The socio-cultural and ethical aspects of participation in a mass drug administration clinical trial for malaria elimination in The Gambia

Fehr, Alexandra Elizabeth Thompson

2022

document version
Publisher's PDF, also known as Version of record

The socio-cultural and ethical aspects of participation in a mass drug administration clinical trial for malaria elimination in The Gambia

Alexandra Fehr

International Doctorate in Transdisciplinary Global Health Solutions
Erasmus Mundus Joint Doctorate Trans Global Health Programme

This dissertation was completed within the Erasmus Mundus Joint Doctorate Program of the European Union for the International Doctorate in Transdisciplinary Global Health Solutions; a consortium consisting of:

- Institute of Tropical Medicine, Antwerp, Belgium
- VU University Amsterdam, Amsterdam, The Netherlands
- University of Barcelona, Barcelona, Spain
- Universiteit van Amsterdam, Amsterdam, The Netherlands
- Academisch Medisch Centrum bij de Universiteit van Amsterdam, Amsterdam, The Netherlands
- Université de Bordeaux, Bordeaux, France

VRIJE UNIVERSITEIT

The socio-cultural and ethical aspects of participation in a mass drug administration clinical trial for malaria elimination in The Gambia

ACADEMISCH PROEFSCHRIFT

ter verkrijging van de graad Doctor of Philosophy

aan de Vrije Universiteit Amsterdam en de Universitat de Barcelona,

op gezag van de rectores magnifici prof.dr. J.J.G. Geurts en prof. Joan Guardia Olmos

in het openbaar te verdedigen

ten overstaan van de promotiecommissie

van de Faculteit der Bètawetenschappen

op vrijdag 18 november 2022 om 13.45 uur

in een bijeenkomst van de universiteit,

De Boelelaan 1105

door

Alexandra Elizabeth Thompson Fehr

geboren te California, United States

promotoren:	dr. T. Zuiderent-Jerak
	dr. A. Bardaji Alonso
copromotoren:	prof.dr. J.G.F. Bunders-Aelen
	prof.dr. K. Peters Grietens
promotiecommissie:	prof.dr. J.E.W. Broerse
	prof.dr. R. Ravinetto
	prof.dr. S. Lees
	dr. D. Kamuya
	dr. S.S. Kane

Dit proefschrift is tot stand gekomen in het kader van het Erasmus Mundus program of the European Union for International Doctorate in Transdisciplinary Global Health Solutions (Specific Grant Agreement 2013-0039), onder toezicht van een samenwerkingsverband bestaande uit: Instituto de Salud Global de Barcelona (ISGlobal) van de Universitat de Barcelona, Spanje; en Athena Instituut, Vrije Universiteit Amsterdam, Nederland;

This thesis has been written within the framework of the Erasmus Mundus program of the European Union for International Doctorate in Transdisciplinary Global Health Solutions (Specific Grant Agreement 2013-0039), under the joint supervision of the following partners: Instituto de Salud Global de Barcelona (ISGlobal), Universitat de Barcelona, Spain; and Athena Institute, VU University, Amsterdam The Netherlands.

Table of contents

Account

The findings of this dissertation are based on articles that are published or currently under review in international peer-reviewed journals.

Chapter 4

Costs and barriers faced by households seeking malaria treatment in the Upper River Region, The Gambia

- Henk Broekhuizen, Alexandra Fehr, Claudia Nieto-Sanchez, Joan Muela, Koen Peeters-Grietens, Tom Smekens, Momodou Kalleh, Esmé Rijndertse, Jane Achan & Umberto D'Alessandro
- Published: Malaria Journal (2021) 20:368, https://doi.org/10.1186/s12936-021-03898-6

Chapter 5

From informed consent to adherence: factors influencing involvement in mass drug administration with ivermectin for malaria elimination in The Gambia.

- Alexandra Fehr, Claudia Nieto-Sanchez, Joan Muela, Fatou Jaiteh, Omar Ceesay, Ebrima Maneh, Dullo Baldeh, Jane Achan, Edgard Dabira, Bakary Conteh, Joske Bunders-Aelen, Tom Smekens, Henk Broekhuizen, Umberto D'Alessandro and Koen Peeters Grietens
- Published: Malaria Journal (2021) 20:198, https://doi.org/10.1186/s12936-021-03732-z

Chapter 6

The role of social cohesion in the implementation and coverage of a mass drug administration trial for malaria control in the Gambia: An in-depth comparison of two intervention villages

- Alexandra Fehr, Joan Muela, Claudia Nieto-Sanchezb, Ebrima Manneh, Dullo Baldeh, Omar Ceesay, Azucena Bardají, Teun Zuiderent-Jerak, Joske Bunders-Aelena
- Published: Social Science & Medicine (2021) 291:114487, https://doi.org/10.1016/j.socscimed.2021.114487

Chapter 7

Doing "reciprocity work": the role of fieldworkers in a mass drug administration trial in The Gambia

- Alexandra Fehr, Claudia Nieto-Sanchez, Joan Muela, Ebrima Manneh, Dullo Baldeh, Omar Ceesay, Umberto D'Alessandro, Edgard Dabira, Patricia Kingori, Koen Peeters Grietens, Azucena Bardají, Joske Bunders-Aelen, and Teun Zuiderent-Jerak,
- Published: Global Public Health (2022), https://doi.org/10.1080/17441692.2022.2125998
    - Part of the special Issue, *Making global health "work": Frontline workers' labour in research and interventions*
        - Guest Editors: Patricia Kingori, and Francis Kombe, and Alexandra Fehr

Chapter 8

Rethinking what it means to "participate" in an MDA clinical trial for malaria elimination in The Gambia: Local strategies for increasing community involvement and coverage

- Alexandra Fehr, Joan Muela, Joske Bunders-Aelen, Ebrima Manneh, Dullo Baldeh, Omar Ceesay, Umberto D'Alessandro, Teun Zuiderent-Jerak, Koen Peeters Grietens, Claudia Nieto-Sanchez.
- Submitted: Social Science & Medicine

Chapter 1

Introduction

Young boys show the herbs that are traditionally used for treating malaria

Malaria has been a major public health concern for centuries and has been the on-and-off focus for control and global elimination campaigns since the 1950s[1,2]. In 2000, reducing malaria incidence and mortality was included in the Millennium Development Goals, thereby securing its status as one of the "Big Three"[1] in global public health and garnering increased projects and funding[1,3]. However, the 2021 World Malaria Report – the most recent at the time of writing – clearly demonstrates the burden of malaria to do this day: 627,000 people died of the disease in 2020[4]. After having followed a general trend of decline since 2000, malaria case incidence and deaths have increased since 2019. This is in part due to the disruption of malaria control services as a result of the COVID-19 pandemic. However, even before the pandemic began, progress towards malaria elimination had stalled since 2015, leading the global malaria community to call for better interventions to combat the disease[4,5].

The Global Technical Strategy for Malaria 2016-2030 [5] is part of that effort. Adopted by the World Health Assembly in 2015, the GTS provides a framework for countries to accelerate their progress towards malaria elimination. The strategy was then assessed and updated in 2021. The current principles of the GTS, as highlighted in the World Malaria Report 2021, increased the focus on community engagement and now include language such as "involvement and meaningful participation of communities" and "interventions tailored to local context" [5]. As will be described in the following sections, this proves to be a markedly different tone than early malaria elimination and eradication efforts[1,2].

1.1. History of malaria and malaria elimination

Biologically, malaria in humans is caused by one of four species of Plasmodium parasites entering the bloodstream through the bite of an infected female mosquito[6]. Early forms of the parasite have been around for half a billion years[1] and its antigen has been found in human remains as far back as 3200 BCE[7]. In 1880, Alphonse Laveran discovered the malaria parasite in human blood and in 1898, Ronald Ross and Giovanni Grassi discovered the transmission of malaria in humans by mosquitos[1].

[1] The other two being HIV/AIDS and Tuberculosis.

However, malaria is a social disease. Human infections began when early efforts to cultivate land created ideal breeding conditions. From there, the global spread of malaria followed the migrations of humans and has been based on their community structures and living arrangements. From the beginning, the epidemiology of the disease has been affected by the social, political, and economic contexts within which the human hosts, malaria parasites, and mosquito vectors simultaneously operate[1]. As such, some public health scientists, as early as Angelo Celli in 1900, have argued that the causes – and, subsequently, the methods of prevention – of malaria were rooted in social and ecological factors as much, if not more so, than biological.

One of the earliest forms of malaria treatment may have been the use of quinine – produced from tree bark – for the treatment of "fever" in 17th Century Peru. Once the technicalities had been determined, quinine, and soon thereafter chloroquine, quickly became the primary forms of treatment. These discoveries followed an overall trend in public health and medicine that focused on eliminating the biological organisms that cause disease (in this case, the malarial parasites and mosquito vectors) rather than addressing social or economic causes. This led to early malaria interventions of vector-control strategies focused on eliminating mosquito breeding sites and the distribution of quinine to targeted populations, especially soldiers during World War I[1,7].

Though often thought of as a "tropical disease," malaria outbreaks have occurred over most of the globe, including as far north as northern Europe, Canada, and Russia. In many of these locations, however, malaria began to decline even before the implementation of any intentional interventions. This was due predominantly to the changing ecological relationship between mosquitos and humans that resulted from changes in agricultural practices and improved living standards [1].

Malaria control interventions in the Global South followed a different trajectory that included a history marked by multiple top-down and externally implemented "magic bullet" interventions[2]. Early efforts were based upon the assumption that international "givers" (donors and

[2] The early interventions also did not target any country in Africa, as it was deemed "premature," even though the continent was and is disproportionately affected by malaria[2].

implementers) knew what was best for the "local receivers" and focused on the technologies available, predominantly insecticides, such as DDT, and anti-malarial medications. This mentality also believed that the given technologies could override any social conditions or processes that may pose as "obstacles" to implementation and clinical success. Therefore, any attempt to understand the cultural beliefs or implement community health education were neglected[2]. Unfortunately, this pattern has continued to repeat itself throughout malaria elimination and eradication history, from the Malaria Eradication Programme in 1955 to the beginnings of Roll Back Malaria in 1998[1,2].

1.2. Mass drug administration for malaria control and elimination

Mass drug administration (MDA) involves administering a complete therapeutic course of a given medication to an entire geographically defined target population, regardless of individual disease or symptom status[8]. MDA is not a new intervention. It was used for the control of soil-transmitted helminths in the southern United States in the early 20th century and was used for malaria elsewhere in the Global North during early elimination efforts[1]. Eventually, multiple studies were conducted to assess whether MDA was an effective strategy – and the results were mixed [9]. Due to concerns regarding its efficacy, sustainability, the possibility of drug resistance, and its "operational feasibility,[3]" the WHO stopped recommending MDA in the 1970s [8,10].

However, MDA returned as a possible malaria control and elimination method in the early 2000s due to the need to diversify strategies outside those typically employed (e.g., pesticides and bed nets)[1,2]. In 2013, a Cochrane Review[11] was conducted on the results of MDA trials for malaria control and elimination, followed by a scoping review by Newby, et al (2015)[10]. These two reviews found that under certain conditions, MDA may indeed be an effective tool for malaria control[10,11]. At present, the WHO recommends the use of MDA for *P. Falciparum* malaria elimination as a time-limited intervention under certain contexts, such as in places approaching elimination and where there is also "good access to treatment, effective

[3] A frequently used code for the acceptance of the intervention among targeted populations.

implementation of vector control and surveillance, and a minimal risk of re-introduction of infection" [8].

Though many have argued MDA is a viable strategy for malaria control and elimination[12,13], it is still not without its criticisms. First, drug resistance is still a concern, and elimination efforts in the past have seen this occur within short periods of time[14,15]. Second, the MDAs that reported success were based on immediate results; few studies have determined whether or not the MDA was still successful more than 6 months after drug distribution[12]. In addition, the indicators that were used for determining success were rarely defined prior to the trial's commencement. When the indicators were defined, there were notable inconsistencies among definitions, making it impossible to compare results across MDAs[10,11,16–18]. Third, the implementation of MDAs is extremely demanding in cost and labour and requires a high number of trained field staff[13].

Lastly, MDAs require high coverage and adherence[10,19 4]. Computer models have suggested that coverage must be at least 80% of the targeted population, and achieving this coverage is likely the most important aspect in implementing a successful MDA – even more so than the type of medication[10]. On a biological level, MDA is based on eliminating the "silent" human reservoir of infection (i.e., killing the parasite in asymptomatic individuals); anyone who carries the parasite but does not take the medication may reintroduce malaria into the community[13]. Furthermore, not achieving the required coverage level to allow for success means that the risks of the medication(s) is now greater than the potential benefits, rendering the MDA ethically invalid[20].

Simply put, MDA for malaria control and elimination is not effective nor ethical without achieving high community coverage or "participation." This makes MDA deeply dependent on non-clinical factors, such as the acceptability among and the social dynamics of the target populations. As the global burden of malaria continues to increase, it is all the more important to

[4] These terms will be further discussed and unpacked in the following chapter. However, in this instance, coverage refers to the percent of the eligible target population that takes the medication at least one time, and adherence refers to the percent of the eligible target population that completes the entire drug regimen.

understand what facilitates better coverage, what affects participation, and how MDAs can work better within – and for – communities.

1.3. The Gambia

"In The Gambia, the epithet that 'Africa is a laboratory' needs to be taken more literally."

- Fairhead, et al 2006 [21]

1.3.1 Overview and brief history of The Gambia and its health system[5]

The Gambia is a small country in West Africa bordered on one side by the Atlantic Ocean and on three sides by Senegal. According to the World Bank, its most recent population estimate is 2.4 million; it is geographically the smallest and one of the most densely populated countries on the continent[22]. Regarding its development indicators, The Gambia has a life expectancy at birth of 62 years[22] and 85% of children under 2 years receive their basic immunizations[23]. There are large differences between the urban (coastal) areas and the rural: in urban areas, the average household size is 7.3 persons and in rural areas it is 10.4; 79% of urban residents have access to electricity compared to 25% of rural residents; and 80% of urban residents use improved sanitation compared to 44% of rural[23]. The official language of The Gambian government is English, but the country hosts multiple other languages, including Mandinka, Fula, Serahule, Wolof, and others. Ninety percent of the population practices Islam[24].

Like its neighbouring countries, The Gambia was deeply affected by the West African slave trade, after which, the British occupied the country and claimed it as a colony. The Gambia gained its independence from Great Britain and became a member of the Commonwealth in 1965[24] and a Republic in 1970. For the next 24 years, The Gambia was headed by its first president, Dawda Jawara. During this time, the country faced severe economic issues and food and fuel shortages that remained in the rural areas even after the coast and capital, Banjul, saw economic improvement. In 1994, Yahya Jammeh staged a coup and came into power; this was confirmed in 1996 when he was elected president. Jammeh's time as president – which lasted until 2016 – was known for its oppression of dissent and human rights violations. In

[5] More details on the specific study setting of this dissertation can be found in Chapter 3.

addition, government healthcare services were nearly non-existent, and Gambians, particularly in rural areas, had to rely on international research for basic medical needs. Then in December 2016, The Gambia held free, democratic elections and Adama Barrow was elected. At the time of writing, he is the current President of the country.

The Medical Research Council Unit The Gambia (MRCG) was one of the international research institutes on which many Gambians relied. MRCG was founded in 1947 and is the United Kingdom's largest international research institution; in February 2018, it became a formal Unit of the London School of Hygiene and Tropical Medicine (LSHTM). As a research institution, the MRCG conducts studies aimed at the major public health burdens facing the country, including malaria, malnutrition, maternal and child health, infectious diseases, and vaccines[25]. During times of political turmoil and a lack of government healthcare services, the MRCG gained a strong presence in The Gambia and became a vital component of the overall healthcare landscape. Multiple studies have shown that due to its provision of ancillary care during clinical trials, as well as care provided through its clinics, many people in The Gambia consider the institution to be one of healthcare provision rather than one of research[26–28].

1.3.2. Malaria and malaria elimination in The Gambia

The Gambia is a malaria endemic country and nearly all cases are caused by the mosquito species *P. Falciparum*. The disease follows a perennial transmission cycle, where approximately 90% of all cases occur during the later months of the rainy season: June-December[29] [6]. Since the early 2000s, The Gambia has experienced an overall decline in malaria incidence and mortality, especially in the coastal region. However, due to increased flooding and rice cultivation[7], the Upper River Region (URR) maintains substantially higher rates [4,29,30].

[6] The rainy season itself starts earlier, typically around June, and peaks in these months. However, climate changed has already affected this cycle, and the rainy season is now more difficult to predict.

[7] These are the reasons the most recent Gambia Malaria Indicator Survey (2017) gave for why the URR experienced higher rates of malaria incidence, but it is worth noting that the area is also one of the poorest and most rural in the country, and access to medical services are far lower than on the coast.

The country also has a long history of interventions to control – with the goal to eventually eliminate – malaria. The National Malaria Control Programme (NCMP) was founded in 1990 and has since worked independently and with the Medical Research Council Unit The Gambia (MRCG) on multiple malaria reduction strategies. At present, interventions in The Gambia include the use of insecticide-treated nets (ITNs), indoor residual spraying (IRS), intermittent preventative treatment during pregnancy, and seasonal malaria chemoprevention (SMC) among children less than five years of age (since 2014 and only in the Central River Region and the URR)[31].

According to the 2019-2020 Demographic and Health Survey (the most recent at the time of writing), 77% of Gambian households have at least one ITN, 95% of which were obtained through mass distribution campaigns. Further, households in rural areas have more ITNs than those in urban (95% vs 72%) and those in the lowest wealth quintile have more than those in the highest (50% vs 23%)[23]. Even with the additional challenges caused by the COVID-19 pandemic, The Gambia was one of only five countries in the WHO African Region to achieve the GTS goal of a 40% reduction in malaria case incidence. The country did not significantly reduce its malaria mortality rate, as it was already low[4].

1.4. The problem

As mentioned at the beginning of this chapter, new and better interventions are required if malaria is ever to be eradicated, and these interventions will require the "meaningful participation of communities." This is particularly pertinent to MDAs that need high levels of participation in order to be clinically successful and ethically valid. Therefore, the main research question of this dissertation is:

How can we understand the socio-cultural and ethical aspects of participation in a mass drug administration trial for malaria elimination in The Gambia?

To answer this question, this dissertation follows a specific MDA clinical trial that took place in the Upper River Region of The Gambia. At this date, the trial has been completed and, according to the final manuscript of its clinical results, it was a success: "mass drug administration (MDA) of ivermectin and

dihydro-artemisinin-piperaquine (DP) reduced malaria prevalence by 60% and malaria incidence by around 80% compared with the standard intervention group…"[32].

However, community participation – or at least coverage – was sub-optimal. As the manuscript states (emphasis mine):

"In 2018, dihydroartemisinin–piperaquine coverage was lower than 60% whereas ivermectin coverage was 50% or less, underlining the challenges to achieve the required WHO target of 70–80% mass drug administration coverage in the eligible population. ***Such coverage was the result of poor community sensitisation and study population involvement due to a delay in obtaining the required approvals and the short time available… One of the main barriers to non-participation and non-adherence in mass drug administration is the short-term mobility****.[27] Residents in villages might not be available during enumeration, consent, or mass drug administration, which resulted in a setup of these processes throughout the trial and implementation of a complex system to ensure that these individuals are registered, provide consent, and are followed up at home"*[32(p. 526)].

Situated within the historical context of malaria elimination efforts and the unique setting of The Gambia, this dissertation aims to explore all the factors that affected participation, both positively and negatively, in this MDA clinical trial. The following chapter describes more of the background information and conceptual framework needed to address this research question.

REFERENCES

1. Packard R. *The Making of a Tropical Disease:A Short History of Malaria*. Baltimore, Maryland: Johns Hopkins University Press; 2011.
2. Cueto M. A return to the magic bullet? Malaria and global health in the Twenty-First Century. In: Biehl J, Petryna A, eds. *When People Come First: Critical Studies in Global Health*. Princeton, New Jersey: Princeton University Press; 2013:30-53.
3. Tichenor M. The power of data: Global malaria governance and the Senegalese Data Retention Strike. In: *Metrics: What Counts in Global Health*. Durham, North Carolina: Duke University Press; 2016:105-124.
4. World Health Organization. *World Malaria Report 2021*.; .
5. World Health Organization, ed. *Global Technical Strategy for Malaria 2016-2030, 2021 Update*.; 2021. https://www.who.int/publications/i/item/9789240031357.
6. Centers for Disease Control and Prevention. Malaria. https://www.cdc.gov/parasites/malaria/index.html.
7. Committee on the Economics of Antimalarial Drugs. *Saving Lives, Buying Time: Economics of Malaria Drugs in an Age of Resistance*. (Arrow K, Panosian C, Gelband H, eds.). Washington, D.C.: National Academies Press; 2004.
8. World Health Organization. Mass drug administration, mass screening and treatment and focal screening and treatment for malaria. In: *Malaria Policy Advisory Committee Meeting*. ; 2015.
9. Eisele TP. Mass drug administration can be a valuable addition to the malaria elimination toolbox. *Malar J*. 2019;18(1):1-5. doi:10.1186/s12936-019-2906-8
10. Newby G, Hwang J, Koita K, et al. Review of Mass Drug Administration for Malaria and Its Operational Challenges. *Am J Trop Med Hyg*. 2015;93(1):125-134. doi:10.4269/ajtmh.14-0254
11. Poirot E, Skarbinski J, Sinclair D, Kachur SP, Slutsker L, Hwang J. Mass drug administration for malaria. *Cochrane Database Syst Rev*. 2013;12(12):CD008846. doi:10.1002/14651858.CD008846.pub2
12. Poirot E, Skarbinski J, Sinclair D, Kachur SP, Slutsker L, Hwang J. Mass drug administration for malaria. *Cochrane Database Syst Rev*. 2013. doi:10.1002/14651858.CD008846.pub2
13. Webster JP, Molyneux DH, Hotez PJ, Fenwick A. The contribution of mass drug administration to global health: past, present and future.

Philos Trans R Soc B Biol Sci. 2014;369(1645):20130434. doi:10.1098/rstb.2013.0434
14. von Seidlein L, Peto TJ, Landier J, et al. The impact of targeted malaria elimination with mass drug administrations on falciparum malaria in Southeast Asia: A cluster randomised trial. Beeson JG, ed. *PLOS Med*. 2019;16(2):e1002745. doi:10.1371/journal.pmed.1002745
15. Kaehler N, Adhikari B, Cheah PY, et al. The promise, problems and pitfalls of mass drug administration for malaria elimination: a qualitative study with scientists and policymakers. *Int Health*. 2019;11(3):166-176. doi:10.1093/inthealth/ihy079
16. Adhikari B, James N, Newby G, et al. Community engagement and population coverage in mass anti-malarial administrations: a systematic literature review. *Malar J*. 2016;15(1):523. doi:10.1186/s12936-016-1593-y
17. Kingori P, Gerrets R. Morals, morale and motivations in data fabrication: Medical research fieldworkers views and practices in two Sub-Saharan African contexts. *Soc Sci Med*. 2016;166:150-159. doi:10.1016/j.socscimed.2016.08.019
18. Peeters Grietens K, Gryseels C, Verschraegen G. Misdirection in the margins of malaria elimination methods. *Crit Public Health*. 2019;29(4):390-400. doi:10.1080/09581596.2019.1597965
19. Whittaker M, Smith C. Reimagining malaria: five reasons to strengthen community engagement in the lead up to malaria elimination. *Malar J*. 2015;14(1):410. doi:10.1186/s12936-015-0931-9
20. Cheah PY, White NJ. Antimalarial mass drug administration: ethical considerations. *Int Health*. 2016;8(4):235-238. doi:10.1093/inthealth/ihw027
21. Fairhead J, Leach M, Small M. Public Engagement with science? Local understandings of a vaccine trail in The Gambia. *J Biosoc Sci*. 2006;38(1):103-116. doi:10.1017/S0021932005000945
22. World Bank. The Gambia.
23. ICF. The Gambia Demographic and Health Survey 2019-20 . 2021. https://www.dhsprogram.com/pubs/pdf/FR369/FR369.pdf.
24. Faal D. *A History of The Gambia: 1000-1965*. Second. Banjul, The Gambia: Toplink; 2014.
25. Medical Research Council Unit The Gambia. *Annual Report 2018*. Fajara, The Gambia; 2019.
26. Leach M, Fairhead J. Being “with the Medical Research Council”: Infant

Care and Social Meanings of Cohort Membership in Gambia's Plural Therapeutic Landscapes. In: Geissler PW, Molyneux CS, eds. *Evidence, Ethos and Experiment: The Anthropology and History of Medical Research in Africa*. New York: Berghahn Books; 2011:508.

27. Kelly A. Remember Bambali: Evidence, Ethics and the Co-production of Truth. In: Geissler WP, Molyneux S, eds. *Evidence, Ethos and Experiment: The Anthropology and History of Medical Research in Africa2*. 1st ed. New York: Berghahn Books; 2011.
28. Geissler PW, Kelly A, Imoukhuede B, Pool R. 'He is now like a brother, I can even give him some blood' – Relational ethics and material exchanges in a malaria vaccine 'trial community' in The Gambia. *Soc Sci Med*. 2008;67(5):696-707. doi:10.1016/j.socscimed.2008.02.004
29. Mwesigwa J, Achan J, Di Tanna GL, et al. Residual malaria transmission dynamics varies across The Gambia despite high coverage of control interventions. Carvalho LH, ed. *PLoS One*. 2017;12(11):e0187059. doi:10.1371/journal.pone.0187059
30. Mwesigwa J, Okebe J, Affara M, et al. On-going malaria transmission in The Gambia despite high coverage of control interventions: a nationwide cross-sectional survey. *Malar J*. 2015;14(1):314. doi:10.1186/s12936-015-0829-6
31. The Gambia, Programme NMC, the Gambia Bureau of Statistics and Utica International. *The Gambia Malaria Indicator Survey 2017*. Columbia, Maryland; 2018.
32. Dabira ED, Soumare HM, Conteh B, et al. Mass drug administration of ivermectin and dihydroartemisinin–piperaquine against malaria in settings with high coverage of standard control interventions: a cluster-randomised controlled trial in The Gambia. *Lancet Infect Dis*. 2022;22(4):519-528. doi:10.1016/s1473-3099(21)00557-0

Chapter 2

Background and conceptual framework

A mother brings her children to take the MDA medication

The previous chapter provided the historical context and current status of malaria elimination efforts, mass drug administration (MDA), and the need for trial implementers and research institutes to better engage with communities. It also introduced the study setting, including the role of the Medical Research Council Unit The Gambia (MRCG) and the work that has taken place to eliminate malaria in The Gambia. This provided the context for the main research question of this study: *"How can we understand the socio-cultural and ethical aspects of participation in a mass drug administration trial for malaria elimination in The Gambia?*

This chapter will now provide the background information and conceptual framework necessary to approach this question. It will begin by discussing the terminology used to measure MDAs and medicinal intake – coverage, compliance, and adherence – as well as some of the challenges with their use. Next, the chapter will include a summary of the current literature regarding the factors that affect MDA participation. These factors are organized according to the "levels" of the socio-ecological model (SEM), the principle conceptual framework of this dissertation, and include: the individual level, the interpersonal level, the community level, and the societal level. Lastly, this chapter will discuss the informed consent process and summarize some of its complications related to conducting clinical research in the Global South.

2.1. MDA Terminology

To be successful, an MDA requires approximately 80% of the targeted population to take the medication as prescribed[1]. In order to determine if this condition is met, MDA studies use three principal indicators: coverage, compliance, and adherence. As briefly introduced in the last chapter, despite the way they are presented, these terms and their definitions are not so straightforward; instead, there is a marked lack of consistency in their formulation, quantification, and reporting[1–4]. Because they are implementation indicators, as opposed to indicators of success (e.g., percent reduction in malaria incidence), they are often adapted and redefined to meet the implementation needs of specific MDAs[1,5].

In general, coverage is considered an indicator for the MDA's reach into the targeted population. However, the value used as the denominator and the

way these calculations were determined has varied across studies. For example, some studies have calculated coverage using the entire targeted population, but maintained varied considerations for eligibility or mobility[6], and others have focused on smaller units of the population, such as the household or compound[7,8]. The definition of these indicators is further complicated if the MDA requires multiple doses to complete the drug regimen, as is frequently the case in malaria MDAs[9], including the MASSIV trial[10]. In this case, compliance and adherence may be used to expand on coverage and indicate the MDA's acceptability within the given population[11,12]. Though frequently used interchangeably, these two terms do not have the same meaning. In the medical literature, compliance is regarded as a passive behavior or acritical obedience to medical advice[13]. Non-compliance, historically, was considered a failure of discipline[14]. Alternatively, adherence has been more-or-less the preferred term since the 1980s. It is considered less paternalistic and more inclusive to patients being active participants in their medical decision making[11,12]. This, however, is more complicated when it is in reference to community-level implementation and the mass administering of a medication rather than a singular patient-doctor relationship.

The complicated and inconsistent use of these terms is problematic. Without clarity or consistency in the definitions, it is not possible to compare MDAs across settings, therefore rendering it impossible to adequately evaluate MDA as an effective tool for malaria control and elimination and justify its implementation in resource-constrained healthcare settings[1,2,4]. Furthermore, the binary nature of these terms does not represent the realities of implementation and medicinal intake. Rather than a singular action, such as consenting to enroll in the MDA trial, taking the full course of the medicinal regimen over several days is better described as a process that can be affected by multiple factors, from individual characteristics to societal pressures[15–18]. These different factors will be discussed in the following section.

2.2. The socio-ecological model and effects on participation

2.2.1. The socio-ecological model

The socio-ecological model (SEM), first developed in the 1970s by Urie Bronfenbrenner, has been used and adapted as a model for understanding

myriad complex health-related studies and interventions[19,20]. In the model, the individual is placed in the center of nesting circles where each circle illustrates a "level" of influence on that individual (typically used to assess influences on the individual's health)[19]. Though the number and specific names of the levels may change based on the adaptation or study, the model, in general, includes the personal level, the inter-personal or relationship level, the community level, and the societal level. Other models also add or specify ecological levels[20], institutional levels, and/or policy levels[19,21].

Figure 2.1. A commonly used/adapted SEM from the Centers for Disease Control and Prevention

2.2.2. Effects on MDA participation

This section summarizes the literature on the factors that affect malaria MDA medicinal intake or participation. The known effects are organized based on the levels of the SEM.

2.2.2.1. Individual-level factors

Coming predominantly from Southeast Asia and sub-Saharan Africa, findings from the literature revealed that most studies that assessed for the effects on medicinal intake in malaria MDAs were focused on individual factors. Similar barriers and facilitators to individuals taking the MDA medication were identified across studies and included the timing of the MDA, work or domestic demands, hesitancy towards the medication or its potential side effects, and personal beliefs regarding the importance of the MDA[17,22–24].

The two most cited barriers to medicinal intake were short- and long-term mobility and work-related demands that coincided with the timing of the MDA[22,25,26]. To be most effective, the medication in MDAs for malaria control

must be administered prior to the peak timing of malaria transmission, which most often occurs at the beginning of the rainy season. In the settings of these studies, this regularly coincided with times of heavy agricultural and farming demands. As most of the target populations relied heavily on agriculture, the timing of the MDA interfered with the busiest time of the year[22,24,26]. Studies showed that men and boys were particularly less likely to take the MDA medication due to these labor demands, and, at the same time, women and girls had increased domestic duties that may also have prevented them from taking the medication. Further, many people, especially young men, were found to travel for work at different times of the year. In The Gambia, for example, it was reported to be common for young men from rural areas to travel to the urban coast for work, or travel with their herds for grazing, and this caused them to be absent around the time of the MDA[25–27].

There were also individual barriers related to the medications themselves. Several studies reported individuals who did not take the MDA medication because they were skeptical of allopathic medication in general and preferred the use of traditional medicine[2]. Others were opposed to taking medication when they were not presently sick[28]. In some studies, the potential for side effects was enough to prevent individuals from seeking the medication in general, or if experienced in an early round, the side effects caused others to stop taking the medication in subsequent rounds[22,24].

How an individual regarded the need for the MDA was also found to affect whether they took the medication. Several studies demonstrated that those who believed malaria to be a health concern in the community and those who knew of the clinical and epidemiological reasons for the MDA were more likely to take the medication[29–31]. Further, individuals who considered the MDA to have additional benefits were more likely to take the medication. Benefits could include the health-related goal of the MDA, to reduce malaria, but could also include access to other goods or services. For example, studies have shown that individuals were more likely to take the MDA medication if they were able to receive ancillary care for themselves or family members, or gain access to transportation or other material goods[23,25,32].

2.2.2.2. Interpersonal factors

Though less is known about how or to what extent, peer and familial relationships were also found to influence participation in malaria MDAs. In

Laos, families were found to value cohesion in decision making, so members of the same family were all likely to either fully participate or not participate at all[22]. In The Gambia, the compound head is vital to the decision-making process of those within his compound, especially as it relates to health matters[27]. Outside the MDA literature, studies have noted the importance of the household or compound head in the decision-making process for clinical trials and have shown that women and children are particularly influenced by older male family members[33–35].

2.2.2.3. Community factors

Community-level consent is often deemed an important part of research and clinical trial ethics, and within the settings of most MDAs, this typically includes permission from the village leader[36–38]. One key mechanism through which this is done is *community engagement*, the importance of which has drastically increased in prominence since the early 2000s[39]. An initial step in community engagement is often for the trial or implementation team to meet with the leader of a community and secure their support for the given trial or intervention[40]; this is often considered the culturally appropriate way to enter a community and begin the community engagement process[38]. Regarding MDAs, there is evidence that the community leader plays an important part in the overall participation of individuals. If the leader is supportive of the MDA, it is expected that those in the community will be more likely to participate as well[38,40–42]. Furthermore, multiple studies have shown that individuals who participated in community engagement activities, such as attending a pre-trial sensitization meeting, were more knowledgeable about the details and justifications of the MDA being implemented and were more likely to take the medication as prescribed[43,44].

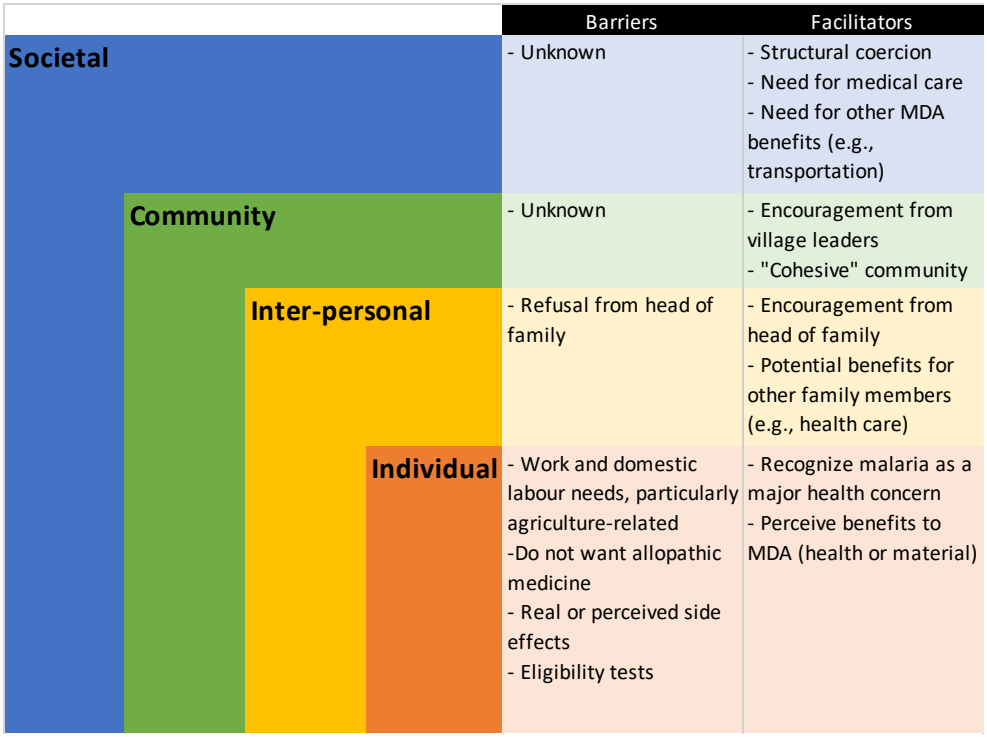
Though they do not develop the concept further, Kajeechiwa, et al (2016) found that villages that "gave the appearance of cohesive communities" had higher coverage than "more fractured" villages in an MDA on the Thai-Myanmar border. They hypothesized that this cohesion within the communities may have been even more causal in the high coverage than the difference in knowledge pertaining to the MDA and the biological causes of malaria[44]. In Laos, MDA study staff also noted that individual decision making was influenced by the general community's support and encouragement of the MDA: "if all participate, I will participate" was the summarized finding of people's attitudes toward participation[31].

2.2.2.4. Societal factors

Fundamental to understanding research participation in low-resource settings or among economically vulnerable populations is structural coercion, the ways in which the "broader social, economic, and political context compels individuals to enroll in research"[45]. Based on Farmer's theory of structural violence, it occurs when aspects such as poverty, illiteracy, or authoritarian leadership impact an individual's ability to decide on participating in a clinical trial[46–48].[8] For many, the access to care for themselves or their families is more important than any of the trial's details[49] (more citations), and there is substantial evidence that people will use MDAs and clinical trials as a resource-seeking strategy[50,51]. This extends beyond the individual-level factor of perceived benefits of the MDA. Instead, benefits, such as access to medical care, are a societal-level factor when the need for them is so great that people perceive participation to be an "empty choice"[52].

