

Factors Associated With Coverage in Community-directed Treatment With Ivermectin for Onchocerciasis Control in Savannah and Forest Areas in Central African Republic: A Cross-sectional Study

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Objectives: The aim of this study was to identify factors associated with coverage in community-directed treatment with ivermectin for onchocerciasis control in savannah and forest areas in the Central African Republic.

Methods: A cross-sectional study was conducted in 2 districts where onchocerciasis is endemic. We employed a pretested and validated questionnaire that included questions about the socio-demographic characteristics of the respondents and variables relevant to coverage assessment. Multivariate logistic regression analyses were performed to identify the associations between surveyed mass drug administration (MDA) coverage and the variables considered, while accounting for potential confounding factors. A p -value < 0.05 was considered statistically significant.

Results: At the district level, the MDA program achieved a reach of 87.29% (95% confidence interval [CI], 86.03 to 88.55) in Bossangoa and 61.74% (95% CI, 59.56 to 63.92) in Kémo, compared to the reported rates of 90.02% and 91.70%, respectively. Women in both Bossangoa and Kémo were 1.28 times more likely to have taken ivermectin than men (95% CI, 1.12 to 1.47; $p=0.008$; 95% CI, 1.09 to 2.00; $p=0.041$, respectively). The age groups of 5-14, 15-24, and 25-34 were statistically associated with better distribution coverage in both districts. Individuals with knowledge of onchocerciasis were more likely to receive ivermectin compared to those without knowledge, with adjusted odds ratios of 1.41 (95% CI, 1.11 to 2.01; $p=0.030$) and 3.19 (95% CI, 2.91 to 4.08; $p=0.001$), respectively.

Conclusions: The authors recommend implementing measures to improve MDA coverage in future campaigns. These measures should include allocating sufficient time for MDA activities, providing health education, and mobilising the entire population.

Key words: Mass drug administration, Ivermectin, Onchocerciasis, Distribution

Received: Jun 7, 2024 Revised: Jul 27, 2024 Accepted: Aug 1, 2024

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INTRODUCTION

Onchocerciasis, or river blindness, is classified as a preventable neglected tropical disease [1]. This disease imposes a significant social burden in endemic regions, leading to reduced life expectancy and causing conditions such as blindness in both adults and children [2-6]. As a result, it remains a critical public health issue in certain sub-Saharan African countries

where it is endemic [7-10]. Recently, national disease control programs have adopted more ambitious objectives, aiming for the complete eradication of the disease in selected African nations by 2020 [11,12] or 2025 [13-15]. To achieve this, endemic countries have received technical support and supervision from the Expanded Special Project for the Elimination of Neglected Tropical Diseases.

The primary strategy of the national onchocerciasis control programmes involved mass drug administration (MDA) of ivermectin and expanding geographical coverage, alongside establishing an enhanced monitoring and evaluation system [16-18]. During each MDA campaign, community drug distributors (CDDs) were tasked with generating routine coverage reports [19,20]. However, the data quality provided by CDDs is often poor. Therefore, it is crucial to conduct community-based post-MDA surveys to accurately estimate drug coverage and confirm the validity of the reported coverage [9,16,19,21].

In the Central African Republic, 4 out of 7 health regions are endemic for onchocerciasis. The World Health Organization (WHO) estimates that by 2020, approximately 2 662 937 people will be residing in these areas and will consequently require medical care [7,22], with a mass treatment coverage of 50% [23]. Residents of the savannah and forest regions in the Central African Republic are particularly vulnerable to onchocerciasis due to the heightened presence of the transmissible agent. In response, the Ministry of Health and Population has initiated an onchocerciasis control program. The challenge lies in devising prevention and treatment strategies that ensure community compliance with the control measures. The purpose of this study was to evaluate the post-distribution coverage of ivermectin and to identify factors that contribute to its successful uptake within the community.

METHODS

Study Design

A cross-sectional study was conducted in 2 districts of the Central African Republic endemic for onchocerciasis—specifically in the city of Bossangoa within the savannah zone and in Kémo, located in the forest. These districts are situated in the north and south of the country, with populations of 140 547 and 189 539, respectively. The study was carried out from November 2, 2022 to June 30, 2023.

