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Population coverage and factors associated with participation following a mass drug administration of azithromycin for trachoma elimination in Amhara, Ethiopia

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Summary

OBJECTIVES Mass drug administration (MDA) with azithromycin is a core component of the WHO-recommended strategy to eliminate trachoma as a public health problem, but low participation rates in MDA campaigns may undermine the effectiveness of this intervention. We explored factors associated with individual MDA participation at the individual, head of household and household levels in Amhara, Ethiopia.

METHODS We conducted four district-level, multilevel cluster random coverage surveys to collect data on self-reported MDA participation and predictors. Random-effects logistic regression modelling was used to identify correlates of MDA participation while adjusting for nesting of individuals at the household and village level.

RESULTS The district-level self-reported participation in the trachoma MDA ranged from 78.5% to 86.9%. Excellent and fair health status (Odds ratio [OR] = 5.77; 95% Confidence interval [CI]: 3.04, 10.95; OR = 7.08; 95% CI: 3.47, 14.46), advanced knowledge of the MDA campaign (OR = 2.93; 95% CI: 2.04, 4.21) and knowledge of trachoma (OR = 1.60; 95% CI: 1.17, 2.19) were all positively associated with MDA participation. When excluding heads of household from the model, correlates retained similar positive associations to participation, in addition to the head of household participation (OR = 3.34; 95% CI: 2.46, 4.54).

CONCLUSIONS To increase the impact of MDA campaigns, MDA mobilisation strategies—including comprehensive trachoma and azithromycin messaging and MDA campaign awareness—should target heads of household, those in poorer health and older age groups.

keywords trachoma, mass drug administration, coverage survey, ethiopia, SAFE strategy

Introduction

Trachoma, a disease caused by an ocular infection, is the primary infectious cause of blindness [1]. Treatment through mass drug administration (MDA) of antibiotics is one component of the WHO-endorsed SAFE (Surgery, Antibiotics, Facial cleanliness and Environmental improvement) strategy for the elimination of trachoma as a public health problem [2]. Trachoma-specific MDA programs, which target all members of a community, aim for a minimum of 80% population coverage. Reluctant or hard-to-reach members of a community, however, may undermine the effectiveness of the resource- and labour-intensive MDA campaigns as these individuals could serve as sources of re-emergent infection [3]. Factors associated with not attending MDA campaigns or not receiving MDA medications for neglected tropical diseases can be categorised at hierarchical levels: individual, head of household, household, community and campaign factors [4–9]. To better target MDA-related health messages and design more inclusive campaigns, further research is needed at each of these levels to better understand drivers of MDA participation.

The Trachoma Control Program in Amhara, Ethiopia has been at scale with the SAFE strategy since 2010, and many districts in the region have received eight or more rounds of annual MDA. Despite the maturity of the program, increased knowledge about the factors which motivate the program's beneficiaries could help improve the effectiveness of the MDA program, and thus increase the chances of achieving the elimination of trachoma as a public health problem faster. We conducted four population-based post-MDA coverage surveys to determine the district-level self-reported coverage after a 2017 trachoma MDA in Amhara. As part of these surveys, we further determined the individual, head of household and household factors associated with participation in the MDA campaign.

Methods

Study location

Between May 14 and May 18, 2017, an MDA of azithromycin and tetracycline eye ointment (for those who declined azithromycin or were not eligible to take azithromycin) for trachoma was simultaneously carried out in 61 eligible districts in the eastern half of Amhara. These districts had a prevalence of trachomatous inflammation—follicular (TF) of at least 5% among children aged 1–9 years; determined from previous trachoma impact surveys. MDAs in Amhara are conducted using a community-based model whereby health extension workers (HEWs), who are village-based governmental health workers, distribute medications at a central point in each village with the help of village volunteers [10].

Four districts were selected to participate in a survey assessing the district-level self-reported coverage of the MDA (Figure 1). These districts were purposively selected based on having a high TF prevalence, ranging from 13% to 52% among children aged 1–9 years (determined at a previous impact survey), or based on previous low reported MDA coverage [10]. Geographic variability was also a consideration. The MDA teams were not aware of which districts were chosen for post-MDA coverage survey. Including the May 2017 MDA, these four districts had each received 10 annual MDA rounds.