[8]Structural violence is one of the three types of "invisible violence" categorized by Bourgois (2009)[48]. With an origin in Marxism and Liberation Theology, structural violence refers to the indirect violence created from political economic forces, unequal international trade terms, and unequal access to services and resources (Bourgois 2009). It is "violence exerted systematically - that is, indirectly - by everyone who belongs to a certain social order"[47]. The other forms of invisible violence are 1) Symbolic violence, initially developed by Bourdieu[64,65] and "refers to the mechanism whereby the socially dominated naturalize the status quo and blame themselves for their domination;" and 2) Normalized violence, an adaptation of Scheper-Hughes' "everyday violence," refers to the routine, institutional practices, cultural values, and daily interactions that harm individuals' health[48].

Figure 2.2. Modified SEM of the effects on MDA participation based on the literature



By organizing the literature on the factors that affect participation in an MDA clinical trial according to the levels of the SEM, it is possible to see the focus on the individual factors and the gaps in understanding factors from the societal or community levels. Further, some of the factors that affect participation may, in fact, also be affecting individual autonomy in the informed consent process. This is discussed in the following section.

2.3. Individual Autonomy

The informed consent process has been the cornerstone of biomedical research for decades[53]. Though the concept of beneficence has been a part of medicine since the Hippocratic Oath, the process of informed consent was formalized as a key principle of the Nuremburg Code after the atrocities of World War II and the gross violations of research with human subjects in Europe and the United States[36,53,54]. Informed consent touches on all four of the main principles of biomedical and clinical research ethics: 1. Autonomy,

2. Non-maleficence, 3. Beneficence, and 4. Justice, though autonomy is considered the most relevant[54,55]. Additionally, informed consent includes three principals within itself: 1. Capacity/competence, 2. Information, and 3. Voluntariness[55].

Researchers have long since debated the many potential complications in conducting informed consent in resource-poor settings in the Global South[36] and argued that consent should be tailored to specific contexts[56]. Points of concern have included mixed evidence that people can recall the specifics of the trial they just consented to[57] and evidence that people decide upon giving consent and participating in research based upon information they gathered from peers prior to the informed consent process taking place[58]. Others have demonstrated complications surrounding gender relationships in certain settings. For example, Princewill, et al (2017) studied the concept of autonomy in relation to a malaria trial in Western Nigeria. In their discussions with women, their husbands, and the research staff, they found that respondents had a strong understanding of "autonomy" as a concept, as well as its complications within their specific context. They concluded that the women in the study had little autonomy when it came to trial participation - that their husbands, as heads of households, gave the final say in all health-related decisions[59]. However, this may be too simplistic a view, and in other settings, women have been shown to be able to strategize ways to make their own informed decisions regarding participation[60].

Still further, the informed consent process has been shown to be affected by other familial relationships and power structures. Women and children, for example, have the potential to be coerced into signing and informed consent document (or providing assent) by a spouse or parent[61], and others may be compelled to provide consent because they were asked to do so by someone in a position of authority[62,63].

2.4. Closing

This chapter has summarized the key background information and conceptual framework necessary for addressing the main research question of this study. It included descriptions of the key indicators used for measuring the percent of people who take the MDA medication as well as the factors that affect participation at different levels of the SEM. These factors were

included in an adapted SEM that also demonstrated the gaps in understanding at the societal and community levels. Lastly, it discussed individual autonomy as it is relevant to the informed consent process for MDA clinical trial participation.

Next, the following chapter discusses the study design and research methodologies used to answer the main research question, *How can we understand the socio-cultural and ethical aspects of participation in a mass drug administration trial for malaria elimination in The Gambia?*

References

1. Newby G, Hwang J, Koita K, et al. Review of Mass Drug Administration for Malaria and Its Operational Challenges. *Am J Trop Med Hyg*. 2015;93(1):125-134. doi:10.4269/ajtmh.14-0254
2. Adhikari B, James N, Newby G, et al. Community engagement and population coverage in mass anti-malarial administrations: a systematic literature review. *Malar J*. 2016;15(1):523. doi:10.1186/s12936-016-1593-y
3. Poirot E, Skarbinski J, Sinclair D, Kachur SP, Slutsker L, Hwang J. Mass drug administration for malaria. *Cochrane Database Syst Rev*. 2013. doi:10.1002/14651858.CD008846.pub2
4. Peeters Grietens K, Gryseels C, Verschraegen G. Misdirection in the margins of malaria elimination methods. *Crit Public Health*. 2019;29(4):390-400. doi:10.1080/09581596.2019.1597965
5. World Health Organization. Mass drug administration, mass screening and treatment and focal screening and treatment for malaria. In: *Malaria Policy Advisory Committee Meeting*. ; 2015.
6. von Seidlein L, Peto TJ, Landier J, et al. The impact of targeted malaria elimination with mass drug administrations on falciparum malaria in Southeast Asia: A cluster randomised trial. Beeson JG, ed. *PLOS Med*. 2019;16(2):e1002745. doi:10.1371/journal.pmed.1002745
7. Okebe J, Ribera JM, Balen J, et al. Reactive community-based self-administered treatment against residual malaria transmission: Study protocol for a randomized controlled trial. *Trials*. 2018;19(1):126. doi:10.1186/s13063-018-2506-x
8. Jaiteh F, Masunaga Y, Okebe J, et al. Community perspectives on treating asymptomatic infections for malaria elimination in the Gambia. *Malar J*. 2019;18(1):39. doi:10.1186/s12936-019-2672-7
9. Kamga G-R, Dissak-Delon FN, Nana-Djeunga HC, et al. Audit of the community-directed treatment with ivermectin (CDTI) for onchocerciasis and factors associated with adherence in three regions of Cameroon. *Parasit Vectors*. 2018;11(1):356. doi:10.1186/s13071-018-2944-z
10. Dabira ED, Soumare HM, Lindsay SW, et al. Mass drug administration with high-dose ivermectin and dihydroartemisinin-piperaquine for malaria elimination in an area of low transmission with high coverage

of malaria control interventions: Protocol for the massiv cluster randomized clinical trial. *JMIR Res Protoc*. 2020;9(11):e20904. doi:10.2196/20904

11. Spencer KL. Transforming Patient Compliance Research in an Era of Biomedicalization. *J Health Soc Behav*. 2018;59(2):170-184. doi:10.1177/0022146518756860
12. Kyngäs H, Duffy ME, Kroll T. Conceptual analysis of compliance. *J Clin Nurs*. 2000;9(1):5-12. doi:https://doi.org/10.1046/j.1365-2702.2000.00309.x
13. Spencer KL. Transforming Patient Compliance Research in an Era of Biomedicalization. *J Health Soc Behav*. 2018;59(2):170-184. doi:10.1177/0022146518756860
14. Whitmarsh I. The Ascetic Subject of Compliance. In: Biehl J, Petryna A, eds. *When People Come First: Critical Studies in Global Health*. Princeton University Press; 2013:302-324.
15. Muela Ribera J, Hausmann-Muela S, Gryseels C, Peeters Grietens K. Re-imagining adherence to treatment from the "other side": local interpretations of adverse anti-malarial drug reactions in the Peruvian Amazon. *Malar J*. 2016;15(1):136. doi:10.1186/s12936-016-1193-x
16. Kaehler N, Adhikari B, Cheah PY, et al. The promise, problems and pitfalls of mass drug administration for malaria elimination: a qualitative study with scientists and policymakers. *Int Health*. 2019;11(3):166-176. doi:10.1093/inthealth/ihy079
17. Vincent R, Adhikari B, Duddy C, et al. 'Working relationships' across difference - a realist review of community engagement with malaria research. *Wellcome Open Res*. 2022;7:13. doi:10.12688/wellcomeopenres.17192.1
18. Krentel A, Fischer PU, Weil GJ. A Review of Factors That Influence Individual Compliance with Mass Drug Administration for Elimination of Lymphatic Filariasis. Addiss DG, ed. *PLoS Negl Trop Dis*. 2013;7(11):e2447. doi:10.1371/journal.pntd.0002447
19. Kilanowski JF. Breadth of the Socio-Ecological Model. *J Agromedicine*. 2017;22(4):295-297. doi:10.1080/1059924X.2017.1358971
20. Mburu CM, Bukachi SA, Shilabukha K, et al. Determinants of treatment-seeking behavior during self-reported febrile illness episodes using the socio-ecological model in Kilombero District, Tanzania. *BMC Public Health*. 2021;21(1):1-11. doi:10.1186/s12889-021-11027-w

21. Lee BC, Bendixsen C, Liebman AK, Gallagher SS. Using the Socio-Ecological Model to Frame Agricultural Safety and Health Interventions. *J Agromedicine*. 2017;22(4):298-303. doi:10.1080/1059924X.2017.1356780
22. Adhikari B, Phommasone K, Pongvongsa T, et al. Factors associated with population coverage of targeted malaria elimination (TME) in southern Savannakhet Province, Lao PDR. *Malar J*. 2017;16(1):424. doi:10.1186/s12936-017-2070-y
23. Adhikari B, Phommasone K, Kommarasy P, et al. Why do people participate in mass anti-malarial administration? Findings from a qualitative study in Nong District, Savannakhet Province, Lao PDR (Laos). *Malar J*. 2018;17(1):15. doi:10.1186/s12936-017-2158-4
24. Atkinson J-A, Vallely A, Fitzgerald L, Whittaker M, Tanner M. The architecture and effect of participation: a systematic review of community participation for communicable disease control and elimination. Implications for malaria elimination. *Malar J*. 2011;10(1):225. doi:10.1186/1475-2875-10-225
25. Dierickx S, Gryseels C, Mwesigwa J, et al. Factors Associated with Non-Participation and Non-Adherence in Directly Observed Mass Drug Administration for Malaria in The Gambia. Sullivan DJ, ed. *PLoS One*. 2016;11(2):e0148627. doi:10.1371/journal.pone.0148627
26. Dial NJ, Ceesay SJ, Gosling RD, D'Alessandro U, Baltzell KA. A qualitative study to assess community barriers to malaria mass drug administration trials in the Gambia. *Malar J*. 2014;13(1):47. doi:10.1186/1475-2875-13-47
27. Jaiteh F, Dierickx S, Gryseels C, et al. 'Some anti-malarials are too strong for your body, they will harm you.' Socio-cultural factors influencing pregnant women's adherence to anti-malarial treatment in rural Gambia. *Malar J*. 2016;15(1):195. doi:10.1186/s12936-016-1255-0
28. Njomo DW, Amuyunzu-nyamongo M, Magambo JK, Njenga SM. The Role of Personal Opinions and Experiences in Compliance with Mass Drug Administration for Lymphatic Filariasis Elimination in Kenya. 2012;7(11). doi:10.1371/journal.pone.0048395
29. Sahan K, Pell C, Smithuis F, et al. Community engagement and the social context of targeted malaria treatment: a qualitative study in Kayin (Karen) State, Myanmar. *Malar J*. 2017;16(1):1-10. doi:10.1186/s12936-017-1718-y

30. Nguyen TN, Thu PNH, Hung NT, et al. Community perceptions of targeted anti-malarial mass drug administrations in two provinces in Vietnam: A quantitative survey. *Malar J*. 2017;16(1):1-12. doi:10.1186/s12936-016-1662-2
31. Peto TJ, Tripura R, Davoeung C, et al. Reflections on a Community Engagement Strategy for Mass Antimalarial Drug Administration in Cambodia. *Am J Trop Med Hyg*. 2018;98(1):100-104. doi:10.4269/ajtmh.17-0428
32. Gooding K, Phiri M, Peterson I, Parker M, Desmond N. Social Science & Medicine Six dimensions of research trial acceptability: how much, what, when, in what circumstances, to whom and why ? *Soc Sci Med*. 2018;213(January):190-198. doi:10.1016/j.socscimed.2018.07.040
33. Okoko BJ, Yamuah LK. Household decision-making process and childhood cerebral malaria in The Gambia. *Arch Med Res*. 2006;37(3):399-402. doi:10.1016/j.arcmed.2005.07.007
34. Browne JL, Rees CO, Delden JJM Van, Agyepong I, Grobbee DE. The willingness to participate in biomedical research involving human beings in low- and middle-income countries : a systematic review. 2018;00(00):1-16. doi:10.1111/tmi.13195
35. Kamuya DM, Molyneux CS, Sally T. Gendered negotiations for research participation in community-based studies: Implications for health research policy and practice. *BMJ Glob Heal*. 2017;2(2):e000320. doi:10.1136/bmjgh-2017-000320
36. Emanuel EJ, Wendler D, Killen J, Grady C. What Makes Clinical Research in Developing Countries Ethical? The Benchmarks of Ethical Research. *J Infect Dis*. 2004;189(5):930-937. doi:10.1086/381709
37. Diallo DA, Doumbo OK, Plowe C V., Wellems TE, Emanuel EJ, Hurst SA. Community Permission for Medical Research in Developing Countries. *Clin Infect Dis*. 2005;41(2):255-259. doi:10.1086/430707
38. Tindana PO, Rozmovits L, Boulanger RF, et al. Aligning Community Engagement With Traditional Authority Structures in Global Health Research: A Case Study From Northern Ghana. *Am J Public Health*. 2011;101(10):1857-1867. doi:10.2105/AJPH.2011.300203
39. George AS, Mehra V, Scott K, Sriram V. Community participation in health systems research: A systematic review assessing the state of research, the nature of interventions involved and the features of engagement with communities. *PLoS One*. 2015;10(10):1-25. doi:10.1371/journal.pone.0141091

40. Lavery J V., Tinadana PO, Scott TW, et al. Towards a framework for community engagement in global health research. *Trends Parasitol*. 2010;26(6):279-283. doi:10.1016/j.pt.2010.02.009
41. Nyirenda D, Sariola S, Kingori P, et al. Structural coercion in the context of community engagement in global health research conducted in a low resource setting in Africa. 2020:1-10.
42. King KF, Kolopack P, Merritt MW, Lavery J V. Community engagement and the human infrastructure of global health research. 2014:1-6.
43. Dierickx S, O'Neill S, Gryseels C, et al. Community sensitization and decision-making for trial participation: A mixed-methods study from The Gambia. *Dev World Bioeth*. 2018;18(4):406-419. doi:10.1111/dewb.12160
44. Kajeechiwa L, Thwin MM, Shee PW, et al. The acceptability mass administrations of anti-malarial drug as part of targeted malaria elimination in villages along the Thai-Myanmar border. *Malar J*. 2016;15(1):1-12. doi:10.1186/s12936-016-1528-7
45. Fisher JA, Fisher JA. Expanding the Frame of "Voluntariness" in Informed Consent: Structural Coercion and the Power of Social and Economic Context. 2020;23(4):355-379.
46. Farmer P. *Infections and Inequalities: The Modern Plagues*. Berkeley, California: University of California Press; 1999.
47. Farmer P. Sidney W. Mintz Lecture for 2001: An anthropology of structural violence. *Curr Anthropol*. 2004;45(3):305-325.
48. Bourgois P. In Barbara Rylko-Bauer, Linda Whiteford, and Paul Farmer, eds. 2009 Global Health in Times of Violence. Santa Fe, NM: School of Advanced Research Press. Pages 18-40. In: *Global Health in Times of Violence*. Santa Fe, NM; 2009:18-40.
49. Ravinetto RM, Afolabi MO, Okebe J, et al. Participation in medical research as a resource-seeking strategy in socio-economically vulnerable communities: Call for research and action. *Trop Med Int Heal*. 2015;20(1):63-66. doi:10.1111/tmi.12396
50. Masiye F, Kass N, Hyder A, Ndebele P, Mfutso-Bengo J. Why mothers choose to enrol their children in malaria clinical studies and the involvement of relatives in decision making: Evidence from Malawi. *Malawi Med J*. 2008;20(2):50-56. doi:10.4314/mmj.v20i2.10957
51. Mfutso-Bengo J, Ndebele P, Jumbe V, et al. Why do individuals agree to enrol in clinical trials? A qualitative study of health research participation in Blantyre, Malawi. *Malawi Med J*. 2008;20(2):37-41.

doi:10.4314/mmj.v20i2.10898
52. Kingori P. The ‘ empty choice ’: A sociological examination of choosing medical research participation in resource- limited Sub-Saharan Africa. 2015. doi:10.1177/0011392115590093
53. Boulton M, Parker M. Informed consent in a changing environment. *Soc Sci Med*. 2007;65(11):2187-2198. doi:10.1016/j.socscimed.2007.08.002
54. Beauchamp T, Childress J. *Principles of Biomedical Ethics*. Fifth. Oxford: Oxford University Press; 1983.
55. Faden R, Beauchamp T. *A History and Theory of Informed Consent*. Oxford: Oxford University Press; 1986.
56. Kalabuanga M, Ravinetto R, Maketa V, et al. The Challenges of Research Informed Consent in Socio-Economically Vulnerable Populations: A Viewpoint From the Democratic Republic of Congo. *Dev World Bioeth*. 2016;16(2):64-69. doi:10.1111/dewb.12090
57. Afolabi MO, Okebe JU, Mcgrath N, Larson HJ, Bojang K, Chandramohan D. Informed consent comprehension in African research settings. *Trop Med Int Heal*. 2014;19(6):625-642. doi:10.1111/tmi.12288
58. Paré Toe L, Ravinetto RM, Dierickx S, et al. Could the Decision of Trial Participation Precede the Informed Consent Process? Evidence From Burkina Faso. Choonara I, ed. *PLoS One*. 2013;8(11):e80800. doi:10.1371/journal.pone.0080800
59. Princewill CW, Jegede AS, Om KN, Lanre-abass B, Elger BS. Factors affecting women's autonomous decision making in research participation amongst Yoruba women of Western Nigeria. *Dev world bioethics*. 2017;17(1):40-49. doi:10.1111/dewb.12112
60. Kamuya DM, Theobald SJ, Marsh V, Parker M, Geissler WP, Molyneux SC. “The One Who Chases You Away Does Not Tell You Go”: Silent Refusals and Complex Power Relations in Research Consent Processes in Coastal Kenya. Seeley JA, ed. *PLoS One*. 2015;10(5):e0126671. doi:10.1371/journal.pone.0126671
61. Millum J. Consent Under Pressure : The Puzzle of Third Party Coercion. 2016;17(1):113-127. doi:10.1007/s10677-013-9419-2.Consent
62. Molyneux CS, Peshu N, Marsh K. Understanding of informed consent in a low-income setting: Three case studies from the Kenyan coast. *Soc Sci Med*. 2004;59(12):2547-2559. doi:10.1016/j.socscimed.2004.03.037
63. Gikonyo C, Bejon P, Marsh V, Molyneux S. Taking social relationships

seriously: Lessons learned from the informed consent practices of a vaccine trial on the Kenyan Coast. *Soc Sci Med*. 2008;67(5):708-720. doi:10.1016/j.socscimed.2008.02.003

64. Bourdieu P. The forms of capital. In: Richardson JG, ed. *Handbook of Theory and Research for the Sociology of Education*. Westport, CT: Greenwood; 1986:241-258.

65. Theory S, Spring N. Social Space and Symbolic Power Pierre Bourdieu Social space and symbolic power. 2007;7(1):14-25.

Chapter 3

Research design and methodology

Members of the social science team meet with members of the clinical team to discuss the current MDA round

The previous two chapters have introduced mass drug administration (MDA) within the history of malaria elimination campaigns and as well as MDA's necessity for high levels of participation and medicinal intake. They have also summarized the current literature and the concepts required for addressing the principal research question of this dissertation:

How can we understand the socio-cultural and ethical aspects of participation in a mass drug administration trial for malaria elimination in The Gambia?

3.1. Research questions

The main research question of this dissertation lends itself to several sub-questions. First, the term "participation" needs to be more thoroughly understood and defined. The first sub-question of this dissertation attempts to clarify this issue. As shown in Chapter 2, the indicators used to measure the proportion of people who took the medication in an MDA trial – coverage, compliance, and adherence – are often poorly defined and used interchangeably. This is problematic for several reasons, including the fact that the binary nature of these indicators neglects the processes that take place each time an individual takes the MDA medication and the different factors that can influence medicinal intake throughout the duration of the trial. Therefore, the first sub-question of this dissertation is:

Sub-question 1: What – and for whom – *is* participation in an MDA clinical trial?

Sub-question 1 demonstrates the complexity of what participation can be understood to mean to the different stakeholders in MDA trials. This understanding creates further nuances in what affects participation. The majority of previous studies focused on the factors that influence MDA trial participation are based on individual factors, including, for example: mobility, agricultural demands, and personal beliefs regarding the use of medication, especially when asymptomatic. Less literature exists on the impact of influences outside the individual – such as the role of family members or community engagement activities – and by using the socio-ecological model (SEM) as a guide, we can see that there are gaps in understanding how factors

in the higher levels affect participation. Therefore, the second sub-question of this thesis is:

Sub-question 2: Based upon the socio-ecological model, what affects participation in an MDA clinical trial at different "levels" (e.g., the individual, familial, community, and societal levels)?

In addition to the above, however, it is necessary to understand what types of activities and involvement from those in the trial community are required to for a successful MDA. Therefore, it follows that this dissertation also asks:

Sub-question 3: What *work*, and by whom, is required for participation in an MDA clinical trial to occur?

Personal autonomy and the informed consent process for research participation are the cornerstones of traditional research ethics, however the use and effectiveness of the informed consent process within economically vulnerable populations has been debated. In understanding the factors that effect participation, it is also important to ask:

Sub-question 4: What factors affect individual autonomy in the decision-making process regarding participation in an MDA clinical trial?

As an overall guide to the rest of this thesis, the following table provides an overview of the research sub-questions as they are most addressed in each chapter.

Table 3.1 Research questions and chapter guide

		Dissertation Chapters				
Question and Sub-questions		4	5	6	7	8
How can we understand the socio-cultural and ethical aspects of participation in a mass drug administration trial for malaria elimination in The Gambia?						
1	What – and for whom – *is* participation in an MDA clinical trial?					
2	Based upon the socio-ecological model, what affects participation in an MDA clinical trial at different "levels" (e.g. the individual, familial, community, and societal levels)?					
3	What *work* is required for participation in an MDA clinical trial to occur?					
4	What factors affect individual autonomy in the decision-making process regarding participation in an MDA clinical trial?					

Throughout the following sections, this chapter will now describe the research design and methods used to answer these research questions. It will start with a description of the MDA clinical trial to which this study ran concurrently as well as the study setting. It will then break down data collection efforts and end with measures taken to ensure validity, as well as ethical considerations.

3.2 The MASSIV trial

This study ran concurrently to the "Mass drug administration of ivermectin and dihydroartemisinin-piperaquine as an additional intervention for malaria elimination (MASSIV)" trial conducted by the Medical Research Council Unit The Gambia at the London School of Hygiene and Tropical Medicine (MRCG)[1]. MASSIV was a Phase III, community-based, cluster-randomized control trial testing the efficacy of MDA with dihydroartemisinin-piperaquine (DP) and ivermectin on interrupting the transmission of malaria in the Upper River Region of The Gambia. It was conducted in 32 villages – 16 control and 16 intervention – with drug distribution taking place between August - October 2018 and July - September 2019. Drug distribution was conducted through

directly observed therapy (DOT). Each month was considered a round of MDA and medication was distributed three days in a row within each round; there were 3 rounds per year. In total, a person who took the full regimen would have taken DP and ivermectin a total of 18 times over the two years of the MDA trial.

The initial stage of the trial took place in November of 2017. A MRCG field team conducted a malariometric survey of all potential study villages, as well as an up-to-date census. The villages with a malaria incidence of > 10% were among those selected for MASSIV. Once 32 were chosen, study villages were randomized into either the intervention or control arm. MRCG staff then went to each village to inform the Alkalo, the village chief, and seek general approval for the MDA trial to take place. No Alkalo turned down the opportunity to participate.

In July 2018, prior to the commencement of the MDA, members of the clinical team went to each village for a sensitization meeting. At these meetings, the village leadership and community would meet at the *bantaba*, the village centre and gathering location, and the field team would present the details of the MASSIV, including its objectives, risks, benefits, voluntariness, and details of the drug distribution. Those in attendance would then have the opportunity to ask questions and give an overall, village-level consent for the MDA trial. In the days between the sensitization meeting and first round of MDA, the field teams would go to their assigned villages and conduct informed consent and enrolment of all willing individuals.

MASSIV was comprised of 4 separate "teams," each of which had their own methods and research objectives.

<u>The clinical team</u>

The clinical team was comprised of the trial PI and co-PIs, the coordinating and clinical doctors, and multiple field nurses and field workers, as well as nursing and field staff coordinators. Their main focus was on distributing the medications and recording the epidemiological data. As the main research focus of the trial, their objectives were to evaluate impact of the MDA on malaria transmission and vector population density.

Entomology team

The entomology team focused on the details of mosquitos captured in the trial villages, including their mortality rate until 21 days post-MDA.

Health economics team

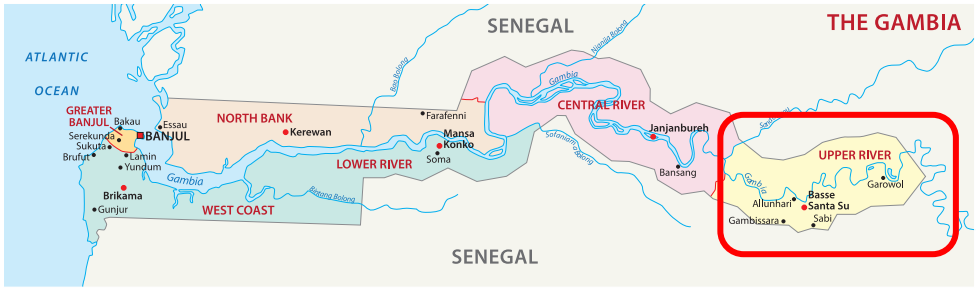
The health economics team conducted an in-depth cost analysis of malaria treatment in the trial area with the objective of determining its cost-effectiveness and potential to be scaled-up to regional levels.

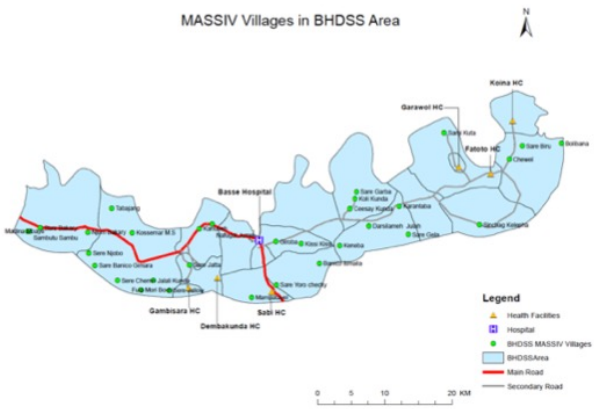
Social science team

The social science team, of which I was a part, had a research objective of understanding the acceptability, coverage, and adherence of the MDA trial in the study area. As such, the methods of this section are the same as the methods employed by the social science team through the MDA.

3.3 Study setting

Figure 3.1 Map of study setting, including The Gambia and trial villages in the Upper River Region





This study took place in the lower bank of the Upper River Region (URR) in The Gambia. The region is the furthest west in the country and surround on 3 sides by Senegal; cross-border movement for trade, grazing cattle, and visiting relatives between the two countries is common. The region's capital, Basse Santa Su (Basse), is the largest city in the area, with a population of approximately 18,000. A busy market brings traders from all around western Africa. Basse is also home to the local MRCG campus and the largest government health facility in the area. Outside Basse, the region is predominantly very rural. The population lives in villages typically comprised on one ethnic group or a single-family lineage. Fula is the largest ethnic group in the area, followed by Mandinka and Serahule, but small groups of other ethnic groups can be found, especially in the larger villages. The majority of people are subsistence farmers and cultivate various grains and ground nuts or herd cattle, though some also participate in the fishing industry or engage in small business (such as running a shop).

The MASSIV villages ranged in size from approximately 140-700 people, with the majority having a population around 250-300. Coinciding with the URR's demographics, the trial villages were predominately Fula and relied heavily on agriculture; the second largest ethnic group was Mandinka, followed by Serahule. All villages were headed by the Alkalo who was most often the oldest male and a direct descendant of the founder of the village. Within the villages, people lived in compounds based on patrilineal relationships and headed by the compound head. The compound would include the compound head's wives and children and the wives and children of either his older sons or younger brothers. Most people in the study area practice Islam.

The study area has a marked seasonal malaria transmission cycle with low vector density and high vector survival (parous rate 81-91% in URR as compared to 27-71% in other regions)[2]. The area also has high coverage of standard malaria control interventions[3], including long-lasting insecticidal nets (LLINs), indoor residual spray (IRS) and seasonal malaria chemoprevention (SMC) for children under 5 years of age. The Gambia, in general, offers free Artemisinin-based combination therapy (ACT) at the government health centers for those with diagnosed malaria. However, even with these measures, the URR has the highest rates of malaria in the country[4–6].

3.4. Study design

"Without a historically deep and geographically broad analysis, one that takes into account political economy, we risk seeing only the residue of meaning."

- Paul Farmer, 2004[7]

3.4.1 Research approach

This study used a transdisciplinary and mixed-methods approach with an emergent and iterative data collection and analysis process. The transdisciplinary approach utilizes theories, concepts, and methodologies from multiple disciplines in order to address complex social phenomena that require a vast range of diverse and critical perspectives to properly address[8,9]. It incorporates multiple stakeholders throughout the data collection process in the hope to co-create knowledge[10]. Because it is not limited by a singular discipline, transdisciplinary approaches have been used in conducting research and creating innovative solutions for a variety of complex problems, such as climate change, poverty and inequality, and healthcare systems. Particularly relevant for this study, a transdisciplinary approach supports research that focuses beyond discrete levels of the socio-ecological framework to address complex issues that stretch across levels.

Because the transdisciplinary approach applies a focus on the knowledge creation process, as opposed to only the resulting data[11], it is particularly useful for an iterative and emergent approach of data collection and analysis combined with extended fieldwork. As will be demonstrated in the following sections, this approach was applied through this study: as new themes and hypotheses emerged, we were able to reflect on how best to further explore them, including changing methodology if needed. With the introduction of new findings, we could adapt our future data collection approaches to ensure they were the most applicable.

This research approach is what led to our specific data collection methods and analysis process.

3.4.2. Data collection and analysis

A note on the field team

The vast majority of the fieldwork was conducted by me and three members from the field team: Omar Ceesay, Dullo Baldeh, and Ebrima Manneh. All three men were well trained and seasoned MRCG fieldworkers with many years of experience working with the institution and in the URR. Dullo and Omar are both native Fula speakers, but are also fluent in Mandinka and English; Ebrima is a native Mandinka speaker also fluent in Fula and English. Ebrima and Dullo had previous social science experience with members of the ITM team on a previous research project also related to a malaria control trial. Other members of the team, Drs. Claudia Nieto-Sanchez and Joan Muela, were also present during various periods of fieldwork. I was present and led all research phases mentioned in this chapter.

3.4.2.1. Ethnographic methods

Ethnographic research involves the study and observations of people in a given setting carrying out their daily lives. It can include participating in the community and always includes the writing of extensive notes that can be used independently for analysis or as to provide greater context and triangulation with data collected through other methods[12]. In this study, ethnographic methods included structured and unstructured observations of all components of the MDA trial, including initial sensitization meetings, the consent and enrollment processes, as well as the MDA drug administration in all trial villages.

In addition, member of the field team and myself observed, and sometimes participated, in staff meetings with other trial teams, including trainings held for the clinical team field staff. We also spent many days and nights living in the trial villages during and in between MDA rounds. In this way, we were able to observe and try to understand the day-to-day life and activities of the villages and their community members. We took part in daily activities, including cooking and eating, and leisure time in the evenings. We were able to hold informal conversations related to malaria, the MDA trial, MRCG, as well as life in general.

We took structured notes on observations. After each event, we sat and discussed our findings as a team and focused on what we learned, what we

still needed to learn, and new findings. For other events, observations were less structured, and each member of the team took their own notes on what they found important; we would then hold meetings after the fact and discuss all that we found. Informal conversations were conducted without taking notes, but detailed summaries of the conversation and any relevant data were recorded in notes as soon as possible.

3.4.2.2. Qualitative methods

Qualitative methods were composed of in-depth interviews (IDIs) and focus group discussions (FGDs). Both methods were conducted with the aid of trained field staff fluent in the local languages and English. Sampling was purposive to allow for maximum variation and ensure that all opinions were collected. Among the IDIs, we included: all intervention and control village Alkalos, those who participated in the MDA trial and took the medication, those who did not participate or take the medication, village leaders and relevant stakeholders (e.g., Village Development Chairs, Traditional Birth Attendants, Village Healthcare Workers, and community group leaders), adolescents (over the age of 12 years), trial field staff, and anyone else deemed relevant by the study team. FGDs were held with groups of similar age and of the same gender: adult men, adult women, adolescent boys, and adolescent girls. All IDI and FGD guides were semi-structured. Questions and translation of questions were reflected on after each activity and edited as appropriate.

Overall, data analysis was a continuous, iterative process. Data were analysed and discussed regularly with the social science team both in the field and in Amsterdam (VU) and Antwerp (ITM). This allowed for constant reflection and the ability to continue conducting research that could confirm or refute preliminary findings and emerging themes until saturation was reached. IDIs and FGDs were recorded and transcribed verbatim by the research team. Raw data were processed in their textual form and coded to generate analytical themes for further analysis using NVivo v. 12 Qualitative Data Analysis software[13].

3.4.2.3. Quantitative methods

A cross-sectional household survey was conducted in all 16 intervention villages and targeted all village members over age 12, regardless of individual involvement in the MDA trial. Surveys were administered using Epi Info v. 7

by trained field workers using Android tables (additional field staff were hired for the purposes of the survey). At the end of each survey day, data were synchronized from each tablet and checked for quality. At the end of the survey period, data were exported into Excel and analyzed using STATA v. 13[14].

The household survey had a calculated target sample size of 850, which we rounded up to 900 for our target number of surveys. This value was calculated to estimate an odds ratio of at least 1.5 as part of a multinomial logit regression for an outcome variable with 3 levels (no adherence, low adherence, and high adherence). Per-village sample size targets were based on the proportion of the village's population size to the total population of all intervention villages. Respondents were randomly selected from census data collected by the MASSIV clinical team in November 2018. If a selected individual was unavailable or declined participation, another individual of the same gender and age bracket was selected. During the analysis stage, the decision was made to combine no and low adherence into one category, resulting in binary logistic regression analysis (no/low adherence and high adherence), which has lower sample size requirements.

Survey questions and possible responses were formulated based on the findings of the exploratory ethnographic and qualitative data during MDA Year 1 (Phase 1 of the research study). The survey focused on: knowledge of malaria; knowledge of the MDA trial, including perceived risks and benefits (both of the trial directly and indirectly); the decision-making process around medicinal intake; social influences; the spread of information; and opinions on MRCG in general. In collaboration with the health economics team, details of and the costs-associated with the last time a respondent (or their child) sought treatment for malaria were also collected.

3.5. Study phases

Table 3.2 Study phases

	2018											
	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
MDA Trial						Team training	Sensitization meetings: Informed consent and enrollment	MDA 1	MDA 2	MDA 3		
Social Science Study			Pre-Phase: Ethics approval	Pre-Phase: Introduction to study setting			Phase 1: Observations and informal interviews: Intervention Alkalo IDIs	Phase 1: MDA observations; IDIs in MDA villages	Phase 1: MDA observations; IDIs in MDA villages	Phase 1: MDA observation; IDIs in MDA villages; Control IDIs		
	2019											
	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
MDA Trial						Sensitization meetings: Informed consent and enrollment	MDA 1	MDA 2	MDA 3		Final analyses	
Social Science Study	Phase 2: Household survey	Phase 2: Household survey; IDIs and FGDs with adolescent girls	Phase 2: IDIs and FGDs with adolescent girls			Phase 3: Observations and informal interviews	Phase 3: In-depth ethnography, Village 1	Phase 3: In-depth ethnography, Village 2	Phase 3: Additional IDIs, FGDs; IDIs with fieldworkers	Phase 3: Additional IDIs, FGDs; IDIs with fieldworkers		

The research for this dissertation fell into three primary phases that corresponded with the sequential mixed-methods qualitative and quantitative approach [QUAL -> quan][15]. After a pre-study phase, it included an exploratory phase qualitative phase, followed by a quantitative household survey, and then a more in-depth and focused qualitative phase.

3.5.1. Pre-phase: 27 March – 14 April 2018

Prior to the commencement of the MDA trial and our research, I traveled to The Gambia for the first time in late March 2018. My principal objective was to present our study at the meeting of the MRCG Scientific Coordinating Committee as part of receiving ethical clearance in-country. The meeting was held at the main campus in Fajara (near the capitol city Banjul). While there, I was also able to meet with key researchers at the MRCG and learn more about the focus and priority areas of their work in The Gambia and the URR, as well as their past and current malaria trials and MDAs.

