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Why onchocerciasis transmission persists after 15 annual ivermectin mass drug administrations in South-West Cameroon

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ABSTRACT

Introduction Onchocerciasis is targeted for elimination mainly with annual community-directed treatment with ivermectin (CDTI). High infection levels have been reported in South-West Cameroon, despite ≥15 years of CDTI. The aim of this study was to assess factors associated with continued onchocerciasis transmission and skin disease.

Methods A large-scale cross-sectional study was conducted in 2017 in 20 communities in a loiasis-risk area in South-West Cameroon. A mixed-methods approach was used. Associations between infection levels, skin disease and adherence to CDTI were assessed using mixed regression modelling. Different community members' perception and acceptability of the CDTI strategy was explored using semi-structured interviews.

Results Onchocerciasis prevalence was 44.4% among 9456 participants. 17.5% of adults were systematic non-adherers and 5.9% participated in ≥75% of CDTI rounds. Skin disease affected 1/10 participants, including children. Increasing self-reported adherence to CDTI was associated with lower infection levels in participants aged ≥15 years but not in children. Adherence to CDTI was positively influenced by perceived health benefits, and negatively influenced by fear of adverse events linked with economic loss. Concern of lethal adverse events was a common reason for systematic non-adherence.

Conclusion CDTI alone is unlikely to achieve elimination in those high transmission areas where low participation is commonly associated with the fear of adverse events, despite the current quasi absence of high-risk levels of loiasis. Such persisting historical memories and fear of ivermectin might impact adherence to CDTI also in areas with historical presence but current absence of loiasis. Because such issues are unlikely to be tackled by CDTI adaptive measures, alternative strategies are needed for onchocerciasis elimination where negative perception of ivermectin is an entrenched barrier to community participation in programmes.

Key questions

What is already known?

- Targeting onchocerciasis elimination rather than morbidity control raises new challenges for community-directed treatment with ivermectin (CDTI), particularly in areas of co-endemicity with *Loa loa* where fear of adverse events negatively impacts on participation and high transmission persists despite long-term CDTI.

What are the new findings?

- Prevalence was high including among high adherers to CDTI (prevalence range 25% to 55% in ≥50 year-olds and 9 to 14 year-olds with self-reported high adherence, respectively), suggesting persistence of high transmission despite 15 rounds of CDTI.
- Low adherence to CDTI and interrupted ivermectin uptake were mostly due to experienced or observed common ivermectin-related adverse events interfering with daily activities as well as their economic consequences.
- Systematic non-adherence was related to fear of death and rumoured severe adverse events, which persisted despite the current very low prevalence and infection intensity of *Loa loa*.
- Participants who were concerned about serious and lethal ivermectin-related adverse events did not directly relate those issues to loiasis.

INTRODUCTION

Onchocerciasis, or river blindness, is a neglected tropical disease caused by the

Key questions

What do the new findings imply?

- CDTI alone, even improved with programme adaptive measures, is highly unlikely to eliminate onchocerciasis in such areas, where the fear of ivermectin adverse events and death is deeply anchored in the population and persists as a reason for systematic non-adherence despite the current quasi absence of high-risk levels of loiasis in the area.
- Other alternative approaches such as vector control with ground larviciding and/or treatments avoiding direct microfilaricidal side effects, such as doxycycline, might be more acceptable in areas not only of current, but also of past co-endemicity with loiasis.

filarial parasite *Onchocerca volvulus*, transmitted by blackflies of the genus *Simulium*.

In 2017, there were an estimated 20.8 million onchocerciasis cases, 99% of which occurred in the poorest and most vulnerable populations of sub-Saharan Africa.[1] Onchocerciasis notably causes potentially irreversible impaired vision but most commonly presents as skin disease, which affects 70% of cases and caused over 90% of years lived with disability due to onchocerciasis in 2017.[1–3]

The WHO strategy against onchocerciasis consists of mass drug administration (MDA) with community-directed treatment with ivermectin (CDTI) and has shifted its goal from morbidity control to disease elimination with a target of 12 (31%) endemic countries verified for interruption of transmission by 2030.[4]

By killing the parasite larvae present in the skin, the microfilariae (mf), regular ivermectin (IVM) treatment both prevents further disease development and transmission to the blackfly vector.[5] WHO recommends that annual MDA for at least 15 to 17 years of high coverage (80%) should reduce transmission and result in decreased skin infection incidence in children.[2 6]

Although 15 to 17 years of CDTI has achieved elimination in some African settings, high transmission levels persist in the face of long-term CDTI campaigns in other areas, particularly in communities living and working close to blackfly vector breeding sites in forested regions where year-round transmission occurs.[7–12] An additional challenge is the risk of severe adverse events (SAEs) following ivermectin treatment in patients harbouring heavy *Loa loa* microfilaraemia, co-endemic with onchocerciasis.[13] Reasons for low participation to CDTI are numerous and may include absence during drug distribution, negative perception of CDTI, fear of side effects and weak community ownership.[9 14 15]

The aim of this work was to document onchocerciasis infection and morbidity levels after 15 years of annual CDTI in previously identified persisting onchocerciasis hot spots, by assessing their association with adherence to CDTI, and identifying drivers of adherence and ivermectin uptake based on the case of these high-risk communities in South-West Cameroon.

METHODS

Study area, design and participants

A community-based cross-sectional study was conducted between June and October of 2017 in 20 communities in the Meme River Basin, South-West region, Cameroon, where onchocerciasis transmission was recorded between 2011 and 2012.[7] The assessments presented here were conducted during the baseline survey of a controlled before-and-after community-based intervention study aiming at assessing the impact of WHO-endorsed alternative strategies to accelerate the elimination of onchocerciasis, that is, 35-day treatment of onchocerciasis cases with 100 mg doxycycline (test and treat with doxycycline), either alone or in combination with ground larviciding with temephos for vector control. Further details are available in the study protocol.[16] First, a census of all study villagers was undertaken in all communities, and those aged ≥5 years and who had lived ≥5 years in the community were eligible.

Parasitological and questionnaire data

Enrolled participants were diagnosed for onchocerciasis with two skin snips taken from each iliac crest using a sterile 2 mm corneo-scleral punch (CT 016 Everhards 2218–15 C, Meckenheim, Germany). Mf counts were expressed as mf per skin snip. *L. loa* infection was diagnosed using a 50 µL thick blood smear prepared with blood collected by finger prick. Microfilariae were identified under light microscope and the counts were expressed as number of microfilariae per millilitre (mf/mL) of blood.[16] Information on socio-demographics, self-reported adherence to CDTI and recent medical history was collected with individual structured questionnaires. Pre-control *O. volvulus* prevalence and community microfilarial load (CMFL) for six of the study communities were obtained from previous reports.[7 17]

Onchodermatitis clinical assessments

Onchodermatitis diagnosis was conducted, using a formal clinical classification and coding system, by district hospital nursing staff specifically trained by an expert dermatologist.[16 18]

Onchocercal skin disease (OSD) was classified as acute papular onchodermatitis (APOD), chronic papular onchodermatitis (CPOD), lichenified onchodermatitis, depigmentation, atrophy or hanging groin.[18] Non-onchocercal skin diseases included scabies, dermatophytes and pyoderma. Severe itching was defined as either itching reported spontaneously with emphasis in response to open-ended questions about general health or reported when prompted with a follow-up probe asking specifically about itching as either troublesome itching disturbing sleep or as severe.[19]

Semi-structured qualitative interviews

To investigate reasons for participation or non-participation in annual CDTI, interviews were conducted with community members who tested negative for

onchocerciasis and were offered IVM as standard treatment, 24 interviewees accepted and 16 declined IVM. Community members were purposefully selected based on demographic characteristics including age, sex and location.[16] Interviews were also conducted with community drug distributors (CDD) (n=26) to gain insight into their experience of community acceptance of CDTI. Interviews were conducted in 9 out of the 10 representative communities because one community could not be accessed (due to a blocked road).

Qualitative data analysis

Interviews were recorded, transcribed verbatim and translated from Pidgin to English. The transcripts and field notes were analysed with NVivo software using a framework approach as described by Ritchie, *et al* 2013.[20] The framework was developed both inductively and deductively. After familiarisation, coding frameworks were developed and all data was coded, charted and synthesised by gender and age groups.

Statistical analysis

Census data was collected with ODK (Open Data Kit, July 2010, http://opendatakit.or) and cleaned in Microsoft Excel. Parasitological and questionnaire data were entered with EpiInfo V.3.5.2 (EpiData Association; Odense, Denmark). Further data management and analysis were performed in Stata V.15.0 (StataCorp LP; College Station, Texas, USA).

Infection status was defined as positive if at least one microfilaria was found in either skin snip, or negative otherwise. The CMFL, that is, infection intensity at community level, was calculated as the geometric mean of the community infection intensity among individuals aged 20 years and above, including the negatives.[21] Self-reported adherence to CDTI was expressed as the proportion of rounds taken out of the maximum of rounds the person could have taken given their age. Variables were categorised as described in online supplemental file 1.

CIs were estimated accounting for the cluster design of the study. Pearson's χ^2 test was used to compare proportions. The association between infection levels or symptoms of onchocerciasis and adherence to CDTI or other variables of interest was assessed using mixed-effects logistic (*O. volvulus* mf prevalence, nodule presence or clinical sign prevalence) or negative binomial (mf load) regression models with community as a random effect. All models were adjusted for factors unevenly distributed between participants enrolled or non-enrolled in the parasitological study. Other variables were selected based on the likelihood ratio test (LRT) at 20% level significance and Akaike's information criterion for correlated variables (see online supplemental file 1 for further details). Two-way and three-way interactions between age, sex and adherence to CDTI, or self-reported adherence and time since last treatment were checked and assessed using the LRT. CIs for interactions were estimated using the Stata 'lincom' command. Marginal probabilities of, and the effect of adherence levels on, *O. volvulus* prevalence, intensity and nodule prevalence were estimated with the respective multivariate models and plotted using the Stata command 'margins' and 'marginsplot'.

Ethics statement

All censused individuals were explained the objectives and procedures of the intervention study. Informed assent was obtained from children and adolescents aged under 18 years with parental consent, and consent was provided by all adult participants (age ≥18 years). All participants diagnosed with *O. volvulus* infection were offered treatment as described in the study protocol paper.[16]

Role of the funding source

The funder (Department for International Development; UK-AID) had no role in study design; in the collection, analysis and interpretation of data; in the writing of the report; or in the decision to submit the paper for publication. The corresponding author confirms that he has full access to all the data in the study and had final responsibility for the decision to submit for publication.

RESULTS

Study population and participation in the baseline survey

Out of a total of 19 915 participants determined by community census at baseline, 1935 were aged <5 years, 8515 were absent, refused to participate or lived <5 years in the community, 9 had incomplete demographic data. As a result, 9456 (52.6% of eligible) participants were included in the parasitological survey. Among those, 238 and 103 participants had none or incomplete adherence to CDTI data, respectively. A study diagram is provided in online supplemental file 2 and participant characteristics are available in online supplemental file 3.

All models were adjusted for unbalanced characteristics between enrolled and non-enrolled participants, that is, age, gender, occupation and education.

Sensitivity analysis of complete cases (presented here) versus missing values for incomplete adherence data addressed using multiple imputation provided the same results, probably due to the low proportion of missing values (data not shown).