Sample design

Between June 10 and June 22, 2017, 3–5 weeks after the MDA, a multi-stage cluster random sample survey was conducted to estimate self-reported MDA coverage within each of the four districts. To adequately estimate MDA coverage of at least 70%, we used an alpha level of 0.05 and a design effect of 4.0 [11]. An anticipated non-response rate of 15% was incorporated into the calculation, which increased the number of required study participants to 1486. According to impact assessments conducted in Amhara, there are 4.1 residents per household and thus 316 households per district would be visited to achieve the estimated sample size.

In each of the four districts, 25 clusters (villages) were selected per district from a geographically ordered list using a probability proportional to estimated size method. From each cluster, one development team (defined as an administrative unit of approximately 30 households) was randomly selected from each village. The development team was divided into two roughly equivalent segments using a sketch map technique and one segment was randomly chosen [10]. All households within the selected segment were eligible for inclusion in the survey. Vacant houses were revisited by the study team, and if still vacant on the second visit were skipped and not replaced. All household members, defined as someone who slept in the house the night before, were eligible to be interviewed. Survey teams returned to households where there were absent individuals for a second attempt at data collection at the end of each day.

Data collection

Data recorders were not involved in the MDA and were trained over 4 days on the survey methodology and survey software. Survey questionnaires were translated into Amharic. Prior to deployment, the survey tools were piloted in two sub-districts that were not included in the main survey. There were two components to the survey: a household-level questionnaire administered to the head of household and an individual-level questionnaire administered to all present and consenting/assenting household members. Non-consenting or absent household members were still enumerated by the survey team. Household members were shown azithromycin (Zithromax®) and tetracycline eye ointment samples to assist in recall. The surveys were recorded electronically on Android tablets using Carter Center ODK-based NEMO software.

The primary outcome was MDA participation, defined as individual self-report of taking the MDA medication (either azithromycin or tetracycline eye ointment). For children who were unable to accurately report about themselves, data recorders asked a household adult respondent. Individuals were asked about their age, sex and self-reported health status (characterised as poor, fair or excellent) during the week of the MDA. Head of household and household factors included head of household age, education level, place of birth (inside or outside the village), having prior knowledge of the MDA campaign (defined as at least 1 day prior to the start of the MDA), trachoma knowledge ('Do you know what