In addition, this trip allowed for me to travel to the URR for the first time. I met with Dullo Baldeh, who would later join our team, and Kebba Naban, the field coordinator for the clinical team. They took me to some of the villages in the area and introduced me to many people. The trial villages had not yet been selected nor had our protocol been approved by the ethics boards, so

Dullo and Kebba took me on informal visits to other villages where MRC regularly worked. I was able to see and discuss with them the differences between Fula and Mandinka villages, as well as have conversations with men, women, and adolescents, including a traditional birth attendant (TBA) and a village health worker (VHW). Conversations were casual and unstructured, and included topics such as the lives of those in the URR, cultural, economic, and other aspects of the area, general concerns regarding health, and what MRCG has done in the villages. Further, I was able to speak with other MRCG staff to understand more about their work and the villages in the area. This pre-phase provided an initial introduction into the context of the study area and helped to prepare for Phase 1.

3.5.2. Phase 1: July-November 2018; MDA Year 1

Focus of data collection

- Exploratory, ethnographic research
- Qualitative research; in-depth interviews

Description

The first phase of the research for this thesis began with exploratory ethnographic and qualitative methods. I returned to The Gambia in early July, prior to the start of any MDA trial activities. The first step was to conduct trainings with our field team and to thoroughly discuss the different phases of the research and how we would approach the early trial activities and the three rounds of the first year of the MDA trial.

Without concrete questions, outside the overall research question and the topics in the social science protocol (acceptability, coverage, and adherence), my team and I attended and observed as many sensitization meetings and informed consent and enrolment processes in as many villages as we could. As many ran concurrently, we specifically choose villages that may provide greater variation. After the first sensitization meeting, we created a structured observation form to ensure we were all observing the many different components taking place, including who attended the meetings, what types of information were shared by the clinical team, and what types of questions or comments community members asked towards the end. After each meeting, we would then conduct informal conversations with those in attendance; we asked what they learned about the trial, their overall

thoughts regarding whether or not they would participate, and why they made that decision. At the end of each observation, we discussed our findings as a group and planned what other topics we would further explore during the next sensitization meeting.

Before the first round of MDA, we also conducted IDIs with the Alkalos of all 16 intervention villages. We asked them to provide a brief history of their village, to discuss their decision-making process for granting the trial permission to take place, the general demographics of the village, its prior work with MRCG, and its general epidemiologic profile and health-seeking behaviours. At the end of Phase 1, we asked similar questions of the Alkalos in all 16 of the control villages.

The rest of Phase 1 consisted of observations and IDIs with those in the trial villages during and in between rounds of the MDA. We purposively tried to observe the drug distribution at each intervention village. Upon entering a village for the day, after first introducing ourselves and our objectives to the Alkalo, we would speak with the clinical field team. Informal observations with the fieldworkers focused on how the MDA was going in general, their challenges throughout the process, their opinions of the village's acceptance of the MDA, and if there was anything they found particularly interesting that we might investigate further. Afterwards, we would introduce ourselves to various villagers and seek their permission to interview them. Early interviews focused on their general knowledge and thoughts regarding the MDA, their decision-making process, and challenges in taking the medication. After more and more "field days," we would hold meetings with the field team and the rest of the team abroad to discuss what we were finding and to agree on topics to explore further. This lasted throughout the first year of the MDA.

We continued analysis throughout fieldwork and once I returned to Amsterdam in November. This early analysis was used to create a quantitative household survey that would then be used in Phase 2. Lastly, with our initial results from Phase 1 we were able to write a report with recommendations for the clinical team. These recommendations were then used to better the implementation and helped secure higher coverage in Year 2 of the MDA.

Output

In addition to observations and informal conversations, by the end of Phase 1, we had conducted:

- 141 IDIs
    - 32 Alkalo interviews (16 intervention, 16 control)
    - 24 interviews in Round 1
    - 31 interviews in Round 2
    - 26 IDIs in Round 3
    - 28 (non Alkalo) interviews in control villages
- 3 FGDs

3.5.3. Phase 2: January-March 2019; Between MDA Year 1 and Year 2

Focus of data collection

- Quantitative household survey in intervention villages
- IDIs and FGDs with adolescent girls

Description

In January 2019, approximately 3 months after the last drug administration of MDA Year 1, I returned to The Gambia to conduct the quantitative survey. Joined by Claudia for the first two weeks, we hired short-term field staff to join our current team and conducted in-depth trainings and piloted the survey. In addition to the subsequent manuscripts and dissertation chapters, results of this survey were presented at the MASSIV Investigators' Meeting held in April 2019 at LSHTM and to guide more focused and in-depth research questions to address in Phase 3.

Phase 2 also included IDIs and FGDs with adolescent girls. Preliminary analysis from Phase 1 showed that this particular group had unique experiences and challenges related to the decision-making process and participation in the MDA. To make the respondents more comfortable (and to ensure better data quality), we hired and trained a young woman fluent in the local languages and English to help conduct the IDIs and FGDs. These activities focused on the perspectives, opinions, and beliefs of the girls regarding the MDA trial, MRCG, and their lives in general.

Output

In addition to observations and informal conversations, by the end of Phase 2, we had conducted:

- A household survey of 864 respondents across the 16 intervention villages
- 9 IDIs with adolescent girls
- 9 FGDs with adolescent girls

3.5.4. Phase 3: June-October 2019; MDA Year 2

Focus of data collection

- In-depth ethnographic research of 2 intervention villages
- Additional qualitative methods
- IDIs, informal conversations, and observations of MASSIV field team members

Phase 3 began immediately prior to the start of Year 2 of the MDA. I returned to The Gambia, and with my field team, observed the new consent and enrolment processes and interviewed villagers on their experiences and opinions regarding the upcoming year. The results of Phases 1 and 2 also provided context and helped frame our research approach. Though we still conducted IDIs and FGDs in other villages, we heavily focused on two theoretically chosen villages for a more in-depth analysis. These two villages were chosen based on our findings from Year 1: in addition to having substantially different coverage rates (determined from the household survey and the clinical team's data) we also observed differences in their engagement with the implementation of the MDA and their own intra-village social dynamics. We spent multiple nights in each village both during and in between MDA rounds. We became very well known and were able to spend time with people and carry out multiple informal conversations. We also participated in "normal life" activities, such as cooking with the women, playing with children, brewing tea and chatting with the men, etc. We focused heavily on the notion of social cohesion, and conducted many IDIs and FGDs on this topic in both communities. While researching social cohesion, we held many team meetings both on the ground and from abroad, to thoroughly unpack the nuances of the findings and to ensure we were asking the right questions and understanding the responses within their context.

Another topic of focus was on the individual fieldworkers of the clinical team. We took our notes from previous informal conversations to make semi-structured interview guides. Outside the villages we already focused on, we purposively selected to interview fieldworkers from different villages and with different qualifications and past experiences.

Output
In addition to observations and informal conversations, by the end of Phase 3, we had conducted:

- 39 IDIs with men, women, adolescent boys, and adolescent girls
- 19 FGDs with men, women, adolescent boys, and adolescent girls
- 11 IDIs with MASSIV clinical field team members

3.6. Validity

Validity refers to the accuracy of data collection tools and the ability to trust the data and research findings (Bernard 2018). In addition to the methods described above, including a transdisciplinary approach and an emergent, iterative analysis process that necessarily triangulated data across methods, this study also employed multiple measures through the study to ensure validity. First, this study had an experienced and trained local field team fluent in the local languages and culture. They were incorporated into all aspects of data collection and analysis to ensure translations and interpretations remained consistent with local understanding. As part of this, we also maintained regular team debriefings and reflection exercises, including involvement with the team abroad. In this way, all emergent themes were thoroughly discussed and action plans for future data collection and analysis were made as part of a group.

In regard to data collection tools, all translations for IDIs, FGDs, and the household survey were done by group consensus and back translated into English. The regular debriefing meetings would include discussions on the translation of questions to ensure we were gathering the data we wanted and that the questions were being asked and interpreted accordingly. Audio files for all qualitative data were transcribed by a different member of the team rather than the person who led the IDI or FGD. In addition, we held regular checks of transcripts for quality and accuracy of transcription and

translation. Any issues were solved by group consensus. Lastly, multiple coders were involved in any of the qualitative analysis.

3.7. Ethical considerations

Respondent and data privacy

IDIs, focus group discussions, and surveys were all conducted with as much privacy as could be managed, and typically took place in the private homes of respondents. If the home was not available, data collection methods were conducted outside, on a shaded platform away from others. All transcripts were transcribed and translated into English verbatim, but names and any identifying information was excluded. All villages and categories of respondents (e.g., adult male, adolescent female, Alkalo, field staff, etc.) were given codes. These codes were used in the naming and filing system of all data and the key, along with the original audio files, were kept on password-protected files that only remained with relevant members of the study team.

Informed consent and assent

All respondents and their guardians (when under 18 years old) were explained the purpose of the study by field staff and gave informed consent or assent before being included in the qualitative or quantitative strands. Considering that the act of signing documents is not common practice for local populations and that it could produce mistrust towards the study team, we favoured verbal over written consent.

Ethics approval

The quantitative and qualitative studies were considered as two separate studies. Both were approved by the Institutional Review Board of the Institute of Tropical Medicine, Antwerp, Belgium, by the Scientific Coordinating Committee and the Gambian Government/MRC Joint Ethics Committee in The Gambia.

References

1. Dabira ED, Soumare HM, Lindsay SW, et al. Mass drug administration with high-dose ivermectin and dihydroartemisinin-piperaquine for malaria elimination in an area of low transmission with high coverage of malaria control interventions: Protocol for the massiv cluster randomized clinical trial. *JMIR Res Protoc*. 2020;9(11):e20904. doi:10.2196/20904
2. Mwesigwa J, Achan J, Di Tanna GL, et al. Residual malaria transmission dynamics varies across The Gambia despite high coverage of control interventions. *PLoS One*. 2017;12(11):1-24. doi:10.1371/journal.pone.0187059
3. Mwesigwa J, Okebe J, Affara M, et al. On-going malaria transmission in The Gambia despite high coverage of control interventions: a nationwide cross-sectional survey. *Malar J*. 2015;14(1):314. doi:10.1186/s12936-015-0829-6
4. ICF. The Gambia Demographic and Health Survey 2019-20 . 2021. https://www.dhsprogram.com/pubs/pdf/FR369/FR369.pdf.
5. Mwesigwa J, Achan J, Di Tanna GL, et al. Residual malaria transmission dynamics varies across The Gambia despite high coverage of control interventions. Carvalho LH, ed. *PLoS One*. 2017;12(11):e0187059. doi:10.1371/journal.pone.0187059
6. The Gambia, Programme NMC, the Gambia Bureau of Statistics and Utica International. *The Gambia Malaria Indicator Survey 2017*. Columbia, Maryland; 2018.
7. Farmer P. Sidney W. Mintz Lecture for 2001: An anthropology of structural violence. *Curr Anthropol*. 2004;45(3):305-325.
8. Leavy P. *The Essentials of Transdisciplinary Research: Using Problem-Centered Methodologies*. New York, New York: Routledge; 2016.
9. Rosenfield PL. The potential of transdisciplinary research for sustaining and extending linkages between the health and social sciences. *Soc Sci Med*. 1992;35(11):1343-1357. doi:10.1016/0277-9536(92)90038-R
10. Bunders-Aelen J, Broerse J, Keil F, Pohl C, Scholz R, Zweekhorst M. How can transdisciplinary research contribute to knowledge democracy? In: In'tveld RJ, ed. *Knowledge Democracy: Consequences for Science, Politics, and Media*. ; 2010:1-397. doi:10.1007/978-3-642-11381-9
11. Bunders-Aelen J, Bunders A, Zweekhorst M. Challenges for Transdisciplinary Research. In: Werlen B, ed. *Global Sustainability*.

Cham: Springer International Publishing; 2015. doi:10.1007/978-3-319-16477-9
12. Emerson R, Fretz R, Shaw L. *Writing Ethnographic Fieldnotes*. Second. Chicago, Illinois: The University of Chicago Press; 2011.
13. NVivo. 2018. https://www.qsrinternational.com/nvivo-qualitative-data-analysis-software/home.
14. Stata Statistical Software. 2011.
15. Teddlie C, Tashakkori A. *Foundations of Mixed Methods Research: Integrating Quantitative and Qualitative Approaches in the Social and Behavioral Sciences*. London: Sage Publications; 2009.

Chapter 4

Costs and barriers faced by households seeking malaria treatment in the Upper River Region, The Gambia

A group of boys and young men take a break from their farming labour to eat breakfast

ABSTRACT

Background and aims: Malaria transmission in The Gambia decreased substantially over the last 20 years thanks to the scale up of control interventions. However, malaria prevalence is still relatively high in eastern Gambia and represents both a health and a financial burden for households. This study aims to quantify the out-of-pocket costs and productivity losses of seeking malaria treatment at household level.

Methods: A household survey was carried out through in-person interviews. Respondents were asked about malaria prevention methods, their treatment seeking behaviour, and any costs incurred for transport, services, food, and/or overnight stays. We used a bottom-up costing approach to calculate the unit cost of treatment and a tobit regression approach to investigate cost drivers.

Results: The survey included 864 respondents, mainly subsistence farmers. Most respondents (87%) considered malaria to be a problem affecting their ability to perform their regular duties. Respondents preferred going to a health facility for treatment. The primary reason for not going was related to costs; 70% of respondents incurred costs for seeking health care, with a median of £3,62 (IQR: £1,73 to £6,10). The primary driver of cost was living in one of the villages that are off the main road and/or far from health facilities. 66% reported productivity loss of 5 working days on average during a malaria episode of them or their child.

Discussion: Although malaria prevalence is decreasing and treatment is provided free of charge, households seeking treatment are confronted with out-of-pocket expenditures and lost working days; particularly in remote villages.

INTRODUCTION

In 2017, the estimated global burden of malaria was 219 million cases and 435,000 deaths[1], 90% of which occurring in sub-Saharan Africa[2]. The Gambia, a small country in western Africa, has been very successful in decreasing the malaria burden: clinical malaria incidence has dropped five-fold, from 275 cases per 1,000 population in 2010 to 57 cases per 1,000 population in 2017. This has been achieved thanks to the scale up by the National Malaria Control Program (NMCP) of malaria control interventions such as insecticide-treated nets, indoor residual spraying (IRS), intermittent preventative treatment during pregnancy, and seasonal malaria chemoprevention (SMC). Nevertheless, malaria transmission is still ongoing, particularly in eastern Gambia, in the Upper River Region (URR)[3]. Asymptomatic malaria cases are often mentioned as the reservoirs for this continued transmission and novel strategies are needed to clear these[2–4]. Several trials are currently underway to investigate if such residual transmission can be reduced with mass drug administration (MDA) based on the endectocidal drug Ivermectin (IVM)[4–6]. To evaluate adoption of such an approach by national or global stakeholders, it is important that its cost-effectiveness is established. Costing studies are an essential component of cost-effectiveness analyses[7,8]. Although various types of costing studies are needed, household costs are a particularly important type of costing study because apart from a health impact, malaria also has a financial impact on households because they incur costs for prevention and for case management. Malaria diagnosis and treatment in The Gambia, as in many other sub-Saharan African countries, is provided free of charge, but indirect costs can still be incurred. Studies from Ghana, Kenya and Ethiopia show that households incur costs for transport, food, and overnight stays in health facilities[9–11]. Unfortunately, household costing data are not available for The Gambia. The aim of this study is to fill this knowledge gap by surveying households in URR about their malaria treatment seeking behaviour and the (in)direct costs they incur whilst doing so.

METHODS

Study setting and respondent selection

This household-level costings study was part of a larger village-level, cluster-randomized trial evaluating the efficacy of MDA with IVM and the antimalarial drug dihydroartemisinin-piperaquine (DP) on residual malaria

transmission (#NCT03576313). It took place in 32 villages (16 control and 16 intervention) with populations of 140-700 located in the South Bank of the URR. The two-year trial consisted of the administration of the medications for three consecutive months prior to the period of peak malaria transmission (November-December); medications were distributed August-October 2018 and July-September 2019. All eligible individuals in the intervention villages were targeted for trial participation.

Separate from, but concurrent to, the RCT, a quantitative household survey on the acceptability of MDA and the costs of seeking care was carried out. The sample size was designed to substantiate inferences concerning trial participation, defined as a multinomial outcome with three levels: no participation, partial participation, full participation. Assuming an effect size of 1.5, an intra-correlation of 1% and 80% power, the required sample size was estimated at 850 individuals, rounded up to 900, in the 16 intervention villages. The target sample size per village was made proportional to the village population size. Participants were randomly selected from the most recent census data collected by the trial field team prior to the trial; all individuals aged 12 and above were eligible to participate in the household survey, regardless of participation in the RCT. If a selected individual was absent or refused to participate, they were replaced by another individual of similar age and gender. In addition to the household survey, village health workers (VHWs) of trial intervention villages were interviewed. The aim was to include all 16 intervention villages.

Data collection

The survey was carried out between January and February of 2019, 2-3 months after the first intervention year. Part of the acceptability survey concerned treatment seeking behaviour and costs. These questions were developed based on the ACT Consortium guidance[12]. Respondents, besides demographic information, general malaria knowledge, owned means of transport, and primary economic activities, were asked questions on their treatment seeking behaviour for malaria, malaria prevention methods employed, and perceived problems associated with malaria. Information on the last episode of malaria experienced by them and by one child of the household was also collected, including the preferred and chosen treatment option and costs incurred. Questions and potential responses of non-economic topics were formulated on the basis of qualitative and

ethnographic data collected prior to and during the implementation of the MDA in 2018. Data were electronically captured in Epi Info v.7 by trained field workers using Android tablets. Data were synced at the end of every field day and checked for quality.

The interviews with VHWs of trial intervention villages were conducted during the summer of 2019. They were asked questions about their background as well as their role in malaria testing and treatment. In addition, they were asked about barriers surrounding malaria testing and treatment facing them as well as the inhabitants of their village.

Analysis of costing data

We followed a bottom-up costing approach to calculate the unit costs incurred by a household of the last malaria episode for an adult and for a child. Direct cost components were defined as costs for testing and treatment while indirect costs were defined as costs of transport, costs of overnight stays and related food. We assumed uncomplicated cases would not incur costs for overnight stays or food. All costs were obtained directly from the respondents. Productivity losses were measured in number of working days missed, either to obtain one's own treatment or to accompany a sick child to a health facility. The total financial impact of malaria care-seeking on households in URR was calculated by multiplying the unit cost of seeking care by the average yearly clinical incidence of malaria based on data obtained from the NMCP.

Costs are reported in 1 January 2020 British pounds. We used the average Gambian Dalasi to British Pound exchange rate during the period October – November 2018 (about 61 Dalasi per 1 GBP), the peak malaria season when malaria-related costs would have been incurred.

To investigate what demographic variables drive the household unit cost of obtaining malaria treatment, we used a tobit regression approach [13]. This approach is particularly well-suited for costing data where a proportion of the sample may have zero costs, leading to highly skewed data.

Ethics

All participants (and their guardians if under 18) were explained the purpose of the study by trained field staff in their preferred language prior to giving

informed consent and/or assent (minors) to participate. The study was approved by the Institutional Review Boards of the Institute of Tropical Medicine Antwerp and by the Gambian Government/MRC Joint Ethics Committee.

RESULTS

The household survey was completed by 864 respondents, 66% of them women. The median age was 29 years (IQR: 19-41). Fulas were the most represented ethnic group (73%) and most respondents (80%) were subsistence farmers. A large proportion of respondents (41%) had not received any formal education (Table 1). In total, 14 VHWs were interviewed. Most had received a 4-week training on testing and treating Malaria in Basse (the major town in URR) and they had 5 years' worth of experience on average.

Perspectives on malaria and healthcare seeking behaviour

A large proportion of respondents (63%) considered malaria a relevant but declining problem while 25% had the opposite view and considered malaria as a current problem. This view was shared by VHWs, of whom 79% indicated malaria was a problem in their village. When asked what non-health problems malaria can cause for the patient or their family, 65% stated missing work, 56% missing household responsibilities, and 50% missing school. Malaria was indicated to cause financial problems due to costs incurred at the health facility (42%), for medicines (46%), or for transport (37%).

The belief that malaria can be prevented by using bed nets was shared by 95% of participants. In addition, almost half of respondents (45%) believed malaria could be prevented by cleaning the environment (e.g., by removing stagnant water or other mosquito breeding sites). Fewer believed malaria could be prevented using sprays (20%), coils (11%), medication (6%), or herbs (13%). Regarding treatment, 85% of respondents believed malaria medication should be taken even if someone was no longer visibly sick. VHWs indicated that the majority of people in their villages used bed nets (33%), environmental cleaning (21%), or coils (16%) to prevent malaria. All VHWs indicated that NMCP prevention activities (bed net campaign, IRS, SMC) had taken placed in their village in 2019. Most VHWs had a role in IRS and SMC (>80%) but this was less so for net distribution (57%).

Malaria in the previous months was reported by 28% of adults; 37% of them reported an episode of malaria among children of their household. All but one VHWs indicated that most villagers with fever came to them first to seek testing and/or treatment. Despite this, the large majority of episodes in adults (89%) and children (91%) reported preferring and having received treatment at a health facility. Very few adults self-treated (4%), received treatment by VHWs (4%), or by a traditional healer (1%). Similarly, most children (91%) were treated at a health facility. Overall, most respondents went to the centrally located - and largest - facility in Basse, despite not being the closest one for many respondents (Figure 1).

Most respondents travelled to the health facility using public transport (36%), followed by motorcycle (24%), walking (12%), or donkey cart (8%). Private or MRC-provided transport were rarely used (1% and <1%, respectively). 15% of respondents used a combination of transport modes. The choice of transport was not different between adult cases versus paediatric cases. The mean distance to the chosen health facility was 37 kilometres (95% CI: 12 to 48).

Barriers to preventing malaria and seeking care

Not getting/having enough bed nets (50%) and financial difficulties (29%) were mentioned by VHWs as most important prevention challenges, followed by a lack of cleaning materials (21%) or coils (14%). The 59 respondents who indicated that they did not go to the health facility for the most recent malaria episode gave as reasons: transport costs (17%), service costs (12%), or that they were treated at home (10%). All VHWs indicated that a lack of supplies prevented them from consistently testing and treating malaria as per their training and the village's needs.

Barriers to accessing care for villagers according to VHWs were the unavailability of RDTs (86%) and antimalarial drugs (93%) at the village level. Although a majority (86%) of VHWs indicated that the coordination between them and the health facilities was good, 64% of them also stated that having to travel to the health facility presented a barrier to accessing malaria care for people in their village.

Cost of seeking treatment at a health facility

More than half (54%) of respondents who attended a health facility incurred out-of-pocket expenditures for transport, with a median cost of £1,07 (IQR: £0,66 to £1,65). When at the health facility, 65% had to pay for services, to the median amount of £3,30 (IQR: £1,65 to £4,94). Only 6% of respondents had to pay for food during the visit to the health facility; the median amount paid was £4,37 (IQR: £1,65 to £5,15). When combined, 70% of respondents incurred out-of-pocket expenses when attending a health facility, the median of which was £3,62 (IQR: £1,73 to £6,10). Regarding productivity losses, 56% of respondents indicated productive work lost during their last malarial episode and 39% indicated productive work lost during the last episode of their child. In both cases, 5 working days were lost on average by the adult.

When we multiply our out-of-pocket cost estimates for seeking care with the historical clinical incidence (of both uncomplicated and complicated malaria) as reported by NMCP we find that the total expected expenditures by households in URR on malaria treatment ranged from £44,000 in 2017 to £164,000 in 2015 (Table 2). Of these costs, 97% would be for uncomplicated cases.

Table 2. Estimation of total costs incurred by households in URR during the years 2013-1017 based on this study and malaria clinical incidence data in URR for these years obtained from the Gambian National Malaria Control Programme.

Years	Complicated cases	Uncomplicated cases	Household costs for seeking treatment
2013	1,515	45,479	£145,021
2014	933	26,806	£85,613
2015	1,273	52,007	£164,288
2016	1,262	34,167	£109,368
2017	526	13,821	£44,293

Drivers of costs

Overall, services constituted the majority of costs (69%) followed by transport (22%) and overnight stays/food (9%). Median costs were higher for adults (£4,20, IQR: £2,02 to £6,70) than for children (£3,54, IQR: £0,41 to £6,18). The average out-of-pocket cost incurred for services differed by the

choice of the health provider; it was the highest for a health facility (£3,91), followed by home treatment (£3,21), village health worker (£2,73), traditional healer (£2,06) or MRC (£2,04). Travelling by public transport to attend a health facility costed an average amount of £1,34 out-of-pocket. This was slightly less for those who travelled by motorbike (£1,21), donkey cart (£0,33), or walking (£0,03). Transport expenditures for respondents who used multiple modes of transport were £1,30 on average.

For the tobit regression analysis, we included the demographic variables in Table 1, with the exception of ethnic group as this is highly correlated with village of residence (most villages are composed predominantly of one ethnic group). The cost of seeking malaria care is reduced significantly by having a Quranic as opposed to no education ($p<0.01$) and having business among one's primary economic activities ($p<0.01$). Compared to the largest village of Giroba (Figure 2), people from some villages (Sare Garba, Koli Kunda, Darsilameh Julah or Sare Gela) bear a significantly higher total cost ($p<0,01$), while villagers from Sare Cherno had a significantly lower cost ($p=0,03$). Age, status in household, and owning particular modes of transport did not significantly impact the total costs of seeking malaria treatment.

DISCUSSION

This study investigated treatment seeking behaviour and expenditures incurred by households in URR, The Gambia, when one of their members contracts malaria. Our results show that most respondents considered malaria a problem that affects their quality of life and their economic productivity. Although in The Gambia malaria treatment is free of charge, many barriers to this actually happening are mentioned. Seventy per cent of respondents reported incurring expenditures for malaria treatment. The health facility is seen as the most efficient way to treat malaria and households incurred a median of £3,72 in out-of-pocket expenses to obtain treatment there, two thirds of which was for services.

The primary cost driver in this study is village of residence. This is not surprising given the fact that the villages where respondents incurred significantly more costs are located between the health facilities surrounding Basse and the health facilities at the eastern tip of URR (Figure 2). Furthermore, they are off the main west-east road and/or have a road

connection that is in bad condition (especially during the rainy season). Village of residence was, in this study, a pragmatic surrogate for travel time because travel times are hard to calculate given the many modes of transport people employ and the varying condition of roads throughout the year.

That travel time (or distance to health facility) is an important driver of costs is also found in earlier malaria treatment costing studies in Ghana, Ethiopia, Malawi, and Uganda[9,11,14,15]. What is different is that in our study costs for services constituted nearly two-thirds of total costs, while in the other studies it was the reverse. Based on earlier qualitative fieldwork in the region, the VHW interviews, and an earlier study in the west of The Gambia [16], we hypothesize that the relatively high expenditure on services is due to regular stock-outs at health facilities that require people to purchase treatment at private pharmacies in the larger towns. This is a cause of frustration for VHWs who despite being trained to test and treat (uncomplicated) malaria, are often not able to do so because of a lack of RDTs and antimalarial drugs. The majority of transport and services costs incurred by households for seeking malaria treatment could be avoided if people could consistently receive treatment locally in their own village. This would require more supplies and better distribution according to need.

Other drivers of treatment-seeking costs found in the literature are relative household wealth, public versus private facility, and availability of drugs at the health facility. We did not collect data on household wealth, but it is reasonable to postulate that involvement in business and educational level (which significantly affects total cost in our sample) are proxies for household wealth. In addition, given the social structure in the Gambia, it is reasonable to assume that healthcare costs are shared by members of a household or a compound. This may mean that, although our results did not show being a household or compound head has a significant effect on costs, *actual* malaria-related costs for these people may be higher as they are expected to pay for the care of others under their care as well. We did not ask specifically if respondents went to a public or private health facility because there are almost no private clinics in URR and we did not have data on stock-outs at health facilities. However, the relatively high costs of services in a system that should in theory provide malaria care for free could be a reflection of the fact that a part of treatment (drug provision) is being taken up by private pharmacies.

A major strength of this study is the large sample of respondents across URR and the inclusion of the VHW perspective. This provides confidence in the reliability of the results. The primary limitation of this study is the cross-sectional approach and the reliance on respondent call-back. Despite practical and financial barriers, the majority of respondents reported seeking biomedical treatment for malaria at a health facility. This is in line with earlier research in The Gambia[16,17] but there are two limitations that put these findings into perspective[17]. First of all, within the local cultural beliefs regarding health, there can be an overlap between (symptoms of) malaria and certain folk illnesses. Though not particularly common, some symptoms of complicated malaria, such as convulsions or losing consciousness, may be perceived to have supernatural causes and result in different treatment-seeking behaviour, such as from a traditional healer. These factors may have led to an overestimation of health facility preference and an underestimation of the total malaria-related cost impact on URR. Relying on respondent recall may also have biased the costing results as respondents may not remember correctly what spent a few months before the interview. As we did not ask about *when* the latest malaria episode occurred, it is hard for us to assess the impact of the recall bias on the results. A related limitation is that this survey was administered in between year 1 and year 2 of the MASSIV trial.

Though great care was taken to ensure participants knew the household survey team was separate from the MDA clinical team, potential benefits derived from access to the study medicines could have added a desirability bias to participants' responses. Another limitation is costs incurred for severe malaria. As this is relatively rare and is sometimes fatal, it is likely that our results mainly reflect costs incurred for uncomplicated malaria. Finally, because we focused on out-of-pocket expenditures, our results primarily reflect financial rather than economics costs. We did collect data on working days lost but converting this to a monetary value was not practical as 80% of the respondents were subsistence farmers and thus had no formal income. There are methods for assessing wealth of subsistence farmers but they are time-intensive and would have carried the risk of respondent fatigue in an already long survey.

CONCLUSION

The residual transmission of malaria in The Gambia's URR region requires households to keep spending money on prevention and treatment. This study has quantified the latter and found that costs are incurred for both transport and services, despite malaria care in The Gambia being provided free-of-charge and VHWs being available in most villages. To reduce malaria transmission in areas with a high coverage of prevention interventions, novel approaches such as mass drug administration with Ivermectin are needed. This study can add to the evidence base that is needed to establish the cost-effectiveness of such approaches for regular use or for malaria elimination. Apart from clinical and costing data, cost-effectiveness studies and policy should take into account health system barriers and local cultural interpretations of disease that may prevent theoretically efficacious interventions from reaching their full potential for vulnerable populations.

TABLES and FIGURES

Table 1. Demographics of the respondent population and results from the multivariate tobit regression against total costs in 2020 GBP
IQR=interquartile range. †: intercepts of model had as estimates 262.64 and 5.30 with standard errors of 68.05 and 0.03; both had p-values <0.01. ‡: standard education was defined as having enjoyed primary, junior, senior, and/or more than senior education. Asterisks denote significance level: *=p≤ 0.05, **=p≤0.01, ***=p≤0.001

Descriptive statistics			Multivariate tobit regression†		
N=864		Median (IQR)	Coefficient	Standard error	p-value
Age		29 (19 to 41)	-0.33	0.78	0.67
		n (%)			
Gender = female		566 (65.8)	-42.547	29.073	0.143
Village					
	Sare Njobo	86 (10.0)	-33,543	41,993	0,424
	Sare Banico Gimara	29 (3.4)	63,784	54,416	0,241
	Sare Cherno	41 (4.8)	-118,192	54,288	0,029*
	Jalali Kunda	36 (4.2)	12,533	57,306	0,827
	Sare Jallow	40 (4.6)	-88,370	50,765	0,082
	Giroba	112 (13.0)	Reference level		
	Sare Yoro Checky	36 (4.2)	-34,612	53,147	0,515
	Keneba	60 (7.0)	17,445	44,617	0,696
	Sare Garba	38 (4.4)	184,352	49,313	0,000***
	Koli Kunda	75 (8.7)	122,425	40,847	0,003**
	Ceesay Kunda	54 (6.3)	79,823	43,878	0,069
	Karantaba	38 (4.4)	66,906	47,185	0,156
	Darsilameh Julah	35 (4.1)	175,121	54,085	0,001***
	Sare Gela	70 (8.1)	92,361	42,767	0,031*
	Sami Kuta	70 (8.1)	2,379	44,953	0,958
	Sare Biru	43 (5.0)	16,819	49,425	0,734
Status					

	Compound head	69 (8.0)	Reference level		
	Household head	24 (2.8)	-8,542	68,700	0,901
	Compound member	226 (26.2)	-56,729	39,243	0,148
	Wife	360 (41.7)	-4,541	44,988	0,920
	Child	182 (21.1)	-69,012	49,361	0,162
	Other	2 (0.2)	-122,171	217,871	0,575
Education					
	None	357 (41.1)	Reference level		
	Standard‡	243 (28.2)	-23.339	25.065	0.352
	Quranic	261 (30.2)	-63.133	21.952	0.004**
	Other	2 (0.2)	-154.831	155.492	0.319
Ethnic group			Not included in regression		
	Fula	626 (72.5)			
	Mandinka	172 (19.9)			
	Sarahule	56 (6.5)			
	Other	9 (1.0)			
Primary economic activity					
	Farming	694 (80.3)	-3,070	29,650	0,918
	Herding	65 (7.5)	-7,989	36,192	0,825
	Business	131 (15.2)	70,759	25,813	0,006**
	Domestic	263 (30.0)	-10,205	20,258	0,614

Table 2. Estimation of total costs incurred by households in URR during the years 2013-1017 based on this study and malaria clinical incidence data in URR for these years obtained from the Gambian National Malaria Control Programme

Years	Complicated cases	Uncomplicated cases	Household costs for seeking treatment
2013	1,515	45,479	£145,021
2014	933	26,806	£85,613
2015	1,273	52,007	£164,288
2016	1,262	34,167	£109,368

2017	526	13,821	£44,293

Figure 1: Map of the Upper River Region in the Gambia showing the health facilities visited for malaria treatment by survey respondents

The width of lines is proportional to the number of respondents from a particular that indicated having gone to a particular health facility

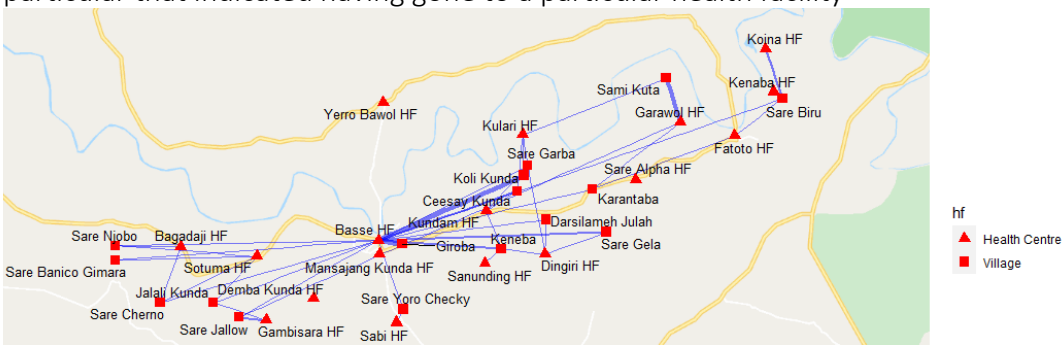
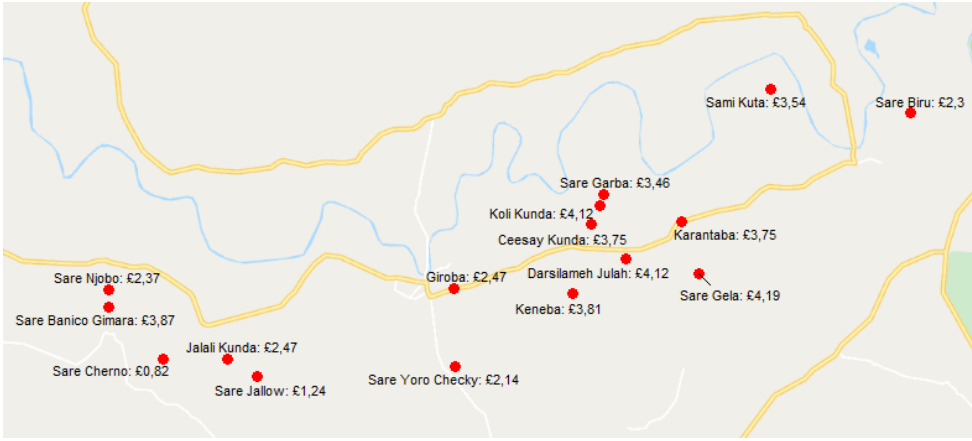


Figure 2: Map of the Upper River Region showing median household costs for seeking, Malaria care during the last transmission season per village as indicated by survey respondents



References

1. WHO. *World Malaria Report*. Geneva; 2018.
2. Cibulskis RE, Alonso P, Aponte J, et al. Malaria: Global progress 2000 – 2015 and future challenges. *Infect Dis Poverty*. 2016;5(1):61. doi:10.1186/s40249-016-0151-8
3. Mwesigwa J, Achan J, Di Tanna GL, et al. Residual malaria transmission dynamics varies across The Gambia despite high coverage of control interventions. Carvalho LH, ed. *PLoS One*. 2017;12(11):e0187059. doi:10.1371/journal.pone.0187059
4. Jaiteh F, Masunaga Y, Okebe J, et al. Community perspectives on treating asymptomatic infections for malaria elimination in the Gambia. *Malar J*. 2019;18(1):39. doi:10.1186/s12936-019-2672-7
5. Slater HC, Walker PGT, Bousema T, Okell LC, Ghani AC. The Potential Impact of Adding Ivermectin to a Mass Treatment Intervention to Reduce Malaria Transmission: A Modelling Study. *J Infect Dis*. 2014;210(12):1972-1980. doi:10.1093/infdis/jiu351
6. The IVM Roadmappers. A Roadmap for the Development of Ivermectin as a Complementary Malaria Vector Control Tool. *Am J Trop Med Hyg*. 2020;102(2s):3-24. doi:10.4269/ajtmh.19-0620
7. Gunda R, Chimbari MJ. Cost-effectiveness analysis of malaria interventions using disability adjusted life years: a systematic review. *Cost Eff Resour Alloc*. 2017;15(1):10. doi:10.1186/s12962-017-0072-9
8. Chaccour C, Rabinovich NR. Ivermectin to reduce malaria transmission III. Considerations regarding regulatory and policy pathways. *Malar J*. 2017;16(1):162. doi:10.1186/s12936-017-1803-2
9. Dalaba MA, Welaga P, Oduro A, Danchaka LL, Matsubara C. Cost of malaria treatment and health seeking behaviour of children under-five years in the Upper West Region of Ghana. Carvalho LH, ed. *PLoS One*. 2018;13(4):e0195533. doi:10.1371/journal.pone.0195533
10. Dixit A, Lee M-C, Goettsch B, Afrane Y, Githeko AK, Yan G. Discovering the cost of care: consumer, provider, and retailer surveys shed light on the determinants of malaria health-seeking behaviours. *Malar J*. 2016;15(1):179. doi:10.1186/s12936-016-1232-7
11. Hailu A, Lindtjørn B, Deressa W, Gari T, Loha E, Robberstad B. Economic burden of malaria and predictors of cost variability to rural households in south-central Ethiopia. Carvalho LH, ed. *PLoS One*. 2017;12(10):e0185315. doi:10.1371/journal.pone.0185315
12. Hansen K, Yeung S. ACT consortium guidance on collecting household costs.
13. Gregori D, Petrinco M, Bo S, Desideri A, Merletti F, Pagano E. Regression models for analyzing costs and their determinants in health care: an introductory review. *Int J Qual Heal Care*. 2011;23(3):331-341.

doi:10.1093/intqhc/mzr010
14. Hennessee I, Chinkhumba J, Briggs-Hagen M, et al. Household costs among patients hospitalized with malaria: evidence from a national survey in Malawi, 2012. *Malar J*. 2017;16(1):395. doi:10.1186/s12936-017-2038-y
15. Matovu F, Nanyiti A, Rutebemberwa E. Household health care-seeking costs: experiences from a randomized, controlled trial of community-based malaria and pneumonia treatment among under-fives in eastern Uganda. *Malar J*. 2014;13(1):222. doi:10.1186/1475-2875-13-222
16. Wiseman V, Scott A, Conteh L, McElroy B, Stevens W. Determinants of provider choice for malaria treatment: Experiences from The Gambia. *Soc Sci Med*. 2008;67(4):487-496. doi:10.1016/j.socscimed.2008.04.007
17. O'Neill S, Gryseels C, Dierickx S, et al. Foul wind, spirits and witchcraft: illness conceptions and health-seeking behaviour for malaria in the Gambia. *Malar J*. 2015;14(1):167. doi:10.1186/s12936-015-0687-2

Chapter 5

From informed consent to adherence: Factors influencing involvement in a mass drug administration with ivermectin for malaria elimination in The Gambia

Community elders wait outside the MDA site to receive the medication

Abstract

Background: The World Health Organization (WHO) recommends consideration of mass drug administration (MDA) for malaria control in low-endemic settings approaching elimination. However, MDA remains a controversial strategy, as multiple individual, social, and operational factors have shown to affect its acceptability at local levels. This is further complicated by inconsistent definitions of key indicators derived from individual and community involvement — coverage, adherence, and compliance— that cast doubts about the actual and potential epidemiological impact of MDA on disease control and elimination. This study aimed to identify limitations and enabling factors impacting involvement at different stages of a large cluster-randomized trial assessing the effect of combining dihydroartemisinin-piperaquine (DP) and ivermectin (IVM) in malaria transmission in The Gambia.