To implement the MDA program, a series of training sessions were conducted during each round of drug distribution in

Bossangoa and Kémo. Prior to the drug distribution in their respective districts, health facilities received either orientation or refresher training, which was followed by several awareness campaigns on onchocerciasis control. Training typically included health education about onchocerciasis and its control, emphasising strong mobilisation and awareness-raising. These sessions were conducted in each village, utilising platforms such as social and religious gatherings.

Study Population and Sampling

We included in the study all individuals over the age of 5 who had resided in each community for more than a year. Residents younger than 1 year and those who declined to participate were excluded, particularly non-residents who had moved from other locations after June 2022. The sample size (n) was calculated using the following formula [24]:

$$n = \frac{(DEFF) (z^2_{\alpha/2}) (p) (1-p)}{\delta^2(1-r)}$$

where n: survey sample size; DEFF: design effect; α : alpha; δ : desired precision; r: non-response rate, and p: reported drug coverage.

According to WHO guidelines [24], we conducted an integrated coverage assessment with a default assumption of 50% coverage for each district. Considering a design effect of 4 and a non-response rate of 10% with 5% precision at a 95% confidence interval (CI), a sample of 1707 individuals from Bossangoa and 1707 from Kémo was estimated as the minimum necessary. This calculated sample size was then proportionally allocated based on the household sizes in the municipalities. Households were systematically sampled by dividing the total number of households in each municipality by the sample size allocated to that municipality, adjusted proportionally to the population size of each municipality. The process for selecting respondents involved listing all occupants of eligible households and then randomly selecting individuals from this list. Data concerning young children were gathered from their primary caretakers. Houses that were inaccessible on the day of the survey and households whose heads declined participation were not replaced in the study.

Tools and Data Collection Methods

We utilised a pretested and validated questionnaire that included questions on the socio-demographic characteristics of the respondents and variables relevant to coverage assess-

ment [25]. The investigators consisted of sixth-year medical students and third-year sociology students, all of whom had received training in onchocerciasis control practices, community distribution of ivermectin, and data collection techniques. Before administering the questionnaire face-to-face, respondents were briefed on the study's purpose, the procedures involved, and the necessity of their consent to participate. To aid in recall, respondents were shown examples of an ivermectin tablet.

Statistical Analysis

Data were collected, recorded in Microsoft Excel (Microsoft, Redmond, WA, USA), and analysed using RStudio version 3.2.3 (R Foundation for Statistical Computing, Vienna, Austria). Descriptive analysis utilised frequencies and proportions for qualitative variables, while quantitative variables were described using means and standard deviations. Ivermectin MDA coverage was calculated as the proportion of individuals in the survey areas who were offered the drug, out of the total number surveyed, regardless of actual ingestion. Reported coverage data were considered validated if they fell within the 95% CI of the surveyed coverage rate. These reported coverage data and population estimates from the MDA were provided by the onchocerciasis/neglected tropical diseases focal person from the respective district health office to facilitate comparison between reported coverage and survey coverage rates. To compare surveyed coverage, researchers utilised reported program coverage data from the eligible population, which was adjusted by excluding children under 5 years old from the denominator. Univariate and multivariate logistic regression analyses were conducted to identify factors associated with MDA survey coverage, taking into account potential confounding factors. The analyses used odds ratios with 95% CIs. A p -value < 0.05 was considered statistically significant.

Ethics Statement

Ethical clearance and administrative authorisations were obtained before data collection began. The study was submitted to and approved by the Ethics Committee of the University of Bangui. For this purpose, an ethical clearance was issued, bearing the number 005/CSERC/UB/2023. We also obtained signed informed consent from the participants.

RESULTS

Baseline Characteristics of Respondents

The study had a total sample size of 4621 participants, with 4576 consenting to participate in the interview, resulting in a global response rate of 99.0%. Of these, 2668 (58.3%) were from the Bossangoa district and 1908 (41.7%) from the Kémo district. The mean age of the respondents was 28.20 years, with a standard deviation of 12.20 years. The proportion of women participants was 51.4% in Bossangoa district and 50.9% in Kémo district, whereas 48.6% and 49.1% of participants were men, respectively. Additional characteristics of the respondents are presented in Table 1.