O. volvulus and *L. loa* infection levels, and adherence to CDTI

The overall prevalence of *O. volvulus* was 44.4% (95% CI: 39.2 to 49.8), ranging between 31.3% (95% CI: 26.5 to 36.6) and 75.5% (95% CI: 69.7 to 80.7) at community level. Three villages were hypoendemic and three were still hyperendemic. Study villages endemicity levels are displayed in figure 1A. The mean CMFL was 2.06 (range across communities: 0.82 to 3.59). A maximum (arithmetic) mean mf count of 538.5 per skin snip was found in a 9-year-old boy. The prevalence of *L. loa* was 3.7% (95% CI: 2.4 to 5.6), range across communities: 1.4% to 11.5%). The mean *L. loa* infection intensity was 49.5 mf/mL and ranged among positives between 0.5 and 1860 mf/mL, this maximum being below the 8000 mf/

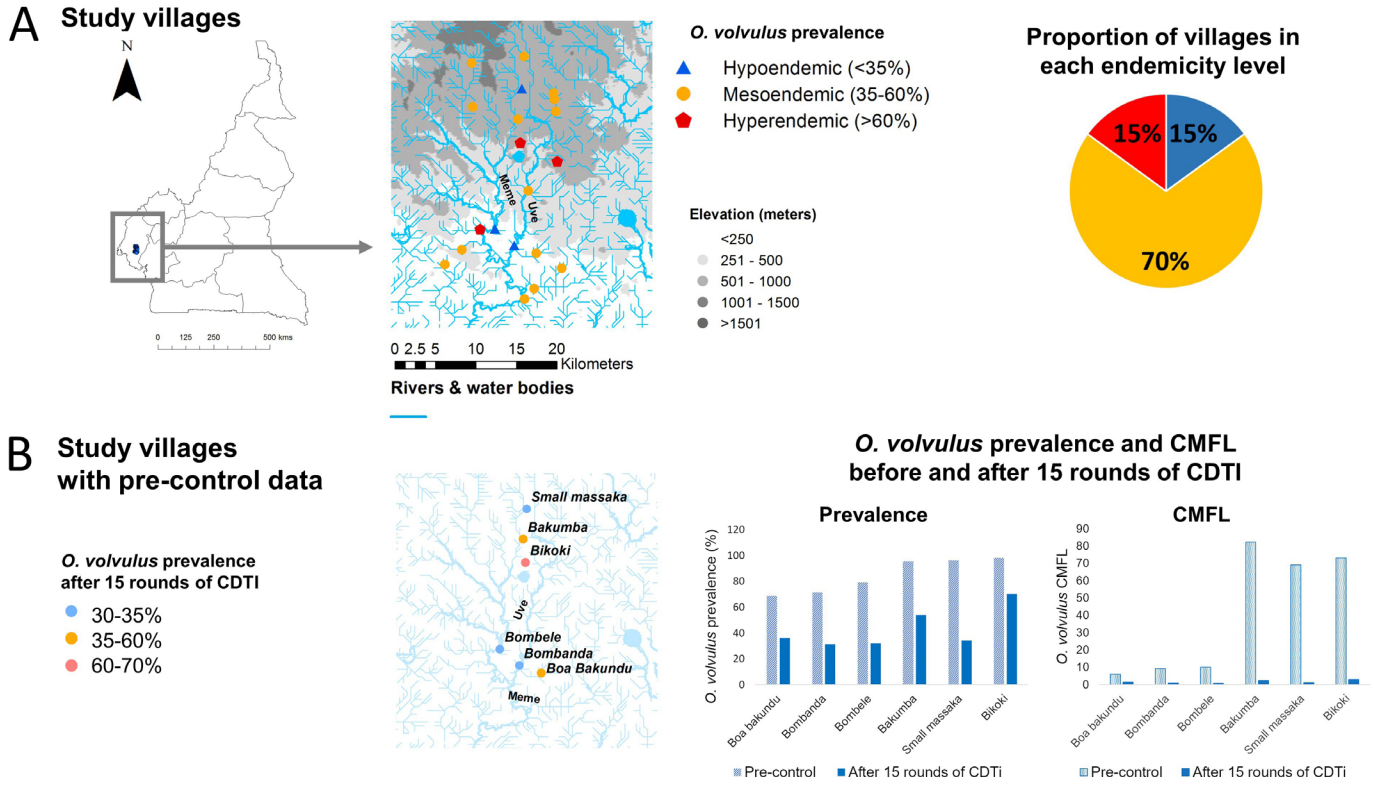

Figure 1 *O. volvulus* prevalence in 20 study communities (A) and *O. volvulus* prevalence and CMFL before and after 15 rounds of CDTI in six study villages (B). A: Geographical location of, and *O. volvulus* prevalence in, the 20 study villages. Data were obtained from 9456 participants aged 5 years and over in a cross-sectional survey conducted in 2017 in 20 villages of South-West Region, Cameroon. This map has been produced in ArcGIS 10.5 specifically for this study. B: *O. volvulus* prevalence and CMFL before and after 15 rounds of CDTI in six of the study villages. Pre-control data were obtained from.[7 17] Data after 15 rounds of CDTI were obtained from a cross-sectional survey conducted in 2017 and including 3062 participants aged 5 years and over (prevalence) and 1703 participants aged 20 years and over (CMFL), living in six villages of South-West Cameroon. CDTI, community-directed treatment with ivermectin; CMFL, community microfilarial load; *O. volvulus, Onchocerca volvulus.*

mL threshold associated with a high risk for ivermectin-related SAEs.

Village level *O. volvulus* prevalence rates and CMFL, as well as *L. loa* prevalence are available in online supplemental file 4.

Most participants (4079/4946, 82.5%) aged ≥20 years (ie, who were ≥5 years when CDTI reached 65% coverage) declared having taken IVM at least once. Over a quarter of participants (17.5%) reported being systematic non-adherers (ie, never took IVM), with similar proportions among men and women. Only 5.89% (95% CI: 3.57 to 8.16) of adult participants (age ≥18 years) reported high adherence (participation in ≥75% of rounds). Figure 2 displays age and gender-specific self-reported adherence levels (2A), and proportion of high adherers (2B). Adherence increased with increasing age and was lowest in the 14 to 29 years, regardless of gender.

Comparison of pre-CDTI and post-CDTI infection levels in a subset of communities

Pre-control and current *O. volvulus* mf prevalence and CMFL estimates are displayed in figure 1B. CDTI had a strong impact on the CMFL. The impact on prevalence was more modest and varied considerably across communities. Although three of those villages are currently the only hypoendemic villages in the area, they still all have prevalence rates above 30% (Bombanda 31.3%, Bombele 32.2% and Small Massaka: 34.3%).

Association between adherence to CDTI, infection levels and presence of nodules

Figure 3 displays *O. volvulus* mf prevalence ((3A), mf load (3B) and nodule prevalence (3C)) estimated as a function of age and self-reported adherence using the mixed-multivariate models presented in table 1. Unadjusted ORs are presented in online supplemental file 5.

Women had lower infection levels (all three outcomes) than men. Recent IVM treatment (≤1 year) was associated with lower odds of mf or nodule prevalence and lower mf loads.

The relationship between self-reported adherence and each of the three outcomes varied across age groups (effect modification), but not across gender. Self-reported adherence to CDTI was associated with lower infection levels in participants aged ≥30 years (figure 3D,E), but not in children, and its protective effect increased with increasing adherence (figure 3A,B).

Our model estimated that, compared with an adherence level of 50% to 75%, adhering to ≥75% of rounds resulted in a significant additional mf prevalence

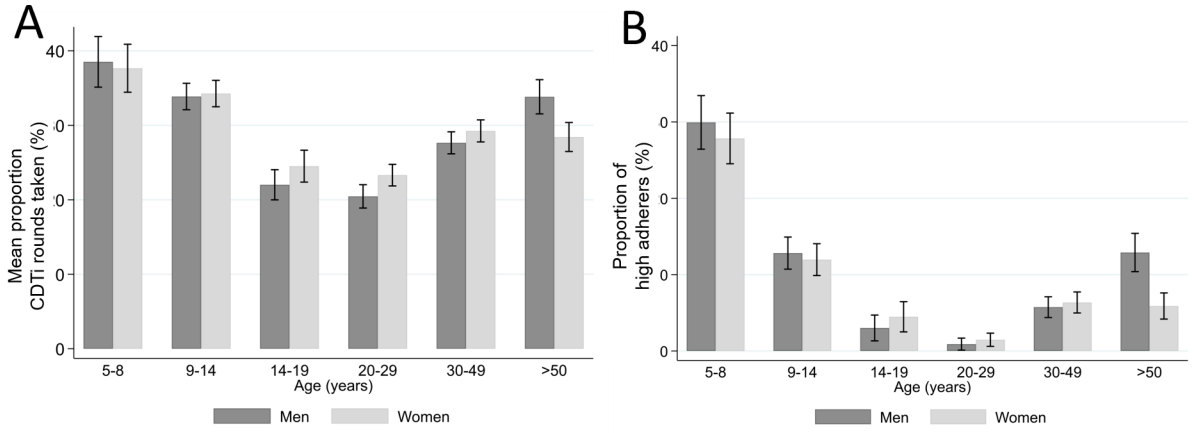

Figure 2 Mean proportion of CDTI rounds participated in (A) and proportion of high adherers (B), by age and gender. High adherers are defined as participants who took ivermectin in ≥75% of rounds. Denominators for the mean proportion of rounds taken are the maximum number of rounds an individual could have participated in given their age. Data were obtained from 9164 participants aged 5 years and over, with available CDTI adherence data, in a cross-sectional survey conducted in 2017 in 20 villages of South-West Region, Cameroon. CDTI, community-directed treatment with ivermectin.

reduction of −9.7% (95% CI: −0.2 to −19.0%) and −15.5% (95%CI: −5.4 to −25.7%) in the 30 to 49 years and the ≥50 years, respectively.