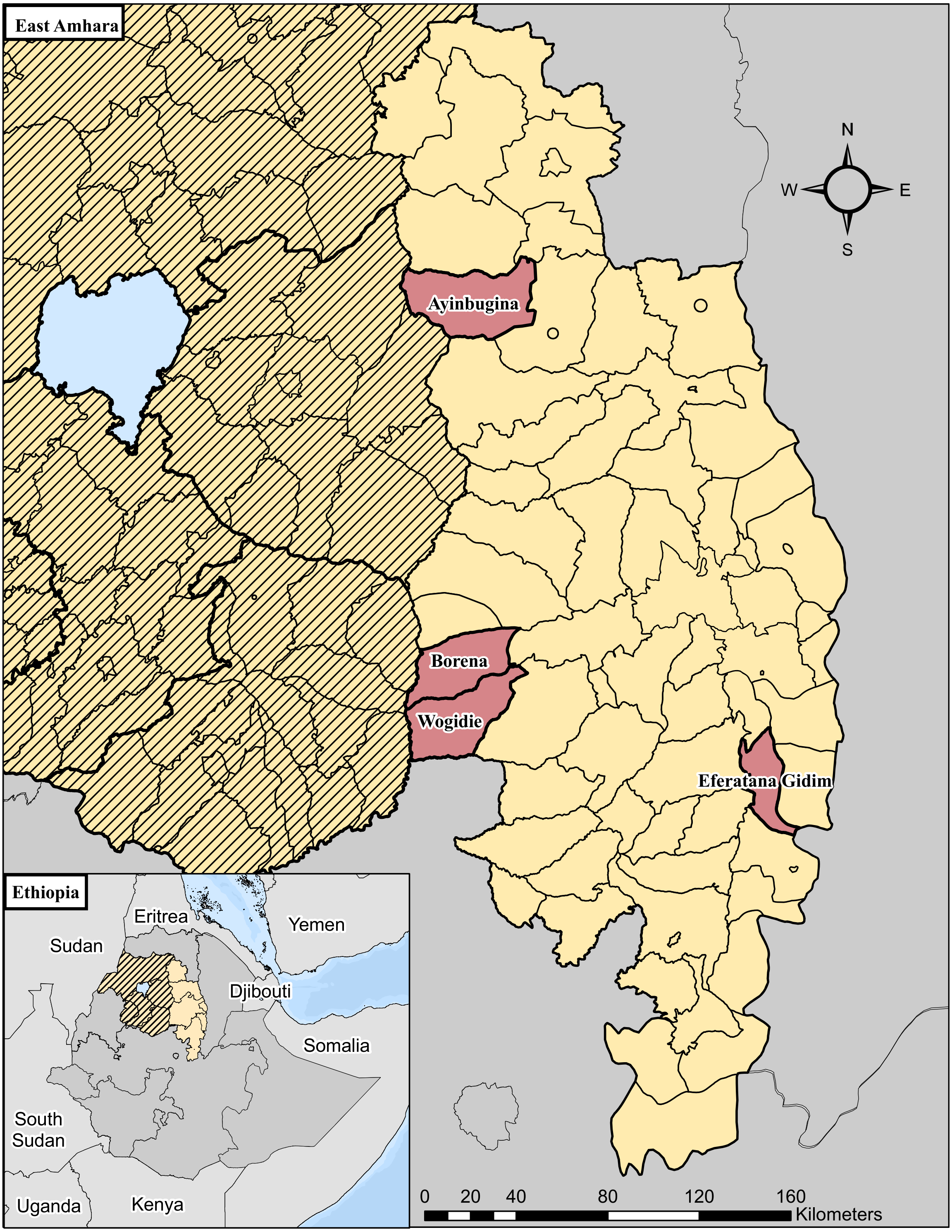

Figure 1 Location of surveyed districts in East Amhara, Ethiopia, 2017. [Colour figure can be viewed at wileyonlinelibrary.com]

trachoma is?') and participation in the MDA. Other household variables included household size, length of household residency (classified as lived in current village for >10 years *vs.* ≤10 years) and social capital (the amount of social time spent with friends, and how many neighbours one could rely on for financial and/or familial assistance if faced with an emergency) [12].

Statistical analysis

Survey data were entered, cleaned and analysed in Stata (Version 15; Stata Corp, College Station, TX, USA). Data from all present and consenting/assenting participants were included in the analysis. District-level self-reported MDA coverage estimates were weighted based on the inverse of the probability of selection at each stage of selection and estimated using the *svy* package. Confidence intervals (CI) were calculated using Taylor linearisation in Stata.

We used exploratory logistic regression analyses to examine bivariate associations between each potential correlate and the outcome of MDA participation. Random-effects logistic regression, using *melogit* in Stata, allowed us to model factors for individual MDA participation while adjusting for nesting of individuals within household and village levels. We built two final models that were informed by existing evidence in the literature and our exploratory bivariate analysis. The first model included all present and consenting/assenting participants, while the second model removed all heads of household so that a head of household MDA participation variable could be added as a predictor. Both models were adjusted for the age and sex of head of household. We reached our final models using backwards stepwise elimination to include factors with a *P*-value <0.05. We calculated the intraclass correlation coefficient (ICC) of MDA participation within households to measure the degree of clustering by running the random-effects model without the independent variables. The map was created in ArcGIS 10.6 (ESRI, Redlands, CA, USA).

Ethics

The study protocol was approved by the Emory University IRB and the Amhara Regional Health Bureau. Informed consent or assent was obtained from everyone responding to the survey. Respondents were allowed to terminate the interview at any point without a need of explanation.

Results

We surveyed 1629 households in four districts. Of the 7200 individuals residing within these households, 586 (8.1%) individuals were absent and one (0.1%) present individual declined to respond, resulting in 6613 (91.8%) present individuals who completed the study (Figure 2). Over half of the respondents were female (52.5%) and the mean age was 24 years.