Table 1. Socio-demographic characteristics of the respondents in Bossangoa and Kémo districts in 2023

Characteristics	Bossangoa (n=2668)	Kémo (n=1908)	Total (n=4576)
Gender			
Women	1372 (51.4)	971 (50.9)	2343 (51.2)
Men	1296 (48.6)	937 (49.1)	2233 (48.8)
Age (y)			
5-14	403 (15.1)	311 (16.3)	714 (15.6)
15-24	718 (26.9)	340 (17.8)	1058 (23.1)
25-34	483 (18.1)	417 (21.9)	900 (19.7)
35-44	375 (14.1)	329 (17.2)	704 (15.4)
45-54	297 (11.1)	301 (15.8)	598 (13.1)
≥ 55	392 (14.7)	210 (11.0)	602 (13.2)
Educational level			
Primary	1072 (40.2)	775 (40.6)	1847 (40.4)
Secondary	1397 (52.4)	1011 (53.0)	2408 (52.6)
University	199 (7.5)	122 (6.4)	321 (7.0)
Profession			
Public	348 (13.0)	676 (35.4)	1024 (22.4)
Private	97 (3.6)	176 (9.2)	273 (6.0)
Farmers/Breeders/Fishermen	2223 (83.3)	1056 (55.3)	3279 (71.7)
Religion			
Christian	1800 (67.5)	1329 (69.7)	3129 (68.4)
Muslim	89 (3.3)	101 (5.3)	190 (4.1)
Other	779 (29.2)	478 (25.0)	1257 (27.5)
Household size (n)			
< 5	2075 (77.8)	1401 (73.4)	3476 (76.0)
5-10	561 (21.0)	444 (23.3)	1005 (22.0)
≥ 11	32 (1.2)	63 (3.3)	95 (2.1)
Knowledge about onchocerciasis			
Yes	2322 (87.0)	1796 (94.1)	4118 (90.0)
No	346 (13.0)	112 (5.9)	458 (10.0)

Values are presented as number (%).

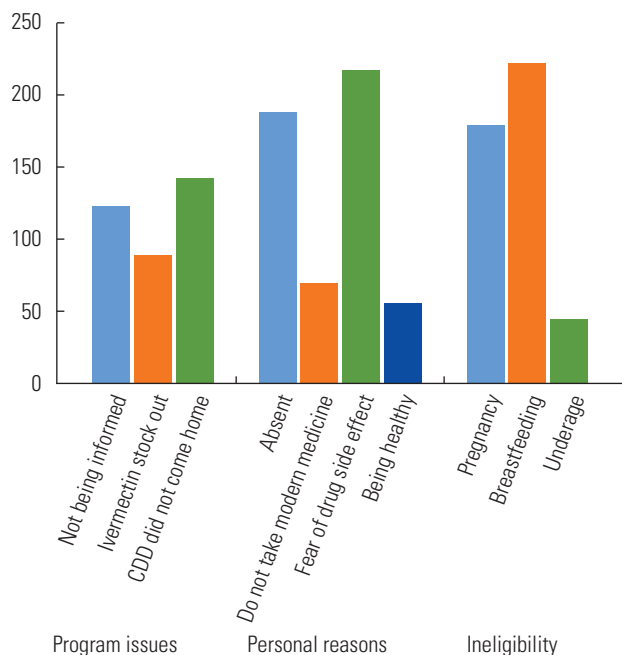


Figure 1. Reasons why eligible people did not take ivermectin in Bossangoa and Kémo during mass drug administration. CDD, community drug distributor.

Survey Coverage and Reasons Why Eligible Respondents Did Not Take Ivermectin

During the 2023 MDA, 3254 respondents (71.11%; 95% CI, 55.07 to 87.15) received ivermectin tablets, while 1322 (28.89%) did not. At the district level, 2329 respondents in Bossangoa and 1178 in Kémo were offered the drug, demonstrating an MDA program reach of 87.29% (95% CI, 86.03 to 88.55) in Bossangoa and 61.74% (95% CI, 59.56 to 63.92) in Kémo. These figures compare to the 90.02% and 91.70% reported by the national onchocerciasis control programme for each district, respectively.