Among high adherers, children had higher infection levels than adults aged ≥30 years and this difference was

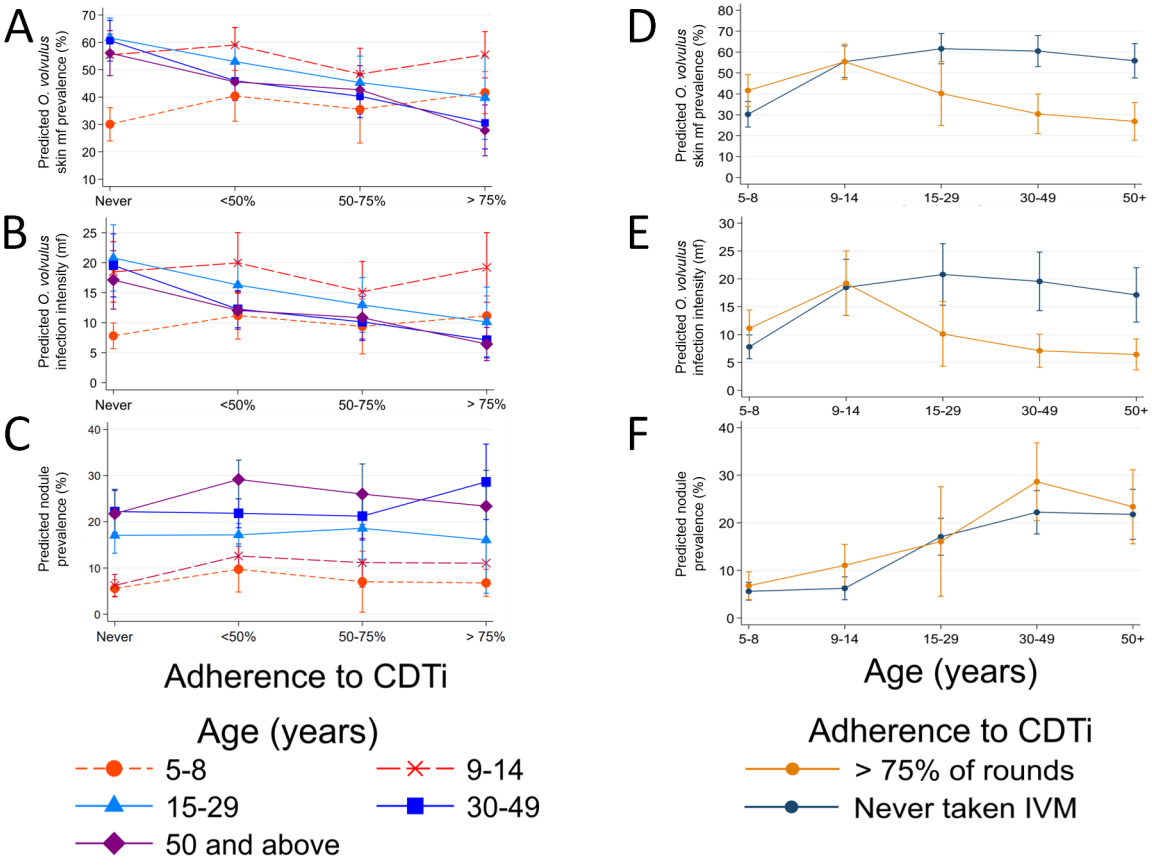

Figure 3 *O. volvulus* skin mf prevalence (A and D), infection intensity (B and E) and nodule prevalence (C and F) by adherence level and age. Those predictions were obtained using the multivariate models presented in table 2. Age groups 15 to 19 and 20 to 39 years had similar infection risk and intensity across adherence levels and were grouped in a larger category (ie, 15 to 29 years) to increase the precision of estimates. Data were obtained from a cross-sectional survey conducted in 2017, including 9115 participants with complete data aged 5 years and over living in 20 communities of South-West Cameroon. CDTI, community-directed treatment with ivermectin; IVM, ivermectin; mf, microfilariae; *O. volvulus, Onchocerca volvulus.*

Table 1 Association between infection levels and adherence to CDTI

		O. volvulus mf prevalence			***O. volvulus*** mf load			**Presence of nodules**		
Variable	Category	OR	95% **CI**	P value	IRR	95% **CI**	P value	OR	95% **CI**	P value
Effect of self-reported adherence in each age group*										
5–8 years	Never taken IVM	1.00			1.00			1.00		
	Up to 50% of rounds	**1.65**	1.13 to 2.41	0.010	**1.43**	1.07 to 1.90	0.017	1.84	0.96 to 3.53	0.066
	50% to 75% of rounds	1.32	0.76 to 2.29	0.325	1.20	0.76 to 1.90	0.426	1.28	0.44 to 3.75	0.649
	>75% of rounds	**1.72**	1.28 to 2.31	<0.0001	**1.43**	1.14 to 1.80	0.002	1.23	0.70 to 2.16	0.472
9–14 years	Never taken IVM	1.00			1.00			1.00		
	Up to 50% of rounds	1.18	0.91 to 1.52	0.213	1.08	0.92 to 1.30	0.354	**2.21**	1.42 to 3.43	<0.0001
	50% to 75% of rounds	0.74	0.50 to 1.10	0.135	0.82	0.62 to 1.10	0.156	1.91	0.99 to 3.70	0.054
	>75% of rounds	0.37	0.70 to 1.42	0.990	1.04	0.82 to 1.30	0.744	**1.89**	1.05 to 3.42	0.034
15–29 years	Never taken IVM	1.00			1.00			1.00		
	Up to 50% of rounds	**0.69**	0.54 to 0.88	0.003	**0.78**	0.68 to 0.90	0.001	1.01	0.75 to 1.36	0.958
	50% to 75% of rounds	**0.50**	0.33 to 0.75	0.001	**0.62**	0.46 to 0.80	0.002	1.11	0.66 to 1.88	0.687
	>75% of rounds	**0.39**	0.19 to 0.77	0.007	**0.49**	0.28 to 0.80	0.009	0.93	0.37 to 2.33	0.873
30–49 years	Never taken IVM	1.00			1.00			1.00		
	Up to 50% of rounds	**0.52**	0.41 to 0.67	<0.0001	**0.63**	0.54 to 0.73	<0.0001	0.98	0.74 to 1.28	0.868
	50% to 75% of rounds	**0.41**	0.29 to 0.57	<0.0001	**0.52**	0.41 to 0.66	<0.0001	0.94	0.64 to 1.38	0.756
	>75% of rounds	**0.26**	0.16 to 0.41	<0.0001	**0.36**	0.25 to 0.53	<0.0001	1.43	0.89 to 2.30	0.139
≥50 years	Never taken IVM	1.00			1.00			1.00		
	Up to 50% of rounds	**0.63**	0.47 to 0.85	0.002	**0.70**	0.58 to 0.90	<0.0001	1.51	1.01 to 1.09	0.741
	50% to 75% of rounds	**0.55**	0.37 to 0.82	0.003	**0.63**	0.48 to 0.80	0.001	1.28	0.82 to 1.99	0.279
	>75% of rounds	**0.26**	0.16 to 0.40	<0.0001	**0.38**	0.25 to 0.60	<0.0001	1.10	0.65 to 1.87	0.721
Effect of age in each self-reported adherence group*										
Never taken IVM	30–49	1.00			1.00			1.00		
	5–8	**0.25**	0.19 to 0.34	<0.0001	**0.40**	0.33 to 0.49	<0.0001	**0.20**	0.13 to 0.30	<0.0001
	9–14	0.80	0.58 to 1.10	0.163	0.94	0.77 to 1.15	0.576	**0.22**	0.14 to 0.36	<0.0001
	15–29	1.05	0.78 to 1.43	0.736	1.06	0.89 to 1.27	0.494	0.71	0.50 to 1.01	0.053
	≥50	0.81	0.59 to 1.12	0.211	0.88	0.72 to 1.07	0.186	0.97	0.68 to 1.40	0.882
up to 50% of rounds	30–49	1.00			1.00			1.00		
	5–8	0.80	0.55 to 1.16	0.234	0.91	0.69 to 1.21	0.520	**0.37**	0.21 to 0.68	0.001
	9–14	**1.79**	1.44 to 2.23	<0.0001	**1.63**	1.40 to 1.89	<0.0001	**0.50**	0.38 to 0.67	<0.0001
	15–29	**1.38**	1.17 to 1.63	<0.0001	**1.33**	1.18 to 1.50	<0.0001	**0.73**	0.60 to 0.90	0.003

Continued

Table 1 Continued

Variable	Category	***O. volvulus*** mf prevalence			***O. volvulus*** mf load			**Presence of nodules**		
		OR	95% **CI**	P value	IRR	95% **CI**	P value	OR	95% **CI**	P value
	≥50	0.98	0.81 to 1.18	0.825	0.98	0.86 to 1.13	0.807	**1.50**	1.22 to 1.85	<0.0001
50% to 75% of rounds	30–49	1.00			1.00			1.00		
	5–8	0.82	0.46 to 1.47	0.508	0.93	0.58 to 1.49	0.751	**0.27**	0.09 to 0.79	0.016
	9–14	1.45	0.96 to 2.21	0.081	**1.50**	1.09 to 2.05	0.012	**0.45**	0.24 to 0.84	0.012
	15–29	1.28	0.84 to 1.96	0.250	1.28	0.92 to 1.77	0.138	0.84	0.49 to 1.44	0.527
	≥50	1.11	0.76 to 1.61	0.600	1.07	0.80 to 1.43	0.657	1.32	0.86 to 2.03	0.207
>75% of rounds	30–49	1.00			1.00			1.00		
	5–8	**1.70**	1.05 to 2.74	0.030	**1.57**	1.06 to 2.32	0.025	**0.17**	0.09 to 0.32	<0.0001
	9–14	**3.11**	1.88 to 5.14	<0.0001	**2.70**	1.82 to 4.02	<0.0001	**0.30**	0.16 to 0.54	<0.0001
	15–29	1.59	0.74 to 3.43	0.233	1.42	0.76 to 2.66	0.269	0.46	0.18 to 1.21	0.116
	≥50	0.83	0.46 to 1.48	0.525	0.90	0.55 to 1.48	0.690	0.75	0.42 to 1.34	0.328
Time since last treatment	Any other case	1.00			1.00			1.00		
	<1 year	**0.60**	0.54 to 0.68	<0.0001	**0.71**	0.65 to 0.77	<0.0001	**0.79**	0.68 to 0.92	0.002
Gender	Men	1.00			1.00			1.00		
	Women	**0.80**	0.74 to 0.88	<0.0001	**0.84**	0.79 to 0.89	<0.0001	**0.64**	0.57 to 0.72	<0.0001
Occupation	Farmer	1.00			1.00			1.00		
	None, child, N/A	0.95	0.79 to 1.16	0.626	0.93	0.81 to 1.06	0.257	1.07	0.86 to 1.35	0.531
	Student/pupil	0.99	0.84 to 1.18	0.939	0.96	0.86 to 1.08	0.528	0.85	0.68 to 1.06	0.143
	Other†	**0.68**	0.54 to 0.86	0.001	**0.71**	0.60 to 0.85	<0.0001	**0.64**	0.47 to 0.87	0.004
Education attainment	No school	1.00			1.00			1.00		
	Primary, secondary	0.85	0.70 to 1.03	0.106	**0.87**	0.76 to 0.99	0.032	0.96	0.77 to 1.20	0.743
	≥High school	0.88	0.74 to 1.05	0.146	**0.87**	0.77 to 0.98	0.019	1.03	0.84 to 1.26	0.771

Results were obtained by multivariate mixed logistic (*O. volvulus* prevalence and presence of nodules) and mixed negative binomial (*O. volvulus* infection intensity) regression models and data from a cross-sectional survey conducted in 2017 among 9115 participants with complete data living in 20 communities of South-West Region, Cameroon.
OR and IRR in bold are significant at 95% level.
*Age was an effect modifier of self-reported adherence.
†Occupation classified as 'other' included small businesses, workers, civil servants and liberal professions.
CDTI, community-directed treatment with ivermectin; IRR, incidence rate ratio; IVM, ivermectin; mf, microfilariae; *O. volvulus*, *Onchocerca volvulus*.

significant for children and adolescents aged 9 to 14 years (figure 3A,B).

Nodule prevalence was not associated with adherence but increased with age and was significantly higher in participants aged above 15 years (figure 3C,F).

Prevalence of clinical signs

OSD affected 10.3% (95% CI: 8.8 to 12.0) of participants, most of them (865/972, 89.0%), being diagnosed with only one OSD, the others having up to three OSDs.

The prevalence of OSD increased with age, ranging for any OSD from 6.57% (95% CI: 5.4 to 8.0) in children and adolescents aged below 15 years to 20.6% (95% CI: 17.0 to 24.7) in adults aged over 50 years. Online supplemental file 6 displays the prevalence of OSD among participants aged above and below 15 years, that is, born before and during the CDTI era. Younger participants mostly suffered from reactive skin disease whereas chronic depigmentation, atrophy, hanging groin (long-term development OSD) were more common among participants aged over 30 years.