The district-level self-reported MDA participation across all ages ranged from 78.5% (95% CI: 68.0, 86.3%) in Wogidie to 86.9% (95% CI: 81.6, 90.9%) in Ayinbugina (Table 1). Children aged 1–9 years had the highest coverage among 10-year age groups, and there was little difference between males and females across all ages. There was evidence of clustering at the household level for MDA participation with an ICC of 0.61 (95% CI: 0.55, 0.66), but less clustering was observed at the village level, ICC = 0.30 (95% CI: 0.23, 0.38).

Initial logistic models were created to test the independent association between each possible predictor with self-reported participation in the MDA (Table 2). Individual-level factors statistically significantly associated with MDA participation included excellent or fair health status (compared to poor) and older age. The head of

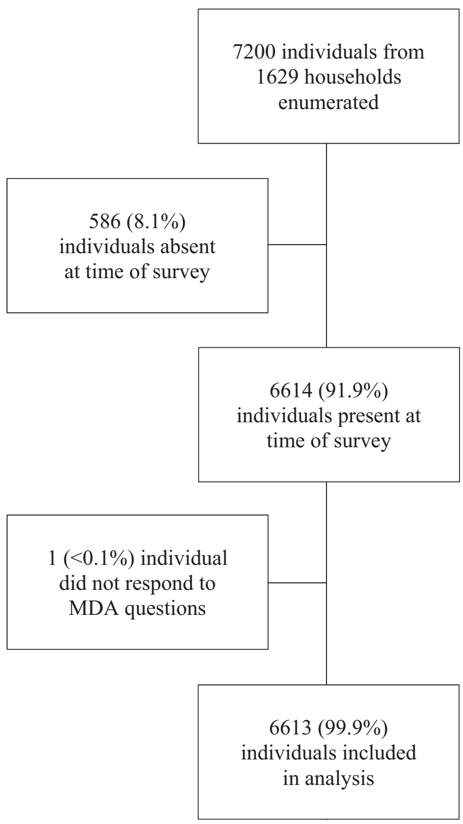

Figure 2 Flow diagram of participation in the post-campaign coverage survey, Amhara, Ethiopia, 2017.

Table 1 District-level self-reported estimates† of mass drug administration coverage, Amhara, Ethiopia, 2017

Zone	District	Total *N*, all	Participated (%), all	95% CI	Total *N*, ages 1–9	Participated (%), ages 1–9	95% CI
North Shoa	Eferatana gidam	1630	83.4	77.3–88.1	356	93.8	89.8–96.3
North Wollo	Ayinbugina	1637	86.9	81.6–90.9	464	93.6	89.8–96.0
South Wollo	Borena	1634	84.7	78.1–89.5	341	92.6	86.4–96.1
South Wollo	Wogidie	1712	78.5	68.0–86.3	441	82.8	70.0–90.8

†Weighted estimate; multilevel survey design accounted for 6613 (99.9%) individuals included in analysis.

household and household factors associated with MDA participation included knowledge of trachoma, having prior knowledge of the MDA campaign and head of household participation in MDA. Residents belonging to households where the head of household was born outside the village were less likely to participate as were residents belonging to a household that had been within the community <10 years *vs.* longer-term residents. Members living in a household that could rely on at least five neighbours in times of emergency, as well as living in a household that was heavily engaged in the community were more likely to participate. Lastly, residents from larger households were more likely to participate in the MDA.

The first multi-variable model (Table 3), which included all study participants (n = 6613), identified several factors associated with self-reported participation in the MDA. After adjustments for the age and sex of heads of household, as well as clustering at the household and village level, prior knowledge of the MDA campaign significantly increased the likelihood of MDA participation (OR = 2.93; 95% CI: 2.04, 4.21) compared to no advanced knowledge. Also, individuals who knew of trachoma were more likely to participate than those who did not. Participants self-reporting fair (OR = 7.08; 95% CI: 3.47, 14.46) and excellent health (OR = 5.77; 95% CI: 3.04, 10.95) were more likely to participate in the MDA than those in poor health. Meanwhile, older residents had a decrease in the odds of participation (OR = 0.98; 95% CI: 0.98, 0.99). Duration of residency in current village, a household's ability to rely on neighbours and household size were not retained in the final model.