Respondents cited several reasons for not taking ivermectin, which generally fell into 3 main categories: program-implementation-related issues, personal reasons, and ineligibility criteria. These categories account for 26.6% (352/1322), 39.9% (527/1322), and 33.5% (443/1322) of the responses, respectively. Figure 1 presents a summary of these reasons.

Factors Associated With Mass Drug Administration Coverage

Multiple logistic regression analysis indicated that women were 1.28 times more likely to have taken ivermectin than men in both Bossangoa and Kémo (95% CI, 1.12 to 1.47; $p=0.008$ and 95% CI, 1.09 to 2.00; $p=0.041$, respectively). The age groups

5-14, 15-24, and 25-34 were statistically associated with better distribution coverage in these 2 districts. Individuals with knowledge of onchocerciasis were more likely to receive ivermectin than those without such knowledge, as indicated by adjusted odds ratios of 1.41 (95% CI, 1.11 to 2.01; $p=0.030$) and 3.19 (95% CI, 2.91 to 4.08; $p=0.001$), respectively. However, factors such as religion or household size did not provide any significant insights into ivermectin intake (Table 2).

DISCUSSION

This study was conducted to estimate ivermectin coverage, compare MDA coverage as reported by CDDs, explore the main reasons for not offering the drug, and identify factors associated with drug intake during the MDA campaign in June 2023. The campaign took place in 2 onchocerciasis-endemic districts in the Central African Republic: Bossangoa, a savannah region, and Kémo, a forest region. The comparison is based on the higher transmission rates of the disease in savannah areas compared to forest areas, attributed to the disease's prevalence [26]. The elimination of onchocerciasis through MDA depends on achieving and maintaining high drug coverage over an extended period. This is necessary to reduce the human reservoir of the parasite and interrupt its transmission, posing a significant challenge for national control programmes [27].

Characteristics of Respondents

Women slightly outnumbered men. Similar findings have been reported by other authors [28,29]. This trend is consistent in the Central African Republic, as in other regions, where the number of women marginally surpasses that of men. The average age was 28.20 years, indicating that the population in rural areas is predominantly young.

Coverage Evaluation and Settings

Evaluation of distribution coverage is a crucial metric for assessing the effectiveness of an onchocerciasis elimination program. Historically, several methods have been employed to assess post-distribution coverage, including the statistical method of lot quality assurance sampling and 2-stage cluster sampling [30]. However, these methods have various limitations. The most appropriate approach, as recommended by the WHO Neglected Tropical Disease Programme Review Group, is the probability sampling with segmentation, introduced in 2016 [24]. In both districts examined, the coverage observed ex-

Table 2. Factors associated with coverage during mass drug administration in Bossangoa and Kémo districts in 2023