Methods: This social science study used a mixed-methods approach. Qualitative data were collected in intervention and control villages through ethnographic methods, including in-depth interviews (IDIs), focus group discussions (FGDs), and participant observation conducted with trial participants and decliners, community leaders, and field staff. A cross-sectional survey was conducted in the intervention villages after the first year of MDA. Both strands of the study explored malaria knowledge and opinions, social dynamics influencing decision-making, as well as perceived risks, burdens, and benefits associated with this MDA.

Results**:** 157 IDIs and 11 FGDs were conducted, and 864 respondents were included in the survey. Barriers and enabling factors to involvement were differentially influential at the various stages of the MDA. Issues of social influence, concerns regarding secondary effects of the medication, costs associated with malaria, and acceptability of the implementing organization, among other factors, differently affected the decision-making processes throughout the trial. Rather than a linear trajectory, involvement in this MDA trial was subjected to multiple revaluations from enrolment and consent to medicine intake and adherence to treatment.

Conclusions**:** This study went beyond the individual factors often associated with coverage and adherence and found that nuanced social dynamics greatly influence the decision-making process at all phases of the trial. These issues need to be consider for MDA implementation strategies and inform discussions about more accurate ways of reporting on critical effectiveness indicators.

Background

Mass drug administration (MDA) is an intervention that aims at reducing the human reservoir of malaria infection by administering a full antimalarial treatment to the whole population, regardless of the individual's infection status. This approach has been successfully implemented to control several neglected tropical diseases[1]. The World Health Organization (WHO) recommends the consideration of MDA for malaria control in endemic island communities and in low-endemic non-island settings approaching elimination, such as The Gambia, where there is minimal risk of re-introduction of infection, good access to treatment, and implementation of vector control and surveillance[2]. However, MDA remains controversial. A Cochrane systematic review concluded that MDA substantially reduces the risk of malaria infection, but few studies have shown a sustained impact beyond six months post-MDA[3]; further, MDA may increase the risk of selecting drug resisistance parasites[4]. Studies have also shown that achieving and sustaining high coverage is likely more important than the treatment used[5]. This requires the involvement of the target populations for as long as necessary in order to achieve the expected epidemiological outcomes, especially as a consistent trend of reduced MDA uptake over time, particularly in multidose regimens, has been observed[6].

Multiple individual, social, and operational factors have shown to influence acceptability and adherence to MDA. These include scepticism towards allopathic medicine[7], reluctance to undergo screening procedures like blood sampling[8] and pregnancy tests[9], concerns on drug adverse reactions[10], and reluctance of taking treatment without any symptoms[11]. Lack of clarity regarding the specific drug regimens administered[12], mobility[9], and mistrust between those who distribute the medications and local populations[13] have also been identified as factors decreasing treatment coverage and compliance. Implementing organizations also play a significant role in facilitating or limiting local involvement in MDA. Operational and implementation issues, such as providing adequate information, designing field staff supervision responsibilities, and preparing health systems for the intervention, heavily rely on management decisions and existing health policies at the national and local levels[14].

Lack of clarity regarding key MDA performance indicators such as coverage, compliance, and adherence contributes to the scepticism on MDA effectiveness. A systematic review on MDA strategies observed methods to estimate coverage and compliance are often not reported [7] or, when reported, definitions vary. Coverage may be estimated by taking the whole population[15], residents in smaller units of analysis (household or compounds)[16], or only those eligible for treatment[17]. Trials also differ on the amount of doses necessary to determine adherence to treatment. This can be as little as receiving treatment at any point in the intervention[17], completing a component of the treatment[18], or taking the full medication regimen[19]. The inconsistencies in the definitions and use of these indicators have a direct impact on the quality of the data collected, and, ultimately, on the arguments used to justify MDA implementation in already constrained health systems[20–22].

It has been recently suggested that ivermectin (IVM), commonly used for the control of onchocerciasis and lymphatic filariasis, may also play a role in malaria control and elimination. Indeed, IVM is toxic to *Anopheles* mosquitoes when they take a blood meal from a host that has recently received the drug. This provides the opportunity of killing mosquitoes that have escaped conventional vector control interventions[23], e.g. those that bite outdoors[24,25]. Combining an efficacious anti-malarial with IVM may have a synergistic effect as the former would reduce the population parasite biomass and provide post-treatment prophylaxis while the latter would reduce vector densities[26,27]. Eventually, IVM would reduce the minimal coverage required by MDA as mosquitoes, by feeding on several individuals over a short period, may also take a toxic dose of IVM from one of them. Transmission models suggest that adding IVM to a MDA intervention may interrupt transmission where standard MDA would be insufficient[28].

Factors influencing the decision-making process at different stages of an MDA implementation process, from enrolment to adherence, were investigated in the framework of a large cluster randomized trial (the MASSIV trial) assessing the effect of MDA with dihydroartemisinin-piperaquine (DP) and IVM in The Gambia.

METHODS

The MASSIV trial

The trial was implemented in the Upper River Region (URR) in eastern Gambia, where the incidence of malaria is 1.7/PYAT[29]. This is an area of marked seasonal malaria transmission, with low vector density and high vector survival (parous rate 81-91% in URR as compared to 27-71% in other regions)[29]. Despite high coverage of standard control interventions—namely long-lasting insecticidal nets (LLINs), indoor residual spraying (IRS), Seasonal Malaria Chemoprevention (SMC), and artemisinin-based combination therapy (ACT)—URR is the Gambian region with the highest burden of malaria[30].

Thirty two study villages with a population between 140 and 700 each were identified in the south bank of the URR and randomly assigned to either the intervention or the control arm. Most villages were inhabited by a single ethnic group, the most common of which was Fula followed by Mandinka. Villages are led by an Alkalo, or village chief, and are made up of compounds, an enclosed space containing one or several households belonging to the same extended patrilineal family. The main economic activity is subsistence farming with a heavily reliance on remittances[31].

Prior to the MASSIV trial's enrolment process, community sensitization meetings took place in all trial villages. Sensitization meetings were events where the trial and its details were introduced to the community by MRC field staff after receiving permission from the village Alkalo. The intervention was implemented with 3 MDA rounds per year, for 2 years, just before and at the beginning of the malaria transmission season. During each round, DP and IVM were administered as pills at the recommended dosage according to body weight over the course of 3 days. The primary endpoint was malaria prevalence determined by molecular methods at the peak of the second transmission season (November 2019)[32]. Data reported in this manuscript correspond to the first year of intervention.

Study design

This social sciences study used a sequential exploratory mixed-methods design [QUAL -> quan][33]. Initial qualitative research was implemented between July and November 2018, starting before the community

sensitization meetings and lasting through the third MDA round. Data were collected in all villages, intervention and control alike, and informed the design of the quantitative component carried out in January-February 2019.

Qualitative strand

Rationale. This strand focused on understanding the decision-making process for both those who accepted and declined being part of the trial, the trial effects on the residents' daily activities, and the barriers and enabling factors facilitating uptake of the intervention at individual, family and community level.

Data collection. Initial qualitative research was conducted through ethnographic observations of all trial components, including sensitization meetings, the consent and trial enrolment processes, as well as treatment administration in all intervention villages. In-depth interviews (IDIs) and focus group discussions (FGDs) were conducted with the aid of trained field workers fluent in local languages.

Sampling strategy. Selection was purposive to allow for maximum variation and to further explore emergent themes. Community leaders, individuals who accepted or declined to take part in the trial, research team, and relevant stakeholders identified by the study team were included in this study.

Data analysis. Qualitative analysis was a continuous, flexible, and iterative process, where data were analysed in the field and further research was conducted to confirm or refute preliminary findings until saturation was reached. All discussions were recorded and transcribed verbatim by the research team. Raw data were processed in their textual form and coded to generate analytical themes for further analysis using NVivo Qualitative Data Analysis software (CITE software).

Quantitative strand

Rationale. The survey focused on knowledge of the trial, decision-making processes around involvement, spread of trial-related information, and social influences, as well as perceived risks, burdens, and benefits. In addition, data were collected on the details and costs associated with the last time the respondents sought treatment for malaria. The questions and potential

responses were framed upon the initial findings of the qualitative research strand.

Data collection. A cross-sectional survey was carried out in all 16 intervention villages and targeted individuals aged at least 12 years, regardless of level of involvement in the trial. Surveys were administered using Epi Info v. 7 by trained field workers using Android tablets. Data were synchronized with each tablet daily and regularly checked for quality. Once all surveys were conducted, data were exported into Excel to be analysed in STATA version 13.

Sampling. A sample size of 850 (rounded up to 900) was calculated in order to estimate an odds ratio of at least 1.5 as part of a multinomial logit regression for an outcome variable with 3 levels (no adherence, low adherence, and high adherence). However, during the analysis stage, the decision was made to combine no and low adherence into one category, resulting in binary logistic regression (no/low adherence and high adherence), which, incidentally, has lower sample size requirements. Per-village sample size targets were based on the proportion of the village's population size to the total population of all intervention villages. Respondents were randomly selected from census data collected by the research team in November 2018. If a selected individual was unavailable or declined to be surveyed, another individuals of the same gender and age bracket was recruited from the census data.

Data analysis

Statistical analysis included frequencies of relevant variables based on survey responses and bi- and multi-variate analysis of selected variables to test for associations and predictors of the main outcome variables. To mirror the general criteria used by the trial, the analysis considered four endpoints:

1. *Consent and enrolment*: the proportion of surveyed individuals who self-reported providing written informed consent to participate in the trial (some of whom signed with their thumbprint);
2. *Coverage*: the proportion of surveyd individuals included in this study who stated having taken the trial medication at least once at any point during the MDA;

3. *Self-reported adherence:* the proportion of individuals self-reporting the number of days having taken the medication, classified as: a) no/low adherence (0-6 times) and b) high adherence (7-9 times);
4. *Clinical card adherence*: the proportion of surveyed individuals with a) no/low adherence (0-6 times) or b) high adherence (7-9 times) according to the clinical cards provided by the trial.

Ethics

All respondents and their guardians (when under 18 years old) were explained the purpose of the study by field staff and gave informed consent or assent before being included in the qualitative or quantitative strands. Considering that the act of signing documents is not common practice for local populations and that it could produce mistrust towards the study team, we favoured oral over written consent. Both studies were approved by the Institutional Review Board of the Institute of Tropical Medicine, Antwerp, Belgium, by the Scientific Coordinating Committee and the Gambian Government/MRC Joint Ethics Committee in The Gambia.

RESULTS

Respondents characteristics

Qualitative strand

There were 157 in-depth and key informant interviews and 11 Focus Group Discussions (FGDs) conducted across the 32 villages. Respondents included village inhabitants, many of them holding community positions such as Alkalos, Chair of the Village Development Committees (VDC), traditional birth attendants (TBAs), village health workers (VHWs), and youth leaders. In addition, village residents, regardless of whether or not they took part in the trial, and MRC field staff were interviewed. Most respondents were women, belonging to the Fula ethnic group, and engaged in farming as their primary activity.

Quantitative strand

The survey included 864 respondents across the 16 intervention villages. There were no refusals. The majority of respondents were female (66%), belonged to the Fula ethnic group (73%), and listed farming as their primary

activity (80%). The median age was 29 (IQR: 19-41); 34% (294/864) reported previous participation in MRCG-affiliated research or programmes (Table 1).

Involvement in the MDA trial

Consent and enrolment, coverage, and adherence

Overall, 722 (84%) survey respondents self-reported to have provided written informed consent/assent and enrolled in the clinical trial; 70% (606) had taken the treatment at least once. Almost two third (62%, 534/864) of respondents self-reported no/low adherence and the rest (38%) high adherence. The trial clinical card was available at the time of the survey for 295 (34%) individuals; about half 45% (134/295) had evidence of low adherence (Table 2). It was possible, with the trial clinical card, to estimate adherence by round. The highest uptake was achieved by the first MDA round, followed by the third round. In addition, during each round, uptake decreased fron dose 1 to dose 3 (Fig. 1). Self-report of treatment (mean 6.9; SD 2.7) was very similar yet significantly higher than the information on the trial card (mean 6.5; SD 2.7) (paired ttest p-value = 0.001), though the values were highly correlated (0.7).

Barriers to individual involvement in the MDA

Multiple factors affected respondents' abilities or desires to take the trial medication. Some factors were more relevant at particular phases of the trial; others, such as farming responsibilities, were reported as relevant in all phases, from enrolment to adherence. Interestingly, of those who had enrolled in the trial, 16% (n=142) did not take the medication. Some of them, though enthusiastic to enrol and promote uptake of the intervention among their communities, never intended to be treated:

"R: We went from one compound to another to inform them to come out [because] the MRC staffs have come.
I: Did you take the medication?
R: I did not take the medicine because of the reason I told you that after I take medicine it makes me sick and makes me vomit." (Village TBA)

"R: Since they [MRC] start to give medication in the village I was the one working with them. I have not had anyone complain that he or she will not drink the medication anymore when the MRC people bring the medication.
I: Do you drink the medication?

R: No, I have not drunk the medication.

I: Why is it that?

R: You know since the MRC people came here, I am the one attached working with them. I had an emergency: one of my sisters was sick in [another village], her husband was not there, and I was the one responsible to take her to the health facility. Before I came back, I found that time has delayed, so that was the reason why I could not drink the medication." (Male adult)

Travel/mobility

Having travelled or temporarily being away from the village was the primary reason for not enrolling in the trial (47% of those who did not enrol) or not taking all nine doses of the study medication (41% of those who took < 9 doses) (Table 3). Those in the age category 18-25 years were significantly less likely to take the medicine at all or have high adherence (Table 4). When asked to elaborate on this finding, respondents explained that this age group was the least likely to take part on the trial because they travel for employment opportunities. Though some may return to assist in farming, young men were the most likely to travel to the coast or abroad during the time of the MDA:

"No, I didn't drink the medication. By then I was at the North Bank doing some electrical work. It seems like I am the guardian, but I don't drink the medication because that very day didn't find me here. But my wife and my children have all taken the medication." (Village mobilizer)

Being away from the village at the time of the MDA round and time constraints related to economic activities - particularly farming - were also important reasons for not enrolling in the trial or not fully adhering to medication: 18% of those who did not enrol and 17% of those who did not complete it stated it was because they were too busy at that time (Table 3). This can be explained by the fact that the timing of the MDA and malaria season overlaps heavily with the rainy season, the most intense period of agricultural production in this region:

"Some people are working on their groundnuts and coos farms, this is what we depend on for survival. We have only two months remaining for the farming period to be completed so we need to work harder." (VDC Chairman)

Implementation issues

Implementation issues impacting medicine uptake included misinterpreting or disagreeing with the conditions or logistics of the MDA, such as distribution times and locations, enrolment opportunities, and eligibility criteria. The requirement to fast for 3 hours before and after medicine intake (for DP) was said to be an obstacle for their regular activities (such as farming) and, for some, was sufficient to refuse taking the medication.

Lack of privacy

As part of the eligibility requirements, women of reproductive age (15-49 years old) were required to undergo a pregnancy test. The implementation of the pregnancy tests varied by village, but it was often a source of concern due to privacy and other issues. In several villages, the location of the MDA lacked a private toilet facility and the results were often read at the same table where people registered. In some cases, women went home to collect their sample, but this required carrying an urine sample across the village. For many, particularly younger women and adolescents, this was a sufficient reason not to enrol or return for additional doses of the medication:

"We all [the entire compound] went to take the medicine, but I was asked to give my urine sample. I told them I am not married, and if it is about pregnancy, I know nothing has happened to me but they insisted that I must give my urine sample before they give me the medicine (…) Because the entire compound was there, and they asked me to give my urine sample, I refused because I am NOT having any relationship with any man, so I would not do it." (Adolescent female)

"R: It [the pregnancy test] was done in the open [space], so people were sitting there. When you come and give them the urine sample, they will place it there and people will be sitting there looking at it (…) It should not happen like that.
I: And when did you decide to stop taking the medicine?
R: I stopped taking the medicine last month.
I: Can you tell us why? Anything that made you to stop taking the medicine?
R: Nothing happened, just on menstruation those days. That is why I did not go there." (Adult female)

Knowledge of medicine and perceived side effects

Respondents' personal beliefs also played a role in determining whether to enrol in the trial or continue taking the medicine. Some stated that they were too old for the treatment and others did not consider allopathic medicine as the most effective course of action for treating malaria:

"Well, it is a long time I don't drink medication; I mostly depend on herbs." (Village TBA)

Among those surveyed, 13% said they did not enrol and 10% said they did not fully adhere due to what they considered side effects of the medication (Table 3). Side effects reported by respondents during IDIs included excessive sweating, diarrhoea, vomiting, rash, dizziness, stomach pain, and burning chest or heart. Respondents reported having stopped the medicine intake as a result of personally experiencing or hearing of other community members with such symptoms:

"I have drunk the medication once, but I don't continue drinking it anymore because since I drink the medication day before yesterday me and my wife vomited a lot, so this is why I will not go and drink the medicine today although I have finished drinking the medication in the first round." (Adult male)

Specific concerns regarding the mosquitocidal effect of ivermectin were also mentioned:

You gave someone medication to take and when mosquito bites you that mosquito dies, it will also kill flies and lice and bedbugs… Will that not affect the person who took that medicine? That is the reason why some refuse." (Alkalo)

However, though rarer, side effects were not always considered to be a negative consequence of the medication: some respondents described those symptoms as a clear sign that the medicine was having its intended effect.

<u>Enabling factors for individual involvement in the MDA</u>

The most significant enabling factors at all stages included: recognizing malaria as a health concern, believing the trial's benefits, and attending the sensitization meetings.

Recognizing malaria as a health concern

Both the qualitative and quantitative data showed that although there is a general perception that malaria has substantially declined in the last few years (63% of respondents), it is still considered the most serious health concern in the intervention area as stated by IDI respondents. Despite being a medically pluralistic population that uses Western biomedicine, herbalists and marabouts, respondents reported that going to health facilities is the preferred (87%) and most common option when they experience malaria symptoms for themselves (60%) or a child (44%) (Table 5).

Inability to perform income-generating activities was cited as the most common non-health impact of malaria (78%), followed by missing household responsibilities (67%), and missing school (57%). However, the costs associated with malaria medication (45%), visiting the health facility (41%), and transport to the health facility (38%) were also named as important consequences of malaria (Table 5). Furthermore, the total self-reported costs of the last malaria-related visit to the health centre (the accumulating costs of medication, fees, food, and transport) were significantly associated with increased adherence to the trial for each outcome variable: those who paid more were more likely to enrol, take the medication at least once, and have high adherence (Table 4).

Local communities examined the costs associated with malaria not only as the result of the direct investment necessary to treat it, but also as the cost derived from having to go to the health facility during the busiest time of the year:

"When [field nurse] and team come here, I gather all my family and ask them to go and take the medicine. I make sure all the children take the medicine for three times. I know I am comfortable when they are healthy. I will not be visiting the healthy facility always, I have been spending two, three hundred dalasi to buy medicine; therefore, when I am to stay healthy without paying a dalasi, do you think I will not take that seriously?" (Adult male)

"When the person develops any health problem is his own responsibility. From here to Basse the fare is seventy dalasi and whilst you are in Basse you cannot stay all day without food; therefore, if you people come all the way from Basse

and bring us medication here if we accept taking the medication is for our own good and whoever refuses to take the medication refuses at his own detriment." (Adult male)

Perceived benefits of the trial

The most common perceived benefits of participating in the trial were "improved health" (70%) and preventing malaria (45%). Believing on the trial's benefits was significantly associated with higher levels of adherence in both bi- and multi-variate analysis (Table 4). Though only a sparse number of respondents cited access to medical personnel or transportation as a benefit on their own, when prompted, 68% and 50%, respectively, said these factors were important trial's benefits (Table 5).

"Our thoughts with MRC are that they are good and they have good medication, and if you are enrolled with the MRC, if you happen to get sick, they give you free transport from your home to the health facility. After treatment they send you home without paying anything and when they give you medication, you will not pay anything either." (TBA female)

Receiving the medication was explained along the same line of thought, not necessarily as an individual health protective measure, but as a benefit some members of the family should receive on behalf of the other:

"My elder brother is a motorcycle mechanic. He works the whole day and before he comes back is already late. My father is also a farmer who goes and chases animals at the farms from morning until evening to make sure that the farm is not invaded by animals, and the other two are women that are in the compound are all breastfeeding, so they can't come. That is why for me as I have time I came to participate in the MDA." (Adult female)

Attending community sensitization meetings

42% of surveyed women and 38% of surveyed men (41%, n=349, of all those surveyed) reported that they attended the sensitization meetings in their villages (Table 6). Based upon the data from those surveyed, 52% of the attendants were 26-49 years of age. Only 3% of sensitization meeting attendees were girls aged 12-17, many of whom reported during interviews that they were too busy with household responsibilities during the meeting times.

Although IDI respondents were not able to report many details about the information provided at the community sensitization meetings — and in some cases mentioned the meeting was held in a different language than the one spoken in the village — they were generally informed about the main focus (malaria) and activities (medicine distribution) of the trial, as well as the fact that they were not obliged to participate. IDI respondents also referred to the sensitization meetings as means to secure access to material benefits potentially available through their long-term collaboration with MRC:

"When studies like this are conducted in a village, try by all means to allow 3 or 4 people from your family to be part of the study (…) I said this because when there is future benefit for example this [other MRC trial in area]*, when your compound is not participating in that project you don't benefit from this project."* (Adult male)

Social influence

Social influence emerged as an essential factor in all phases of the trial - as both a barrier and facilitating factor. Respondents mentioned they waited to decide on whether or not to take the medication until after they saw the potential side effects it had on other people they know. Physical and social closeness within these villages facilitates this logic. Several respondents mentioned that when external visitors come to the village to introduce a specific intervention, they prefer to postpone their decision to take part on it until the announced services are actually provided, and they can learn from other villagers' experiences. In this particular case, community members' experiences with the first rounds of MDA influenced respondents' decision-making processes subsequent rounds:

"Early on we were scared to drink the medicine because some people were not talking good about the medicine (…) Some were saying that the medicine is good, others were saying that if you drink the medicine it will make you vomit, dizzy, you can have diarrhoea and weak body from it. This is what scared us in taking the medication at the initial stage (…) All this information comes out from our conversations because sometimes during our conversations you will meet with your good friends who will attest to you that this medication is very good, and it is very effective." (Adult female)

Unanimously agreeing with a particular course of action was reported as a sign of cohesion at the village, compound, and household levels, in that order of authority and decision-making power. It was believed that these authority figures should act as caretakers and enforce their decisions as a way to benefit the entire village.

"Well in this situation if the whole village decides on something, I can't dispute it. I will just agree to the decision made by the village leaders, because wherever the village stands that is where I will be." (Adult male)

"When a whole village is doing something, and you are not doing the same, they consider you differently." (Adult female)

IDI respondents often reported not having information about those not taking the medication, or referred to decliners as isolated cases or negative examples of community members that could be internally addressed:

"Yes, a few numbers of them didn't want to participate in the study. (…) But in general, all the compounds are participating (…) the lost people whom you know that they are not educated, and they don't listen to what the educated people are preaching to them, they are the people who spread bad rumours that MRC takes people's blood (…) In any community those kinds of people exist. Even in our village, there are a few of them here, but people will not listen to them because everyone knows what is good and bad, and in such a situation we know how to handle such people in our community." (VDC Chairman)

Although following the decisions of the majority is a well-established social norm, our data also show instances of disagreement among heads of household and village leaders. In those cases, heads of household used their authority to prevent members of their families from taking part in the study:

"I went to [the coast]. When I came back, my elder daughter, I saw the card with her, she went and drink the medicine. I asked my daughter, 'How you got this paper?' and she said, 'it was giving to me by MRC people." I asked the mother, the mother said she was not aware. I was very angry that time, I took the card from my daughter and I keep it. I told the mother that 'I think I told you that I do not have interested of this program, so why in the absence of me

you sent my daughter to go and take the medicine?' So, I was angry." (Adult male)

Having a spouse adhere to the trial was significantly associated with increased adherence for both men and women (Table 6). Women and minors, regardless of their age or marital status, were expected to consult with their husbands or caretakers (or their representatives in case of absence) about their potential adherence to the trial prior to providing informed consent. Women were significantly more likely to require permission to enrol in the trial and needing permission was significantly associated with increased adherence (Table 6).

"I: As a woman, do you agree with reason given by your household head about not to participate in the trial?
R: I will discuss with my husband, try to convince him to participate because it is good. When I discuss with him, if he agrees, we will join, but if he did not agree then I will not join the trial." (Adult female)

"When they came for enrolment in this compound my mother was not around - she went to Basse to sell. The field worker found me here and asked me to come and enrol. I told him that I can't give you my consent in the absence of my mother, because I need to seek consent from her first. Then the field worker reacted and said to me 'you are a grownup person you can decide for yourself.' I was not happy about that reaction from the fieldworker and I still insisted that I can't give consent without my mother (…) Your elder is just your elder, and you know everyone has a position in a family, and for her, she is my parent. And the rest of the children, I am also their elder. Anything I am supposed to do I need permission from her. If she authorizes, I proceed with it; if she doesn't give me permission, I stop it, so I can't go beyond her decision."
(Adult female)

Respondents mentioned their capacity to influence their social environment by advising others about the benefits of working with MRC, which was seen as a form of protecting the interests of the village. Acknowledging that elders act as role models for the village, fieldworkers strived to involve this sector of the population from early stages of the process by physically bringing them to their distribution point and having them motivate others to participate:

"Since the beginning of the MDA when the Alkalo and the village elders came, all the elders came as one group and the drugs were given to them (…) He was the first person who came (…) Because they see their elders taking it, why not them? I think this is the step they are following. Seeing their elders taking it, their grandfathers, fathers taking it in front of them, then they should be behind them." (MRC Field Nurse)

The role of MRC

MRC's long-standing presence in the study area also held considerable influence in trial decision-making and adherence. Respondents expressed high appreciation for receiving —what they consider— health care in their own village and mentioned MRC's presence as an important facilitating factor to increased access to healthcare in general. This appreciation was reported to be retributed with unconditional support and trust in MRC activities. In fact, those who were first told of the trial by an MRC employee were significantly more likely to take the study medicine at least once (Table 4):
"For me and my family, I will never step back when it comes to MRC work." (VDC Chairman)

"Yes, I always tell my people to go and take the medicine, I tell them all the time, I always tell them that MRC does not give medicine that would make people sick; they give medicine to improve our health." (Adult male)

In some cases, community members assumed a more active role and became advocates for the organization:

"My concern regarding the study is that there are people who know why they are drinking this medication, but there are others whom you know they are drinking this medication, but they don't know why they are drinking this medication. They are just drinking it for the sake of drinking. So that being the case, I will take that responsibility before the second round. I will go and meet with these people within the compound and talk to them about why they are drinking this medication so that they will know. If not, in the second round when it is time for the MDA, they will start to take excuses by saying 'I am going to the garden and other places.' But if they are informed, the second round will be much better." (Village mobilizer, male)

Negative past experiences, widely spread rumours regarding MRC financially gaining from the sell of people's blood, and questions regarding research practices also acted as arguments to decline involvement with this particular initiative:

"We were looking at MRC. Like when you participate in an MRC study, they will come for you, but when they find a sick person in the compound, they will not attend to the patient, but they will be interested in taking the healthy person and leave the sick one at home, and that is where we think is faulty. Secondly, we were thinking like when they recruit children in their study, they will take them and bleed them, and you know? People who eat sorrel don't have a lot of blood. This was the problem. We started discussing with them all that, but they just passed us and left. We didn't, this was the issue." (Adult male)

DISCUSSION

MDA requires active individual and community involvement to secure efficacy of treatment[6,7]. This mixed-methods study builds upon previous literature by showing that adherence to MDA is influenced by a multiplicity of individual, social, and implementation considerations constantly interacting and influencing decision-making at each and every stage of the MDA process. The results of this study show that rather than a linear trajectory, involvement is subjected to multiple revaluations from enrolment and consent to medicine intake and adherence to treatment[34,35]. Issues of social influence, concerns regarding secondary effects of the medication, costs associated with malaria, and acceptability of the implementing organization, among other factors, differently affect decision-making processes throughout the trial.

The role that family and community members play on decision making is well known within The Gambian context[8]. These results support the notion that people's level of involvement with and adherence to the trial is heavily influenced by the opinions, perceptions, and actions of their spouses, parents, compound heads, and community leaders. Respondents reported that unanimously supporting a particular course of action or decision made at the village level is a highly valued social norm; therefore, people are further

influenced by social pressure to comply with what has been agreed upon by the community as a whole. Taking part in this particular intervention was described as an expression to support the communal decision of receiving the MRC and the trial medication - a decision that could render benefits not only for the individual, but also for the household, compound, and the entire village, both immediately and in the future [36].

However, this social influence is expressed differently between genders and across the different positions individually held within the village and the household. For women in particular, social factors were highly influential. Women who required permission to take part in the trial, for example, were significantly more likely to enrol, take the medication at least once, and self-report high adherence than those who reported not needing permission. Later on, however, women that initially accepted to enrol and attempted medicine intake, reported having stopped the medication due to a lack of privacy during the process of the pregnancy tests as it might elicit rumours within the village. Social influence acts in this case as a facilitating factor for enrolment, but also as a deterrent for further adherence to treatment. Similarly, having a spouse take the medication was significantly associated with increased enrolment, coverage, and high adherence for both men and women. However, men were still less likely to report high adherence, supporting previous arguments about men's hesitations regarding MDA[37]. These findings highlight the importance of MDA community strategies that target gender-specific contextual factors to address the particular concerns and needs of the local population [6]. Beyond their direct impact on coverage and adherence, issues of privacy and autonomy should be analysed in their ethical dimension as predictors of inclusion among particularly vulnerable populations, such as women of child-bearing age, in implementation research [37–39].

Similarly, attending the sensitization meeting was found to be associated with consenting to enrol in the trial, taking the medication the medications at least once, and adherence to treatment. Although this association may be linked to the importance of information provision on individual decision-making, this conclusion is overly simple. For example, 60% of respondents sampled did not attend sensitization meetings, but 84% consented to enrolment in the trial. Attending the sensitization meeting loses significance with enrolment and coverage in the multi-variable analysis, demonstrating

that other factors - such as perceived benefits - are concurrently involved in the decision-making process.

Previous studies have shown that the decision to take part in a trial in low-income settings often precedes information provision[40] and is made on the basis of non-health related arguments[41]. Expectations generated through the informal spread of information has been identified as particularly relevant, also in The Gambian context[8]. The political connotations of the sensitization process from the respondents' point of view exemplify these dynamics. In this study, community members reported to use sensitization meetings to make themselves and their families visible in the village and MRC-supporting members, as this may render them eligible for any potential benefits. Additionally, by being present at the meetings, community members expressed their political power as part of an internal decision-making processes in the village and could demonstrate their position as supporters of the community's decision.

Local village dynamics should also be considered while explaining the behaviour of those who enrolled in the intervention but had no intention of taking the medication, as well as those who were willing to just partially adhere. This can be interpreted as a non-confrontational and contextually-appropriate resistance strategy that allows villagers to remain autonomous in their personal decision-making in the context of power imbalances existing among community members and sparked by MRC's presence. MRC's particular influence and importance within The Gambia has been extensively documented[41–43] and this study supports this: respondents at large expressed trust in the organization and the desire to accept what they had to offer, particularly as they viewed essential services like transportation and access to increased medical care as benefits of the trial. This close interplay between individual decision-making and larger social dynamics should be considered when explaining enrolment and consent that does not translate into actual medicine intake[35].

Concerns about the potential side effects of the medication were reported as one of the main reasons to reject or interrupt treatment at different stages of the MDA. Although the data do not support a direct association between symptoms reported by the study respondents and the specific medications used in this MDA (all adverse events were reported regardless of their

relation to the medication), it is important to point out that symptoms such as fever, headache, nausea, vomiting, dizziness, and itching have been previously reported for the medications used in this trial[15,44]. Community concerns regarding safety of IVM's mosquitocidal effect in humans should be seriously considered and adequately addressed in existing communication spaces with local communities, as they can overlap with those reported side effects and influence the uptake of and adherence to interventions.

Adding to the complexity of the decision-making process, the data support that the direct and indirect costs associated with having malaria (particularly the cost of the last malaria-related visit to the health facility) are of importance throughout all phases of the trial[11]. This continues to hold true when all other factors, such as social influences and individual demographics are considered. The possibility of receiving preventative treatment directly in their villages to avoid these expenses acts as an important justification to individually take part in the trial and motivate others, especially within the same family unit, to do the same.

There are important limitations in this study. At the moment of writing this manuscript, access to final figures of coverage and adherence for the general trial that could serve as reference to contrast the results has not been possible. Although this study only aimed to capture trends in coverage and adherence that could inform future MDA rounds, both coverage and adherence data were below the ones originally targeted for this trial during the first year of implementation. The data hereby presented, however, cannot be extrapolated to the general trial as this study could not include eligibility criteria in the calculations.