We ran a second multi-variable model excluding the heads of household (n = 4969). Overall, model 2 yielded similar results to our first model (Table 4) with the exception that head of household knowledge of trachoma was no longer statistically significant. We found head of household self-participation in the MDA to be statistically significantly associated with an increased odds of participation by other household members (OR = 3.34; 95% CI: 2.46, 4.54).

Discussion

These four population-based post-MDA coverage surveys demonstrated that between 79% and 87% of the population self-reported having participated in the 10th annual round of MDA. These results were similar to other recent reports from the Amhara and Tigray regions [7, 8, 10] demonstrating that a large majority of the population reports being reached by trachoma MDA campaigns in Ethiopia. Despite the longevity of the MDA program in Amhara and the overall support for these campaigns among the population there are still some community members not receiving MDA treatments. It is critical to fully examine head of household and household factors associated with participation as these factors likely affect all members of the household, especially the most vulnerable, children, whose healthcare is dependent upon the head of household [5]. Improvements in targeted MDA messaging could increase the coverage of MDAs within communities, which could possibly lead to an accelerated reduction of trachoma particularly in high-burden districts.

General knowledge of trachoma and having knowledge of the MDA prior to the campaign were important correlates of MDA participation in this population. A generalised understanding of the causes, symptoms and consequences of a disease may strongly motivate participation in MDAs [13–15]. In The Gambia, for example, communities had persistent non-participation in trachoma MDAs because of a lack of health education [6]. In our study, despite the overall high coverage, only 54.1% of respondents who participated in the MDA had a general understanding of trachoma, suggesting the need for greater health messaging in these communities. Community awareness of upcoming MDAs has consistently been shown to be an important factor for trachoma MDA participation in Ethiopia [7, 8, 10]. Beyond the clear

Table 2 Individual, head of household and household factors for participation in mass drug administration (MDA) *vs.* no participation in MDA, Amhara, Ethiopia 2017

Categorical variables	Participated (%)	Did Not Participate (%)	OR	95% CI
Age				
0–9	26.6	17.4	1.00	
10–19	28.2	23.6	0.84	0.69–1.01
19–29	10.9	17.0	0.47	0.38–0.58
30–39	11.5	11.9	0.64	0.51–0.80
40–49	7.6	8.4	0.68	0.53–0.89
50–59	6.2	7.8	0.54	0.41–0.70
60–69	4.8	6.3	0.49	0.37–0.66
70+	4.3	7.6	0.38	0.28–0.50
Sex				
Female	51.8	54.4	1.00	
Male	48.2	45.6	1.01	0.89–1.15
Health†				
Poor	0.8	3.8	1.00	
Fair	10.1	8.2	3.75	2.36–5.95
Excellent	89.1	88.1	3.45	2.30–5.17
Highest level of household education				
None	34.0	32.8	1.00	
Religious	3.0	3.2	1.04	0.74–1.48
Primary school	10.7	11.9	0.82	0.67–1.00
Junior secondary	25.5	21.8	0.98	0.83–1.16
Senior secondary	15.1	21.9	0.78	0.64–0.94
College/university	2.0	2.3	0.78	0.49–1.22
Non-formal education	9.6	6.1	1.36	1.03–1.78
Head of household's place of birth				
Within the village	59.4	50.8	1.00	
Outside the village	40.6	49.2	0.80	0.71–0.91
Years of residency‡				
Greater than 10 years	90.4	86.5	1.00	
10 years or fewer	9.6	13.5	0.68	0.56–0.81
Prior knowledge of MDA campaign§				
No	59.8	78.8	1.00	
Yes	40.2	21.2	2.83	2.42–3.31
Knowledge of trachoma§				
No	45.9	60.1	1.00	
Yes	54.1	39.9	1.51	1.33–1.72
Social capital: social time spent with friends§				
Zero times (in a month)	19.9	22.6	1.00	
1–4 times a month (< weekly)	29.9	33.3	1.12	0.94–1.35
5–8 times a month (< biweekly)	16.0	13.9	1.13	0.91–1.40
9–29 times a month (< monthly)	26.5	26.3	0.87	0.72–1.04
Every day	7.7	4.0	1.80	1.18–2.75
Social capital: ability to rely on neighbors§				
No one	29.3	31.2	1.00	
1–2 people	16.9	23.5	0.70	0.59–0.83
3–4 people	20.0	19.4	0.75	0.63–0.89
5+ people	32.5	24.7	1.20	1.01–1.44
Don't know	1.4	1.2	1.18	0.61–2.25
Travel time from household to distribution site§				
0–30 min	94.6	93.9	1.00	
31–60 min	5.2	5.4	0.86	0.58–1.27
>60 min	0.3	0.7	0.34	0.10–1.20
Head of household participated in MDA§				
No	10.5	55.4	1.00	
Yes	89.6	44.6	11.06	9.37–13.05