Variables	Bossangoa						Kémo					
	Ivermectin (n)		cOR (95% CI)	p-value	aOR (95% CI)	p-value	Ivermectin (n)		cOR (95% CI)	p-value	aOR (95% CI)	p-value
	Yes	No					Yes	No				
Gender												
Women	1030	342	1.42 (1.20, 1.69)	<0.001	1.28 (1.12, 1.47)	0.008	603	368	1.78 (1.48, 2.14)	<0.001	1.29 (1.09, 2.00)	0.041
Men	880	416	1.00 (reference)	-	1.00 (reference)	-	449	488	1.00 (reference)	-	1.00 (reference)	-
Age (y)												
5-14	360	43	8.81 (6.07, 12.79)	<0.001	3.24 (2.86, 6.59)	0.001	225	86	2.38 (1.65, 3.43)	<0.001	1.91 (1.61, 2.01)	0.021
15-24	487	231	2.22 (1.72, 2.86)	<0.001	1.91 (1.76, 2.09)	0.004	251	89	2.56 (1.78, 3.69)	<0.001	1.97 (1.44, 2.30)	0.036
25-34	397	86	4.86 (3.58, 6.60)	<0.001	2.59 (1.99, 3.21)	<0.001	320	97	3.00 (2.11, 4.27)	<0.001	2.19 (1.99, 2.88)	0.009
35-44	188	187	1.06 (0.80, 1.40)	0.348	-	-	180	149	1.32 (0.93, 1.88)	0.054	-	-
45-54	168	129	1.37 (1.01, 1.86)	0.020	1.01 (0.86, 1.99)	0.078	179	122	1.33 (0.93, 1.90)	0.056	-	-
≥55	191	201	1.00 (reference)	-	1.00 (reference)	-	100	110	1.00 (reference)	-	1.00 (reference)	-
Educational level												
Primary	893	179	2.77 (1.99, 3.85)	<0.001	1.80 (1.31, 2.22)	0.010	699	76	3.41 (2.14, 5.42)	<0.001	2.40 (2.01, 3.06)	0.029
Secondary	1026	371	1.53 (1.12, 2.09)	0.004	1.22 (1.06, 1.99)	0.081	894	117	2.83 (1.82, 4.41)	<0.001	1.87 (1.06, 2.99)	0.043
University	128	71	1.00 (reference)	-	1.00 (reference)	-	89	33	1.00 (reference)	-	1.00 (reference)	-
Profession												
Public	151	197	1.00 (reference)	-	1.00 (reference)	-	302	374	1.00 (reference)	-	1.00 (reference)	-
Private	83	14	7.73 (4.23, 14.16)	<0.001	3.69 (2.87, 4.82)	0.002	99	77	1.59 (1.14, 2.22)	0.003	1.09 (0.97, 1.89)	0.062
Farmers and others	1689	534	7.13 (3.26, 5.21)	<0.001	2.79 (1.99, 3.46)	0.001	929	127	9.06 (7.13, 11.51)	<0.001	3.79 (2.19, 4.47)	0.002
Religion												
Christian	1458	342	1.00 (reference)	-	-	-	805	524	1.00 (reference)	-	1.00 (reference)	-
Muslim	72	17	0.99 (0.58, 1.71)	0.480	-	-	74	27	1.78 (1.13, 2.81)	0.005	1.27 (0.87, 2.03)	0.098
Other	621	158	0.92 (0.75, 1.14)	0.224	-	-	312	166	1.22 (0.98, 1.52)	0.034	-	-
Household size (n)												
<5	1407	668	1.10 (0.53, 2.30)	0.391	-	-	961	440	0.62 (0.34, 1.14)	0.060	-	-
5-10	397	164	1.27 (0.59, 2.69)	0.267	-	-	397	164	0.69 (0.37, 1.28)	0.122	-	-
≥11	21	11	1.00 (reference)	-	1.00 (reference)	-	49	14	1.00 (reference)	-	-	-
Knowledge about onchocerciasis ¹												
Yes	1802	520	1.91 (1.50, 2.43)	<0.001	1.41 (1.11, 2.01)	0.030	1287	509	8.79 (5.57, 13.88)	<0.001	3.19 (2.91, 4.08)	0.001
No	223	123	1.00 (reference)	-	1.00 (reference)	-	25	87	1.00 (reference)	-	1.00 (reference)	-

cOR, crude odds ratio; aOR, adjusted odds ratio; CI, confidence interval.
¹Vector, transmission and prevention.

ceeds the WHO's recommended threshold of 90% or higher. Nonetheless, the coverage noted after field evaluations falls below the averages reported by distributors. These findings align with those reported by other researchers [31-33], but also differ from others [28]. Despite these discrepancies, the variation between reported and observed coverage remains within the WHO's acceptable range of 15% [24].

The surveyed coverage in the 2 districts did not meet the recommended minimum threshold of 90% for the elimination of onchocerciasis. However, the National Onchocerciasis Control Programme in the Central African Republic must intensify its efforts to achieve better coverage in future MDAs. This is crucial because both districts reported drug coverages that exceeded the survey estimates and fell outside the 95% CIs, casting doubt on the accuracy of these coverage reports. This discrepancy could stem from inaccurate census data or potential biases aimed at meeting program objectives, which might lead to the intentional inflation of reported coverage [34].