Severe itching affected 5.85% (95% CI: 4.57 to 5.45) of participants. Visual impairment/vision problem was reported by 2.32% (95% CI: 1.29 to 4.15) of participants.

Non-onchocercal skin disease was rare, with 160 cases of infection with dermatophytes (prevalence: 1.69%, 95% CI: 1.06 to 2.68), 76 cases of pyoderma (prevalence: 0.08%, 95% CI: 0.06 to 1.07) and 32 cases of scabies (prevalence: 0.34%, 95% CI: 0.013 to 0.086).

The prevalence of palpable nodules was 17.1% (95% CI: 15.3% to 19.0%) and most participants (94.2%) had one to three nodules. The maximum number of palpable nodules, 20, was observed in a 65-year-old woman.

Association between onchocercal skin disease, infection status and adherence to CDTI

Age-specific OSD prevalence rates were estimated using mixed–multivariate regression models. They are presented in online supplemental file 7 and illustrated in online supplemental file 8. The results of the bivariate analysis (unadjusted ORs) are presented in online supplemental file 9. The association between OSD was stronger with nodule number than with nodule presence (data not shown). Only depigmentation, atrophy and severe itching were associated to some extent with infection levels (either mf presence or load).

In the multivariate analysis, only depigmentation and severe itching (borderline non-significance) were associated with *O. volvulus* infection while APOD, CPOD and depigmentation were positively associated with nodule number (online supplemental file 7).

Men and women had similar risks of suffering from any OSD. The odds of suffering from depigmentation (OR=3.39 (95% CI 2.61 to 4.40) for the 50+ years age group compared with participants aged 30 to 49 years) or atrophy (OR=2.51 (95% CI 1.56 to 4.05) for the 50+ years age group compared with participants aged 30 to 49 years) increased with age. With regard to adherence to CDTI, early onset OSD tended to be positively associated with increasing adherence but the association was significant for APOD only. High adherence appeared to be associated with decreased risk of depigmentation and atrophy in participants aged 50 years and above, although not significantly, probably due to the low proportion of high adherers in this setting resulting in small sample size for these cross-categories.

Severe itching was more likely to be reported by participants aged ≥15 years, women and participants who ever took IVM, particularly high adherers. All three forms of reactive skin disease were associated with severe itching, with an increasing strength of association across APOD (OR=3.79, 95% CI (2.58 to 5.56), CPOD (OR=6.63 95% CI 4.91 to 8.96) and lichenified onchodermatitis which exhibited the strongest association (OR=8.11, 95% CI: 4.42 to 14.87) (online supplemental file 10).

Perception and acceptability of CDTI

Interviews were conducted with 40 community members and 26 CDDs to understand perceptions around IVM (online supplemental file 11).

Exposure and awareness

Many community members understood that IVM (commonly referred to as '*Mectizan*') was used to treat '*filaria*' (common name for onchocerciasis) which was transmitted by '*Mbitti*' (blackfly), and caused itching, skin disease, discolouration of the skin, skin nodules ('*mabo*' or *'horns'*), itching eyes and blindness. Most participants (of all ages) suggested that '*filaria*' was very common in their communities. All participants reported getting bitten by flies (or mosquitoes) frequently and this was often associated with being near water or on their farm. Other beliefs about transmission included through intercourse or sharing clothes, with some rare reports that it was hereditary. Measures taken to prevent bites included; covering skin as much as possible, especially feet; use of medicated soap, improved hygiene and not sharing clothes.

'It is because I always mask myself from my head, all my skin, except my neck that I do not cover' (Community member, man aged 15 to 20 years).

Acceptance of CDTI

There were many structural, social, economic and health factors identified by the communities which contributed to adherence or non-adherence to IVM which are outlined in table 2.

The most prominent barriers and facilitators for CDTI were centred around acceptability, including affordability of taking IVM. CDDs reported that the acceptability of '*Mectizan*' varied in households with some accepting and others not. The main driver identified by community members for taking '*Mectizan*' was its perceived health benefits of reducing symptoms and treating 'hidden disease'. Older adults (aged >40 years) were the most likely to recognise health benefits from taking '*Mectizan*',

Table 2 Summary table of barriers and motivators for uptake of CDTI

Thematic areas	Barriers to CDTI uptake	Motivators/facilitators for CDTI uptake
Awareness	**Lack of understanding about blackfly vector specific transmission**	**Understanding of transmission, prevention and treatment of onchocerciasis** (education in school)
	Limited understanding of prevention and treatment	**Observed reduction in community morbidity** *'The benefit of this Mectizan programme is that it has helped the community from blindness. …many people would have been blind and parents in those days and even youths had leopard legs…'* (CDD, man, aged 31–40 years)
Availability	**Distribution timing of CDTI** (community members being absent from community as on the farm)	**Regular distribution with supplies available from other sources if missed distribution or symptomatic.** *'They distribute it from house to house. But if you have itches you can go to the pharmacy and pay a 100 FRS to get Mectizan'* (Community member, man, aged 15–20 years)
	Demotivation from CDDs due to lack of intrinsic and/or extrinsic motivation	**Financial and/or non-financial motivational structures in place**
Accessibility	**Seasonality of CDTI** (CDDs being unable to access rural communities because of lack of resources such as umbrellas and boots) *'What I find very difficult in the task is, transportation is difficult especially during the rainy season when we must use materials like)umbrellas, shoes etc.'* (CDD, man, aged 41–50 years)	**Medication is free'** *The benefit to the community is that we benefit the Mectizan for free. So, we do not pay transport and if we were to be paying transport to go and get it, am not sure that even twenty people would go and get the Mectizan'* (Community member, woman, aged 41–50 years)
		House to House distribution
Acceptability	**Side effects**(experienced, observed in others or rumoured) (see online supplemental file 12 for more details)	**Health benefits** (experienced or observed in others / preventative and symptom control) *'Sometimes my eyes cannot really open but when I take the mectizan, my eyes will open. So, it depends as every person has its own benefits just as I just said mine. I have benefits in mectizan and that is why I now trust mectizan'* (Community member, woman, aged 41 to 50 years)
	Fears of 'hidden' disease or provoking disease *'When Mectizan just came I heard many people say that "you people should not take Mectizan oh… Mectizan will wake up all diseases in your body. Sometimes it can generate a sick in you when you don't have money and that is how you will die'* (Community member, woman aged 41–50 years).	**Encouragement from parents** (especially mothers) or other members of the community

Continued

Table 2 Continued

Thematic areas	Barriers to CDTI uptake	Motivators/facilitators for CDTI uptake
	Association with witchcraft	**Belief ivermectin will treat multiple diseases**' *The benefit is that we should drink it and it should stop any illness that is filarial in anybody's body.'* (Community member, woman, aged 41 to 50 years)
	Perceived exclusion criteria of ineligibility to take Mectizan due to other health conditions (such as pregnancy, epilepsy, hernias, alcohol consumption) *'We were told not to give epileptic patients mectizan, and equally some men who complained that they have Hernia and that they cannot take mectizan'* (CDD, woman, aged 31–40 years)	**Medication to treat side effects is free**
	Discouragement from others (eg, family or palm wine makers)	**Being able to receive free treatment for side effects from CDDs or be referred to a health facility** *'Most of them go to the health centre and they are given drugs to cold down all the pains.'* (Community member, man, aged 41–50 years) (see online supplemental file 12) for more details)
	Fear of death *'Some people take the drugs while others do not mainly because of the side effects like swollen bodies, itches and rashes. Some people in the community when you have witchcraft and you take mectizan, you will die. So, some people too refuse taking it because one may have witchcraft and is not aware of it. So, they prefer not to take it at all.'* (Female community member 15–20 years)	
	'Some people decide that they will never take Mectizan again· For example, an old man said that he took Mectizan and it almost killed him and concluded that he will never take it again in his lifetime' (Community member, man, aged 31–40 years)	
	Costs of treating side effects, especially hernias	
	Economic costs of missing work or school because of side effects *'I said no· because I am in a rural area and if I take all at once and it gives me a severe side effect that will disturb me from going to my farm, then I will have to absent from my farm.'* (Community member, man, aged 41–50 years)	

CDD, community drug distributor; CDTI, community-directed treatment with ivermectin.

which mostly included improvement in eyesight and reduction in blindness.

The main barrier to accepting '*Mectizan*' for community members was fear of adverse events (online supplemental file 12). Even if community members perceived associated health benefits, for some this was over-ridden by fear of adverse events, such as swelling and increased itching, or fear of 'provoking' other sickness. Some had

taken '*Mectizan*' in the past and experienced a negative reaction and therefore would not accept it again, while others had heard of negative effects in the community and therefore would not take it at all. Fear around side effects of '*Mectizan*' and associations with death were highlighted both by community members and CDDs. Fears of death were reported as '*Mectizan*' was thought to make the conditions worse or provoke other diseases or activate malaria, typhoid, rheumatism and especially hernias. which were perceived to worsen when taking '*Mectizan*'. Several community members reported that they never participated in CDTI due to rumoured reports of deaths or observed side effects.

'I have not been taking because I am afraid because some people say when they take, they get swollen and others die. So that has made me never to take mectizan, and I have never taken mectizan.' (Male community member 31 to 40 years).

Fear of economic consequence of adverse events, such as needing treatment or missing work was given as a justification for not accepting *'Mectizan'*, particularly for those who worked on farms, especially around the cocoa season. An older man reported that *'It disturbs them from going to the farm and carry out other personal, social and commercial activities'*. (Community member, man, aged 60+ years).

Not having the money to pay for healthcare or treatment created fears that they could die from side effects if they took '*Mectizan*'.

Other social, economic and health consequences of adverse events was also noted by CDDs and community members (online supplemental file 12), such as fear of fertility problems or causing miscarriage, fear of hernias needing surgery as well as becoming a burden to the family by being unable to attend work or school, or being unable to socially interact due to adverse events, particularly itching or reduced mobility.

It makes me to feel uncomfortable when I want to sit with my friends… Because I cannot go and sit among my friends and be scratching my skin (Community member, man, aged 15 to 20).

Those that did accept '*Mectizan*' may try to mitigate potential adverse events through changing how it was consumed, for example, it was reported that some community members would grind '*Mectizan*' and add it to '*rubbing oil*' therefore instead of ingesting the medication, it was applied directly to their skin. This was seen by a few to reduce the severity of adverse events.

DISCUSSION

After over 15 years of CDTI with ≥65% programmatic therapeutic coverage, we report *O. volvulus* prevalence as high as 44.4% in a sample of over 9000 individuals aged 5 years and above and living in 20 villages of South West Region, Cameroon.[7] Only three villages were found to be hypoendemic, and prevalence was above 30% in all 20 communities.

CDTI has been an effective control measure

The low CMFL in all communities and its dramatic drop even in communities with very high pre-control indicators, show a strong impact of CDTI on infection intensity, similarly to other settings, and suggests that CDTI has been an effective control measure.[7 10 17] Additionally, there was an overall low prevalence of late onset OSD mostly affecting older participants when compared with various pre-control studies.[22–26] The reduction of severe morbidity was also perceived by community members, especially the older participants and CDDs who reported that they observed a reduction of blindness and severe skin disease since CDTI began.