Continuous variables	Mean (95% CI)	Mean (95% CI)		
Household size¶	4.9 (4.8–5.0)	4.6 (4.4–7.8)	1.06	1.02–1.10
Head of household's age	42.1 (41.0–43.1)	42.7 (41.1–44.2)	0.99	0.98–1.00

†Self-reported.
‡Number of years the household has lived in their current village.
§Reported by the head of household.
¶Number of individuals living in the household.

communication of logistical information and the purpose and possible side effects of MDAs, which have been shown to increase participation [13, 16], the benefits to the individual and the community should be made explicit [17]. Comprehensive messaging may reduce panic and fear about the disease and the intervention to control it, and ultimately may lead to a successful reduction of trachoma and to healthier children [5, 16, 18, 19].

In this population, perceived health status was strongly associated with MDA participation. Prior research in the trachoma and lymphatic filariasis contexts has shown that people perceive medication as a health maintenance method and thus regularly participate in MDAs [20, 21]. Our study demonstrated that those having a higher self-rated health score had higher participation in the MDA than residents with 'poor' health. Those in poor health, however, may have had less opportunity to participate in MDA campaigns. An earlier coverage survey conducted in Amhara found that a primary reason individuals did not participate in the recent trachoma MDA was due to physical difficulties in reaching the distribution site. This may have resulted from or been exacerbated by poor

Table 3 Adjusted† random-effects logistic model for mass drug administration (MDA) participation among all study participants (n = 6613), Amhara, Ethiopia, 2017

	Model 1a		Model 1b‡	
	OR	95% CI	OR	95% CI
Age	0.98	0.98–0.99	0.98	0.98–0.99
Health§				
Poor	1.00		1.00	
Fair	7.06	3.46–14.38	7.08	3.47–14.46
Excellent	5.72	3.02–10.83	5.77	3.04–10.95
Years of residency¶	1.28	0.84–1.96		
Prior knowledge of MDA campaign††	2.89	2.01–4.17	2.93	2.04–4.21
Knowledge of trachoma††	1.60	1.17–2.18	1.60	1.17–2.19
Social capital: ability to rely on neighbours				
No one	1.00			
1–2 people	0.96	0.66–1.40		
3–4 people	0.85	0.56–1.29		
5+ people	1.01	0.66–1.53		
Don't know	1.62	0.48–5.52		
Household size‡‡	1.02	0.95–1.11		

†Adjusted for head of household's age and sex and clustering at the household and village level.
‡Model containing only significant correlates (P-value < 0.05).
§Self-reported.
¶≥10 years *vs.* <10.
††Yes *vs.* no.
‡‡Number of individuals living in the household.

Table 4 Adjusted† random-effects logistic model for mass drug administration (MDA) participation among household members excluding heads of household (n = 4969), Amhara, Ethiopia, 2017

	Model 2a		Model 2b‡	
	OR	95% CI	OR	95% CI
Age	0.98	0.98–0.99	0.98	0.98–0.99
Health§				
Poor	1.00		1.00	
Fair	7.25	3.02–17.40	7.44	3.10–17.85
Excellent	6.06	2.82–13.00	6.21	2.89–13.34
Years of residency¶	1.13	0.75–1.71		
Guardian participated in MDA††	3.33	2.45–4.53	3.34	2.46–4.54
Prior knowledge of MDA campaign††	1.73	1.26–2.38	1.73	1.27–2.36
Knowledge of trachoma††	1.20	0.91–1.60		
Social capital: ability to rely on neighbors				
No one	1.00			
1–2 people	1.32	0.92–1.89		
3–4 people	1.09	0.74–1.59		
5+ people	1.24	0.86–1.80		
Don't know	3.04	0.89–10.43		
Household size‡‡	0.97	0.90–1.05		