Coverage surveys were helpful for identifying reasons that influenced participation in MDA campaigns against neglected tropical diseases (NTDs) [35] including onchocerciasis [9,36,37], to implement tailored effective strategies to improve the programmes. Among the 4576 respondents from both districts, 1614 individuals were not offered the drug during the June 2022 drug distribution campaign; specifically, 758 from Bossangoa and 856 from Kémo district. Some respondents who were not offered treatment reported that they were absent from their homes and/or community during the campaign. This issue may stem from the insufficient time allocated for the MDA campaign, which only lasted a few days for mobilisation, education, and drug distribution in the study areas. Consistent with the findings of the current study, absenteeism from homes or villages at the time of drug distribution has been identified as a major reason for missing the drug [28,36,38,39]. In both districts, 35.3% (120/340) of the ivermectin non-recipients reported a lack of information about the MDA campaign. Therefore, it is necessary to reduce the number of non-recipients by allocating a sufficient number of days for the MDA campaign and by effectively mobilising communities before distributing the drug.

Reasons given by respondents for not taking ivermectin were related to issues with program implementation, personal reasons, and ineligibility criteria, such as not being informed, being absent, fear of drug side effects, or breastfeeding. Similar findings have been reported by other authors, although for

different reasons [14,36]. In our case, insufficient time was allocated to raising awareness, and not all community members received the same information regarding the importance of using ivermectin.

Factors Associated With Ivermectin Intake

Identification of factors associated with ivermectin intake is helpful for sustaining and enhancing the implementation of MDA programs. An analysis of factors believed to affect MDA coverage revealed that women had significantly higher coverage rates than men in both districts studied ($p < 0.05$). These findings support those of another author [36] but contrast with different studies [28,33]. Such discrepancies may stem from variations in perceived treatment benefits, health-seeking behaviours, socio-cultural beliefs, or the sizes of the study samples. In this study, respondents aged 15-24 years and 25-34 years exhibited significantly better coverage rates compared to those over 54 years old. This suggests that the younger age groups, less likely to have experienced morbidity attributed to onchocerciasis, may not perceive the disease as a threat in their community, or they may participate less in village meetings discussing the benefits of ivermectin treatment. Addressing these issues could involve enhancing community education and actively involving both adults and youths in village meetings and community health education programs. Researchers from Uganda have noted that young adults and middle-aged individuals are more inclined to take ivermectin than older adults [27]. Knowledge about onchocerciasis (vector, transmission, prevention) has significantly encouraged ivermectin uptake. This is particularly evident in the Bossangoa district, where there is a care centre for many individuals blinded by onchocerciasis.

The surveyed coverage was lower than that reported by distributors in both districts, although this discrepancy remained within the 15% range recommended by the WHO. A higher proportion of young people than adults received ivermectin, and awareness of onchocerciasis contributed to the drug's distribution in both districts. This study recommends that future MDA rounds should include efforts to expand coverage, such as proper planning and implementation of MDA activities, allocating adequate time for these activities, health education, and mobilisation of the entire population. It is important for such studies to be extended to other MDA programs targeting different NTDs.

Limitations of the Study

The responses analysed in this study were not obtained from CDDs; instead, their responses were used to compare the reasons for not taking ivermectin with those identified in our own research. This study utilised self-reported data from household respondents who participated in the MDA campaign in June 2022. Therefore, the accuracy of the responses was contingent upon the respondents' ability to recall events accurately, which may have introduced recall bias into the study.

NOTES

Conflict of Interest

The authors have no conflicts of interest associated with the material presented in this paper.

Funding

None.

Acknowledgements

We are thankful to the administrative and health districts of Bossangoa and Kémo, the village leaders, and the residents of the studied communities for their cooperation. We are also grateful to the Ministry of Public Health and Population of Central African Republic for allowing this study.

Author Contributions

Conceptualization: Worumogo SH, Longo JDD. Data curation: Ngouyombo AD, Doyama-Woza RH. Formal analysis: Worumogo SH. Funding acquisition: None. Methodology: Worumogo SH, Ngouyombo AD. Project administration: Longo JDD. Visualization: Garoua-Adjou SI, Doyama-Woza RH. Writing – original draft: Worumogo SH, Garoua-Adjou SI, Diemer HSC, Doyama-Woza RH. Writing – review & editing: Worumogo SH, Longo JDD, Ngouyombo AD.

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