Using the same OSD classification, pre-control data and current OSD estimates in the Kumba district, the prevalence of nodules, depigmentation, early onset skin disease and severe itching were found to be 46%, 29.8%, 21.7, % and 21.4% in the late 90s and dropped to 17%, 3.4%, 5.4% and 5.8%, respectively, in 2017.[18 22] Reduction in OSD and severe itching prevalence following several years of CDTI has also been reported in African Programme for Onchocerciasis Control (APOC) sentinel sites, with declining rates varying with therapeutic coverage.[3 24 27] IVM treatment within a year before the study was associated with lower infection levels as well as with lower odds of having nodules, the latter possibly reflecting the partial macrofilaricidal activity of repeated doses.[28]

Adherence was associated with lower infection levels in participants aged ≥15 years only, and increased participation resulted in increased protective effect of treatment, reflecting the impact of long-term ivermectin uptake.[2 29]

Effectiveness is suboptimal and CDTI alone is unlikely to achieve elimination in this setting

In addition to high onchocerciasis prevalence, over one-third (35.8%) of adults and 15.9% of children born in the CDTI era had nodules and/or suffered from OSD and/or severe itching, indicating a suboptimal impact of treatment and persisting transmission.[10] The prevalence of early onset skin disease (acute or chronic papular onchodermatitis) was similar in participants aged below or above 15 years.

Challenge 1: transmission and exposure

Children (age <15 years, that is, born in the 'CDTI era') had overall similar mf prevalence and mf loads as participants aged ≥15 years. Low or absent infection levels in young children would be supportive of a decrease or block in transmission following implementation of CDTI, but this pattern was not supported by our findings. The only group with significantly lower infection levels than adults were children aged 5 to 8 years who never took ivermectin. While the absence of association between treatment and infection levels in children could be due to reporting bias, we found that systematic non-adherence was highest in this age group (52.6%), probably because children aged 5 to 6 years might not have yet

participated into CDTI due to their age versus distribution timing. This high reported non-participation would be in favour of accurate reports, even more so since children were assisted by their parents in answering questionnaires. Additionally, children aged 5 to 8 years identified as high adherers were more likely to exhibit OSD symptoms than others, suggesting that the presence of symptoms might have led parents to give them treatment. This result would be in line with the assessment of association (which go both ways) and not causality.

As a comparison, reported systematic non-adherence by older children aged 9 to 14 years was much lower (21.6%) and might more likely result from response bias due to social desirability. This absence of association between ivermectin uptake and infection levels in participants aged less than 15 years has previously been reported in the area and has been attributed to response bias as children tend to give answers that they think are expected from them.[30 31] Yet, this bias might have been mitigated by parents assisting children up to 15 years in answering questions. Another reason, suggesting high transmission in the area, could be behaviour favouring exposure of children and adolescents, as previously reported in Cameroon.[7 32]

In participants aged over 15 years, self-reported adherence to CDTI was associated with decreased incidence of skin infection. Yet, our fully adjusted models estimated that the lowest prevalence rates remained at over 25%, among older adults with high adherence. High prevalence rates in high adherers might relate to the local high transmission potential. Although this will need to be corroborated by entomological studies, blackfly biting rates appeared high as community members reported frequent bites on their farms or while at the river for social or domestic activities. The Meme River basin was previously found to have the highest entomological indices in the area, with over 1000 infective larvae/man/month in some communities.[7] Participants lived and worked extremely close to the rivers and attempts to prevent exposure through clothing was often insufficient in preventing bites. Our results indicate that the CDTI strategy had suboptimal impact in suppressing skin infections to prevent transmission in both children and adults although with contrasting self-reported adherence patterns. A second factor contributing to persistent high prevalence could be the selection of *O. volvulus* more refractory to ivermectin occurring in areas with higher drug pressure due to long-term CDTI, which has previously been documented in Cameroon and Ghana.[33–35]

Model-based treatment duration requirements for breaking transmission in hyperendemic settings with annual CDTI at coverage above 65% range between 10 years (for a 62% pre-control prevalence) and >25 years.[6] The comparison of pre-control and current estimates for one-third of our study villages indicate that they are far below the more optimistic targets, with only one being within model-based prediction ranges and current estimates being more in line with elimination not occurring even after 25 years of CDTI.[6]

Challenge 2: adherence

Adherence was particularly low in our study setting. Only half (52.8%) of adults participated in CDTI the year preceding the study, and as few as 5.7% reported having participated in at least 12 of 16 (ie, ≥75%) CDTI rounds (high adherers). We also found that adherence was lowest in adolescents and young adults (aged 15 to 29), which is in line with findings from West Cameroon.[9] In the present study, low participation of the youth was mostly due to a lack of perceived need based on an absence or lack of awareness regarding associated morbidities such as chronic skin and ocular disease. While perceived health benefits or seriousness of disease have been reported as an important driver of adherence in Cameroon and Nigeria, in some settings, consequences of adverse events outweighed perceived health benefits.[14 36] Lower perceived benefits in the young might lead to decreasing adherence in further rounds, both by this generation and their children in settings where morbidity declined due to successful control of onchocerciasis.[9 37 38]

Systematic non-adherence, 17.6% among adults, was extremely high, even compared with other areas of Cameroon, and is of major concern as model-based predictions suggest that elimination cannot be achieved in originally hyperendemic communities with 5% of systematic non-adherence.[9 14 29] Reasons for suboptimal uptake of CDTI are variable and include systemic as well as individual factors.[8 9 14 15 39] Programmatic factors associated with low adherence in this setting included limited access and availability of CDTI due to the timing and seasonality of distribution, which is in line with other findings in West Cameroon.[9] However, the recommended strategy of biannual or pluriannual CDTI in areas of low adherence would unlikely overcome adherence issues in this setting, as acceptability of IVM treatment appeared to be the main driver of (non-)adherence.

An important finding is that the nature of adverse events reported as reasons for interrupted participation (low adherence) and systematic non-adherence were different. Low adherence appeared to relate to the fear of common and non-serious ivermectin-related AEs interfering with daily activities, a cause of low adherence that has been reported by many studies, including in Cameroon.[9 37] We also found that an important deterrent to participation was the fear around the economic consequences of AEs, including treatment affordability, work incapacity and subsequent loss of income and difficulties in accessing health facilities. With recognition that onchocerciasis affects the world's poorest and marginalised people the economic consequences of adverse events from IVM may continue to perpetuate poverty, and therefore should not be overlooked.[40]

Systematic non-adherence appeared to be associated to the fear of rumoured reports of deaths or observed adverse events (ie, not personally experienced), which

are likely linked to SAEs that occurred in regions of *L. loa* co-endemicity, which is the case in South-West Cameroon.[13 41 42] The fear of adverse events is a common reason for low adherence to CDTI in areas of loiasis co-endemicity and recommendations to tackle this issue include; lengthy communication strategies with communities, rapid epidemiological assessments, materials development, training, advocacy, community sensitisation and mobilisation, case management and counselling, supervision, monitoring and evaluation.[41] Additionally, in areas where the population associates ivermectin-related SAEs and deaths with loiasis, the use of the LoaScope-based Test and Not Treat strategy to identify and exclude from treatment *L. loa* cases at risk for SAEs might help increase adherence.[43]

Yet, our findings suggest that none of those solutions might help overcome low adherence to CDTI and achieve elimination in this area. First, the Test and Not Treat strategy might not help reassuring the population as it would not lead to the exclusion of any individuals in these communities due to the current low intensity of loiasis in this region.[44 45] Importantly, while participants reported fear of SAEs (and death) that are known to be related to ivermectin treatment in case of heavy infection with loiasis, they did not directly associate them with loiasis. Rather, they associated those SAEs with witchcraft, or as revealing severe diseases previously 'hidden' in the body such as malaria, typhoid or hernias. Therefore, it appears unlikely that CDTI adaptive measures would overcome deeply anchored fears and beliefs partly relating to historical memory of SAEs in this area with a history of low-to-moderate endemicity.[45] This persistence of the fear of SAEs and death in areas where the actual risk of ivermectin SAEs is virtually non-existent, could be a major obstacle to onchocerciasis elimination. Indeed, it might also affect populations who are not directly at risk for SAEs but live in settings where historical memories of SAEs and deaths have been perpetuated including when originating from other communities. This issue should not be overlooked as it might affect up to 79 million persons living in the areas of currently low-to-moderate loiasis risk within the 11 APOC countries.[45]

Limitations

Our study has several limitations. First, the low enrolment rate, a common issue with skin snipping, likely resulted in an underestimation of our infection and morbidity estimates as low or non-adherers, who are also more likely to be infected and suffer from OSD, might be less inclined to participate in studies.[46] Yet estimates produced by regression models were adjusted for imbalanced characteristics due to non-participation and therefore unbiassed. Second, the cross-sectional design of this work cannot infer causality and longitudinal studies are needed to adequately quantify the impact of adherence to CDTI on infection levels and morbidity. Third, adherence to CDTI was assessed through self-reporting, which is known to be subject to recall bias. Still, some studies have established that most CDTI participants (>60%) are able to correctly recall their number of treatment and comparisons have indicated that reported coverage is overall similar to surveyed coverage.[47 48] Although response bias from children is likely, the clear inverse relationship between self-reported adherence expressed in broad percentage categories and infection levels in adults suggests that the recollection of participation in CDTI over 15 annual rounds by adults was generally an accurate reflection of adherence. Additionally, systematic non-adherence is likely to be adequately reflected as it is not subject to memory recollection.[9]

CONCLUSION

CDTI is facing major issues to achieve elimination of onchocerciasis in this area of current very low, but past low-to-moderate loiasis co-endemicity. In those originally hyperendemic communities located close to breeding sites, onchocerciasis transmission is still high despite 15 rounds of CDTI, with high prevalence persisting among high adherers. Of particular concern is the extremely high systematic non-adherence, with over one in six adults reporting having never taken ivermectin. Despite the current very low prevalence of loiasis in the area, an important reason for systematic non-adherence was the fear of ivermectin-related SAEs or death which were historically reported in the region.[42] Yet those SAEs were not perceived as associated with loiasis by community members. It therefore appears unlikely that CDTI alone will achieve elimination in areas where both parasites have long co-existed and deeply rooted negative perception of ivermectin persisted despite the quasi disappearance of high-risk levels of loiasis, even if access, community sensitisation and management of adverse events were to be improved. Other alternative approaches such as vector control with ground larviciding or treatment with doxycycline, a macrofilaricidal antibiotic that avoids adverse events due to the absence of direct microfilaricidal activity, might be more acceptable to these communities.[49] Additionally, CDTI effectiveness might potentially be further impacted by the selection of *O. volvulus* that are less sensitive to IVM following long-term treatments. Alternative strategies are needed to tackle onchocerciasis in regions of persisting high prevalence and low CDTI adherence, particularly in areas of current but also past co-endemicity with loiasis.[50–54]

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Supplemental File 1. Variable categorization and selection

Variable categorization

Age was categorized into six classes: (*i*) 5-8 years, (*ii*) 9-14 years, (*iii*) 15-19 years, (*iv*) 20-29 years, (*v*) 30-49 years and (*vi*) ≥50 years.