There were also methodological challenges to accurately assess individual involvement in MDA. This study utilized two different approaches to assess the surveyed respondents' consent and enrolment, coverage, and adherence: self-reported data and in-hand trial participation cards. Both approaches showed important limitations. In the case of self-reporting, it was difficult to frame survey questions in such a way that accurately responded to specific medication intake during each administration, in each one of the days that it was provided, and during the three rounds of MDA. The fact that this MDA included two different medications—often not distinguished by respondents— in each administration further complicated matters. The

question was finally posed as "*How many times did you take the medication during the MDA*?"; this question cannot assess the sequence of intake or allow for us to calculate per-round coverage, but reflects the recollection of single times in which it happened. Field workers were trained on how to deal with questions or confusion from respondents. For the latter approach, difficulties derived from the possession of participation cards by village members. Many respondents reported that their cards were either lost or collected by MRC personnel after the trial. In addition, there were discrepancies between some respondents having self-reported not taking the medicine but having clinical cards with recorded doses. Although only minor differences emerged from the data collected through these different approaches, these discrepancies highlight the need to improve the data collection methods of trials and their concurrent studies to accurately measure progress towards elimination[21].

Of note, the word 'participant' was purposely avoided in this manuscript. The rationale for this decision is two-fold: first, there is a need to avoid any confusion between individuals involved in this sub-study (respondents) and individuals involved the trial in general; second, and more important, this study made evident that local populations have a broader understanding of what participating in a trial of this nature means. It can include activities such as being in touch with clinical teams to replicate information at the village level or cleaning and organizing the space where the medicine administration will take place. Since assessing participation in its political and social dimensions is beyond the scope of this paper, the decision was made to avoid the term and to report on this subject in upcoming manuscripts.

CONCLUSION

Factors discussed in the previous sections demonstrate the complexity of interactions influencing adherence to multidose MDA regimens. From consent to medicine intake, local residents constantly revaluated their involvement with the trial based on multiple individual and social factors, including potential or actual side effects of the medication, the timing of the MDA in regard to economic demands, previous information regarding the intervention, as well as perceptions and experiences of other family members and community members in relation to the medication and its providers. In the same vein that authors have proposed to reimagine malaria treatment,

diagnostics, and surveillance during this elimination era[45,46], this study demonstrates the need to invest resources to improve critical indicators and more accurately report adherence to emerging elimination tools. In the case of MDA, it is essential that more complex ideas about individual and community involvement are incorporated in the understanding of the internal heterogeneity that could significantly limit the effectiveness of the intervention.

TABLES AND FIGURES

Table 1. Demographic information of surveyed respondents

N=864		n (%)
Age	Median (IQR)	29 (19-41)
	Mean (SD)	32.5 (16.1)
Gender	Male	295 (34)
	Female	566 (66)
Ethnic group	Fula	626 (73)
	Mandinka	172 (20)
	Serahule	56 (5)
	Other	9 (1)
Marital status	Never married	240 (28)
	Married	580 (67)
	Separated/divorced	9 (1)
	Widowed	31 (4)
Primary activity	None	65 (8)
	Farming	694 (80)
	Herding	65 (8)
	Business/trade	131 (15)
	Domestic work	263 (30)
	Other	56 (6)
Education	None	357 (41)
	Standard	243 (28)
	Quranic	261 (30)
Household status	Compound head	69 (8)
	Household head	24 (3)
	Compound member	226 (26)
	Wife	360 (42)
	Child	182 (21)
	Other	2 (0)
Previous MRC experience	Yes	294 (34)
	None	547 (64)
	Doesn't know	10 (1)
	Doesn't remember	3 (0)

Table 2. Consent and enrolment, coverage, and adherence of surveyed respondents based on self-report and clinical cards

	Of total surveyed n=864 n (%)	Of those consented /enrolled n=722 n (%)	Of those who took medicine 1+ times n=606 n (%)	Of those with clinical card n=295 n (%)
Based on self-report				
Consent and enrolment	722 (84)	-	-	-
Coverage (1 or more doses)	606 (70)	606 (84)	-	-
No/low adherence (0-6 doses)	534 (62)	392 (54)	276 (46)	115 (40)
High adherence (7-9 doses)	330 (38)	330 (46)	330 (55)	173 (60)
Based on clinical card				
No/low adherence (0-6 doses)	134 (16)	133 (18)	130 (21)	134 (45)
High adherence (7-9 doses)	161 (19)	160 (22)	158 (26)	161 (55)

Figure 1. Percent of surveyed respondents with clinical cards who took trial medication by dose and round

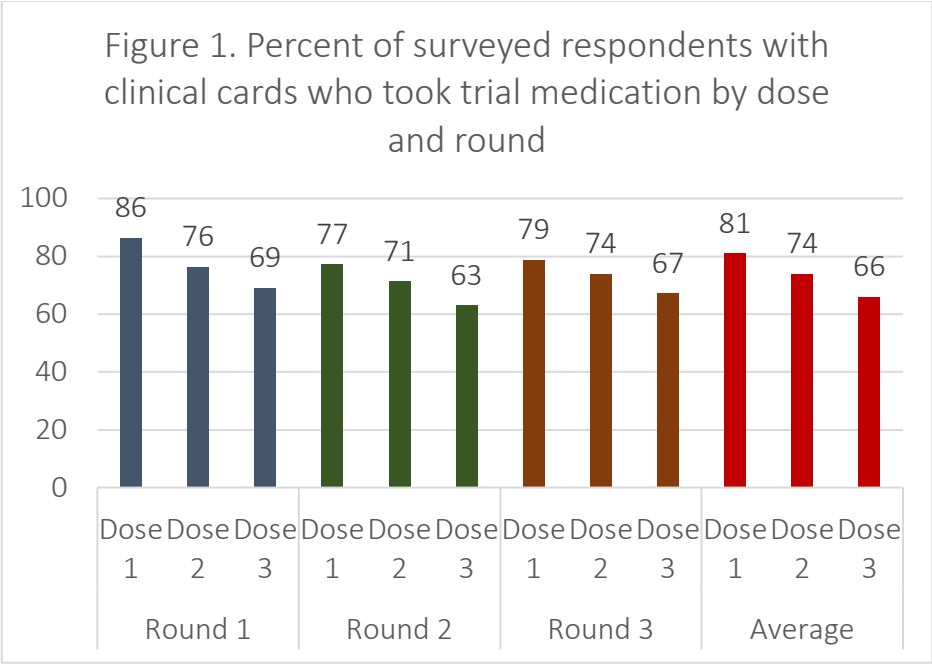


Table 3. Reasons for not enrolling in trial or completing full regimen based on surveyed respondents

Reasons for not enrolling in trial	n=140 n (%)	Reasons for not taking full regimen	n=566 n (%)
Didn't know reason for medicines	5 (4)	Didn't know more than 1 dose/round	4 (1)
Pregnant	14 (10)	Didn't know MRC was coming	10 (2)
Sick at time	6 (4)	Told to come later	4 (1)
Away from village	66 (47)	Ate before	1 (0)
Wouldn't be here for MDA	1 (1)	Away from village	234 (41)
Busy at time	25 (18)	Too busy	96 (17)
Afraid of side effects	18 (13)	Side effects of medication	59 (10)
Healthy; Doesn't need meds	2 (1)	Meds made others sick	12 (2)
Too much medicine	1 (1)	Too much medicine	11 (2)
Did not attend sensitization	2 (1)	Didn't like taste	17 (3)
Does not like medicine	10 (7)	Got malaria	2 (0)
Medicines don't work	0 (0)	Took too much time	0 (0)
Did not want to fast	1 (1)	Other	34 (6)
Doesn't know	6 (4)	Doesn't know	7 (1)
No answer	1 (1)	No answer	5 (1)

Table 5. Trial beliefs and malaria health-seeking behaviours of surveyed respondents

n=864		n (%)
Believe malaria to be a problem		
	Yes	220 (25)
	Yes, but less now than in past	544 (63)
	No	32 (4)
	Doesn't know	35 (4)
	No answer/missing	33 (4)
Non-health impacts of malaria, prompted, could choose multiple (n=561)		
	Costs of health facility	229 (41)
	Costs of medicines	251 (45)
	Costs of transport	215 (38)
	Missed work	440 (78)
	Missed school	359 (57)
	Missed household responsibilities	374 (67)
	None	6 (1)
	Doesn't know	14 (3)
	Other	2 (0)
Benefits to trial, unprompted, could choose multiple		
	None	58 (7)
	Access to study medicine	49 (6)
	Access to medical personnel	7 (1)
	Access to other medicines	4 (0)
	Improved health	609 (70)
	Access to transportation	1 (0)
	Material benefits	1 (0)
	Prevents malaria	389 (45)
	Doesn't know	61 (7)
	No answer	5 (1)
Benefit: Access to medical personnel, prompted		

	Yes	586 (68)
	No	122 (14)
	Doesn't know	81 (9)
	No answer/missing	75 (9)
Benefit: Access to transportation, prompted		
	Yes	431 (50)
	No	277 (32)
	Doesn't know	84 (10)
	No answer	72 (8)
Preferred treatment for malaria		
	Nothing	7 (1)
	Treat at home	27 (3)
	Village health worker	7 (1)
	Health facility	748 (87)
	MRC	61 (7)
	Other	3 (0)
	Doesn't know	6 (1)
	No answer	5 (1)
Treatment sought for last malaria: Self, could choose multiple		
	Nothing	1 (0)
	Treat at home	23 (3)
	Go to VHW	23 (3)
	Go to health facility	518 (60)
	Go to traditional healer	3 (0)
	Go to MRC	26 (3)
	Other	4 (0)
	Doesn't know	7 (1)
	No answer	1 (0)
	Non-applicable	281 (33)
Treatment sought for last malaria: Child, could choose multiple		
	Nothing	0 (0)
	Treat at home	10 (1)
	Go to VHW	8 (1)

	Go to health facility	383 (44)
	Go to traditional healer	1 (0)
	Go to MRC	12 (1)
	Other	6 (1)
	Doesn't know	1 (0)
	No answer	0 (0)
	Non-applicable	188 (22)

Table 6a. Gender differences in social influence factors of surveyed respondents

	Men n (%)	Women n (%)	Total n (%)	p-value
Needed permission to participate	156 (60)	436 (82)	592 (75)	**< 0.0001**
Husband/Wife took medication	121 (41)	195 (35)	316 (37)	0,066
Compound head took medication	158 (54)	334 (59)	492 (58)	0,11
Attended sensitization meeting	112 (38)	237 (42)	349 (41)	0,268

Table 6b. Associations between social influence factors and outcome variables across genders

	Consent/Enrolment		Coverage		Self-Reported: High adherence	
Social influence	Men	Women	Men	Women	Men	Women
Needed permission	0.8 (0.4-1.6)	**4.4 (2.2-9.1)**	**1.3 (0.7-2.4)**	**3.7 (2.3-6.2)**	1.5 (0.8-2.6)	**2.12 (1.3-3.5)**
Spouse took meds	**3.5 (1.8-6.9)**	**2.6 (1.3-5.0)**	**2.5 (1.4-4.5)**	**1.5 (1.0-2.3)**	**2.6 (1.5-4.5)**	**2.3 (1.6-3.3)**
Compound head took meds	1.1 (0.6-1.9)	**2.0 (1.1-3.3)**	**1.9 (1.1-3.3)**	**1.5 (1.0-2.2)**	1.1 (0.7-2.0)	1.2 (0.8-1.8)

References

1. Webster JP, Molyneux DH, Hotez PJ, Fenwick A. The contribution of mass drug administration to global health: past, present and future. *Philos Trans R Soc B Biol Sci*. 2014;369(1645):20130434. doi:10.1098/rstb.2013.0434
2. World Health Organization. Mass drug administration, mass screening and treatment and focal screening and treatment for malaria. In: *Malaria Policy Advisory Committee Meeting*. ; 2015.
3. Poirot E, Skarbinski J, Sinclair D, Kachur SP, Slutsker L, Hwang J. Mass drug administration for malaria. *Cochrane Database Syst Rev*. 2013. doi:10.1002/14651858.CD008846.pub2
4. Kaehler N, Adhikari B, Cheah PY, et al. The promise, problems and pitfalls of mass drug administration for malaria elimination: a qualitative study with scientists and policymakers. *Int Health*. 2019;11(3):166-176. doi:10.1093/inthealth/ihy079
5. Newby G, Hwang J, Koita K, et al. Review of Mass Drug Administration for Malaria and Its Operational Challenges. *Am J Trop Med Hyg*. 2015;93(1):125-134. doi:10.4269/ajtmh.14-0254
6. Whittaker M, Smith C. Reimagining malaria: five reasons to strengthen community engagement in the lead up to malaria elimination. *Malar J*. 2015;14(1):410. doi:10.1186/s12936-015-0931-9
7. Adhikari B, James N, Newby G, et al. Community engagement and population coverage in mass anti-malarial administrations: a systematic literature review. *Malar J*. 2016;15(1):523. doi:10.1186/s12936-016-1593-y
8. Dierickx S, O'Neill S, Gryseels C, et al. Community sensitization and decision-making for trial participation: A mixed-methods study from The Gambia. *Dev World Bioeth*. 2018;18(4):406-419. doi:10.1111/dewb.12160
9. Dierickx S, Gryseels C, Mwesigwa J, et al. Factors Associated with Non-Participation and Non-Adherence in Directly Observed Mass Drug Administration for Malaria in The Gambia. Sullivan DJ, ed. *PLoS One*. 2016;11(2):e0148627. doi:10.1371/journal.pone.0148627
10. Pell CL, Adhikari B, Myo Thwin M, et al. Community engagement, social context and coverage of mass anti-malarial administration: Comparative findings from multi-site research in the Greater Mekong

sub-Region. Rutebemberwa E, ed. *PLoS One*. 2019;14(3):e0214280. doi:10.1371/journal.pone.0214280
11. Jaiteh F, Masunaga Y, Okebe J, et al. Community perspectives on treating asymptomatic infections for malaria elimination in the Gambia. *Malar J*. 2019;18(1):39. doi:10.1186/s12936-019-2672-7
12. Dial NJ, Ceesay SJ, Gosling RD, D'Alessandro U, Baltzell KA. A qualitative study to assess community barriers to malaria mass drug administration trials in the Gambia. *Malar J*. 2014;13(1):47. doi:10.1186/1475-2875-13-47
13. Parker M, Allen T. Does mass drug administration for the integrated treatment of neglected tropical diseases really work? Assessing evidence for the control of schistosomiasis and soil-transmitted helminths in Uganda. *Heal Res Policy Syst*. 2011;9(1):3. doi:10.1186/1478-4505-9-3
14. World Health Organization. Mass Drug Administration for Falciparum Malaria: A practical field manual. *Who*. 2017.
15. von Seidlein L, Peto TJ, Landier J, et al. The impact of targeted malaria elimination with mass drug administrations on falciparum malaria in Southeast Asia: A cluster randomised trial. Beeson JG, ed. *PLOS Med*. 2019;16(2):e1002745. doi:10.1371/journal.pmed.1002745
16. Okebe J, Ribera JM, Balen J, et al. Reactive community-based self-administered treatment against residual malaria transmission: Study protocol for a randomized controlled trial. *Trials*. 2018;19(1):126. doi:10.1186/s13063-018-2506-x
17. Kamga G-R, Dissak-Delon FN, Nana-Djeunga HC, et al. Audit of the community-directed treatment with ivermectin (CDTI) for onchocerciasis and factors associated with adherence in three regions of Cameroon. *Parasit Vectors*. 2018;11(1):356. doi:10.1186/s13071-018-2944-z
18. Patouillard E, Conteh L, Webster J, Kweku M, Chandramohan D, Greenwood B. Coverage, adherence and costs of intermittent preventive treatment of malaria in children employing different delivery strategies in Jasikan, Ghana. Braga EM, ed. *PLoS One*. 2011;6(11):e24871. doi:10.1371/journal.pone.0024871
19. Pongvongsa T, Phommasone K, Adhikari B, et al. The dynamic of asymptomatic Plasmodium falciparum infections following mass drug administrations with dihydroarteminisin–piperaquine plus a single low dose of primaquine in Savannakhet Province, Laos. *Malar J*.

2018;17(1):405. doi:10.1186/s12936-018-2541-9
20. Kingori P, Gerrets R. Morals, morale and motivations in data fabrication: Medical research fieldworkers views and practices in two Sub-Saharan African contexts. *Soc Sci Med*. 2016;166:150-159. doi:10.1016/j.socscimed.2016.08.019
21. Peeters Grietens K, Gryseels C, Verschraegen G. Misdirection in the margins of malaria elimination methods. *Crit Public Health*. 2019;29(4):390-400. doi:10.1080/09581596.2019.1597965
22. Cheah PY, White NJ. Antimalarial mass drug administration: Ethical considerations. *Int Health*. 2016. doi:10.1093/inthealth/ihw027
23. Steketee RW, ter Kuile FO. Editorial Commentary: Ivermectin as a Complementary Strategy to Kill Mosquitoes and Stop Malaria Transmission? *Clin Infect Dis*. 2015;60(3):366-368. doi:10.1093/cid/ciu802
24. Foy BD, Kobylinski KC, Silva IM da, Rasgon JL, Sylla M. Endectocides for malaria control. *Trends Parasitol*. 2011;27(10):423-428. doi:10.1016/j.pt.2011.05.007
25. Reddy MR, Overgaard HJ, Abaga S, et al. Outdoor host seeking behaviour of Anopheles gambiae mosquitoes following initiation of malaria vector control on Bioko Island, Equatorial Guinea. *Malar J*. 2011;10(1):184. doi:10.1186/1475-2875-10-184
26. Alout H, Foy BD. Ivermectin: a complimentary weapon against the spread of malaria? *Expert Rev Anti Infect Ther*. 2017. doi:10.1080/14787210.2017.1271713
27. Seaman JA, Alout H, Meyers JI, et al. Age and prior blood feeding of Anopheles gambiae influences their susceptibility and gene expression patterns to ivermectin-containing blood meals. *BMC Genomics*. 2015;16(1):797. doi:10.1186/s12864-015-2029-8
28. Slater HC, Foy BD, Kobylinski K, et al. Ivermectin as a novel complementary malaria control tool to reduce incidence and prevalence: a modelling study. *Lancet Infect Dis*. 2020;20(4):498-508. doi:10.1016/S1473-3099(19)30633-4
29. Mwesigwa J, Achan J, Di Tanna GL, et al. Residual malaria transmission dynamics varies across The Gambia despite high coverage of control interventions. Carvalho LH, ed. *PLoS One*. 2017;12(11):e0187059. doi:10.1371/journal.pone.0187059
30. Mwesigwa J, Okebe J, Affara M, et al. On-going malaria transmission in The Gambia despite high coverage of control interventions: a

nationwide cross-sectional survey. *Malar J*. 2015;14(1):314. doi:10.1186/s12936-015-0829-6

31. Dierickx S, Gryseels C, Mwesigwa J, et al. Community barriers for the implementation of a mass drugs administration for malaria in the Gambia. *Am J Trop Med Hyg*. 2015;93(4):197. https://www.embase.com/search/results?subaction=viewrecord&id=L613370625&from=export.
32. Dabira ED, Soumare HM, Lindsay SW, et al. Mass drug administration with high-dose ivermectin and dihydroartemisinin-piperaquine for malaria elimination in an area of low transmission with high coverage of malaria control interventions: Protocol for the massiv cluster randomized clinical trial. *JMIR Res Protoc*. 2020;9(11):e20904. doi:10.2196/20904
33. Abbato S. Book Review: Foundations of Mixed Methods Research: Integrating Quantitative and Qualitative Approaches in the Social and Behavioral Sciences. *Eval J Australas*. 2009;9(2):60-63. doi:10.1177/1035719X0900900213
34. Adhikari B, Phommasone K, Kommarasy P, et al. Why do people participate in mass anti-malarial administration? Findings from a qualitative study in Nong District, Savannakhet Province, Lao PDR (Laos). *Malar J*. 2018;17(1):15. doi:10.1186/s12936-017-2158-4
35. Muela Ribera J, Hausmann-Muela S, Gryseels C, Peeters Grietens K. Re-imagining adherence to treatment from the “other side”: local interpretations of adverse anti-malarial drug reactions in the Peruvian Amazon. *Malar J*. 2016;15(1):136. doi:10.1186/s12936-016-1193-x
36. Jaiteh F, Okebe J, Masunaga Y, et al. Understanding adherence to reactive treatment of asymptomatic malaria infections in The Gambia. *Sci Rep*. 2021;11(1):1746. doi:10.1038/s41598-021-81468-1
37. Rilkoff H, Tukahebwa EM, Fleming FM, Leslie J, Cole DC. Exploring Gender Dimensions of Treatment Programmes for Neglected Tropical Diseases in Uganda. Gyapong M, ed. *PLoS Negl Trop Dis*. 2013;7(7):e2312. doi:10.1371/journal.pntd.0002312
38. Gopichandran V, Luyckx VA, Biller-Andorno N, et al. Developing the ethics of implementation research in health. *Implement Sci*. 2016;11(1):161. doi:10.1186/s13012-016-0527-y
39. Kamuya DM, Molyneux CS, Theobald S. Gendered negotiations for research participation in community-based studies: implications for

health research policy and practice. *BMJ Glob Heal*. 2017;2(2):e000320. doi:10.1136/bmjgh-2017-000320
40. Paré Toe L, Ravinetto RM, Dierickx S, et al. Could the Decision of Trial Participation Precede the Informed Consent Process? Evidence From Burkina Faso. Choonara I, ed. *PLoS One*. 2013;8(11):e80800. doi:10.1371/journal.pone.0080800
41. Yavuz H, Akgöl S, Say R, Denizli A. Affinity separation of immunoglobulin G subclasses on dye attached poly(hydroxypropyl methacrylate) beads. *Int J Biol Macromol*. 2006;39(4-5):303-309. doi:10.1016/j.ijbiomac.2006.04.009
42. Geissler PW, Kelly A, Imoukhuede B, Pool R. 'He is now like a brother, I can even give him some blood' – Relational ethics and material exchanges in a malaria vaccine 'trial community' in The Gambia. *Soc Sci Med*. 2008;67(5):696-707. doi:10.1016/j.socscimed.2008.02.004
43. Fairhead J, Leach M, Small M. Where techno-science meets poverty: Medical research and the economy of blood in The Gambia, West Africa. *Soc Sci Med*. 2006;63(4):1109-1120. doi:10.1016/j.socscimed.2006.02.018
44. Vanamail P, Ramaiah KD, Subramanian S, Pani SP, Yuvaraj J, Das PK. Pattern of community compliance with spaced, single-dose, mass administrations of diethylcarbamazine or ivermectin, for the elimination of lymphatic filariasis from rural areas of southern India. *Ann Trop Med Parasitol*. 2005;99(3):237-242. doi:10.1179/136485905X29666
45. Chaccour CJ, Kobylinski KC, Bassat Q, et al. Ivermectin to reduce malaria transmission: a research agenda for a promising new tool for elimination. *Malar J*. 2013;12(1):153. doi:10.1186/1475-2875-12-153
46. Beisel U, Umlauf R, Hutchinson E, Chandler CIR. The complexities of simple technologies: re-imagining the role of rapid diagnostic tests in malaria control efforts. *Malar J*. 2016;15(1):64. doi:10.1186/s12936-016-1083-2

Chapter 6

The role of social cohesion in the implementation and coverage of an MDA trial for malaria control in The Gambia: An in-depth comparison of two intervention villages

The women's group informs and entertains everyone with music, dancing, and a song about the MDA

ABSTRACT

Mass drug administration (MDA), used increasingly in malaria eradication efforts, involves administering medication to an entire target population regardless of individual-level disease status. This strategy requires high levels of coverage and compliance. Previous studies have assessed individual and structural factors affecting MDA coverage, but there is a need to better understand the influence and expressions of community dynamics and social structures, such as social cohesion. We conducted a social science study concurrent to an MDA clinical trial for malaria control in The Gambia; ethnographic research was conducted prior to, throughout, and between MDA implementation July-November 2018, January-March 2019, and July-November 2019. We assessed how social cohesion, as expressed by the trial population, affects trial coverage through an in-depth ethnographic analysis of two trial villages, using observations, interviews, and focus group discussions with community members who took the trial medication and those who did not. We found that the villages had unique expressions of social cohesion. This was reflected through community participation in the trial implementation and may have affected coverage and compliance. The village with low coverage expressed a form of social cohesion where members followed advice to participate through a hierarchal system but did not actively participate in the MDA or its implementation. The village with high coverage expressed social cohesion as more participatory: individuals took the directive to participate but contextualized the trial implementation to their needs and wants. We analyse these different expressions of social cohesion and the important differences they make for the coverage and compliance levels reached in the two different villages.

INTRODUCTION

Mass drug administration (MDA) has been used for the reduction and elimination of multiple neglected tropical diseases and is increasingly being used in malaria eradication efforts.[1–3] This strategy involves the administration of medication to an entire target population regardless of individual-level disease status. Computer models suggest that a minimum coverage – in this case, the percent of targeted individuals who complete the MDA drug regimen – of 80% must be reached to achieve the desired clinical and epidemiological outcomes.[4] Achieving high coverage is also an ethical necessity, as it is required to ensure that the benefits of MDA are greater than the risks.[5] Multiple studies have been conducted to better understand causes of high or low coverage across many geographies, particularly Southeast Asia and sub-Saharan Africa.[6,7] With respect to low coverage, findings have shown that people are less likely to comply to MDA when the timing overlaps with harvesting season or a time of high mobility;[8] when there are concerns about the potential side effects of the medication(s);[9] when there is a lack of acceptance of taking medication, especially when asymptomatic;[7,10] or where there is a reluctance to undergo screening procedures such as pregnancy tests.[8,11] Conversely, since many MDAs take place in low-resource settings, it has been well established that people are more apt to enrol and comply in clinical trials when there are additional benefits to participation, such as ancillary medical care or financial or material incentives.[6,7,12–14] There is also evidence that the socio-political environment and social and familial relationships have a great impact on enrolment and compliance.[11,12]

These studies, however, do not thoroughly elaborate on the ways in which - or how - community dynamics and social structures affect trial coverage and compliance. Particularly relevant in this setting is the community dynamic of social cohesion, "a state of affairs concerning both the vertical and the horizontal interactions among members of society as characterized by a set of attitudes and norms that includes trust, a sense of belonging and the willingness to participate and help, as well as their behavioural manifestations."[15] A systematic review found that all definitions of social cohesion contain three main components: 1. The relations and social networks between people, 2. The sense of belonging and attachment of people to a particular group, and 3. A common orientation towards the

"common good."[16] Additionally, when speaking of requirements for social cohesion in South Africa, Burns, et al [17,18] state that an African social cohesion must include five elements: 1. A feeling of belonging 2. Cooperation within the group, 3. Institutional trust, 4. Social and kin relationships, and 5. A shared identity. Regarding health, some studies have shown that social cohesion may help improve individual health and lead to more successful implementation of global health projects within sub-Saharan Africa.[19,20] Yet, much like many of the decision-making models regarding coverage, these studies were focused on the individual level and did not assess the larger impacts of social cohesion at the community level.[20]

In The Gambia, political, familial/kinship, social relationships, and a sense of belonging impact the acceptance, implementation, and success of clinical trials.[11,21–23] These relationships also influence individual decision making and may lead to social pressure.[11] Further, though it is often considered an important part of successful and ethical global health research[24,25] and may lead to increased MDA coverage, the consequential social pressure from community engagement activities may actually coerce individuals to participate in a clinical trial and, therefore, undermine ethical research practice.[26,27] Some of this social pressure may stem from those in positions of leadership who are traditionally incorporated into community engagement activities.[28] Due to their positions of power within communities, village leaders may apply pressure to their community members to participate, which may lead to structural coercion.[26,27] Strong social pressure to comply with research has been shown in the literature regarding community engagement,[26] but little is known on how social pressure stemming from social cohesion may affect research participation and overall MDA coverage.

"Participation" has become increasingly proceduralized and pervasive in medical (and other) contexts that its power as a concept has decreased.[29] Rather than enacting another critique, it may be more beneficial to explore novel understandings of participation that connect to conceptual strands embedded within the communities themselves. Relatedly, as Global Health as a discipline begins efforts to decolonize its practice and research,[30] it is imperative to increase global epistemic justice[31] and recognize the importance of communities' internal logics in creating models of participation in clinical trials, particularly as they relate to the underlying

social dynamics of trial communities.[32] Besides paying attention to the neo-colonial consequences of efforts to achieve diverse inclusion in clinical trials,[33] increasing importance is given to mobilizing non-Western conceptual approaches and epistemologies[34] in global health scholarship. Using a lens of African philosophy concerning communitarianism could be particularly important here, given its wide-ranging societal consequences. Therefore, the purpose of this study is to understand how villages' enactments of social cohesion elicit specific forms of community participation that may impact MDA coverage. We do so by conducting an in-depth comparison of two trial villages with vast differences in coverage during an MDA trial in The Gambia.

METHODS

Study Design, Data Collection and Analysis

The MASSIV Trial and Social Science Research

This study is part of a larger social science study that took place concurrently to the "Mass drug administration of ivermectin and dihydroartemisinin-piperaquine as an additional intervention for malaria elimination (MASSIV)" trial (clinicaltrials.gov, NCT03576313). MASSIV is a Phase III, community-based, cluster-randomized control trial testing the efficacy of MDA with dihydroartemisinin-piperaquine and ivermectin on interrupting the transmission of malaria in the Upper River Region of The Gambia. It was conducted by the Medical Research Council Unit The Gambia (MRC-Gambia) and took place in 32 villages, 16 control and 16 intervention; the overall targeted population in the intervention villages was approximately 5400. Medication was distributed between August - October 2018 and July - September 2019.[35]

The social science study was a mixed-methods ethnographic study focused on understanding the acceptability, coverage, and compliance of MASSIV. In-depth interviews (IDIs), informal conversations, and focus group discussions (FGDs) were conducted among trial participants, trial decliners, village leaders, and trial field staff. In total, 210 IDI and 29 FGDs were conducted.

This paper focuses on two specific trial intervention villages. During the first year of the trial, we noticed two villages with substantially different levels of coverage. Upon further investigation, we noticed that they also had unique social dynamics that seemed to influence populations' involvement with the

trial. For the second year of the MDA, the social science study theoretically chose these two villages for further research to understand how social dynamics impact trial coverage in both a high- and low-coverage village.[36] Therefore, we conducted additional ethnographic research over the months of the MDA, living in each village and observing and participating in the daily lives of its inhabitants during medication distribution times and otherwise. As part of this, the team compiled extensive structured and non-structured observational field notes that were discussed and reflected on regularly. Additional IDIs, informal conversations, and FGDs were held with individuals and groups purposefully selected to represent all opinions and include those who took or did not take the trial medication. Several respondents were interviewed multiple times and regular reflexive discussions were held with the social science team in the field and abroad. The team in the field included three Gambians from the local area (but not the trial villages), two of whom are Fula and one of whom is Mandinka. These team members were intricately involved in all discussions on the emergence and development of relevant themes, and especially on how the terms related to social cohesion were defined, translated, and used throughout data collection and analysis. Analysis was a continuous, flexible, and iterative process designed to ensure a thorough understanding of emerging themes and definitions of concepts until saturation was reached. All IDIs, KIIs, and FGDs were recorded and transcribed and translated verbatim with the aid of trained field workers. Qualitative data were analysed with the use of NVIVO v12 software.

Study Setting

The trial population is located in a rural area of the Upper River Region, The Gambia, a region with highly-seasonal malaria transmission patterns. It is an area of low mosquito vector density, but high vector survival. This indicates that there are groups of mosquitoes not killed by traditional vector control, making the area ideal for the implementation of MDA. Further, despite reported use of other control methods (e.g. long-lasting insecticidal nets, indoor residual spraying, etc.), the Upper River Region has the highest rate of malaria in The Gambia.[37] Trial villages range in size from 140-700 people. Each village is headed by the Alkalo, the village chief, and is further divided into compounds. Each compound is led by the compound head, the oldest male, and is comprised of his family and those of his eldest sons or younger brothers; polygamy is actively practiced. The population practices Islam and each village has a mosque or designated place to pray and study the

Quran. The primary economic activity in the area is subsistence farming. Villages are often located a prohibitive distance from the main paved road and the difficulties and costs of transportation were often cited as a limitation in accessing health care services. Community-level social cohesion is enacted in specific physical and organizational spaces. The first of these is the village bantaba. A bantaba is a shared communal space maintained by the whole village. It is a place for the village to gather for formal meetings and for people to gather informally for regular social interactions. Similarly, all villages in the region have three principal community groups: the Village Development Council, the Women's Group, and the Youth Group. These groups are involved in making decisions regarding the functioning of the village, as well as carrying out economic and other activities, such as village cleaning and social events. Further details on the two study villages are found in the Results section.

Ethics

All components of this study were approved by the Institutional Review Board of the Institute of Tropical Medicine in Antwerp, Belgium and the Scientific Coordinating Committee and Ethics Review Board of the Medical Research Council Unit The Gambia. All participants provided verbal informed consent or assent (when under 18) prior to participation in any component of the research.

RESULTS

Our results focus on two main components: 1. Enactments of social cohesion in the two study villages, and 2. How local expressions of social cohesion and dissent are reflected in the villages' involvement with the MDA implementation

1. Enactments of social cohesion

Ethnographic research revealed unique attributes in each village that either influenced or were influenced by the types of social cohesion found within them. Definitions of social cohesion were initially found to be similar in both Village A and Village B. The Fula words used in Village A, *kongol gotol*, mean "same voice." And in Village B, the Mandinka word used for social cohesion, *Kangbengo*, means "people who speak the same voice; come to agreement."

Social cohesion was described as when the whole community comes together to make an agreed decision. Respondents in both villages reported that social cohesion was present before anyone in the village was born – it was passed down to them from their ancestors – and that this social cohesion stemmed from the fact that all members of the village were descendants of the same family. One of the most important reasons mentioned for having strong social cohesion was that it is the mechanism through which good things happen to the village. In addition to more abstract notions such as group harmony, this could also mean very specific village development projects (e.g. getting electricity, access to water, better roads, etc.).

"This is something we have inherited from our great grandparents; we are one people born from the same village. This social cohesion has been existing in this village since when we were not yet born and it will continue like that." Adult female, Village B, FGD

Village A and Village B had similar definitions of social cohesion, but there were stark differences in the ways in which this was enacted through the way they were organized, understood leadership, and expressed dissent in public spaces.

1.A. Social organization and leadership

Village A

At the time of the study, the village included 13 compounds and had a population of nearly 200, all of whom identified as part of the Fula ethnic group. The primary economic activity was farming. However, due to the village's location near the border with Senegal, several villagers, predominately young men, were involved with supplying lumber for the illegal logging trade, and this substantially added to their overall income (lumber was collected in The Gambia and moved to Senegal to be shipped abroad). In general, each family or compound had their own land to farm. This land was owned by the oldest male of the family who then maintained control of money earned through selling crops, though other men and women contributed their time and labour. Importantly, working in the lumber trade was viewed as an individual activity that increased a single person's income, whereas farming, the traditional economic activity, was viewed as communal and beneficial to the whole compound.

Village A was the only village included in the trial that did not have a village bantaba. Instead, meetings were held at the compound of either the Alkalo, the Imam, or another member of the village. People tended to socialize at one another's compounds. Like all villages, Village A had the expected community groups, but we saw less of their involvement in village activities; most visible was boys and young men playing soccer as part of the Youth Group.

The role of leaders, especially the Alkalo, is an important component of village social cohesion. The Alkalo of Village A was described as being "everyone's father," so people listen to what he says. When describing the social cohesion of their village, many said it was evident because they all follow what their authority figure tells them to do. At the village level, this means people follow the direction of the Alkalo, and at the compound level, they follow the compound head.

"And in this village, we all look up to the Alkalo as he is the head of the village and a parent to us. Whatever he said to us to follow we will follow it, and if he also said let us not follow something, we as a village will do exactly as he said. No one will challenge or argue about it and this line of respect to village authority will always be continued to be adhered to in our community."
Adult male, Village A, IDI

This notion was reflected in interviews, regardless of age. As one older man said, to show respect to the elders and the Alkalo is "to be under them completely." Members of the community are expected to obey what the elders say, and adhere to their advice, regardless of individual feelings about the matter. This man further explained that to go against the advice of the Alkalo or elders was not only bad for that individual, but also for the society as a whole; going against the Alkalo or your elders was on par with disrespecting the whole community.

"R: The way you should respect your elders, not only the Alkalo, is like whatever they assign you to do, you do it without no hesitation or complaint. You should be a good listener to them, meaning to be under them completely, but most of the time if the Alkalo or village elders give authority, and you are always opposing them, they will see it as you are disrespecting them and it is bad for the society.

I: Why is it bad for the society?
R: That is like if you are supposed to respect these elders and you don't respect them, it is like you disrespect the person and the community as a whole, so for that reason you are affecting yourself and you are affecting the people, and whatever good thing that is about to happen for you, people will not be very much interested about it which is going to affect you in one way or the other."
Adult male, Village A, IDI

Village B

The village had a population of approximately 350 across 14 compounds, nearly all of whom identified as part of the Mandinka ethnic group. Village B is located near the Gambian River and, therefore, in addition to subsistence farming, fishing was also a common additional source of income. Each compound had designated farming land divided into the husband's plot and the wives' plot. Though the men were typically engaged with farming foods for family consumption (e.g., coos and millet) and women were engaged with farming foods to sell (e.g., groundnuts), each was in ownership of the money generated.

During FGDs and IDIs with adolescent girls, it was common for them to discuss what produce they sold and how they chose to spend their money. In fact, as part of their cultivating and money-making, women would give "charity" to their husbands when they were earning more money. The money earned by women was most often spent on goods or healthcare needed by the whole compound, but they also contributed substantially towards "feast money," money that would be used for different ceremonies. Ownership of their financial means also meant that women in Village B seemed to have a greater say in compound decision making than in Village A, where the norm was for the compound head to be the principal decision maker.