†Adjusted for head of household's age and sex and clustering at the household and village level.
‡Model containing only significant correlates (P-value < 0.05).
§Self-reported.
¶≥10years *vs.* <10.
††Yes *vs.* no.
‡‡Number of individuals living in the household.

health conditions [10]. Conversely, other studies have demonstrated that 'healthy' individuals can perceive themselves as not at risk for a particular disease, and thus choose not to participate in MDAs [5]. In Vanuatu, for example, healthy individuals were the primary non-compliant and non-participatory members of lymphatic filariasis MDAs because they saw no reason to be adherent [22]. Our data demonstrated that those reporting 'excellent' health had a smaller odds ratio than those with 'fair' health, which may in some ways be capturing this phenomenon.

The results from our second model demonstrated that heads of household played an influential role in the MDA participation of other household members. These findings are similar to those of other trachoma studies on the authority of head of household's control over their children's healthcare [5, 6, 9]. In a study covering two countries, Ssemanda *et al.* [9] demonstrated that non-compliance with a trachoma MDA was not random rather it was clustered within households. Household-level clustering of MDA participation was also found in our study. Furthermore, in a previous report from Amhara, the prevalence of zonal self-reported coverage was similar whether one considered the responses from all household members or the responses of heads of household only [10]. Messaging aimed at household-level healthcare decision-makers that reinforces trachoma knowledge, MDA program benefits and MDA activity timelines is likely the most important way to ensure improved MDA coverage to effectively reduce trachoma.

Several variables, chosen for modelling based on the existing literature, were found not to be associated with MDA participation in our study population; namely household community engagement (a measure of social capital), years of residency in current village and household size. Those who have had the time to integrate and develop a sense of belonging to the community may be more likely to participate in MDAs than newer and/or less engaged residents. Ssemanda *et al.* [5, 23] found evidence of this in trachoma studies in Tanzania where there is a strong kinship system. Having a connection and/or role to serve within a community may outweigh the concerns of medication side effects and the time-intensive nature of MDA participation [5, 14]. It is possible that the degree of community engagement was not well captured by the questions used in this survey. Further research within groups or sub-populations considered marginalised within their communities would benefit from a multi-faceted approach, which includes both quantitative and qualitative data collection. Identifying, understanding and reaching these groups may be necessary for countries to reach elimination of trachoma as a public health problem.

Although post-MDA coverage surveys are advocated for program use by the Strategic and Technical Advisory Group for NTDs [24], there are some well characterised limitations of this methodology. For this study we attempted to mitigate recall bias by keeping the time frame between the MDA and the survey short (between 3 and 5 weeks) and by showing azithromycin tablets and tetracycline eye ointment samples to every respondent. Furthermore, no other MDA medication was distributed to these districts during this time period. Despite these efforts, surveys such as ours are still at risk for desirability bias. Although the response rate for this study was 91.9%, respondents who were present at the time of the study may have been more likely to also be present for the MDA campaign itself, compared to absent household members. This could have led to an overestimation of the MDA coverage. Our study was cross sectional and directly followed an MDA thus some survey responses may have been influenced by the act of MDA participation, such as knowledge of trachoma. The study questionnaire included several novel health and social capital questions that have yet to be validated with our study population, and the questionnaire did not evaluate the MDA campaign-level factors, which may have been important. Lastly, the list of communities considered for our survey were derived from the list of communities used for MDA planning, and therefore it is possible that some communities were unintentionally excluded from the sampling frame. It is unlikely that many villages would be excluded given that the MDA program has been in effect annually for 10 years. Despite these limitations, coverage surveys remain a common tool used in monitoring NTD programs. Further monitoring methodologies need to be developed and made scalable so that large programs, such as the one in Amhara, have better ways of understanding their MDA coverage [25].

According to the self-report of its beneficiaries, the Trachoma Control Program in Amhara achieved district-level coverage between 79% and 87% after a trachoma MDA. Further analysis demonstrated that increasing efforts to reach those in poor health and improving awareness of trachoma knowledge and MDA logistics, particularly among heads of household, may help close the gap in non-participation. Evidence-based improvements in MDA interventions could help shorten the timeline for eliminating trachoma as a public health problem.

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