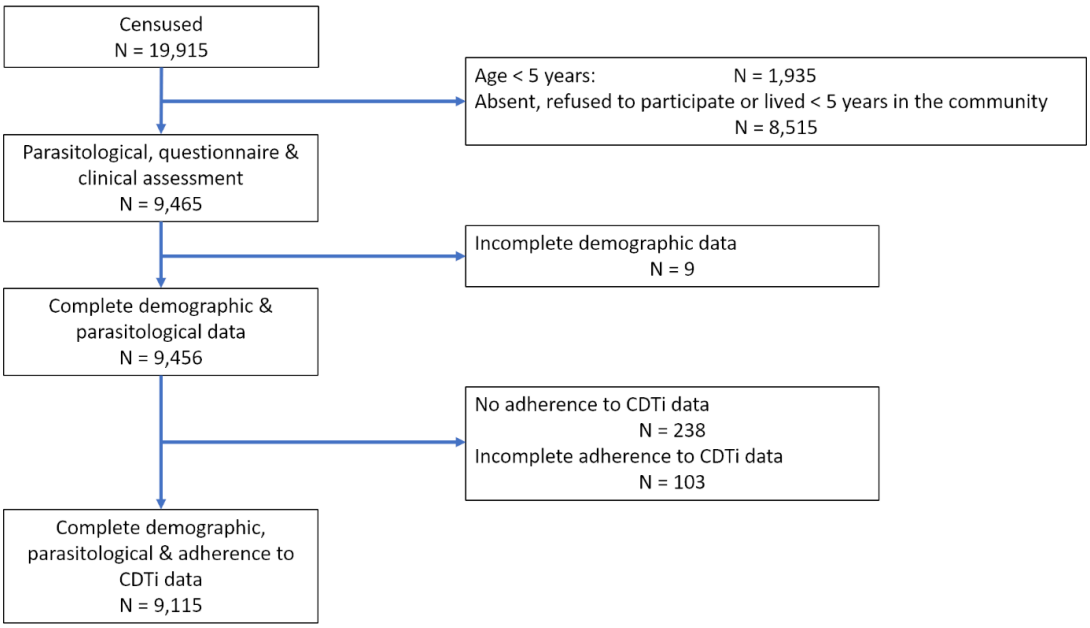
The age cut of 8 years was estimated empirically from the data as delimiting the age group with the lowest *O. volvulus* prevalence, both graphically and statistically using logistic regression. The cut at 15 years was chosen to have participants born before and after CDTI reached 65% coverage (Wanji, Kengne-Ouafo et al. 2015).

Self-reported adherence to CDTI was expressed as the proportion of rounds taken out of the maximum of rounds the person could have taken given their age, i.e. (*i*) Never taken IVM, (*ii*) taken ≤ 50% of rounds, (*iii*) taken 50-75% of rounds and (*iv*), taken ≥ 75% of rounds. Self-reported time since last IVM treatment was categorized as (*i*) IVM taken in the last year *vs.* (*ii*) any other case. For other variables original categories with frequencies below 5% were merged with similar categories.

Variable selection

Mixed-effects regression models were used to assess the association between each outcome and explanatory variables at a 15% significance level using the Likelihood Ratio Test (LRT). Various cut-offs as well as continuous forms where applicable were considered for age and variables pertaining to adherence to CDTI and albendazole treatment. The variable (and) categorization that (*i*) was associated at 15% level in the bivariate analysis, (*ii*) yielded the lowest Akaike Information Criterion (AIC), (*iii*) where applicable did not result in empty cross categories in the multivariate and (*iv*) did not yield collinearity in the multivariate model was selected for inclusion in the final multivariate model.

Supplemental File 2. Study diagram



Supplemental File 3. Participant characteristics

Variable	Category	Enrolled	Not enrolled	All censused
		n (%)	n (%)	n (%)
Age	5-8	1385 (14.7)	1149 (13.5)	2534 (14.1)
	9 -14	1962 (20.8)	1254 (14.7)	3216 (17.9)
	15-29	2206 (23.3)	2994 (35.1)	5200 (28.9)
	30-49	2430 (25.7)	2142 (25.1)	4572 (25.4)
	≥50	1473 (15.6)	983 (11.5)	2456 (13.7)
Gender	Men	4577 (48.4)	4496 (52.8)	9073 (50.5)
	Women	4879 (51.6)	4026 (47.2)	8905 (49.5)
Occupation	Farmer	3946 (41.7)	3792 (44.5)	7738 (43.0)
	None, child, NA	1385 (14.7)	535 (6.3)	1920 (10.7)
	Student/Pupil	3711 (39.2)	3567 (41.9)	7278 (40.5)
	Other: worker, service, liberal	414 (4.4)	628 (7.4)	1042 (5.8)
Education attainment	No school, NA	1849 (19.6)	786 (9.2)	2635 (14.7)
	Primary or secondary school	1524 (16.1)	1517 (17.8)	3041 (16.9)
	High school and higher	6083 (64.3)	6219 (73.0)	12302 (68.4)
Ever taken Albendazole	No	2570 (27.2)	-	-
	Yes, >1 year	1222 (12.9)	-	-
	Yes, < 1 year	5409 (57.2)	-	-
	Missing, no answer	255 (2.7)	-	-
Self-reported adherence to CDTI	Never	2,203 (23.3)	-	-
	up to 50% of rounds	5073 (53.7)	-	-
	50-75% of rounds	937 (9.9)	-	-
	> 75% of rounds	951 (10.1)	-	-
	missing	292 (3.1)	-	-
Time since last treatment	Any other case	4060 (42.9)	-	-
	< 1 year	5055 (53.5)	-	-
	missing	341 (3.6)	-	-
How many times participated in CDTI	missing	292 (3.1)	-	-
		Median; IQR	-	-
		2; 4	-	-

Data were obtained from 9,456 participants aged 5 years and over in a cross-sectional survey conducted in 2017 in 20 villages of Southwest Cameroon.

Supplemental File 4. Village-level *O. volvulus* prevalence and CMFL and *L. loa* prevalence

	O. volvulus				*Loa loa*		
Community	**N**	**Prevalence**	**95%CI**	**CMFL**	**N**	**Prevalence**	**95%CI**
Bakumba	547	53.75	49.6 - 57.9	2.43	539	2.6	1.4 - 4.3
Betenge	211	53.55	46.8 - 60.3	2.79	211	2.8	1.1 - 6.1
Big Butu	544	39.71	35.6 - 43.8	1.31	538	1.5	0.6 - 2.9
Big Massaka	585	58.97	55.0 - 63.0	2.85	576	3.1	1.9 - 4.5
Big Ngwandi	1004	35.66	32.7 - 38.6	1.10	995	2.0	1.2 - 4.9
Bikoki	217	70.05	63.9 - 76.2	3.08	216	2.8	1.0 - 5.9
Boa Bakundu	1249	36.19	33.5 - 38.9	1.43	1224	3.0	2.1 - 4.1
Bombanda	335	31.34	26.4 - 36.3	1.06	328	6.4	4.0 - 9.6
Bombele	373	32.17	27.4 - 36.9	0.82	359	2.2	1.0 - 4.3
Dienyi	727	53.37	49.7 - 57.0	2.02	720	10.6	8.4 - 13.0
Kombone	805	37.64	34.3 - 41.0	1.57	800	1.8	1.0 - 2.9
Kumu Kumu	92	61.96	51.9 - 72.1	3.59	89	6.7	2.5 - 14.1
Kwa Kwa	785	41.78	38.3 - 45.2	1.57	776	2.1	1.2 - 3.3
Lifenja	122	57.38	48.5 - 66.3	3.36	121	1.7	0.2 - 5.8
Lokando	131	58.78	50.2 - 67.3	1.97	130	3.8	1.3 - 8.7
Metoko Bekondo	423	48.70	43.9 - 53.5	1.99	410	11.5	8.5 - 15.0
Nake	495	37.58	33.3 - 41.9	1.26	489	3.1	1.7 - 5.0
Njombe	221	57.92	51.4 - 64.5	2.55	221	1.4	0.3 - 3.9
Small Butu	249	75.50	70.1 - 80.9	3.24	247	4.5	2.2 - 7.8
Small Massaka	341	34.31	29.3 - 39.4	1.29	338	2.4	1.0 - 4.6

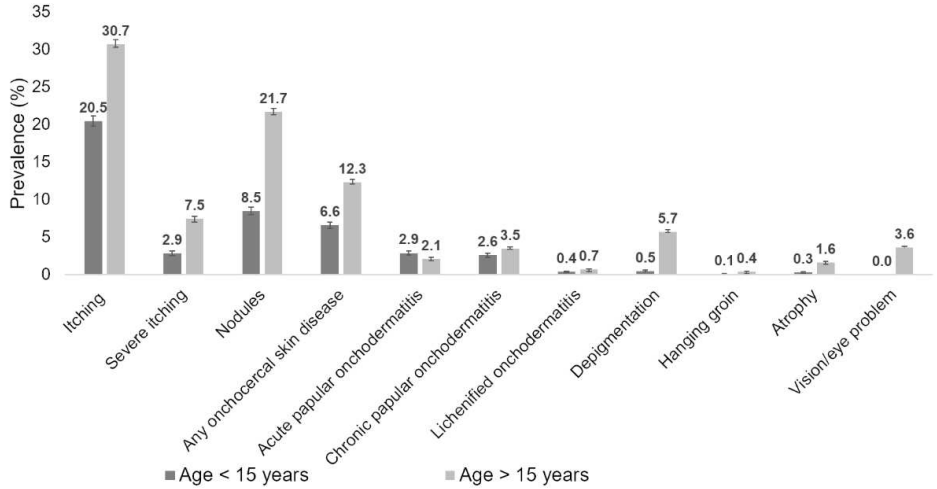
CI: confidence interval

Supplemental File 5. Unadjusted Odds Ratios for mf prevalence & intensity, and nodule prevalence (bivariate models)

		Prevalence			Infection intensity			Nodule prevalence		
Variable	**Category**	**OR**	**95% CI**	**p-value**	**IRR**	**95% CI**	**p-value**	**OR**	**95% CI**	**p-value**
Gender	Men	1.00			1.00			1.00		
	Women	**0.83**	0.76-0.90	<0.0001	**0.86**	0.81-0.91	<0.0001	**0.68**	0.61-0.75	<0.0001
Age (years)	30-49	1.00			1.00			1.00		
	5-8	**0.63**	0.54-0.72	<0.0001	**0.72**	0.65-0.81	<0.0001	**0.22**	0.17-0.27	<0.0001
	9-14	**1.47**	1.30-1.66	<0.0001	**1.39**	1.27-1.51	<0.0001	**0.39**	0.33-0.46	<0.0001
	15-29	**1.31**	1.16-1.48	<0.0001	**1.25**	1.14-1.36	<0.0001	**0.70**	0.60-0.81	<0.0001
	>=50	1.00	0.87-1.14	0.995	1.01	0.92-1.11	0.84	**1.30**	1.12-1.51	<0.0001
Self-reported adherence [(a)]	Never	1.00			1.00					
	<50%	**0.76**	0.68-0.84	<0.0001	**0.80**	0.74-0.85	<0.0001	**1.30**	1.13-1.49	<0.0001
	50-75	**0.48**	0.41-0.57	<0.0001	**0.57**	0.51-0.65	<0.0001	1.14	0.92-1.41	0.228
	>75	**0.04**	0.38-0.53		**0.56**	0.50-0.63	<0.0001	**0.77**	0.61-0.97	0.028
Time since last treatment	Any other case	1.00			1.00			1.00		
	< 1 year	**0.60**	0.55-0.65	<0.0001	**0.69**	0.65-0.73	<0.0001	**0.78**	0.70-0.87	<0.0001
Occupation	Farmer	1.00			1.00			1.00		
	No occupation, child	1.10	0.97-1.25	0.14	1.09	0.99-1.19	0.069	**0.75**	0.64-0.88	<0.0001
	Student/Pupil	1.03	0.94-1.13	0.544	1.04	0.97-1.11	0.246	**0.38**	0.33-0.43	<0.0001
	Other: worker, service, liberal	**0.70**	0.57-0.87	0.001	**0.74**	0.62-0.87	<0.0001	**0.52**	0.39-0.69	<0.0001
Education attainment	No school	1.00			1.00			1.00		
	Primary or secondary school	0.88	0.76-1.01	0.072	**0.89**	0.81-0.99	0.029	1.10	0.93-1.30	0.278
	High school and higher	0.93	0.84-1.04	0.216	0.94	0.87-1.01	0.099	**0.73**	0.63-0.83	<0.0001

OR: Odds ratio, CI: confidence interval; OR in bold are significant at 5% level.
[(a)]: self-reported adherence was expressed as the proportion of rounds taken out of the maximum rounds a person could have taken given their age.