"Men cultivate coos and women cultivate groundnut. The coos is used for the family consumption and the groundnuts cultivated by women would be sold by the women and spent on feast money to buy the ingredients… When we cultivate the groundnut, we bag the groundnut and every nine bags belong to the woman, the tenth bag goes to the husband as charity to the husband. The woman decides what she want to do with her nine bags; the husband has nothing to do with that."

Adult female, Village B, IDI

Village meetings and social gatherings were most often held at the village bantaba or the village mosque. The mosque, a source of pride in the village, was built from donations of village members living abroad. The community groups in Village B were very active and held regular meetings and events, several of which - unrelated to the MDA - took place while we stayed in the village for data collection, including a meeting of the Youth Group on preparing for the next village clean-up.

"That would be a very difficult community [one without active community groups]… A community must have a common goal and that is to develop the community. In the absence of these structures, it would be difficult to bring the people together to focus on development… [Without community groups], there is no social cohesion existing in that village and they would be faced with challenges they would not be able to address because they are not organized. This mosque in this village was built by the youth who travelled to Europe, this and the like can bring social cohesion to the village. In the absence of this, it would be difficult for social cohesion to exist within the community."
Adult male, Village B, IDI

The role of the Alkalo as a decision maker is important in all trial villages, as he (always a male) has the final say in all village-related matters. However, the Alkalo in Village B believed that it is the village as a whole that should make decisions together. He credited this communal involvement in their success in solving problems or bringing in new development projects.

"I am the Alkalo of this village, but the way and manners we operate here is this: we allow the people to lead and we follow. When villagers finally make their decision, then you can support their decision and advise them accordingly, but I would not want them to confront me for not disseminating information… I am the eldest man in this village. I have children and grandchildren in this village. The reason we are one people and speak the same voice is I allow them to lead. When I have visitors, I inform everyone about it, and we sit and discuss. Whatever you discuss with them I would comply, but I must allow my people to express their opinion first. They are my family."

Village B Alkalo, IDI

The Alkalo frequently holds meetings at the village bantaba to elicit feedback and make the decisions about common subjects.

"When projects come to a village, they first introduce the project to the village head and Village Development Chairman. Then the entire village would be informed about the project and a meeting would be organized in the village, and when the leaders accept the project, we accept too and participate."
Adult female, Village B, FGD

Another aspect of the social cohesion as expressed in Village B was the importance of active participation of the individual. When asked questions regarding how one could tell someone is a leader or what qualities a leader possesses, respondents always described a leader as one who was involved in all aspects of village life:

"Villagers respect him. Whatever activity is happening in the village, he is involved."

"She is a good leader because whatever happens in the village, she would participate. When you go to meetings at the bantaba or anywhere in the village, she would participate fully."

- *Adolescent girls, Village B, describing leaders in their village during an FGD*

2. Village involvement in MDA implementation

Despite fluctuations, Village A had one of the lowest rates of coverage during the first year of the trial and the largest drop in coverage between the first and second rounds of the second year. Village B, on the other hand, had the highest trial coverage—nearly 100% of those eligible—of all intervention villages throughout the MDA. In this section, we explore how the local dynamics previously expressed are related to the communities' involvement with the MDA.

2.A. Initial decision making, dissemination of information, and location

The villages of the Upper River Region are accustomed to the implementation of MRC-Gambia programs and trials, and the introduction of MASSIV was designed as a standardized process across villages. Once selected to be part of MASSIV, MRC-Gambia field staff travelled to each village to discuss the trial with the Alkalo and get his permission for it to be conducted in that village. No selected village declined participating in MASSIV. MRC-Gambia field staff conducted sensitization meetings in each village to provide details about the importance of compliance, the timing of the distribution, number of days to take the medicine, etc. prior to enrolment and informed consent of participants.

Each village, with the aid of the MRC-Gambia field team assigned to it, was able to choose the location of the MDA. The main requirements were that the location was available to everyone, large enough to accommodate the necessary supplies, and had shelter against the rain, the wind and the sun. Furthermore, each village needed a location to conduct the pregnancy test required for eligibility purposes of women and girls of reproductive age. This test proved challenging; there are cultural issues surrounding asking unmarried women to take the test, especially by the all-male MRC-GAMBIA staff, and it was difficult to ensure adequate privacy.[11]

In Village A, prior to the commencement of MASSIV, the Alkalo reported being *told* by MRC-Gambia that they would be coming soon to distribute malaria medications and post a nurse in the village. He was happy they were coming, but as such, did not consider accepting MASSIV to be a decision that necessarily needed to be made: the MDA was something that was to happen to the village rather than something that needed to be decided upon.

"The MRC[-Gambia] has been visiting this village for a long time now – it wasn't this year they started visiting the village. But this time they came during the dry season, and when they came, they informed us why they came to this village… They also said they were going to post a nurse in here, so since then we are waiting. They also said they will give us malaria medicine and worm medicine."
Village A Alkalo, IDI

In the same pre-trial interview, the Alkalo said that when MRC-Gambia shared the details of the MDA, he would send his son around the village to

inform everyone, as this is how information is typically distributed throughout the village. From that point on, the son told the village to participate. Individual compound heads may have told their families to go and take the medication. There was no additional formalized system of obtaining information; however, on the first day of the MDA, we observed a compound head, a well-known man active in the daily life of the village, taking it upon himself to inform people that MRC-Gambia had arrived with the medication.

Because Village A did not have a central bantaba or designated mosque in a shared space, the trial medication was distributed at an individual family's compound. This compound was one of the larger ones in the village and had a covered porch area for the MDA field staff. The compound was located at the entrance of the village. The pregnancy test was also conducted there; an MRC-Gambia nurse had a small table inside, and women and girls were able to use the compound's toilet facilities behind the main house.

Unlike Village A, the majority of Village B was involved from the beginning of the implementation process. The Alkalo and his son called a meeting with the village leaders and all compound heads to discuss the details MRC-Gambia provided them. As a collective, the leaders decided that the entire village would benefit from the MDA and made the decision to participate as a whole.

"We accepted the MRC-Gambia because we have support from the villagers. I am the leader, but I cannot do it alone; we accepted to participate in this study because we all agreed to participate…"
Village B Alkalo, IDI

This kind of village-level decision making is common in Village B. In this case, information regarding MASSIV was passed throughout the community in multiple ways. First was the sensitization meeting held by MRC-Gambia. Second, from the initial meeting with the Alkalo, compound heads were expected to share the trial details with their families and to emphasize the importance of participation. Additionally, the Women's Group was heavily involved. On their own initiative, they moved through the village and performed songs and dances telling of the MDA details in the days preceding each round. The Village B mosque served as the venue for the MDA. It was centrally located and contained a large space and an open and covered

courtyard. The pregnancy tests were conducted and read at a neighbouring compound away from the medication distribution site.

Beyond the Alkalo, social cohesion was also linked to the leadership of the compound heads and the strength of the compound. One way compound heads could demonstrate their strong leadership abilities was by having their entire compound fully adhere to the MDA. The ability to lead within one's compound was relevant when that man may want to take on a leadership role within the village.

"Every compound head in the village tells their family, 'if you hear anything that will bring development to the village, you become the first to participate.' Any activity here, each compound head wants their compound to participate, and this is something they are very proud of. If a compound does not get involved, [the compound head] loses respect and they are not allowed to talk in village meetings. Because they cannot control their families, they have no say here."
Adult male, Village B, IDI

2.B. Involvement of community groups and individuals
Having active community groups working for the same goals was not only important for the success of the MDA, but was a central component of the overall social cohesion. The trial protocol included directions for involving an impartial witness in each village to be present during the informed consent process, but did not include formal methods of community engagement. As such, the involvement of individuals, including the Alkalo, or the community groups in the implementation varied from village-to-village.

Due to his health status, the Alkalo of Village A was not eligible for MASSIV. As a consequence, he was not involved in the trial activities unless specifically requested. After an initial low turnout during one round, the MRC-Gambia field team appealed to the Alkalo to use his power and position to encourage those in the village to take the medication. At their request, the Alkalo called an impromptu meeting on his compound reiterating the importance of compliance. Immediately after, there was an increase in people taking the medication.

After the meeting at the Alkalo's compound, the Women's Group performed songs and dances at the MDA site to encourage people to attend and to provide a fun atmosphere. Though some girls told us they would mobilize their peers from their own compounds, neither the Village A Youth Group nor individual youths were involved in MASSIV's implementation. As one teenage girl noted:

[Regarding mobilizing others in the village] "Simply because we are young, and this is a function of the elders. So whatever directives the elders give us, we do that accordingly."
Adolescent girl, Village A, FGD

To our knowledge, the implementation details of the MDA were not discussed in communal spaces during or after implementation, and, therefore, the MDA was carried out as proposed by the MRC-Gambia field team for the most part.

In contrast, the community groups in Village B, already very active in village activities, played a visible role in the trial's implementation. In addition to spreading information, the Women's Group came together and decided to conduct the pregnancy tests themselves. The Traditional Birth Attendant and her assistant were trained by the MRC-Gambia field nurse on how to properly perform the test and they conducted it away from the MDA site. In this way, women and girls were able to be tested for pregnancy by trusted women from their village, without having to risk showing their urine or the results to others. The Youth Group was also heavily involved. Prior to the distribution of medication, they were responsible for cleaning the MDA site and setting up the tables and chairs. During the MDA, youth would go around the village or out to the farms and help mobilize those who had not yet taken the medication.

Additionally, the Village B Alkalo's son was an active coordinator and advocate for the trial. He was involved in the communication between the village and the MRC-Gambia, mobilized village members, and was present at the distribution site throughout the duration of the trial, helping the MRC-Gambia team with anything they needed. The compound heads were also involved by individually leading and strongly encouraging their families to participate. Some explained to us that they would make it a point to receive

the medication in the morning and then wait in their compound (before heading to their farms) until they knew all their family members took the medication.

2.C. Social pressure and expressing dissent

Social pressure — especially to follow the overall decision of the village — was present in both Village A and Village B and affected individuals of all ages and genders. In interviews, respondents explained the consequences of someone going against the group decision, a sign that the social cohesion is "not strong," and something that is looked down upon. When this occurs, villagers, often led by the Alkalo, will try and "bring back" the person to the community.

"People will view that person [who went against the group decision] as an individual who is not good, because if you are asked to participate in something that the whole village agreed to and you disagree to that, people will not see you as a good person… Going against the decision of the entire village is bad. When you were born, people washed you and took care of you, and when you die, people will take care of your body and bury you."
Adult female, Village A, IDI

Often, those who refused to participate (excluding those with justifiable reasons, such as traveling or illness) were described by participants as "selfish," "stubborn," or "disrespectful" because they did not follow their elders' advice. If an individual is not interested in participating in the MDA, a decision the village made as a group, then it is important that their reason is deemed acceptable to the rest of the village. In Village A, adolescent girls spoke of the social pressure they experience from their village and apply to their own peer group. When together, girls give advice, often related to how they should act towards their parents and elders. If the girls do not adhere to the advice of their friends, the friends will discontinue their friendship with the girl in question:

R1: "The village elders will not be happy for her if the girl is not respectful to her parents and elders of the community… nothing good will follow her…What is going to happen in that situation is that I will advise my friend to stop disrespecting her parents; if she doesn't abide by it, I will stop moving with her because I will know that she is not a good friend."

I: "Why is it that you will stop befriending a person who is not respectful to her parents?"
R2: "Because we don't want people in the village to classify us under the same category, because if they see us moving with this disrespectful girl others might think that we are all having the same habit."
Adolescent girls, Village A, FGD

This is particularly relevant to trial compliance, as girls were both perceived and shown in the clinical data to have taken the medication significantly more than boys across all trial villages. When asked why this was the case, respondents in all of the FGDs said it is because girls "respect their parents more" than boys. As part of showing respect, girls are more likely to obey the requests of their parents and elders when told to take the trial medication. Though other reasons included "being healthy" and "absent for work," "disobedience" was emphasized as the main reason for boys' lack of participation.

Unique to Village A among all trial villages was that several people, mostly women and girls, said they had or feared having epilepsy, making them ineligible for MASSIV. This was not found in any other trial village, and, according to MRC-Gambia medical staff, the diagnostic capabilities required to confirm the illness did not exist in the area. The illness was described to us as having two causes: one biological and present since birth, and the other spiritual and related to not having a "clean heart." Due to gender-specific roles, men and boys were able to invoke farming or traveling as an acceptable way of evading the MDA. Conversely, the principal responsibilities of women and girls were on the compounds where their whereabouts and actions could be regularly monitored. By claiming epilepsy, women and girls were giving an "acceptable" way of declining participation in the MDA without having to go against the communal decision. In this way, they did not have to take the medication, but they were still not viewed by their community as a "bad" person.

Dissent, however, was not "all-or-nothing," and room for acceptance of individual opinions and decisions did exist. But even with this nuance, there was still a focus on and importance of rejoining the overall group and village as a whole. As one man explained:

"Well those people will just be seen as how they behave because you know people are different - some people like to share and some people doesn't, but that doesn't mean they should be isolated, as some people like community work but others don't, so in this this situation if they don't agree to the Alkalo's decision and the majority of the community, as time goes on if they see any benefit, if they are convinced, they might join the majority of the village to participate in whatever activity that is ongoing in the village."
Adult man, Village A, IDI

DISCUSSION

This study has sought to identify local enactments of social cohesion and the relationship to community participation in the implementation of an MDA trial in The Gambia. After identifying and theoretically selecting two villages with unique social dynamics and drastically different coverage rates in the first year of the MDA trial, this study builds on previous findings that show social, not just individual, factors are intrinsically important to understanding high and low MDA coverage and compliance.[11]

Both study villages expressed their forms of social cohesion through their unique involvement in the MDA. Further, we believe these expressions of social cohesion can be elaborated on and understood through the lens of African communitarian discourse, of which social cohesion is a core value.[38] Most familiarly referred to as Ubuntu, multiple definitions of African communitarianism exist and its principal components can be found throughout much of sub-Saharan Africa.[3940–42] At its core are concepts of solidarity, reciprocity, and of understanding oneself through relations with others and one's community.[43,44] Participation in society is also a key component. According to Shutte (1993) as stated in Louw (2006), communitarianism unites the individual in a "particular web of reciprocal relations" where "I think, therefore I am," is substituted for "I participate, therefore I am."[45,46(p168)] For the life of the community, individuals morally must participate in the rituals, norms, and traditions that contribute to the community; a component of this is respecting one's elders and place in the social hierarchy.[38] Further, there is a long-standing debate on the extent to which individuals exist in relation to their communities. Some believe that the individual does not and cannot exist without the community,[47–49] and that all members must come to a common consensus and agreement, while

others have argued that this can result in hyper social pressure that may lead to "promoting groupthink and uncompromising majoritarianism."[50]

Part of Village A's expression of social cohesion was the importance of respecting the authority of the Alkalo, to be "under him completely." The initial agreement to participate in the MDA trial was initiated by the Alkalo and those in the village were expected to follow the hierarchal decision-making process. This created pressure to comply, potentially leading to structural coercion.[26] In fact, the importance of power dynamics in certain contexts - such as The Gambia - have been recognized as strong enough for others to suggest limiting the role of authority figures in trial implementation.[51] In this light, it is possible that the social pressure to partake in the MDA as part of the group decision may have been great enough to lead to such reasons for declining as potentially having epilepsy (especially among women and girls).

In Village B, social cohesion was expressed in a way that not only the Alkalo, but all leaders, were active participants in all components of village life. They too reflected a communitarian view of working towards the benefit of the whole group, but the social cohesion of the village was not a result of the leadership of one man. Instead, the active participation expected of all leaders was a result of the type of social cohesion expressed in this village. Further, social cohesion in Village B was expressed through the active participation of all community members throughout the MDA implementation. Participation in a trial, and compliance to the medications was not a one-time activity, but a continuous process,[52] and the members of Village B were involved in the implementation from the initial decision-making until the end. Even when describing leadership roles, Village B conveyed the importance of participation: it is not only good for the community, but it benefits the individual in that their leadership skills and strong character are recognized. It is possible then that this expression of social cohesion was able to minimize the effect of structural coercion and maintain more autonomy in the decision-making process - even while respecting the authority of the Alkalo and the decision of the village as a whole.

Active participation as a form of their definition of social cohesion greatly affected trial coverage in these villages. Community participation is often

described as being "top-down" or "bottom-up," but by focusing on the expressions and logics of the respondents, this study has demonstrated that social cohesion impacts community participation in more complex ways than traditional theories have explained.[6] Particularly in Village B, community participation was a mix of both vertical and horizontal processes. The role and power of the Alkalo is very strong, and community members showed their respect to him and to their compound heads by complying to their requests. However, the individual is respected within their role in the community, and active participation is a form of their social cohesion; the individuals and community groups in Village B were able to modify and contextualize the MDA in a way that best suited their needs and wants, and it is possible this led to greater MDA coverage.

These findings expand upon the previous literature and demonstrate that social factors, especially unique forms of social cohesion at the village level, can prohibit or facilitate high MDA coverage. Additionally, this study shows that many of the individual factors used to describe MDA coverage in previous research, such as farming obligations,[8,12] may, in fact, be a result of more complex social dynamics. For example, with strong social pressure resulting from a particular expression of social cohesion, being too busy with farming activities, or even having a severe illness, may in fact actually be socially acceptable reasons that allow for village members to not partake in the MDA while not outwardly going against the communal decision to participate. It is possible this decreased the overall social pressure to participate and may have led to the lower coverage in the village. In contrast, social cohesion, when expressed via the approach of Village B, may also provide ways to overcome individual factors prohibiting high coverage, such as the hesitation to screen for pregnancy.[8,11]

Implications for future trials

This study has shown that participation in a trial, especially an MDA that targets the entire community, is part of a much more complex social system beyond merely consenting and taking the trial medication. People's ability and interest to "participate" are nuanced and highly influenced by the community around them and their place within it. Further, many African philosophies of communitarianism regard the decision to act in a way that "connects" or betters the community, not only as important, but the morally right thing to do. This is in conflict with the assumptions of individual

autonomy that proliferate in traditional research ethics and trial design. Because of this, future trials need to be aware of the potential impact they may have upon entering a community that makes it socially and morally difficult for an individual to make an autonomous decision. By demonstrating the role of social cohesion and social pressure in MDA implementation and coverage, this study has found that it is imperative for implementing organizations to move beyond the more traditional forms of community engagement and create greater, more meaningful bidirectional understanding and conversation. As part of this, it is important to understand local enactments of critical social dynamics such as cohesion and their particular influence on trials' implementation, as well as the epistemological stances and socio-political systems under which they are framed. In doing so, implementation can be made more community-friendly by allowing trial communities to contextualize the implementation to their needs. Similarly, trials can be made more ethical by understanding how social forces like social pressure and components of structural coercion may undermine the ethical practices already in play. This may be crucial in achieving the coverage necessary for MDA to be successful.

African epistemological frameworks have been largely left out of the discourse surrounding global bioethics in favour of Western philosophies.[50] Within philosophy, this is considered a global epistemic injustice, and there is a need to increase its use to understand problems within sub-Saharan Africa.[31] African philosophy as a whole has already been used as a lens for understanding multiple disciplines in this context, such as economic development,[53] social work,[54] and management practice and leadership,[55] and there has been a growing movement to include African communitarian discourse as an alternative (to Western) ethical framework, particularly for decision making, in global bioethics and public health.[38,44,50,56] This study, by assessing different expressions of social cohesion and its relation to participation, provides a small, first step in empirical application of African philosophy in global public health.

Limitations

This study shows the importance of locally expressed social cohesion in the implementation and success of an MDA trial. However, it is not to say that other factors may not also contribute to a trial's success. Other forms of structural coercion, such as not otherwise having access to medical care, may

greatly impact the decision-making process.[14,26] The role of the field nurses stationed in each intervention village highly impacted implementation outcomes and their role will be the focus of future analyses.

CONCLUSION

Much prior research on MDA coverage has focused on the effects of individual and structural factors. Such studies thereby risk using a lens of interpretation from the Global North to analyse and improve MDA practices. In this study, we focus on community-level social systems as emically understood and practiced. We compared two trial villages, one with high coverage and one with low, and analysed how their unique expressions of social cohesion influenced their involvement in an MDA trial. Both villages' expression of social cohesion involved a leadership style that followed a form of hierarchal order. In Village A, social cohesion was expressed in a top-down, hierarchal form where the Alkalo gave the initial directive to take the MDA medication and those in the village were expected to comply. The community was not actively involved in the implementation and the overall coverage and compliance of the MDA was comparatively low. Conversely, Village B enacted a form of social cohesion where not only the Alkalo, but individuals and community groups were actively involved at each step, allowing them to contextualize the MDA to better fit their needs and wants. This led to much higher coverage and compliance. An African philosophy regarding communitarian discourse provided a guide for interpreting the expressions of social cohesion in the two focus villages. Though this philosophical lens has been used as a framework in other disciplines, this study is one of the first to use it as a way to explore and understand the nuances of MDA participation. This, in turn, sheds light on new implications for future studies to further decolonize global health by demonstrating the importance of non-Western philosophies and logics, including their different manifestations and expressions, in the design and implementation of MDA programs and trials.

REFERENCES

1. World Health Organization. Mass Drug Administration for Falciparum Malaria: A practical field manual. *Who*. 2017.
2. Poirot E, Skarbinski J, Sinclair D, Kachur SP, Slutsker L, Hwang J. Mass drug administration for malaria. *Cochrane Database Syst Rev*. 2013;12(12):CD008846. doi:10.1002/14651858.CD008846.pub2
3. Webster JP, Molyneux DH, Hotez PJ, Fenwick A. The contribution of mass drug administration to global health: past, present and future. *Philos Trans R Soc B Biol Sci*. 2014;369(1645):20130434. doi:10.1098/rstb.2013.0434
4. Newby G, Hwang J, Koita K, et al. Review of Mass Drug Administration for Malaria and Its Operational Challenges. *Am J Trop Med Hyg*. 2015;93(1):125-134. doi:10.4269/ajtmh.14-0254
5. Cheah PY, White NJ. Antimalarial mass drug administration: ethical considerations. *Int Health*. 2016;8(4):235-238. doi:10.1093/inthealth/ihw027
6. Atkinson J-A, Vallely A, Fitzgerald L, Whittaker M, Tanner M. The architecture and effect of participation: a systematic review of community participation for communicable disease control and elimination. Implications for malaria elimination. *Malar J*. 2011;10(1):225. doi:10.1186/1475-2875-10-225
7. Adhikari B, James N, Newby G, et al. Community engagement and population coverage in mass anti-malarial administrations: a systematic literature review. *Malar J*. 2016;15(1):523. doi:10.1186/s12936-016-1593-y
8. Dierickx S, Gryseels C, Mwesigwa J, et al. Factors Associated with Non-Participation and Non-Adherence in Directly Observed Mass Drug Administration for Malaria in The Gambia. Sullivan DJ, ed. *PLoS One*. 2016;11(2):e0148627. doi:10.1371/journal.pone.0148627
9. Pell CL, Adhikari B, Myo Thwin M, et al. Community engagement, social context and coverage of mass anti-malarial administration: Comparative findings from multi-site research in the Greater Mekong sub-Region. Rutebemberwa E, ed. *PLoS One*. 2019;14(3):e0214280. doi:10.1371/journal.pone.0214280
10. Jaiteh F, Masunaga Y, Okebe J, et al. Community perspectives on treating asymptomatic infections for malaria elimination in the

Gambia. *Malar J*. 2019;18(1):39. doi:10.1186/s12936-019-2672-7
11.
12. Adhikari B, Phommasone K, Kommarasy P, et al. Why do people participate in mass anti-malarial administration? Findings from a qualitative study in Nong District, Savannakhet Province, Lao PDR (Laos). *Malar J*. 2018;17(1):15. doi:10.1186/s12936-017-2158-4
13. Mfutso-Bengo J, Ndebele P, Jumbe V, et al. Why do individuals agree to enrol in clinical trials? A qualitative study of health research participation in Blantyre, Malawi. *Malawi Med J*. 2008;20(2):37-41. doi:10.4314/mmj.v20i2.10898
14. Kingori P. The ' empty choice ': A sociological examination of choosing medical research participation in resource- limited Sub-Saharan Africa. 2015. doi:10.1177/0011392115590093
15. Chan J, To H, Chan E, Social S, Jan N. Reconsidering Social Cohesion : Developing a Definition and Analytical Framework for Empirical Research RECONSIDERING SOCIAL COHESION : DEVELOPING A DEFINITION AND ANALYTICAL FRAMEWORK. 2006;75(2):273-302. doi:10.1007/sl
16. Schiefer D, Noll J Van Der. The Essentials of Social Cohesion : A Literature Review. *Soc Indic Res*. 2017;132(2):579-603. doi:10.1007/s11205-016-1314-5
17. Burns J, Lefko-everett K, Njozela L. From definition to measurement : constructing a social cohesion index for South Africa. (217).
18. Burns J, Hull G, Lefko-everett K, Njozela L. Defining social cohesion. (216).
19. Pronyk PM, Harpham T, Busza J, et al. Social Science & Medicine Can social capital be intentionally generated ? A randomized trial from rural South Africa q. 2008;67:1559-1570. doi:10.1016/j.socscimed.2008.07.022
20. Lippman SA, Leslie HH, Neilands TB, et al. Health & Place Context matters : Community social cohesion and health behaviors in two South African areas. *Health Place*. 2018;50(March 2017):98-104. doi:10.1016/j.healthplace.2017.12.009
21. Leach M, Fairhead J. Being "with the Medical Research Council": Infant Care and Social Meanings of Cohort Membership in Gambia's Plural Therapeutic Landscapes. In: Geissler PW, Molyneux CS, eds. *Evidence, Ethos and Experiment: The Anthropology and History of Medical Research in Africa*. New York: Berghahn Books; 2011:508.

22. Geissler PW, Kelly A, Imoukhuede B, Pool R. 'He is now like a brother, I can even give him some blood' – Relational ethics and material exchanges in a malaria vaccine 'trial community' in The Gambia. *Soc Sci Med*. 2008;67(5):696-707. doi:10.1016/j.socscimed.2008.02.004
23. Jaiteh F, Dierickx S, Gryseels C, et al. 'Some anti-malarials are too strong for your body, they will harm you.' Socio-cultural factors influencing pregnant women's adherence to anti-malarial treatment in rural Gambia. *Malar J*. 2016;15(1):195. doi:10.1186/s12936-016-1255-0
24. Emanuel EJ, Wendler D, Killen J, Grady C. What Makes Clinical Research in Developing Countries Ethical? The Benchmarks of Ethical Research. *J Infect Dis*. 2004;189(5):930-937. doi:10.1086/381709
25. Organizations I, Sciences M. *International Ethical Guidelines for International Ethical Guidelines For.*; 2016.
26. Nyirenda D, Sariola S, Kingori P, et al. Structural coercion in the context of community engagement in global health research conducted in a low resource setting in Africa. 2020:1-10.
27. Fisher JA, Fisher JA. Expanding the Frame of "Voluntariness" in Informed Consent: Structural Coercion and the Power of Social and Economic Context. 2020;23(4):355-379.
28. Tindana PO, Rozmovits L, Boulanger RF, et al. Aligning Community Engagement With Traditional Authority Structures in Global Health Research: A Case Study From Northern Ghana. *Am J Public Health*. 2011;101(10):1857-1867. doi:10.2105/AJPH.2011.300203
29. Kelty C. *The Participant: A Century of Participation in Four Stories*. Chicago, Illinois: University of Chicago Press; 2020.
30. Büyüm AM, Kenney C, Koris A, Mkumba L, Raveendran Y. Decolonising global health : if not now , when ? 2020:1-4. doi:10.1136/bmjgh-2020-003394
31. Chimakonam JO. African philosophy and global epistemic injustice African philosophy and global epistemic injustice. 2017;9626. doi:10.1080/17449626.2017.1364660
32. Geissler W, Molyneux C. Studying trial communities: Anthropological and historical inquiries into ethos, politics and economy of medical research in Africa. In: *Evidence, Ethos, and Experiment : The Anthropology and History of Medical Research in Africa*. Berghahn Books; 2011. doi:10.26530/OAPEN_478050
33. Epstein S. *Inclusion: The Politics of Difference in Medical Research*. 1st

editio. Chicago, Illinois: University of Chicago Press; 2007.
34. de Sousa Santos B. *Epistemologies of the South: Justice Against Epistemicide*. 1st editio. Oxfordshire: Routledge; 2014.
35. Dabira ED, Soumare HM, Lindsay SW, et al. Mass drug administration with high-dose ivermectin and dihydroartemisinin-piperaquine for malaria elimination in an area of low transmission with high coverage of malaria control interventions: Protocol for the massiv cluster randomized clinical trial. *JMIR Res Protoc*. 2020;9(11):e20904. doi:10.2196/20904
36. Willems D. Ingebouwde normen, medishe technieken doorgelicht. In: Berg M, Mol A, eds. Utrecht; 2001.
37. Mwesigwa J, Achan J, Di Tanna GL, et al. Residual malaria transmission dynamics varies across The Gambia despite high coverage of control interventions. Carvalho LH, ed. *PLoS One*. 2017;12(11):e0187059. doi:10.1371/journal.pone.0187059
38. Chuwa LT. *African Indigenous Ethics in Global Bioethics*. New York: Springer; 2014. doi:10.1007/978-94-017-8625-6
39. Ramose MB. *African Philosophy through Ubuntu*. Harare: Mond Books; 1999.
40. Eze MO, Eze MO. What is African Communitarianism ? Against Consensus as a regulative ideal. 2013;0136. doi:10.4314/sajpem.v27i4.31526
41. Louw D. Power sharing and the challenge of ubuntu ethics. 2009. http://uir.unisa.ac.za/bitstream/handle/10500/4316/Louw.pdf.
42. Gade CBN. What is Ubuntu ,? Different Interpretations among South Africans of African Descent. 2013;0136. doi:10.1080/02580136.2012.10751789
43. Mkhize N. Ubuntu and harmony: an African approach to morality and ethics. In: Nicolson R, ed. *Persons in Community: African Ethics in a Global Culture*. Scottsville: University of KwaZulu-Natal Press; 2008:35-44.
44. Sambala EZ, Cooper S, Manderson L. Ubuntu as a Framework for Ethical Decision Making in Africa : Responding to Epidemics Ubuntu as a Framework for Ethical Decision Making in Africa : Responding to Epidemics. 2020;8422. doi:10.1080/10508422.2019.1583565
45. Shutte A. *Philosophy for Africa*. Capte Town: UCT Press; 1993.
46. Louw D. The African concept of ubuntu and restorative justice. In: Sullivan D, Tifft L, eds. *Handbook of Restorative Justice: A Global*

Perspective. London and New York: Taylor & Francis; 2006:161-171.
47. Menkiti IA. Persona and Community in African traditional thought. In: Wright RA, ed. *African Philosophy: An Introduction*. Lanham: University Press of America; 1984.
48. Mbiti JS. *African Religion and Philosophy*. London: Heinemann; 1969.
49. Gyekye K. Person and Community in African Thought. In: Coetzee PH, Roux APJ, eds. *Philosophy from Africa*. Johannesburg: ITP; 1998:317-336.
50. World D, Issn B, Metz T, Metz T. AFRICAN AND WESTERN MORAL THEORIES IN A BIOETHICAL CONTEXT. 2010;10(1):49-58. doi:10.1111/j.1471-8847.2009.00273.x
51. Adhikari B, Pell C, Cheah PY. Community engagement and ethical global health research. *Glob Bioeth*. 2020;31(1):1-12. doi:10.1080/11287462.2019.1703504
52. Muela Ribera J, Hausmann-Muela S, Gryseels C, Peeters Grietens K. Re-imagining adherence to treatment from the "other side": Local interpretations of adverse anti-malarial drug reactions in the Peruvian Amazon. *Malar J*. 2016;15(1):136. doi:10.1186/s12936-016-1193-x
53. Mosima P. Inclusive Development: Some Perspectives from African Communitarian Philosophy. *Filos Theor J African Philos Cult Relig*. 2019;8(1):69-94.
54. Mugumbate J, Chereni A. NOW , THE THEORY OF UBUNTU HAS ITS SPACE IN SOCIAL WORK. *African J Soc Work*. 2020;10(1).
55. Guma PK. Rethinking Management in Africa : Beyond Ubuntu. 2012:1-12.
56. Ewuoso C, Hall S. Core aspects of ubuntu : A systematic review. 2019;12(2):93-103.

Chapter 7

Doing “reciprocity work”: the role of fieldworkers in a mass drug administration trial in The Gambia

The moto-bikes of the MASSIV clinical team are parked in an intervention village during a round of MDA

ABSTRACT

In their roles as nurses, data collectors, or other, fieldworkers undertake myriad tasks working intimately with and on the bodies of others - a type of work called 'body work.' This work further includes the micro-political relations shaping these interactions, and studies have shown the importance of these relationships in the success of clinical trials, particularly in The Gambia. This study seeks to expand the concept of body work to understand the roles and interactions of fieldworkers within the trial community, and the effect on a mass drug administration clinical trial (MDA). We conducted a mixed-methods social science study alongside the MDA in 2018-2019, including in-depth interviews, focus group discussions, and semi-structured observations with the population involved (and not) in the MDA, as well as the MRC fieldworkers. We found that fieldworkers participated in what we call 'reciprocity work.' Through their regular tasks and interactions, they necessarily showed respect and established trust in a way that formed and contributed to reciprocal relationships, the results of which impacted the trial and individuals' autonomy in the decision-making process. Understanding the role of fieldworkers and their reciprocity work is a vital component in comprehending how research ethics are made and conducted in global health research.

INTRODUCTION

The recent rise in literature regarding the decolonization of global health research and practice has helped to highlight the strong and historic power and colonial relationships that exist in the discipline, particularly between large health institutions (often based in the Global North) and the communities in which they work (most often based in the Global South)[1]. Much continues to be written about how global health organizations and institutions can change the current power paradigm, and many of the recommendations include greater involvement of target communities in the design and decision-making of health interventions or clinical trials[2,3]. Regardless of which community engagement strategies are used to carry this out, greater involvement of the local communities will require the work and skills of the frontline and fieldworkers who are often saddled with the task of mediating between research institutions and communities as is[3,4].

Fieldworkers can include data collectors, field nurses, and others who work on the 'frontline' of doing and generating Global Health research and knowledge. Due in part to their positions 'in the field,' fieldworkers remain an underrepresented cadre of the Global Health workforce, out of view from the gaze of the discipline's leadership and policy makers[4–7] During clinical trials, the specific work required of fieldworkers causes them to be intimately involved in and with the lives and bodies of potential trial participants, a type of work referred to as 'body work'[8]. Body work is a form of paid labour undertaken by a vast variety of healthcare and social workers focused on the 'assessing, diagnosing, handling, treating, manipulating, and monitoring' of bodies[8]. In this sense, body work is the type of labour that most fieldworkers are trained and hired to do in the context of clinical trials; they take necessary body measurements, administer doses of medication, and respond to and record any reactions of trial participants.

However, beyond the corporal, body work also includes the emotions, time, and space required of this work, as well as the 'micro-political relations' between those doing the work and those being worked on[8]. Just as essential to their positions as the physical components, fieldworkers must also work within the micro-political relations of body work. They do this, in part, by maintaining regular face-to-face interactions with those from the trial communities and working within the context of their own relationships with

the individuals in them[5,9]. This requires fieldworkers to have unique skillsets, including tacit skills and 'local knowledge.' This is not only desired by research institutions[10], but also requires fieldworkers to navigate the everyday ethics of clinical trials, managing – and potentially compromising – their own ethical beliefs[4,11]. Studies have demonstrated that these additional skills – which may include participating in relationships of reciprocity, establishing trust, and showing respect – are not skills included in job descriptions or trainings, but are nonetheless essential to the success of clinical trials[12,13].

Within The Gambia, and the Medical Research Council Unit The Gambia (MRCG) in particular, the role of the fieldworkers is paramount[14–17]. The MRCG, a faculty of the London School of Hygiene and Tropical Medicine, was founded in The Gambia in 1947 – 18 years before the country's independence – and is the United Kingdom's largest international research institution[18]. Working with academic and government partners, MRCG's mission is to improve the health of West Africa by focusing on disease control and elimination, nutrition, vaccines and immunity, and maternal and child health, as well as to provide clinical and scientific training[18].

Social science studies, often conducted concurrent to the institution's clinical trials, have demonstrated the unique and complex history and relationship MRCG has in The Gambia and with the villages where studies and interventions are conducted[14,16,17]. Within its history, MRCG has been present through times of turmoil and insufficient government resources, including the political and economic crises of the 1990s. During this time, there was a decline in government-provided healthcare and an increase in foreign scientific research – particularly through the MRCG. By way of its clinics and the ancillary care provided during clinical trials, the MRCG has been the *de facto* healthcare option most readily available to many Gambians, especially those in rural areas[13,17]. Therefore, most of those enrolled in MRCG trials regard the institution as one of healthcare provision or foreign aid rather than of research[13,17]. For those living in trial villages, clinical trials are not necessarily viewed as specific and time-bound activities; rather, people see the work of MRCG as a continuous effort to 'work with' the village and provide necessary medical care that is otherwise inaccessible[13,16,17].

