatment. *Trop. Med. Int. Health* 17, 920–930.
- Chavasse, D., Whitworth, J., Lemoh, P., Bennett, S., Davies, J., 1995. Low level ivermectin coverage and the transmission of onchocerciasis. *Trans. R. Soc. Trop. Med. Hyg.* 89, 534–537.
- Crump, A., Omura, S., 2011. Ivermectin, 'wonder drug' from Japan: the human use perspective. *Proc. Jpn. Acad. Ser. B* 87, 13–28.
- Frempong, K.K., Walker, M., Cheke, R.A., Tete, E.J., Gyan, E.T., Owusu, E.O., Wilson, M.D., Boakye, D.A., Taylor, M.J., Biritwum, N.-K., 2016. Does increasing treatment frequency address suboptimal responses to ivermectin for the control and elimination of river blindness? *Clin. Infect. Dis.* 62, 1338–1347.
- Garms, R., Badu, K., Owusu-Dabo, E., Baffour-Awuah, S., Adjei, O., Debrah, A., Nagel, M., Biritwum, N., Gankpal, L., Post, R., 2015. Assessments of the transmission of *Onchocerca volvulus* by *Simulium sanctipauli* in the Upper Denkyira District, Ghana, and the intermittent disappearance of the vector. *Parasitol. Res.* 114, 1129–1137.
- Hoerauf, A., Specht, S., Büttner, M., Pfarr, K., Mand, S., Fimmers, R., Marfo-Debrekyei, Y., Konadu, P., Debrah, A.Y., Bandi, C., 2008. Wolbachia endobacteria depletion by doxycycline as antifilarial therapy has macrofilaricidal activity in onchocerciasis: a randomized placebo-controlled study. *Med. Microbiol. Immunol.* 197, 295–311.
- Kutin, K., Kruppa, T., Brenya, R., Garms, R., 2004. Efficiency of *Simulium sanctipauli* as a vector of *Onchocerca volvulus* in the forest zone of Ghana. *Med. Vet. Entomol.* 18, 167–173.
- Lakwo, T., Garms, R., Rubaale, T., Katabarwa, M., Walsh, F., Habomugisha, P., Oguttu, D., Unnasch, T., Namanya, H., Tukesiga, E., 2013. The disappearance of onchocerciasis from the Itwara focus, western Uganda after elimination of the vector *Simulium neavei* and 19 years of annual ivermectin treatments. *Acta Trop.* 126, 218–221.
- Lamberton, P.H., Cheke, R.A., Walker, M., Winskill, P., Osei-Atweneboana, M.Y., Tirados, I., Tetteh-Kumah, A., Boakye, D.A., Wilson, M.D., Post, R.J., 2014. Onchocerciasis transmission in Ghana: biting and parous rates of host-seeking sibling species of the *Simulium damnosum* complex. *Parasite Vectors* 7, 511.
- Nuwaha, F., Okware, J., Ndyomugenyi, R., 2005. Predictors of compliance with community-directed ivermectin treatment in Uganda: quantitative results. *Trop. Med. Int. Health* 10, 659–667. <http://dx.doi.org/10.1111/j.1365-3156.2005.01436.x>.
- Oguttu, D., Byamukama, E., Katholi, C.R., Habomugisha, P., Nahabwe, C., Ngabirano, M., Hassan, H.K., Lakwo, T., Katabarwa, M., Richards, F.O., 2014. Serosurveillance to monitor onchocerciasis elimination: the Ugandan experience. *Am. J. Trop. Med. Hyg.* 90, 339–345.
- Sékétéli, A., 2002. APOC at mid-point: so far so good. *Ann. Trop. Med. Parasitol.* 96, S3–S4.
- Turner, H.C., Walker, M., Churcher, T.S., Basáñez, M.-G., 2014. Modelling the impact of ivermectin on River Blindness and its burden of morbidity and mortality in African Savannah: EpiOncho projections. *Parasite Vectors* 7, 241.
- UNICEF, 1996. UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases Community-Directed Treatment With Ivermectin: Report of a Multicountry Study. World Health Organization Report No: TDR/AFT/RP/96.1, Geneva.
- WHO, 2017. Onchocerciasis World Health Organization; Fact Sheet Updated January 2017.