Supplemental File 6. Prevalence of OSD and itching in participants aged below and above 15 years.



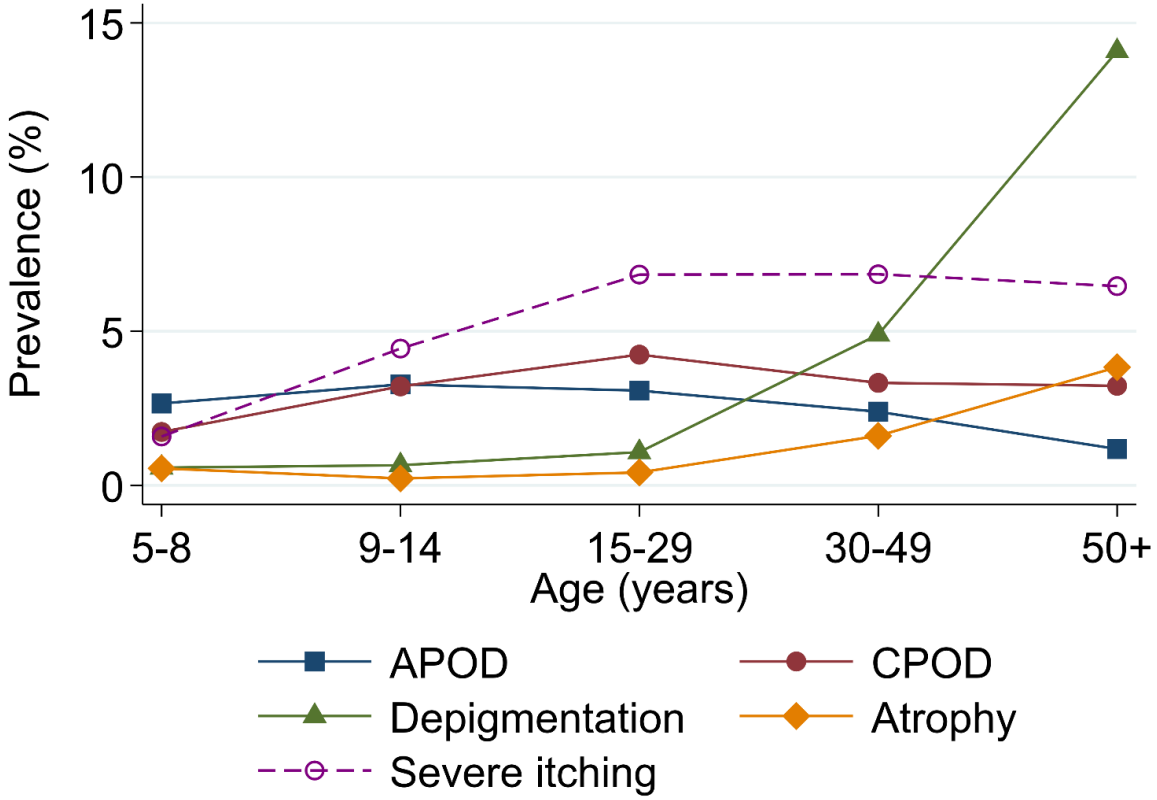
Data were obtained from a 2017 cross-sectional survey of 9,456 participants aged 5 years and over living in 20 communities of Southwest Cameroon.

Supplemental File 7. Association between OSD, adherence to CDTI and *O. volvulus* infection (adjusted ORs / multivariate model)

		APOD			CPOD			Depigmentation			Atrophy		
Variable	Category	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
O. volvulus infection status	-	n.a.			n.a.			n.a.			1.28	0.85-1.94	0.241
O. volvulus mf load	-	n.a.			n.a.			**1.01**	1.00-1.01	0.001	n.a.		
Number of nodules	-	**1.18**	1.03-1.34	0.014	**1.12**	1.00-1.25	0.047	**1.45**	1.27-1.66	<0.0001	1.08	0.92-1.27	0.319
Number of nodules, squared	-	n.a.			n.a.			**0.99**	0.97-1.00	0.043	n.a.		
Age (years)	30-49	1.00			1.00			1.00			1.00		
	5-8	1.12	0.58-2.14	0.735	**0.51**	0.28-0.93	0.027	**0.11**	0.04-1.29	<0.0001	0.35	0.10-1.12	0.089
	9-14	1.39	0.78-2.48	0.259	0.96	0.59-1.58	0.886	**0.12**	0.05-0.30	<0.0001	**0.13**	0.03-0.53	0.004
	15-29	1.30	0.82-2.07	0.264	1.29	0.89-1.86	0.174	**0.20**	0.12-0.36	<0.0001	**0.25**	0.10-0.62	0.003
	≥50	**0.48**	0.27-0.87	0.015	0.97	0.66-1.44	0.881	**3.39**	2.61-4.40	<0.0001	**2.51**	1.56-4.05	<0.0001
Gender	Men	1.00			1.00			1.00			1.00		
	Women	1.18	0.89-1.55	0.251	0.95	0.74-1.20	0.644	0.82	0.65-1.04	0.106	0.93	0.62-1.41	0.742
Self-reported adherence [(a)]	Never	1.00			1.00			1.00			1.00		
	up to 50% of rounds	**1.79**	1.14-2.82	0.011	1.18	0.82-1.69	0.374	0.81	0.59-1.11	0.198	0.99	0.58-1.73	0.999
	50-75% of rounds	**2.36**	1.28-4.36	0.006	1.33	0.78-2.25	0.292	0.80	0.50-1.27	0.345	0.87	0.38-2.01	0.749
	> 75% of rounds	**2.20**	1.20-4.03	0.011	1.63	0.96-2.78	0.07	0.64	0.36-1.15	0.136	0.48	0.15-1.54	0.255
Time since last treatment	Any other case	1.00			1.00			1.00			1.00		
	< 1 year	0.73	0.51-1.04	0.08	0.76	0.56-1.03	0.077	0.86	0.65-1.14	0.298	0.75	0.45-1.24	0.260
Occupation	Farmer	1.00			1.00			1.00			1.00		
	No occupation, child, N/A	0.91	0.47-1.78	0.787	1.43	0.88-2.32	0.144	0.77	0.54-1.10	0.153	0.82	0.43-1.57	0.555
	Student/Pupil	1.31	0.78-2.20	0.315	1.04	0.67-1.60	0.858	0.86	0.42-1.77	0.676	1.27	0.43-3.71	0.662
	Other: worker, service, liberal	0.67	0.28-1.58	0.356	1.34	0.78-2.29	0.29	1.11	0.63-1.98	0.714	1.08	0.38-3.07	0.884
Education attainment	No school	1.00			1.00			1.00			1.00		
	Primary or secondary school	0.70	0.35-1.40	0.314	0.83	0.49-1.40	0.477	**0.39**	0.26-0.57	<0.0001	0.56	0.28-1.10	0.092
	High school and higher	0.83	0.45-1.53	0.557	1.10	0.70-1.72	0.686	**0.60**	0.45-0.82	0.001	0.61	0.35-1.07	0.083

APOD: acute papular onchodermatitis, CPOD: chronic papular onchodermatitis; n.a.: non-applicable
OR: Odds ratio, CI: confidence interval; OR in bold are significant at 5% level
[(a)]: self-reported adherence was expressed as the proportion of rounds taken out of the maximum rounds a person could have taken given their age
No models were run for lichenified onchodermatitis and hanging groin due to the small sample size (58 lichenified onchodermatitis and 31 hanging groin cases, respectively).

Supplemental File 8. Marginal predictions of OSD and itching prevalence by age group.



Marginal predictions obtained with the multivariate models presented in SupplementalSupplemental File 7 (OSD) and SupplementalSupplemental File 10 (severe itching). Data were obtained from a 2017 cross-sectional survey of 9,115 (9,094 for severe itching due to missing data for albendazole treatment) participants aged 5 years and over living in 20 communities of Southwest Cameroon.

Supplemental File 9. Unadjusted Odds Ratio for skin disease and severe itching (unadjusted odds ratio / bivariate models)

		APOD			CPOD			Depigmentation			Atrophy			Severe itching		
Variable	Category	OR	95%CI	p-value	OR	95%CI	p-value	OR	95%CI	p-value	OR	95%CI	p-value	OR	95%CI	p-value
O. volvulus infection status	NA	1.06	0.81-1.38	0.677	1.08	0.86-1.37	0.510	1.42	1.14-1.76	0.001	1.44	0.98-2.13	0.060	0.98	0.82-1.17	0.799
mf load (nb/snip)	NA	1.00	1.00-1.01	0.189	1.00	1.00-1.01	0.461	1.01	1.00-1.01	<0.0001	1.00	0.99-1.01	0.88	1.00	1.00-1.01	0.037
Nodule number	NA	1.11	0.97-1.26	0.13	1.13	1.02-1.26	0.024	1.53	1.41-1.66	<0.0001	1.23	1.08-1.41	0.002	1.16	1.07-1.26	<0.0001
Gender	Men	1.00	NA	NA	1.00	NA	NA	1.00	NA	NA	1.00	NA	NA	1.00	NA	NA
	Women	1.12	0.86-1.47	0.386	0.96	0.76-1.21	0.751	0.95	0.77-1.17	0.648	1.08	0.74-1.58	0.701	1.27	1.07-1.52	0.007
Age (years)	30-49	1.00	NA	NA	1.00	NA	NA	1.00	NA	NA	1.00	NA	NA		NA	NA
	5-8	1.21	0.78-1.89	0.394	0.57	0.36-0.90	0.016	0.10	0.04-0.23	<0.0001	0.37	0.16-0.84	0.018	0.16	0.10-0.27	<0.0001
	9-14	1.55	1.06-2.26	0.024	1.01	0.72-1.41	0.973	0.11	0.06-0.21	<0.0001	0.14	0.05-0.40	<0.0001	0.47	0.36-0.62	<0.0001
	15-29	1.38	0.95-2.02	0.093	1.28	0.94-1.75	0.117	0.20	0.12-0.32	<0.0001	0.26	0.12-0.57	0.001	0.86	0.69-1.08	0.206
	>=50	0.55	0.32-0.95	0.033	0.96	0.66-1.40	0.845	4.02	3.14-5.13	<0.0001	2.81	1.81-4.36	<0.0001	1.02	0.80-1.30	0.89
Self-reported adherence [(a)]	Never	1.00	NA	NA	1.00	NA	NA	1.00	NA	NA	1.00	NA	NA		NA	NA
	<50%	1.42	0.99-2.04	0.058	1.17	0.87	0.313	0.94	0.73-1.21	0.628	0.91	0.58-1.43	0.688	1.69	1.33-2.15	<0.0001
	50-75	1.56	0.93-2.60	0.091	1.13	0.72	0.586	1.08	0.74-1.58	0.701	0.92	0.46-1.88	0.829	1.60	1.13-2.27	0.009
	>75	1.65	0.99-2.76	0.055	1.13	0.72	0.595	0.50	0.30-0.82	0.006	0.35	0.12-1.01	0.051	1.55	1.09-2.20	0.014
Time since last treatment	Any other case	1.00	NA	NA	1.00	NA	NA	1.00	NA	NA	1.00	NA	NA		NA	NA
	< 1 year	1.11	0.84-1.46	0.471	0.87	0.69	0.268	0.62	0.50-0.77	<0.0001	0.56	0.38-0.84	0.005	1.07	0.89-1.28	0.471
Occupation	Farmer	1.00	NA	NA	1.00	NA	NA	1.00	NA	NA	1.00	NA	NA		NA	NA
	No occupation, child	1.18	0.77-1.81	0.446	1.31	0.94	0.11	0.68	0.51-0.91	0.008	0.83	0.50-1.38	0.473	0.84	0.66-1.07	0.169
	Student/Pupil	1.71	1.27-2.31	<0.0001	0.95	0.73	0.703	0.07	0.05-0.12	<0.0001	0.18	0.10-0.33	<0.0001	0.43	0.35-0.54	<0.0001
	Other: worker, service, liberal	0.89	0.40-1.94	0.763	1.35	0.80	0.26	0.46	0.26-0.79	0.005	0.53	0.19-1.47	0.221	0.64	0.41-1.00	0.049
Education attainment	No school	1.00	NA	NA	1.00	NA	NA	1.00	NA	NA		NA	NA		NA	NA
	Primary or secondary school	0.86	0.52-1.42	0.554	0.76	0.51	0.174	0.40	0.29-0.56	<0.0001	0.49	0.27	0.016	1.01	0.77	0.967
	High school and higher	1.31	0.91-1.88	0.142	0.89	0.67	0.414	0.31	0.24-0.39	<0.0001	0.32	0.21	<0.0001	0.71	0.57	0.002