This historical setting of power and resource inequities has created complex relationships between the MRCG and the trial villages, but how this relates to and impacts the fieldworkers themselves is under explored. As part of their role, MRCG fieldworkers are engaged in complex relationships with the individuals in trial communities. This includes relationships of 'exchange'[13], that have been shown to directly impact trial enrolment, informed consent, and continued trial participation[16,19]. The relationships between institutions and communities are bound to change as Global Health works to decolonize its research and practice. As these relationships are mediated through the fieldworkers, it is ever more important for research institutions and those who make Global Health ethics and policy to understand the complex roles of the fieldworkers, and how their body work may be affected, as they navigate these changing dynamics. Working within this context, the objective of this study is to expand the notion of body work, particularly the micro-political relationships it includes, to understand the roles, interactions, and effects of the fieldworkers on the individual participants and overall success of a mass drug administration (MDA) trial for malaria elimination in The Gambia.

METHODS

Study setting

This study took place in the southern bank of the Upper River Region (URR) of The Gambia, an area with seasonal malaria transmission patterns, and the highest rates of malaria in the country. In this setting, each village is headed by the Alkalo, the village chief, and is further divided into compounds, each led by the compound head (usually the oldest male of the family). Subsistence farming is the most prevalent economic activity in the area, though some villagers also engage in herding, fishing, or small businesses. Importantly, government-provided healthcare is difficult to access, and private healthcare is virtually unattainable. Trial villages are located far from government health facilities, and transportation is a prohibitive factor in terms of access. Further, health facilities are often subject to stock-outs, forcing people to try and obtain expensive treatments from private pharmacies.

Study design

We conducted a mixed-methods ethnographic social science study concurrent to the 'Mass drug administration of ivermectin and dihydroartemisinin-piperaquine as an additional intervention for malaria elimination (MASSIV)' trial, a community-based, cluster-randomized control trial that took place in 2018-2019[20]. The objective of the overall social science study was to understand social factors influencing the effectiveness of the MDA intervention, including acceptability and its effects on coverage and adherence. This paper focuses on the roles of the fieldworkers and their interactions in the trial villages.

The MASSIV trial was conducted by the MRCG and international partners, including the London School of Hygiene and Tropical Medicine and the Institute of Tropical Medicine Antwerp. The MDA trial took place in 16 control and 16 intervention villages. The overall target population for the MDA was approximately 5400 people; each trial village ranged in size from 140-700 people. In the intervention villages, the trial consisted of directly observed therapy (DOT) of the two MDA trial medications. Medication was to be taken three days in a row for three consecutive months prior to the peak of malaria transmission season (August-October in 2018 and July-September in 2019). In the control villages, those who opted to enrol were asked to provide a blood sample for malaria testing. No trial medications were distributed in the control arm except in the event of malaria positive cases. Outside the sensitization meeting, the MASSIV trial had no formal community engagement activities.

Data collection

This study included in-depth interviews (IDIs) and focus group discussions (FGDs), as well as informal conversations with who those did and did not take the MDA medications, village leaders and stakeholders, and MASSIV field staff in both the control and intervention arms of the trial. Sampling was purposive to ensure maximum variation in level of involvement in the trial. Structured and semi-structured observations of all components of the MDA trial also took place, from pre-trial sensitization meetings through the final drug distribution.

For this specific study, additional IDIs were conducted with fieldworkers throughout the duration of MASSIV. Though the population of interest

included nurses of different levels and specialities, data collectors, and others, we have chosen to use the general term 'fieldworker' throughout the manuscript to protect the anonymity of respondents. Interviews took place where convenient and private, such as in the evening after drug distribution in the trial villages, or in between distribution rounds. In addition, the social science team spent multiple days and nights living with trial fieldworkers in the intervention villages during the MDA and conducted multiple additional structured observations and informal conversations. At the end of each day with the fieldworkers, the social science team in the field held in-depth discussions on their observations and informal conversations. Detailed notes were taken during these discussions and typed up to be included in the analysis process.

Data Analysis

The analysis of data was a continuous, flexible, and iterative process, and regular reflexive discussions were held with the social science team in the field and abroad. These methods ensured a thorough understanding of emerging issues and concepts; they lasted throughout data collection and analysis until data saturation was reached and no new themes emerged. IDIs and FGDs with those in the trial villages were conducted in the local language (either Fula or Mandinka) and were recorded, transcribed verbatim, and translated into English with the aid of trained field staff. IDIs and informal conversations with the fieldworkers were conducted in English; IDIs were recorded and transcribed verbatim. Qualitative data were analysed using NVIVO v12 software (NVivo, 2018).

Ethics

Ethical approval for this study was granted by the Institutional Review Board of the Institute of Tropical Medicine in Antwerp, Belgium, and by the Scientific Coordinating Committee and Ethics Review Board of the Medical Research Council Unit The Gambia. All respondents provided verbal informed consent prior to participation.

RESULTS

Results are based on over 200 IDIs and 29 FGDs, as well as many informal conversations and non-recorded interviews. These included 12 formal IDIs, 1

FGD, and myriad informal conversations and observations specifically with and of the MASSIV field staff.

The MASSIV fieldworkers

With the exception of one fieldworker in Year 1 of the MDA, all MASSIV fieldworkers were men. They ranged in age from early-20s to mid-50s and originated from all regions of The Gambia (though very few were from the specific trial area, and none originated from the trial villages). Most, but not all, fieldworkers were trained as nurses, and all of them had previously worked with MRCG in similar roles on other clinical trials; a few had worked with MRCG for several decades. Importantly, due to their long-term employment with MRCG, some of the fieldworkers had experience in several of the MDA trial villages and were already familiar with the families and individuals who lived there.

Throughout the MDA trial, fieldworkers had many roles, responsibilities, and tasks that expanded well beyond the summary of only their physical body work that is depicted here. At the beginning of the trial, one of their first tasks was to visit the intervention and control villages and speak to the Alkalos about the trial and what they could expect for their village. The intent of this meeting was also to get the Alkalos' permission for the trial to take place in their village; no Alkalo turned down participating in the MDA trial. At these initial meetings, the Alkalos and fieldworkers would also confirm a time for the fieldworkers to return to the villages and conduct the sensitization meetings. During sensitization meetings, fieldworkers used the participant information sheet as a speaking guide to ensure they told the communities consistent information about all aspects of the MDA trial. At the end, they would answer any questions posed by the community members or leaders. A few days after the sensitization meetings, fieldworkers returned to the villages in teams (the size of which was dependent on the village population) and, traveling compound-to-compound, conducted the informed consent and enrolment processes. This included providing detailed information on the MDA trial to the individuals of the compound; the audience was often comprised of the compound head, his sons, and first wife. Once they gave their initial consent, the fieldworkers obtained informed consent and enrolled the rest of the compound members who were willing to take part in the MDA trial.

On the days of DOT in the intervention villages, fieldworkers continued to engage in much of the physical aspects of their body work. They would arrive, set up their distribution centre, distribute medications, and record all the trial data into a tablet. At the beginning of the trial, this included height and weight for dose calculations, as well as medical histories to determine eligibility. At the start of each round, this also included pregnancy tests for women and girls of reproductive age. If necessary, some fieldworkers would try and encourage those in the villages to come take the medication or would move compound-to-compound with the medication in an attempt to catch those who had not yet taken it. Importantly, in Year 2 of the MDA, fieldworkers were instructed by trial leadership to be much more present in the trial villages. Therefore, fieldworkers lived, slept, and ate with hosts throughout the DOT – engaging in the physical and non-physical aspects of body work – and one or two would stay in the village the following week to be present in the event of any adverse events.

Fieldworkers and the MRCG-Community relationship

On the surface, the long-lasting relationship between the MRCG and the trial villages was readily apparent. Though respondents were aware of the details of the specific MDA that was taking place, most did not differentiate it as a separate trial and, in fact, viewed it as MRCG continuing to '*work with*' their village. Important to respondents in a context where access to medical care is limited or non-accessible, many in the villages expressed that MRCG has long been their primary source of healthcare. Respondents provided numerous examples of how MRCG had treated a sick child or provided transport to the health facility for pregnant women in labour – all without charge to the individual.

Respondents nearly always referred to the institution as being the one to provide resources and work with the village; there was no particular role of individual fieldworkers. And though there were many people more 'senior' than them in the MDA trial leadership and implementation of the trial, it was evident in their day-to-day interactions that the individual fieldworkers in the villages represented the whole of the MRCG for the villagers. We will describe several instances reflecting this perception.

First, due to its history of providing care, many respondents expressed a need to reciprocate to the MRCG by participating in the MASSIV trial. For example,

one man in a control village recounted an incident from several years' ago when his son was suffering from severe malaria. After not being able to access care or medication at the local health facility, the MRCG successfully treated the boy, free of charge. When asked of his motivations for providing a blood sample as part of the control arm of the trial (where he would not receive the MDA medication), the man responded, '*because MRC[G] saved my son, I will do whatever they ask of me*.' In this case, the fieldworker asking for the blood sample was a representation of the MRCG, and by complying with his request to provide a blood sample, the man felt he could give back to the institution for having cared for his son.

In addition, respondents thought about the effects of their present interactions with the MRCG on their future, as well as the future of the villages'. In interviews throughout the study, it was common for respondents to answer our final questions – '*is there anything else you would like to add?*' and *'do you have any questions for us?'* – by saying how grateful they were for the work of MRCG and that they hoped MRCG would continue '*working with*' their village. Many further specified that they wanted MRCG to notice the high levels of participation in the MDA trial with the expectation that the institution would later reciprocate with additional projects. For example:

Interviewer: 'Besides the benefit of the medicine, are there any other reasons why [Village] had many people come and take the medicine?'
Respondent: 'We like the MRC[G] and we would like our village to develop. We trust the MRC[G]… It is good to take the medicine because it is in our own interest so that MRC[G] would continue operating in this area.

- *Focus group discussion with adolescent-aged girls*

Second, the historical representation of MRCG was also true in the event of negative behaviour or trial-related problems. In the first year of the MDA, communication issues meant it was not guaranteed that the fieldworkers would be provided with extra medications, such as paracetamol, to alleviate potential side effects of the trial medication (e.g., headache) (this issue was later addressed and remedied in subsequent rounds). The fieldworkers recognized this as problematic for several reasons. First, not providing these medications could erode the communities' trust in them and affect their relationships with individuals during the course of this MDA trial. Second, it could also erode the communities' trust in the MRCG, which could affect

future trials. Therefore, there were multiple examples of fieldworkers purchasing these medications with their own money.

'When you are doing research, there are certain drugs available for you to counter any reaction or anything that your people complain about - at least you should give them those - because you are using them… paracetamol or anything like that sort thing that they can use to relieve whatever pain they encounter. As far as whenever you are doing a trial on a drug, whatever you issue to them, whatever condition they have, it is really associated with the [trial] drug… [Having paracetamol, etc.] encourages them to continue taking the drug and it will also have them accept any other drug that is going to be tried in their village here, because when we do good to them and make sure we're taking care of them, they are happy - whatever drug is being brought in for trial in to their community, they will really accept, because they will think about the past situation that they encountered. If that was good, they will take it up, but when it is bad, you will start seeing some refusals.

- *Fieldworker*

Third, just as fieldworkers represented MRCG, the Alkalos represented their villages in the MRCG-Village reciprocal relationship. In many interviews with our team, Alkalos emphasized the ongoing relationship their village has with MRCG and that MASSIV was another project with which they were happy to be involved. This message was echoed at the pre-trial community sensitization meetings, where they would speak on behalf of the village to the fieldworker(s) communicating on behalf of MRCG. During these events, the Alkalos would emphasize the villages' general support and appreciation for MRCG, as well as their expectations of high MDA coverage from the community. Like those in their village, the Alkalos directed expressions of hope to the fieldworkers that this would lead to continued interventions, particularly those focusing on other development projects (periodically including those outside the functions of MRCG, such as provision of water and electricity).

<u>Fieldworkers and individual relationships</u>

Fieldworkers spent a lot of time and occasionally resided in trial communities during the MDA (especially during DOT). As such, they developed individual relationships with people in the villages and it was important they interacted in socially appropriate ways. While carrying out the full responsibilities of

their corporal body work – predominantly administering and recording MDA medication – they also balanced these social expectations and micro-political relations. Two of the most important expectations for peacefully living in the villages and achieving high MDA coverage were showing respect and establishing trust.

Showing respect

Showing respect was vital to the success of the MDA trial and began even before the first sensitization meeting took place. As representatives of MRCG, it was essential for fieldworkers to show respect to the Alkalo, as the village leader, in their very first meeting. Often this meant bringing a small offering of kola nuts, a traditional gesture of respect, and greeting him properly. If respect was not shown at these initial meetings, and the Alkalo was not happy with the initiation of the relationship, the trial would never begin in the first place, and the Alkalo may *'chase you out of the village.'* For each subsequent visit to the village, it was then expected that the fieldworkers would first greet the Alkalo before any other work took place.

After the Alkalo, appropriately and respectfully entering individual compounds was another essential aspect of showing respect; this process included recognizing the leadership role of the compound head. Multiple compound heads told us during Year 2 of the trial that they noticed and highly appreciated the increase in respect they were shown by the fieldworkers and that this increased their likelihood of participating in the trial. A prime example of this occurred during the informed consent and enrolment process (which was conducted again before the start of Year 2). When a fieldworker entered a compound and found that the compound head was not at home, rather than consenting and enrolling those adults and children who were present – as was stated in the trial protocol – they would skip the compound all together and only return when the compound head was present. This allowed the compound head to give his consent for the compound as a whole before anyone else gave their consent. As one compound head reported at the beginning of the second year:

'The consenting this year is very good as I was made to understand that all the project is about malaria, and this time the fieldworker or the nurse who talked to me spoke good Fula. And this time around, they waited for me to come and discussed with me rather than what they did last year – they

entered my compound without my consent… This year the consenting is done the way I wanted it, as they have shown me that I am the compound head and waited for me till I came [back to the compound] and talked with me, rather than doing what they did last year - talking with my wives – which I don't agree with. I am the compound head; I give orders to what my family should do.'

- *Compound head, MDA Year 2*

In the event a fieldworker did not follow these social norms, even if they contradicted the trial protocol, village members would be unhappy and the relationship would potentially be disrupted; further, it would risk an individual's participation. For example, one young woman over the age of 18 explained that a fieldworker came to her compound for the informed consent and enrolment process when her mother was not at home. The woman told the fieldworker that she could not give consent to enrol in the trial without first asking her mother. The fieldworker then told the woman that because she is an adult, she can provide consent on her own. The woman was very unhappy with the lack of respect in this response and declined participation. When her mother returned, the woman told her of the incident and they both declined any further involvement in the MDA trial.

This respect continued to be crucial throughout the MDA trial activities and each time a fieldworker interacted with a village member – especially if they were new to the trial. As one fieldworker explained to us, this initial greeting, '*the approach*,' required respect and acknowledging the importance of the individual's role in the trial:

'[Regarding] the respect that we show to the participants [during our] approach [in asking them to participate in the trial], you know, [is to focus on] their importance of participating in this program. When they come, we approach them in a respectful manner. We receive them and then we try to educate them more and [explain] to them their importance of participating in this program and what participation is for them and for the project, overall, for the community at large. So, their role as far as activities is concerned is of great importance and they deserve that respect to be given to them. So, we treat them as participants who are providing very valuable information for the project, who are contributing to the success of the project.'

- *Fieldworker*

The inequalities between fieldworkers and those in the villages was widely recognized. Fieldworkers were far more likely to be educated and have steady employment, and they had greater access to material goods and resources. An important way of showing respect was for the fieldworkers to not act '*too big*' and to '*come to their level;*' it was important to behave in a way that demonstrated they were not somehow better than those in the villages. This could have been a strategic move by a fieldworker or a way to increase a sense of belonging. Regardless, this required work and knowledge beyond what was stated in their job description. Common ways for fieldworkers to show this type of respect included making it a point to be more actively involved in the community and the lives of the individuals in 'their' villages. For example, a (non-trial related) death occurred between MDA rounds in one of the villages. The fieldworkers of that village attended the funeral in their own time and made the customary monetary donations from their own salaries. The village greatly appreciated this sign of respect and the fieldworkers' involvement with and care of the village. At other times, fieldworkers would attend naming ceremonies or other village activities, or during slow times of the MDA, fieldworkers would engage in playful activities, making jokes and entertaining those in the village. These actions, this extra body work, helped secure the fieldworkers' positions as part of the communities and were vital to the success of the MDA trial.

Establishing trust

'*If there is no respect, there is no trust*,' was a highly acknowledged sentiment among the MASSIV fieldworkers. But establishing trust required much more than showing respect on behalf of the institution they represent. For some fieldworkers, this included maintaining an active, continuous dialogue with community members throughout the trial. This could include providing details of the MDA, the importance of the medication, or the greater implications of the trial results. It was also an opportunity for community members to ask questions and for fieldworkers to dispel rumours.

'…Another thing, like the day before the actual MDA, I would be going to compounds telling them about the project so that they can understand, because what I have realized on the way is like most of them, they just think that this thing is for treatment not realizing that is research. They do not understand what is the difference between research and treatment. So, you

need to make them to understand and the benefit of this trial… So, with that, many people started to understand. They all post their questions to me; the ones I can answer, I answer. The ones I cannot answer, I refer them to a later date and when I have answers for that, I would answer them. I would also show them the potential side effects expected because these are some of the things that makes them to withdraw, because if you do not tell them the side effects, if they got it they would think that the drug is giving them problems, but if you tell them prior to the MDA, if they see the side effect, they would expect that this was the side effect this man was telling us.'

- *Fieldworker*

Fieldworkers would also utilize their 'localness' to establish trust in the trial villages. Though most were from elsewhere in the country, there was a shared idea that '*we are all Gambian.'* Historically, rumours have existed in The Gambia that the MRCG steals and sells blood to white foreigners. We were told these rumours have substantially declined, and they were rarely acknowledged among respondents, with the exception of their existence in the past or among small groups of '*uneducated*' people. Being part of the same national identity, however, garnered trust in the fieldworkers and a knowingness that they would not cause harm to their fellow brothers and sisters. In addition to not stealing blood, this also implied the safety – and potential efficacy – of the MDA medications and may have encouraged some to take part in the MDA trial.

Fieldworkers are often employed through project or trial-specific contracts, and many of the MASSIV fieldworkers had worked continuously for years moving from one contract to the next. They strongly felt the need to demonstrate that they had successfully completed their work to ensure they were in good standing and, therefore, able to easily move to the next contract and continue their employment without interruption. These additional strategies and extra-job activities used to show respect and establish trust were recognized by the MASSIV fieldworkers as essential to achieving the indicators of job success, such as high enrolment and coverage rates.

'I think respecting the community can make them to come out and drink the medicine which I think the MRC staff are practicing by respecting the elders, by giving them seats when they come to take the medicine, and we always

greet them anywhere we meet… That has a good effect for the coverage, because if we don't entertain them by talking to them, we will not have a good relationship with them which could affect our work in the village. But by knowing each other, that relationship has contributed immensely for people to come and take the medicine. For example, by knowing each other, any of them who pass nearby, and I asked him or her to come and drink the medicine, he will come and take it.'

- *Fieldworker*

As demonstrated in the quote, fieldworkers knew the nuances of their relationships with the individuals in the communities was key to a successful trial. '*Greeting*' and '*entertaining elders*' in the ways that were appropriate to this specific context and to these specific villages were some of the learned, tacit skills fieldworkers developed as a way to do their job well. The success of MASSIV – and to some extent the security of the fieldworkers' jobs – was dependent on trial indicators such as enrolment and coverage/compliance numbers. In this way, many fieldworkers felt the trial villages held considerable power. To paraphrase one fieldworker from an informal discussion: *The fieldworkers do not hold power; the communities hold all the power. The only power a fieldworker has is his attitude and using that to get the communities to trust him so that they take the medication.*

In addition, it became apparent through our ethnographic research that an individual fieldworker's ability to influence people to take the medication varied across trial villages and was affected by the social dynamics of the given village. In certain villages with strong leadership from the Alkalo and the compound heads, the fieldworkers could rely on internal social dynamics, such as social and familial pressures, to help increase and maintain MDA involvement. However, in villages where the direction of the Alkalo and compound heads was not as impactful, the interpersonal relationships the fieldworkers established with the community members were all the more important in encouraging individuals to take the medication. Had the fieldworkers not built up these relationships – through showing respect and establishing trust – people in these villages would be less inclined to participate in the MDA.

DISCUSSION

This study has demonstrated the complexities of the body work conducted by fieldworkers in the context of an MDA clinical trial for malaria elimination in The Gambia. As is often the case, fieldworkers did far more than administering, recording, and monitoring the trial medication on the bodies of the individuals in the trial villages: they manoeuvred, shaped, and maintained nuanced, reciprocal relationships among themselves, the trial participants, the MRCG, and the trial villages. Working within the micro-political relations of body work [8], they showed respect and established trust through their day-to-day labour and activities on the bodies of participants in a manner that can be defined as 'reciprocity work.'

Much of the literature regarding reciprocity as it relates to health research and clinical trials focuses on the informed consent process and the role of the (foreign) individual researcher and the (local) individual participant. It emphasizes how creating a reciprocal dialogue makes the relationship more equal and can increase autonomy in the informed consent process and aid in creating more ethical research[22,23]. Further, reciprocity has been established as essential to the success of clinical trials, particularly within low-resource contexts in the Global South[12,24]. Especially in more communal cultural settings, reciprocity is a way to ensure there is not overdependence on one person or group. It is a way to share in good fortune, grief, and material goods; there is an expectation that if one shares with you, you will share with them at a later time[25]. Within the context of clinical trial research in The Gambia, where relationships of reciprocity are integral to maintaining individual relationships as well as overall community social cohesion[14,15], studies have demonstrated the existence of relationships of 'exchange,' where trial participation was given for medical care[13]. In these instances, the reciprocity work conducted by the fieldworkers was a critical element of the trials' success.

This study elaborates on previous research by demonstrating that reciprocal relationships, and the reciprocity work conducted to maintain them, are formed within a greater historical context, and are imbued in – existing and trial induced – power dynamics amongst all actors within the greater trial community, including the MRCG, the fieldworkers, and the individuals in the

trial villages. These power dynamics are not a characteristic of a particular person or group, but are produced within the relationship itself, as well as the 'material, social, and normative' context[26–28]. Within research relationships in particular, power is created – and reinforced – by making it a part of the 'norm'[24,28].

In this study, relationships of power and of reciprocity operated in several directions based upon the actors involved. The most obvious holder of power is the MRCG, a large institution with international ties and access to funding. Within this context, where basic healthcare is difficult to access, the MRCG is able to contribute to the reciprocal relationship by providing ancillary care through trials and treatment through their clinics. This has been a reason for some individuals in the trial villages to participate in the MRCG trials or do '*whatever they ask*.' Between the MRCG and the fieldworkers, the MRCG is a provider of highly sought-after employment and a steady income. But, as shown by Kingori and Gerrets (2019), fieldworkers also hold power in their 'localness.' Institutions, including the MRCG, rely upon fieldworks to conduct their reciprocity work in such a way that also allows them to operate as cultural or linguist 'brokers' and 'intermediaries' between the institution and the trial villages [10].

There was, however, nuance in the perspectives of who held power in these relationships and how or in what point of time that power was more prevalent. Several of the MASSIV fieldworkers, as fieldworkers in other studies[4,29] recognized how they may hold positions of power the dynamics between themselves and the individuals in the trial villages, furthered by knowing that they had greater access to wealth and material goods. This was reflected by their need to show that they are '*on their level*' and not acting '*too big*' – small aspects of conducting reciprocity work. Further, through their employment with MRCG, fieldworkers may also have held power in the villages as the individual suppliers of healthcare. Though not noticed in this study, this particular power differential creates the potential for exploitation: in order to reach the coverage 'quota' required by their employer, fieldworkers could potentially take advantage of the villagers' need for healthcare. On the other hand, many fieldworkers believed that the villagers wield considerable power. If villagers showed no or limited inclination to participate and take the MDA medication, the fieldworkers would not be able to do their jobs successfully and may lose future employment, and the MRCG

may not be able to conduct the clinical trials required to maintain their standing within the Global Health community.

The reality in the field is complex and relationships of reciprocity – and the actions of reciprocity work – strongly affect individual and communities' autonomy to participate in clinical trials. By providing paracetamol with their own money, for example, fieldworkers increased trust in the communities and also increased participation in the MDA. In addition to recognizing this as a necessity, as well as a justice issue, the fieldworkers knew that if they were unable to provide medication to alleviate the side effects, people would not continue taking the medications in this trial and would be less likely to participate in future trials. As a single event representing the historical context and power/resource imbalances, reciprocity work in the sense of providing additional care may have increased participation, but may have also undermined autonomy by making those who received medical care feel they 'must' participate to continue to have access. In other trials conducted by MRCG in The Gambia, there was an expectation that by providing, for example, blood samples, study participants and their families would be given medical care[13]. In this context, it is possible that a lack of healthcare infrastructure has led to an expectation of reciprocity in the form of immediate and tangible trial benefits[16], which could lead to structural coercion[30,31].

Like all research institutions following international research ethics guidelines, the MRCG operates its trials with the policy of individual informed consent free of undue influence. The disconnect between ethics guidelines and what actually takes place 'in the field' has been documented in many settings[4,11,29,32]. However, it is the fieldworkers who must navigate the tension between what they are expected to do per protocol and what is more 'culturally appropriate' in order to meet trial demands (such as securing adequate coverage). In this way, fieldworkers often have to 'make ethics'[4] in a way that contradicts those formalized in Global Health research. For example, as part of their reciprocity work, some fieldworkers were involved in continuous dialogue with community members and gave them a space to ask questions regarding the trial and its medications. But by strengthening the interpersonal relationships, these acts of reciprocity work may also undermine autonomy in that the individuals in the trial village may feel they 'owe' the fieldworker their participation[3]. Additionally, in the event of the

young woman who wanted to wait for her mother's approval, the fieldworkers were following ethical protocol: she was over the age of 18 and did not need parental consent to participate in the trial. In theory, she had the agency to make her own decision regarding participation. In pushing her enrolment, the fieldworkers lost a potential trial participant, and the woman lost the potential benefits of trial participation. Had the fieldworkers done the more culturally appropriate thing – and showed respect by allowing her to consult with her mother for her approval first – the woman may have enrolled in the trial. On the other hand, however, they may have also undermined the trial protocol and general research ethics.

CONCLUSION

By beginning with the concept of body work as it relates to the roles of fieldworkers in an MDA clinical trial, this study has demonstrated that fieldworkers partake in a multitude of day-to-day interactions, job responsibilities, and balancing of complicated relationships in what can be called reciprocity work. There are three main components of this relationship. First, the fieldworkers are obligated to the trial and to their employer to achieve high MDA coverage. Second, fieldworkers need to maintain personal relationships with the individuals in the trial villages. In doing so, they must act in accordance with the social norms and expectations that this reciprocity entails. For their work to be fulfilled, they rely upon the individuals to comply with their requests of participation. In return, they may supply individuals with the vital healthcare and medications they need and cannot otherwise easily access. Third, fieldworkers act as representatives of the MRCG and maintain the long-standing reciprocal relationship between the institution and Gambian villages. Reciprocity work has implications for both trial coverage and individual autonomy in the informed consent process, as it can both increase and decrease autonomy in participation. The nuanced roles and myriad skills of the fieldworkers shape not only the success of the specific trial itself, but also research ethics in general. In addition to studying the ethics of neo-colonial relations in Global Health research, studying the reciprocity work of fieldworkers is also important for understanding how research ethics are shaped on the ground.

REFERENCES

1. Chaudhuri MM, Mkumba L, Raveendran Y, Smith RD. Decolonising global health: beyond 'reformative' roadmaps and towards decolonial thought. *BMJ Glob Heal*. 2021;6(7):e006371. doi:10.1136/bmjgh-2021-006371
2. Khan M, Abimbola S, Aloudat T, Capobianco E, Hawkes S, Rahman-Shepherd A. Decolonising global health in 2021: a roadmap to move from rhetoric to reform. *BMJ Glob Heal*. 2021;6(3):e005604. doi:10.1136/bmjgh-2021-005604
3. Vincent R, Adhikari B, Duddy C, et al. 'Working relationships' across difference - a realist review of community engagement with malaria research. *Wellcome Open Res*. 2022;7:13. doi:10.12688/wellcomeopenres.17192.1
4. Kingori P. Experiencing everyday ethics in context: Frontline data collectors perspectives and practices of bioethics. *Soc Sci Med*. 2013;98:361-370. doi:10.1016/j.socscimed.2013.10.013
5. Kamuya DM, Theobald SJ, Munywoki PK, Koech D, Geissler WP, Molyneux SC. Evolving Friendships and Shifting Ethical Dilemmas: Fieldworkers' Experiences in a Short Term Community Based Study in <scp>K</scp> enya. *Dev World Bioeth*. 2013;13(1):1-9. doi:10.1111/dewb.12009
6. Molyneux S, Kamuya D, Marsh V. Community Members Employed on Research Projects Face Crucial, Often Under-Recognized, Ethical Dilemmas. *Am J Bioeth*. 2010;10(3):24-26. doi:10.1080/15265161003708623
7. Maes K. "Volunteers Are Not Paid Because They Are Priceless": Community Health Worker Capacities and Values in an AIDS Treatment Intervention in Urban Ethiopia. *Med Anthropol Q*. 2015;29(1):97-115. doi:10.1111/maq.12136
8. Twigg J, Wolkowitz C, Cohen RL, Nettleton S. Conceptualising body work in health and social care. *Sociol Heal Illn*. 2011;33(2):171-188. doi:10.1111/j.1467-9566.2010.01323.x
9. Gikonyo C, Bejon P, Marsh V, Molyneux S. Taking social relationships seriously: Lessons learned from the informed consent practices of a vaccine trial on the Kenyan Coast. *Soc Sci Med*. 2008;67(5):708-720. doi:10.1016/j.socscimed.2008.02.003
10. Kingori P, Gerrets R. The masking and making of fieldworkers and data in postcolonial Global Health research contexts. *Crit Public Health*. 2019;29(4):494-507. doi:10.1080/09581596.2019.1609650
11. Kamuya DM, Theobald SJ, Marsh V, Parker M, Geissler WP, Molyneux SC. "The One Who Chases You Away Does Not Tell You Go": Silent Refusals and Complex Power Relations in Research Consent Processes in Coastal Kenya.

Seeley JA, ed. *PLoS One*. 2015;10(5):e0126671. doi:10.1371/journal.pone.0126671
12. Dada S, McKay G, Mateus A, Lees S. Lessons learned from engaging communities for Ebola vaccine trials in Sierra Leone: Reciprocity, relatability, relationships and respect (the four R's). *BMC Public Health*. 2019;19(1):1-13. doi:10.1186/s12889-019-7978-4
13. Geissler PW, Kelly A, Imoukhuede B, Pool R. 'He is now like a brother, I can even give him some blood' – Relational ethics and material exchanges in a malaria vaccine 'trial community' in The Gambia. *Soc Sci Med*. 2008;67(5):696-707. doi:10.1016/j.socscimed.2008.02.004
14. Fehr A, Nieto-Sanchez C, Muela J, et al. From informed consent to adherence: factors influencing involvement in mass drug administration with ivermectin for malaria elimination in The Gambia. *Malar J*. 2021;20(1):198. doi:10.1186/s12936-021-03732-z
15. Fehr A, Muela J, Nieto-Sanchez C, et al. The role of social cohesion in the implementation and coverage of a mass drug administration trial for malaria control in the Gambia: An in-depth comparison of two intervention villages. *Soc Sci Med*. 2021;291:114487. doi:10.1016/j.socscimed.2021.114487
16. Kelly A. Remember Bambali: Evidence, Ethics and the Co-production of Truth. In: Geissler WP, Molyneux S, eds. *Evidence, Ethos and Experiment: The Anthropology and History of Medical Research in Africa2*. 1st ed. New York: Berghahn Books; 2011.
17. Leach M, Fairhead J. Being "with the Medical Research Council": Infant Care and Social Meanings of Cohort Membership in Gambia's Plural Therapeutic Landscapes. In: Geissler PW, Molyneux CS, eds. *Evidence, Ethos and Experiment: The Anthropology and History of Medical Research in Africa*. New York: Berghahn Books; 2011:508.
18. Medical Research Council Unit The Gambia. Annual Report 2018. https://www.mrc.gm/wp-content/uploads/2019/05/Annual-Report-2018.pdf. Published 2018. Accessed March 28, 2022.
19. Kelly AH, Ameh D, Majambere S, Lindsay S, Pinder M. "Like sugar and honey": The embedded ethics of a larval control project in The Gambia. *Soc Sci Med*. 2010;70(12):1912-1919. doi:10.1016/j.socscimed.2010.02.012
20. Dabira ED, Soumare HM, Lindsay SW, et al. Mass drug administration with high-dose ivermectin and dihydroartemisinin-piperaquine for malaria elimination in an area of low transmission with high coverage of malaria control interventions: Protocol for the massiv cluster randomized clinical trial. *JMIR Res Protoc*. 2020;9(11):e20904. doi:10.2196/20904
21. NVivo. 2018. https://www.qsrinternational.com/nvivo-qualitative-data-analysis-software/home.

22. Bourdieu P. The forms of capital. In: Richardson JG, ed. *Handbook of Theory and Research for the Sociology of Education*. Westport, CT: Greenwood; 1986:241-258.
23. Maiter S, Simich L, Jacobson N, Wise J. Reciprocity: An ethic for community-based participatory action research. *Action Res*. 2008;6(3):305-325. doi:10.1177/1476750307083720
24. Kerasidou A. Trust me, I'm a researcher: The role of trust in biomedical. *Med Heal Care Philos*. 2017;20(1):43-50. doi:10.1007/s11019-016-9721-6
25. Ujewe SJ. Ought-onomy and mental health ethics: From "respect for personal autonomy" to "preservation of person-in-community" in African ethics. *Philos Psychiatry Psychol*. 2018;25(4). doi:10.1353/ppp.2018.0032
26. Broer T, Nieboer AP, Bal R. Mutual powerlessness in client participation practices in mental health care. 2012:1-12. doi:10.1111/j.1369-7625.2011.00748.x
27. Tourney G. Michel Foucault: Beyond Structuralism and Hermeneutics. *Am J Psychiatry*. 1983;140(8):1087-a-1090. doi:10.1176/ajp.140.8.1087-a
28. Heroux E. Power. Vol. 3 of The Essential Works of Foucault, 1954-1984. *SubStance*. 2001;30(3):143-150. doi:10.1353/sub.2001.0025
29. Gikonyo C, Bejon P, Marsh V, Molyneux S. Taking social relationships seriously: Lessons learned from the informed consent practices of a vaccine trial on the Kenyan Coast. *Soc Sci Med*. 2008;67(5):708-720. doi:10.1016/j.socscimed.2008.02.003
30. Nyirenda D, Sariola S, Kingori P, et al. Structural coercion in the context of community engagement in global health research conducted in a low resource setting in Africa. 2020:1-10.
31. 31. Fisher JA, Fisher JA. Expanding the Frame of "Voluntariness" in Informed Consent: Structural Coercion and the Power of Social and Economic Context. 2020;23(4):355-379.
32. Kingori P. The 'empty choice': A sociological examination of choosing medical research participation in resource- limited Sub-Saharan Africa. 2015. doi:10.1177/0011392115590093.

Chapter 8

Rethinking “participation”: Local strategies for increasing coverage and community involvement in an MDA clinical trial for malaria elimination in The Gambia

A MASSIV fieldworker explains the details of the MDA to a group of women and children in the courtyard of their compound

ABSTRACT

Mass drug administration (MDA), increasingly used for the control and elimination of malaria, requires approximately 80% of the targeted population to take medication(s) as prescribed. The key implementation indicators used to evaluate MDA– coverage, compliance, and adherence – are applied inconsistently and redefined across programmes, therefore preventing comparisons and the ability to evaluate MDA's overall benefits. Further, these indicators are often used to describe issues of community participation, a technical construction that enables implementers to impose an overly reductionist operational gaze over social and political processes that are complex in nature. This study aims to explore emic definitions of "participation" from the perspective of trial communities and describe strategies deployed by village members to increase local involvement in an MDA trial that took place in The Gambia between 2018 and 2019. We conducted a mixed-methods, ethnographic study concurrent to a community-based, cluster-randomized MDA trial. Data includes structured observations of all trial components, informal conversations, 210 in-depth interviews, and 29 focus group discussions. Our results indicate that the social values of the trial communities, particularly social cohesion, communal decision-making, and acting for the betterment of the community, created a supportive environment for participating in the MDA. Furthermore, our results show that "participation" is far more nuanced from the perspective of the community than the act of taking the medication or not. We intend to contribute to the debate on MDA effectiveness by first making visible communities' contributions to the intervention beyond what is commonly reported, and by expanding understanding of the social mechanisms that increase medicinal intake.

INTRODUCTION

Mass Drug Administration (MDA) has been used for the control and elimination of several infectious diseases, and is currently one of the available tools deployed in contexts approaching malaria elimination[1–3]. To successfully reduce malaria transmission and lower malaria case prevalence, approximately 80% of the targeted population must take the MDA medication as prescribed, including asymptomatic and healthy individuals. Critical to determining the effectiveness of MDAs are three key indicators: coverage, compliance, and adherence. These indicators are generally used to measure the extent to which intervened communities follow the treatment protocol[2] and, as a consequence, assess the potential effectiveness of the intervention.