APOD: acute papular onchodermatitis; CPOD: chronic papular onchodermatitis;
OR: odds ratio, CI: confidence interval; NA: not applicable; OR in bold are significant at 5% level.
(a): self-reported adherence was expressed as the proportion of rounds taken out of the maximum rounds a person could have taken given their age.

Supplemental File 10. Factors and symptoms associated with severe itching (adjusted ORs / multivariate model)

Variable	Category	OR	95%CI	p-value
Infection intensity (mf load)		1.00	1.00-1.01	0.057
Presence of nodules	No	1.00		
	Yes	1.23	0.98-1.55	0.074
Age (years)	30-49	1.00		
	5-8	**0.21**	0.11-0.37	<0.0001
	9-14	**0.60**	0.40-0.89	0.012
	15-29	0.99	0.75-1.30	0.918
	≥50	0.94	0.72-1.24	0.66
Sex	Men	1.00		
	Women	**1.28**	1.06-1.55	0.01
Self-reported adherence [(a)]	Never	1.00		
	up to 50% of rounds	**1.40**	1.01-1.93	0.041
	50-75% of rounds	1.35	0.87-2.11	0.18
	> 75% of rounds	**2.06**	1.32-3.23	0.002
Time since last treatment	Any other case	1.00		
	< 1 year	1.03	0.74-1.42	0.866
APOD	No	1.00		
	Yes	**3.79**	2.58-5.56	<0.0001
CPOD	No	1.00		
	Yes	**6.63**	4.91-8.96	<0.0001
LOD	No	1.00		
	Yes	**8.11**	4.42-14.87	<0.0001
Depigmentation	No	1.00		
	Yes	1.40	0.95-2.04	0.086
Atrophy	No	1.00		
	Yes	1.14	0.56-2.35	0.717
Hanging groin	No	1.00		
	Yes	1.20	0.34-4.30	0.779
Non-onchocercal skin disease [(b)]	No	1.00		
	Yes	1.41	0.88-2.26	0.149
Occupation	Farmer	1.00		
	No occupation, child, N/A	1.01	0.71-1.43	0.972
	Student/Pupil	0.79	0.56-1.13	0.198
	Other [(c)]	0.68	0.42-1.10	0.114
Education attainment	No school	1.00		
	Primary or secondary	0.97	0.68-1.40	0.889
	≥ High school	0.94	0.68-1.30	0.721
Taken albendazole	Never	1.00		
	Yes, > 1 year ago	0.82	0.59-1.13	0.229
	Yes, < 1 year ago	0.83	0.63-1.10	0.202

OR: Odds ratio, CI: confidence interval; OR in bold are significant at 95% level.
APOD: acute papular onchodermatitis; CPOD: chronic papular onchodermatitis, LOD: lichenified onchodermatitis;
[(a)] self-reported adherence was expressed as the proportion of rounds taken out of the maximum rounds a person could have taken given their age.
[(b)] non-onchocercal skin diseases included scabies, pyoderma and dermatophytes.
[(c)] occupation classified as "other" included small businesses, workers, civil servants and liberal professions
Results were obtained by a multivariate mixed logistic regression model and data from a cross-sectional survey conducted in 2017 among 9,115 participants with complete data living in 20 communities of Southwest Cameroon.

Supplemental File 11. Participants in the qualitative assessments

	Community members who accepted IVM		Community members who refused IVM		Community Drug Distributors	
Age (years)	Men	Women	Men	Women	Men	Women
15-20	2	1	1	2	0	0
21-30	2	2	1	4	4	3
31-40	2	2	2	3	8	4
41-50	2	3	1	1	1	3
51-60	2	3	0	0	2	0
60+	2	1	0	1	1	0
Sub totals 1	12	12	5	11	16	10
Sub totals 2	24		16		26	
Total	66					

Supplemental File 12. Perceived adverse events of Ivermectin

Reported adverse event	Perceived causes of adverse events	Consequences of adverse events	Prevention and Management of adverse events
• Swelling • Increased itching Making other diseases worse especially hernias and epilepsy *'Because there was a man who was having hernia. The hernia was not yet visible.. It was just hiding in his body but immediately he took Mectizan, the hernia became worse until he couldn't walk'*. (Community member, woman, aged 15-20 years) • Infertility • Miscarriage *'I was refusing to drink Mectizan because*) *they said it aborts pregnancies, I feared drinking the Mectizan; I said I will never drink Mectizan, I was scared'* (Community member, woman, aged -31-40 years) • Boils • Rashes • Death	• Meeting unknown disease in the body • Meeting filaria in the body • Witchcraft	• Having economic expense due to needing operation to treat hernias • Economic costs of missing work • Economic costs of getting treatment from a pharmacy • Being a burden on your family • Being unable to socially interact due to side effects (especially itching or mobility problems) *It makes me to feel uncomfortable when I want to sit with my friends… Because I cannot go and sit amongst my friends and be scratching my skin* (Community member, man, aged 15-20)	• Taking Mectizan as a lotion *'Because when they swallow it they have rashes and their arms or legs get swollen. So they prefer to put it in their lotion to avoid the side effects.*' (Community member, man, aged 15-20 years) • 'Cooler' for minor symptoms *'Some people are afraid, but I do my best to enlighten them saying, if they drink it and it leads to fever, what I can give them to cool the fever is Paracetamol and that is what we were taught but if the effects are more than me to handle, I can send them to the health centre'.* (CDD, man, aged 31-40 years) • Grinded gentamicin for boils • Traditional medicine *'There are traditional medicines that they used, There are traditional medicines that they used, dropping it in the eyes. There are others who use just the Gentamicin eye drop'* (CDD, man, aged 21-30 years) • 'Medicated soap' • Bathing • Treating the 'sickness' that it has provoked. • Surgery • Hospital/clinic visit

CDD: Community Drug Distributor.

Supplemental File 13. STROBE Statement

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract In the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found.
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported Page 6. All introduction except last sentence.
Objectives	3	State specific objectives, including any prespecified hypotheses Page 6-7. Last sentence of the introduction.
Methods		
Study design	4	Present key elements of study design early in the paper Methods, section #1 "Study design and participants". Page 7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection Methods, section #1 "Study design and participants". Page 7 Data collection: Methods, section #2 "Parasitological and questionnaire data"; section #3, "Onchocerciasis clinical assessments"; section #4 "Semi-structured qualitative interviews". Page 7-8.
Participants	6	Give the eligibility criteria, and the sources and methods of selection of participants. Methods, section #1 "Study design and participants"; section #4 "Semi-structured qualitative interviews". Page 7-8.
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable. Methods, section #2 "Parasitological and questionnaire data" Page7.; section #3, "Onchocerciasis clinical assessments" Page 8; section 6 "Statistical analysis"; Page 9-10. Supplemental file 1.
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group. Methods, section #2 "Parasitological and questionnaire data" Page 7; section #3, "Onchocerciasis clinical assessments"; Page 8. section #4 "Semi-structured qualitative interviews". Page 8.
Bias	9	Describe any efforts to address potential sources of bias Methods section 6 "Statistical analysis" Page 9-10; Supplemental file 1. Results section 1 "Study population and participation in the baseline survey", paragraph 2. Page 11.
Study size	10	Explain how the study size was arrived at Results section#1 "Study population and participation in the baseline survey", paragraph 1. Page 10. Supplemental File 2. Study diagram.
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why Methods section 6 "Statistical analysis" Page 9-10. Supplemental file 1. Results section 1, paragraph 2" Page 11.
Statistical methods	12	*(a)* Describe all statistical methods, including those used to control for confounding Methods section 6 "Statistical analysis" Page 9-10.; Supplemental file 1
		(*b*) Describe any methods used to examine subgroups and interactions Methods section 6 "Statistical analysis" Page 9-10.
		(c) Explain how missing data were addressed Methods section 6 "Statistical analysis" Page 9-10.; Supplemental file 1. Results section 1, paragraph 2" Page 11.
		(*d*) If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses

		Results section 1 "Study population and participation in the baseline survey" paragraph 2, Page 11; Supplemental file 1.
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. Results section 1 "Study population and participation in the baseline survey", paragraph 1, Page 10-11. Supplemental File 2 & 3.
		(b) Give reasons for non-participation at each stage Results section 1 "Study population and participation in the baseline survey", paragraph 1, Page 10. Supplemental File 2.
		(c) Consider use of a flow diagram Supplemental File 2
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders. Supplemental File 3. Figure 2.
		Indicate number of participants with missing data for each variable of interest Supplemental File 3
Outcome data	15*	Report numbers of outcome events or summary measures Results, Section #2, "*O. volvulus* infection levels, adherence to CDTI and prevalence of *Loa loa*", Page 11; Section #4 "Prevalence of disease", Page 14.; Supplemental Files 4 & 6.
Main results	16	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included Unadjusted estimates: Supplemental Files 5 & 9. Confounder adjusted estimates: Table 1, Supplemental Files 7 & 10.
		Report category boundaries when continuous variables were categorized Tables 2, 3 and 4. Supplemental Tables 2 & 3.
		If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—e.g. analyses of subgroups and interactions, and sensitivity analyses Results section 1 "Study population and participation in the baseline survey", paragraph 2. Page 11.
Discussion		
Key results	18	Summarise key results with reference to study objectives Done throughout the discussion. Page 20-25
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias Paragraph "Limitations". Page24
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence Done for each specific topic of the discussion. Page 20-25
Generalisability	21	Discuss the generalisability (external validity) of the study results Conclusion page 25
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based Footnote on Funding Page 31.