In contrast to the ways they are usually presented, these indicators are far from straightforward measures. As 'implementation indicators'[4], measures of coverage, compliance, and adherence are constantly redefined and adapted to specific MDA strategies in terms of doses, target population, and means of distribution[5,6]. Coverage, for example, is commonly defined as the proportion of individuals reached by the MDA in a particular setting[7] (10). The methods used to define the numerators and denominators necessary to calculate this figure often rely on a single source of reference, such as census data, which can easily lead to the over or underestimation of coverage rates[8,9]. This problem has already been identified in relation to traditional malaria control methods (e.g., insecticide-treated bed nets-ITN, and indoor residual spray-IRS). Since calculation methods are rarely reported in publications, researchers have highlighted the potential for decontextualized interpretations of coverage data misleading public policy[10].

Compliance and adherence usually elaborate on coverage to indicate acceptability — and potential sustainability — of the intervention[11]. Although often used interchangeably, these terms do not have the same meaning. In the past, the term *compliance* was used within the medical literature, and its antonym, non-compliance, was alluded to as a deviance that needed to be corrected: "failure to comply is a failure of discipline"[12]. To counter this connotation of irrational disobedience to medical advice[8,9], since the 1980s, many in the field began to prefer the term *adherence*, arguing that it is less paternalistic and includes patients as actors critically assessing their medicine

intake through individual rational decision-making processes[11,13]. As a result, while compliance is commonly used to describe medicine intake as a 'yes' or 'no' behaviour, adherence indicators are designed to describe uptake throughout treatment and show variations in this process[14]. What transpired from this debate to the MDA field is the historic tension between medical advice and individual decision-making. Unlike most clinical encounters where the patient is in a dyadic relationship with the doctor when medication is prescribed, the relationships between providers and target populations in MDA settings, particularly those involving community-level implementation, are not private or even direct. As a result, continuing with the suggested medicine regimens or not can be influenced by multiple factors. Previous studies on adherence to MDA in malaria elimination show that completion of treatment can be impacted by individual factors such as scepticism towards MDA as a control method[15–17], fear of adverse drug reactions, and low perception of risk[18,19]. Other effects may include interpersonal factors, such as a lack of trust in the implementation team or agency[20], and material/physical obstacles, such as distribution strategies that do not fit the socio-cultural context or people's mobility and productive needs[21]. Larger social and cultural dynamics, such as social cohesion [22,23] or a sense of responsibility towards family members and village authorities [24] have also been identified as relevant in this context. However, most adherence indicators are reported to assess interventions' fidelity and, as such, are rarely modified to reflect social realities identified throughout the course of a trial.

In addition to their limitations to assess what they intend to measure, these indicators are also used to describe another level of intervention uptake: *community participation*. Individuals who received the medication (coverage) or continued with it for some time (compliance, adherence), are usually referred to as 'participants'. In these cases, the person is said to have 'participated' or 'not participated' in the MDA based on their status in relation to medicine intake[18,22,25–29]. Since community participation is reported as a function of the behaviours performed by the local population in relation to medicine intake, health education campaigns and community sensitization activities are often designed to increase participation in MDA projects. In practice, community participation is then transformed into an implementation indicator and also approached by means of coverage and compliance.

In all these cases, researchers and implementers pay little attention to the impact of existing dynamics, outside program-led activities, on the course of the intervention. To our knowledge, little is known, for example, about the intra-village and intra-household pressures to participate, with its internal moral tensions and contradictions, which may be a key element for projects to succeed. This remains an important knowledge gap, as several studies have questioned how power imbalances between implementing institutions and villagers, the pressure derived from the need to access vital healthcare and other services or goods, and multiple subtle ways of resisting institutional pressure to participate in interventions impact the idea of "individual participation" that lies at the heart of MDA strategies.

We explored these local tensions in a social science study ancillary to an MDA trial conducted in The Gambia. In this manuscript, we will describe the experience of participation as interpreted by local communities in three ways: (i) contextualizing the intervention through the lens of local structures of power and social values; (ii) defining the practices of interaction with this MDA in relation to medicine intake as characterized by local communities, and (iii) describing emic-generated strategies to encourage community involvement with the intervention beyond its programmatic objectives. By doing so, we intend to demonstrate the limitations of existing implementation indicators used to capture the complexity of intervention realities, as well as the problematic nature of applying an operational gaze to processes that are social and political in nature, i.e. community participation.

METHODS

The MASSIV trial

Mass drug administration of ivermectin and dihydroartemisinin-piperaquine as an additional intervention for malaria elimination (MASSIV) was a two-year, community-based, cluster-randomized clinical trial led by the Medical Research Council Unit The Gambia at London School of Hygiene and Tropical Medicine (MRCG)[30,31]. The trial included 16 intervention and 16 control villages, with populations between 140 to 700 people. MDA campaigns were carried out each month from August to October 2018 and July to September 2019, prior to the peak of malaria transmission. Each round consisted of three consecutive days of drug administration conducted through directly

observed therapy (DOT). Medication included both ivermectin and dihydroartemisinin at the same time, with considerations for eligibility and doses based on body weight. Though they changed from the initial protocol, in this MDA, coverage and compliance were in the end defined for implementation purposes as follows:

1. Coverage: the percent of the eligible population that took the medication at least once[31], and
2. Compliance: the percent of those who took the medication that completed the regimen (internal communication).

Study setting

The MASSIV trial and social science study took place in the Upper River Region of The Gambia. This region is appropriate for MDA because it is approaching elimination levels of malaria incidence, and the uptake of traditional control methods - such as ITN and IRS - is high (Cite Julie's paper?). Villages included in the MASSIV trial were familiar with the leading institution, as multiple MRCG trials operate in the area. As it is relevant to the findings, the study setting is further described in the Results section.

Study design.

The social science study. The mixed-methods, ethnographic social science study was conducted concurrently to the MASSIV trial. Fieldwork took place in 2018 and 2019, before, during, between, and after the MDA implementation periods.

Data collection. Observations were conducted of all components of the trial, from the pre-trial sensitization meetings, enrolment, and informed consent processes, and every round of DOT. Observations were structured and included informal conversations with the trial team and people present in the villages at the time (including those who took and did not take the medication). The study also included in-depth interviews (IDIs) and focus group discussions (FDGs) with villagers and trial staff. IDIs and FGDs were carried out in Fula or Mandinka and translated into English by trained field workers; they were recorded, translated, and transcribed verbatim. Informal conversations and interviews with MASSIV nurses and fieldworkers were conducted in English.

Sampling. Sampling was purposive and designed to allow for maximum variation. Community leaders, people who took the medication or declined enrolment in the trial, trial personnel, and other social actors deemed relevant by the study team were included.

Data analysis. Data analysis was a continuous, flexible, and iterative process. Data were analysed in the field so emerging themes could be further researched until saturation was reached. Analysis was technically supported by NVivo Qualitative Data Analysis software [32].

Ethics

All components of this study were approved by the Institutional Review Board of the Institute of Tropical Medicine in Antwerp, Belgium and the Scientific Coordinating Committee and Ethics Review Board of the Medical Research Council Unit The Gambia. All participants provided verbal informed consent or assent (when under 18) prior to participation in any component of the research.

RESULTS

In total, 210 IDIs and 29 FGDs were completed over the two-year period of the study. Based on the data collected, the results are presented in two sections. The first section contextualizes practices of participation within the larger social and cultural environments of village life (beyond trial implementation demands) as identified during our ethnographic fieldwork. The second section identifies different forms of engagement with the MDA in terms of medicine uptake as characterized by respondents, as well as the strategies developed within the village social structures to increase involvement in the MDA based on the emic definitions of participation.

1. Social values and internal structures of power

1.1 The village context

The social values upheld by the community provide the moral framework that explain, justify, and legitimate individual behaviours. In interviews, respondents tended to use the term "participation" as linked to "duty" and "responsibility." They differentiated between two poles of a continuum: "collective interest," related to social responsibility and an obligation to the

whole community, and "individual interest," a term linked to personal desires.

This can be explained though the social context in which ties, mostly based on kinship, are pivotal in the constitution of the villages. The *Alkalo* is the village head, a political role traditionally inherited through the male line of succession from the founder of the village. Characteristics cited as necessary for a strong Alkalo included that he (always a male) is *"prepared to bring development to the doorstep of the people" (Women's FGD).* Consequently, as the leaders of their villages, the Alkalos had the responsibility to accept (or not) the MDA trial and demonstrate to the MRCG that the villagers were willing to participate. Something commonly expressed by the Alkalos interviewed was that they and their village demonstrated a willingness to "work with" the MRCG to maintain an often already long-term relationship. A continued MRCG presence in the village, especially of nurses and access to healthcare, was often deemed beneficial for the community and interpreted as a sign of strong leadership.

Under the *Alkalo* are the *kabilos*, or the council of elders, the traditional political authority and well-established socio-political institution based on lineage. Though most villages included in this trial were mono-ethnic, if there were more ethnic groups, each had representatives at the village level. The religious authority is the Imam. In many of the trial villages, these stakeholders were involved in the initial decision making regarding the MDA trial, as they were also in charge of keeping the traditional political order and maintaining peace within the village. In a context where social cohesion is seen as a key pillar of society, the idea of conflict nearly always was expressed under negative connotations; resolution was described as conducted through negotiation, social pressure, and mediation of the Alkalo or elders. Under a logic of obligation to the village, the Alkalo and elders can assert various pressures to correct an individual's behaviour when it does not comply with the overall good of the community. Therefore, "participation" in the MDA was often described as contribution to the "common good:"

"We thank God now because the Alkalo and the villagers have taken this program seriously. When they come here, the Alkalo will ask every compound head to gather their family and ask them to go and take the medicine. Every compound head would go and gather their family members and ask them to

go and take the medicine by force. We are not taking it lightly; every compound must make sure all your compound members take the medicine by force." Adult female, Mandinka.

Village health workers (VHWs) and traditional birth attendants (TBAs) are the local frontline health workers. They are elected by the village but are trained and officially recognised by the Gambian Government. Together with the *village development committee (VDC),* VHWs and TBAs play a key role in the implementation of health and health research projects led by the Government, the MRCG, and different NGOs. The *kafos*, or *community groups*, are another community organization. *Kafos* include women's and youth groups but, in contrast to the other social structures, are politically horizontal. These groups, along with the VDC, are involved in internal community activities such as collective farming, organizing social events (e.g., marriages and naming ceremonies), implementing small infrastructure repairs (maintaining the roads, repairing water pumps, or taking care of the mosque), cleaning the village (*set setal*), and implementing other external development projects. During the MDA, these organizations played a key part in several villages by helping spread information, set up the drug distribution points, and mobilizing village members.

Respondents stated that they live in a "culture of helping" defined by religious (Islam) and cultural norms around social cohesion. In this way, the good of the community comes before individual interest. According to a respondent, adhering to the MDA was both in one's best "*personal interest*," and was also a "*responsibility towards yourself, your family, and the village.*" Taking the MDA medication to protect one's family and community from malaria was sometimes described as a "*small sacrifice.*" Because certain social pressures are applied, reproduced, and experienced by the individuals in the community, a person who renounced individual interest for the benefit of all was looked upon highly and held social prestige, while the opposite was often regarded as selfish and as an undesirable behaviour that should be corrected.

"Yes, a few of them didn't want to participate in the study… In any community those kinds of people exist. Even in our village, there are a few of them here, but people will not listen to them because everyone knows what is good and

bad, and in such a situation we know how to handle such people in our community." Village Development Chairman, Fula

These values and structures, however, are not free of debate and internal contradictions. The individual behaviour of those who did not take or refused the MDA medication without a "justifiable" reason was explained as either appealing to the different character of people (e.g. "*some people are stubborn*," "*rebellious*," or "*selfish*") or to the idea that people have the free will to decide for themselves. According to several respondents, all adults are free to make their own decisions and to express their opinions in compound and village matters but are expected to act with responsibility towards the group.

"People can decide what they want, as far as this decision matches well with our culture and values." Compound head, Mandinka

1.2 The compound: residence and production unit

Villagers live in compounds, defined by enclosed spaces with one or several households belonging to the same extended patrilineal family. Social position and power distribution, as well as roles and obligations, are assigned mainly based on position within the family, gender, and age. The *compound head* leads the compound as a production unit based predominantly on agricultural work. Most compounds in the study villages were engaged in small cash-crop production or raised cows and goats. Although both men and women are engaged in agricultural work, men are considered the primary money earners and some of them are involved in complementary jobs (mostly during the dry season). Remittances are an important source of revenue, particularly from long-term migration to Europe or the United States.

This particular model of production reinforces the ideal of having "big" and "cohesive" compounds. Like at the village level, conflicts in the compound are not negligible. In interviews, compound heads argued that conflicts not only disturb social life but can have a negative impact on intra-compound collaboration for domestic and farm work, reduce productivity, and eventually split the compound into two or more weaker units. Therefore, the role of compound heads in conflict management is as valued as their role as work organisers. Important decisions were often taken after consultation

with compound members. Although compound heads had the 'last-word,' women often participated in decision-making and could be very influential, particularly the first wife of the compound head. In the event of a compound head being young, his mother may be heavily involved in decision making.

In words of the interviewees, a compound head must first demonstrate "strong leadership" at the compound level to rise to a position of leadership in the village. He would be seen as "strong" by keeping internal order and peace; making the family "speak with one voice" (referring to social cohesion, unity and consensus) and establish "shared interests." As a manager, he should survey that all compound members "*perform properly their tasks, otherwise the compound will collapse*" (Adult Female, Fula).

Related to the MDA, a sign of strong leadership often meant the compound head could ensure his whole compound took the trial medication. Therefore, compound heads were under pressure from the village level to produce compound-level familial pressure. Compound-level pressure is pyramidal in nature: pressure flows from the compound head "down" in a hierarchical structure of power relations to the other members of the compound. It is also public, at least within the boundaries of the compound, socially legitimated, and reproduced and amplified, at different degrees, by people in positions of authority and peers. The compound heads are a key intermediary part of the mechanism by which community leaders can exert pressure on individual villagers. They play an important role in mobilising people from their compounds and use terms such as "*convince*," "*explain*," or, sometimes, "*force*" to describe the influence they exert on family members to participate in the MDA. In the local narrative, the pressure to take the trial medication is lower, or less effective, in *"weak compounds*" than in "*strong compounds*."

1.3 Conjunctures of vulnerability

These relationships are, of course, enacted in the larger socio-political, economic, and healthcare landscapes of the trial communities. Limited access to healthcare also affected how villagers related to the trial. Respondents commonly mentioned that even if they were able to get to the health facility and pay for an appointment, they were frequently unable to pay for the medication (malaria medication is free-of-charge in government

facilities, but stock-outs are common, forcing people to purchase medications at private pharmacies).

The MRCG has been operating in the study area for decades. Though primarily a research institution, the MRCG is often locally viewed as a provider of free-of-charge healthcare through its studies and clinics (no major differences are perceived) to people in this region. When the MRCG enters a local village to implement a trial during peak malaria season, especially if the implementation strategy includes a nurse stationed to the village, community members may view participating in the trial as a way to access much needed healthcare and medication.

"When [MRCG] first informed me about drinking the medication, I also know that it is true – as the saying in Fula says, 'if you are to climb up a tree for something but it finds you on the ground, you just need to pick it up and get the benefit of it.' That is what is good and that is what people like." Compound head, Fula

The timing of the MDA also fell during the most intensive part of the agricultural season when nearly all eligible individuals were required to spend ample time working on the farms (a pressure made worse by environmental changes making dry seasons longer and harsher). This time is also one of strong rains, which lead to an increase in illnesses and further complicate transport. If illness, particularly malaria, occurs at this time, people in the trial communities described that they risk not only increased difficulties in accessing medical care, but a loss of income due to missed labour and domestic needs. This created pressure to participate in the MDA to prevent or alleviate the financial and lost labour-related burdens of malaria. This pressure was most strongly felt by the compound heads, as they were the ones responsible for funding compound members' medical needs. Mothers, too, felt, replicated, and amplified this pressure.

"The reasons girls take the medication is they are asked by their mother to take the medication. Mothers know when the girl child is sick, the mother suffers a lot. That is the reason we force the girls to go and take the medication." Adult female, Mandinka

Overall, the socio-political context of the trial communities and the poverty-related vulnerability were felt by everyone in the village. This created pressure, but the pressures were felt and acted on differentially based upon an individual's status and position.

2. Practices of participation and community strategies to increase medicinal intake

Respondents described taking the MDA medication and their practices of participation in relation to these social values and larger structures of power. These practices of participation were described as active or passive behaviours, enacted accordingly to how "hard" or "soft" people's determination was, or how easy it was to convince them to act otherwise in subsequent rounds. Through these practices of participation, opportunities to exert influence and change people's behaviour were also identified.

Active medicine intake, community mobilization, and narratives of evidence

Those who took the MDA medication were thought to do so either actively or passively. Individuals who actively took the medication were described as "responsible." They often emphasised their willingness to take the medication, even if it was difficult: they would wait in the queue, even under heavy farming-related pressures. Narratives by these individuals frequently focused on the opportunity derived from the convenient presence of the MRCG in the village, and expressed pride in doing what was requested from them to have access to the medication.

"I said [what] I am happy about this project is when you bring food for a hungry person, what do you expect to see? This person will eat the food. That means you are healthy. When someone comes to treat you, you should be happy about that."

- *Adult male, Fula*

A decisive aspect of "actively participating" in the MDA was promoting it among others in the village, particularly if one had a high social status, and mobilizing villagers and family members to take the medication. Importantly, this practice of participation was not based on medicinal intake. Many "active participants" were compound heads who were ineligible to take the medication. Nonetheless, they still *participated* in the trial by utilizing

different strategies to increase medicinal uptake among their community and family.

One common strategy prior to the start of the second year of the MDA was the use of *narratives of evidence* by research participants. The pressures exerted from the socio-economic context of the trial area created a mechanism of increasing medicinal uptake through the spread of "evidence" regarding the trial's effectiveness in preventing malaria. This included the positive effects of the medication on the villagers' health, as well as the economic benefits of fewer medical expenses or loss in productivity for those who did not have malaria. The narratives of evidence were elaborated by comparing the results of Year 1 with previous years, and comparing those who had refused the MDA with those who took the medication:

"I decided for my family to participate because the medicine had benefitted us a lot last year. All those who took the medicine last year did not have malaria, but there is one compound head who refused to participate last year - most of his family members had malaria last year. He has been carrying them to the health facility for treatment. That is why when we were informed by Alkalo and village assistant that the MRC is visiting the village for consenting, I informed everyone about it in my compound and they were all consented." Village Development Committee Chair, Fula

Some respondents, in their role of community mobilisers, mentioned they were using these narratives of evidence as a strategy to convince others to engage in the MDA or to let their family members take part. Rather than health and suffering *per se*, what village leaders emphasised was the need to create awareness on the economic impact of the disease. They targeted all adults, especially compound heads, and strongly emphasised how important it is to take the medication to avoid malaria and protect the economic stability of the compound.

<u>Passive medicine intake and pyramidal pressure</u>

A large percentage of those who took the medication were described as "those who obey," "those who follow," and "those who understand." Most often, this included people in subordinate social positions, such as young women or adolescents and children. Taking the medication because they were told to was often an aspect of demonstrating "respect" for their elders.

However, as this practice of participation was deemed "soft," it required constant reinforcement and "surveillance" by those in greater positions of authority.

The opposite, those who resisted taking the medication, were described as "those who don't obey," "those who don't follow [the community]," "those who don't understand," and "those who are selfish." These individuals were usually identified as young males and described as having "studies but no wisdom", as they were reluctant to follow traditions that required listening to elders' advice. Relatedly were individuals described as "those who avoid taking the medication," and characterized as "not responsible," "those who forget," or "those who are lazy." For example, a local stakeholder involved in the trial described some people, "when it is time for the MDA, they will start to make excuses, saying 'I am going to the garden and other places'" (Adult male, Fula). This was also most often young men and boys who have relative freedom to move about as they please and also have work-related obligations that could provide opportunities to avoid being in the village at the time of the MDA.

Like passively taking the medication, passively not taking the medication was deemed a soft practice. Because they did not out-right refuse the trial, this group could eventually be persuaded to participate, but it would require the efforts of those in positions of authority. Consequently, many compound heads developed strategies to exert pyramidal pressure and increase medicine uptake among these individuals. For example, sometimes they blamed or reprehended those who did not take the medication in front of others to amplify pressure through shame. In other cases, compound heads described how they looked for compound members who did not take the medication, and "forced" them to go to the distribution point.

"The compound head can apply force. My daughter is a student, she took the medicine once, and she said she had a headache after taking the medicine. She decided to refuse to take the medicine for the second time, but my husband shouted on her and advised her to go and take the medicine. She accepted and took the medicine all the rounds." Adult female, Mandinka

Other strategies were more subtle. For example, some compound heads would go to the MDA distribution point with the family to ensure they all took the medication.

"When I wake up in the morning, I mobilise them all by collecting all the participant cards and lead the way to the MDA site. The team would identify everyone by their names of the participant card. When they call their name by turn, I ask them to give each of them the medicine to take in front of me. When they all take and disperse then I would take last. After taking the medicine in the morning, those supposed to go to school would go and those going to the farms would go and work." Adult male, Fula

However, compound heads usually described non-coercive forms of pyramidal social pressure based on motivation and encouragement. For example, they would talk with family members who were reluctant, explain the benefits of the trial, and advise them to participate as a cohesive and united compound. Commonly mentioned was "teaching by example" (or the "exemplary role"), where the compound head would be the first to take the medication in front of other compound members. Lastly, some compound heads and village leaders described more subtle and successful strategies to achieve compliance:

"(…) *when the* [entomology team] *comes here to catch mosquitoes, they all* [the boys] *rush to grab this opportunity. These boys would work from 7.00pm to 7.00am because they are paid. Now I have a strategy: I tell them that if any of these boys refuse to take the medicine, they would not be hired by the entomology team. That will give me no other option than to hire the girls to replace the boys. Now the boys are complying, they are taking the medication".*

- Village Development Committee Chair, Mandinka

Another practice of participation refers to "those who have a justifiable reason for not drinking the medicines," and includes two sub-categories. First, the eligibility requirements prevented some individuals from taking the medication due to pregnancy, current illness, or a pre-existing medical condition (e.g., hypertension). Second, there were socially acceptable, but not trial-related reasons as to why someone may not take the medication. Those reasons included being absent from the village during any part of the

trial (e.g., consent/enrolment or a distribution day), having to work, being "too old," or having had side effects (e.g., nausea, dizziness, etc.) in a previous round. Lack of privacy during the pregnancy tests was also considered a 'valid reason' for many women and girls, particularly unmarried adolescents. Providing a valid reason also meant those in this group were exempt from additional attempts or strategies to convince them to participate.

Lastly, there were those who declined any level of participation in the MDA trial. Though a small minority, people with this practice of participation were considered "*stubborn*" or described as "*those who don't interact with people*" (this was most common among people new to the village). This was deemed a hard position, as this group was considered very difficult or impossible to convince otherwise, regardless of strategy. Although some in this group may be singled out by the community (usually those who already experience some form of social exclusion for other reasons), it was sometimes possible for this behaviour to be justified as an expression of free will, particularly in adult men. If this position was taken by the compound head, it was also possible that his decision to refuse the MDA would be carried down and applied to his whole compound.

"The Alkalo's son came here at night, explained everything to me, said 'your family is lucky to be among the program.' I told him 'I am not interested in this program.' I do not mean the other program but the research program. So, the second time also, I went [out of the village], I came back… I saw the card with [my daughter] – she went and drink the medicine. I ask the daughter 'how you got this paper?' she said 'it was given to me by MRC people.' I ask the mother, the mother said she was not aware. I was very angry that time, I took the card from the daughter." Compound head, Mandinka

DISCUSSION

Our results describe how community participation is locally understood, performed, and encouraged in the MASSIV trial communities. Social values, particularly those of social cohesion, communal decision-making, and acting for the betterment of the entire community, as well as the pyramidal structure of power historically built to enforce authority, created a supportive environment for communities to participate in this MDA trial. Difficulties to asses issues of coverage and adherence in this particular setting

have been reported elsewhere[23,33], but this study has further elaborated on the limitations of these indicators to describe "community participation", a social process far more nuanced than the act of taking medication.

In this study, respondents described social dynamics facilitating or discouraging village members' uptake of the medication using their situated knowledge. Their narratives account for a highly dynamic process in which medicine intake is only one of many elements associated with the idea of being a 'participant' in the intervention. Actions such as allowing the trial to happen in a particular village, disseminating 'narratives of evidence' or encouraging others to take the medication, were also considered concrete ways of participating in the MDA, regardless of whether or not one took the medication.

Consequently, the strategies internally deployed to increase others' acceptance of the proposed treatment responded to contextualized exercises of soft and hard power that work differently at different moments in the trial: members of a compound might approach the MDA distribution site when the compound head is around, but not necessarily complete the treatment without his close surveillance; a mother might be able to secure access to medication by bringing her younger children, but might be limited in her capacity to do so with older or more independent kids; or a member of the community might feel entitled to tell others to take the medication while clearly refusing to do so herself.

The strategies deployed within the villages also demonstrated the value of the trial for community members in positions of power. The compound heads, those described as being the most affected by malaria, believed that participating and taking the trial medication would benefit the whole compound as it was a way to avoid losing valuable farm labour or using money for treatment. Therefore, they often enacted pyramidal social pressure within their compounds to ensure everyone in their family took the trial medication. Due to their socially-defined position as head of the family, those "below" them would not only obey, but also reproduce this pressure. Similarly, the need to reduce the financial strains of malaria triggers complex responses in which mechanisms to exercise internal pressures within the villages are enforced [24,34].

In the case of the MASSIV trial, these practices were particularly visible in the second year of the MDA, when communities themselves deployed their own strategies to facilitate involvement with the trial after the first year's implementation problems, substantially impacting the results finally reported. Studied under an operational gaze, these different social dynamics are generally presented as 'barriers' to implementation and addressed through 'community-based' activities focused on 'sensitizing authorities' and 'convincing individuals' of taking the medication. However, thinking of these local dynamics as 'barriers' – e.g. that some people prioritize work obligations to queuing for medications – carries negative connotations that demonstrate the utilitarian use of the term 'participation' in these cases: it is only relevant to the extent to which it contributes to the goals of the intervention in the specific form of medicine intake. All what happens outside that framing, i.e., the processes of negotiation, knowledge dissemination, and community organisation involved in the success or failure on these interventions, are hardly ever reported or studied.

While using the term 'participant' as binary and individualistic in nature, implementers are taking a simple observable action (medicine reception/intake) to report on a "multifaceted, fluid, and context-bound phenomena"[35], i.e. 'community participation.' For example, 'hard refusers' are already considered different or "difficult to manage," and therefore, de facto excluded from the regular mobilization channels used to promote the MDA. The fact that the trial infrastructure highly relies on existing forms of organisation in which context-specific inclusion and exclusion practices are ingrained, demonstrate how contextual factors closely impact the potential outcome of the intervention. In this case, standard sensitization practices might be able to reach community members that more closely act upon commonly accepted courses of action but fail to capture the practices of those that think of themselves as outside these structures (often times, the ones that would benefit more from the intervention).

We contend that reporting on MDA indicators (e.g., coverage and adherence) using the framing of 'community participation', is misleading. Well beyond semantics, this practice is problematic in—at least—two ways: first, the binary behaviour described by these indicators rarely corresponds with implementation realities, where apparently straightforward *actions* could be better described as *processes* subjected to multiple instances of

interpretation and revaluation against individual and communal factors[36–39]. Second, 'community participation' in disease control and elimination strategies is so loosely defined and overused that seems to lose its meaning and purpose[40]. Using implementation indicators to report about community participation in MDA strategies overstretches the conceptual boundaries of this expression and contributed to this confusion. Both problems result in reductionist practices that prevent exploration of more effective implementation models in which complex interventions are evaluated.

As it happens with any indicator, coverage and adherence are meant to be explanatory devices. However, in global health, indicators are used as much more than that[35]. In Vincanne Adams' words, "(m)etrics enable certain kinds of medical practices while impeding others. They generate forms of knowledge and certainty about some things even while effacing others"[41]. In this case, attention is drawn to implementation efforts focused on encouraging medicine intake while ignoring contextual factors that contribute to this and many other effects surrounding the intervention. By using the term 'participant' to refer to those who take the medication at any point in time and extending their individual involvement to describe a community effect, implementers use a dramatically reductionist approach to interpret local social realities in ways that are only relevant under intervention logics. By doing so, the elements that contribute to the intervention but cannot be counted or are specific to a particular context, are systematically ignored.

A recent Cochrane review emphasized the need to carefully assess issues of coverage and human mobility, among other factors, to determine the viability of MDA in malaria transmission settings, as evidence about this form of intervention is still insufficient, and studies often result in imprecisions and biases[42]. The data hereby presented supports this statement. We expect this study to contribute to understanding the methodological limitations of the approaches currently used to assess MDA and to better understand participation in these interventions. This is particularly important given the precarious realities of the health systems in which these interventions usually take place (and the meaningful staff and material demands of MDA)[37].

CONCLUSION

Participation is a multidimensional concept with important social and political connotations that involves not only individual actions, but also the cultural mechanisms that give meaning to such actions at a community levels. It entails the symbolic character of the perception of 'belonging,' as well as the norms and values that regulate such belonging (such as social pressure and cohesion). In addition, participation is always enacted from the particular position held by an individual in relation to immediate and distant social structures, represented in family groups and specific institutions.

In this study, we shifted the common research focus on adherence to MDA medication in two new directions. First, implementation research and project evaluations tend to emphasise the role of the project's strategy and implementers, but what communities do to form their own initiative to improve uptake is unexplored. Second, we focused on understanding the social mechanisms that increase medicine intake rather than the reasons for non-adherence - a far more common approach. This switch of focus can generate theoretical contributions in terms of the systemic impact of apparently "simple" interventions and provides additional insights into the value of qualitative methodologies to expand on quantitative indicators.

References

1. World Health Organization. *Malaria Eradication: Benefits, Future Scenarios and Feasibility. A Report of the Strategic Advisory Group on Malaria Eradication*.; 2019. https://www.who.int/publications-detail/strategic-advisory-group-malaria-eradication-executive-summary.
2. World Health Organization. Mass drug administration, mass screening and treatment and focal screening and treatment for malaria. In: *Malaria Policy Advisory Committee Meeting*. ; 2015.
3. Poirot E, Skarbinski J, Sinclair D, Kachur SP, Slutsker L, Hwang J. Mass drug administration for malaria. *Cochrane Database Syst Rev*. 2013. doi:10.1002/14651858.CD008846.pub2
4. Newby G, Hwang J, Koita K, et al. Review of Mass Drug Administration for Malaria and Its Operational Challenges. *Am J Trop Med Hyg*. 2015;93(1):125-134. doi:10.4269/ajtmh.14-0254
5. Jaiteh F, Ribera JM, Masunaga Y, et al. Complexities in Defining the Unit of Intervention for Reactive Community-Based Malaria Treatment in the Gambia. *Front public Heal*. 2021;9:601152. doi:10.3389/fpubh.2021.601152
6. Hetzel MW, Genton B. Mass drug administration for malaria elimination: Do we understand the settings well enough? *BMC Med*. 2018. doi:10.1186/s12916-018-1230-4
7. World Health Organization. Mass Drug Administration for Falciparum Malaria: A practical field manual. *Who*. 2017.
8. Nice J, Nahusenay H, Eckert E, Eisele TP, Ashton RA. Estimating malaria chemoprevention and vector control coverage using program and campaign data: A scoping review of current practices and opportunities. *J Glob Health*. 2020;10(2):20413. doi:10.7189/jogh.10.020413
9. Adhikari B, James N, Newby G, et al. Community engagement and population coverage in mass anti-malarial administrations: a systematic literature review. *Malar J*. 2016;15(1):523. doi:10.1186/s12936-016-1593-y
10. Gryseels C, Uk S, Sluydts V, et al. Factors influencing the use of topical repellents: implications for the effectiveness of malaria elimination strategies. *Sci Rep*. 2015;5:16847.
11. Spencer KL. Transforming Patient Compliance Research in an Era of Biomedicalization. *J Health Soc Behav*. 2018;59(2):170-184. doi:10.1177/0022146518756860

12. Whitmarsh I. The Ascetic Subject of Compliance. In: Biehl J, Petryna A, eds. *When People Come First: Critical Studies in Global Health*. Princeton University Press; 2013:302-324.
13. Kyngäs H, Duffy ME, Kroll T. Conceptual analysis of compliance. *J Clin Nurs*. 2000;9(1):5-12. doi:https://doi.org/10.1046/j.1365-2702.2000.00309.x
14. De las Cuevas C. Towards a Clarification of Terminology in Medicine Taking Behavior: Compliance, Adherence and Concordance are Related Although Different Terms with Different Uses. *Curr Clin Pharmacol*. 2011;6(2):74-77. doi:10.2174/157488411796151110
15. Adhikari B, Phommasone K, Kommarasy P, et al. Why do people participate in mass anti-malarial administration? Findings from a qualitative study in Nong District, Savannakhet Province, Lao PDR (Laos). *Malar J*. 2018;17(1):15. doi:10.1186/s12936-017-2158-4
16. Jaiteh F, Masunaga Y, Okebe J, et al. Community perspectives on treating asymptomatic infections for malaria elimination in the Gambia 11 Medical and Health Sciences 1117 Public Health and Health Services 11 Medical and Health Sciences 1103 Clinical Sciences. *Malar J*. 2019. doi:10.1186/s12936-019-2672-7
17. Peto TJ, Tripura R, Sanann N, et al. The feasibility and acceptability of mass drug administration for malaria in Cambodia: a mixed-methods study. *Trans R Soc Trop Med Hyg*. 2018;112(6):264-271. doi:10.1093/trstmh/try053
18. Dial NJ, Ceesay SJ, Gosling RD, D'Alessandro U, Baltzell KA. A qualitative study to assess community barriers to malaria mass drug administration trials in the Gambia. *Malar J*. 2014;13(1):47. doi:10.1186/1475-2875-13-47
19. Dierickx S, O'Neill S, Gryseels C, et al. Community sensitization and decision-making for trial participation: A mixed-methods study from The Gambia. *Dev World Bioeth*. 2018. doi:10.1111/dewb.12160
20. Keys H, Ureña K, Reyes J, et al. Rapid ethnographic assessment for potential anti-malarial mass drug administration in an outbreak area of Santo Domingo, Dominican Republic. *Malar J*. 2021;20(1):76. doi:10.1186/s12936-021-03594-5
21. Broekhuizen H, Fehr A, Nieto-Sanchez C, et al. Costs and barriers faced by households seeking malaria treatment in the Upper River Region, The Gambia. *Malar J*. 2021;20(1):368. doi:10.1186/s12936-021-03898-6

22. Kajeechiwa L, Thwin MM, Shee PW, et al. The acceptability mass administrations of anti-malarial drug as part of targeted malaria elimination in villages along the Thai-Myanmar border. *Malar J*. 2016;15(1):1-12. doi:10.1186/s12936-016-1528-7
23. Fehr A, Muela J, Nieto-Sanchez C, et al. The role of social cohesion in the implementation and coverage of a mass drug administration trial for malaria control in the Gambia: An in-depth comparison of two intervention villages. *Soc Sci Med*. 2021;291:114487. doi:10.1016/j.socscimed.2021.114487
24. Jaiteh F, Okebe J, Masunaga Y, et al. Understanding adherence to reactive treatment of asymptomatic malaria infections in The Gambia. *Sci Rep*. 2021;11(1):1746. doi:10.1038/s41598-021-81468-1
25. Adhikari B, Phommasone K, Pongvongsa T, et al. Factors associated with population coverage of targeted malaria elimination (TME) in southern Savannakhet Province, Lao PDR. *Malar J*. 2017;16(1):424. doi:10.1186/s12936-017-2070-y
26. Hsiang MS, Ntuku H, Roberts KW, et al. Effectiveness of reactive focal mass drug administration and reactive focal vector control to reduce malaria transmission in the low malaria-endemic setting of Namibia: a cluster-randomised controlled, open-label, two-by-two factorial design trial. *Lancet*. 2020;395(10233):1361-1373. doi:10.1016/S0140-6736(20)30470-0
27. Nguyen TN, Thu PNH, Hung NT, et al. Community perceptions of targeted anti-malarial mass drug administrations in two provinces in Vietnam: A quantitative survey. *Malar J*. 2017;16(1):1-12. doi:10.1186/s12936-016-1662-2
28. Dierickx S, Gryseels C, Mwesigwa J, et al. Factors Associated with Non-Participation and Non-Adherence in Directly Observed Mass Drug Administration for Malaria in The Gambia. Sullivan DJ, ed. *PLoS One*. 2016;11(2):e0148627. doi:10.1371/journal.pone.0148627
29. Pell CL, Adhikari B, Myo Thwin M, et al. Community engagement, social context and coverage of mass anti-malarial administration: Comparative findings from multi-site research in the Greater Mekong sub-Region. Rutebemberwa E, ed. *PLoS One*. 2019;14(3):e0214280. doi:10.1371/journal.pone.0214280
30. Dabira ED, Soumare HM, Lindsay SW, et al. Mass drug administration with high-dose ivermectin and dihydroartemisinin-piperaquine for malaria elimination in an area of low transmission with high coverage of malaria

control interventions: Protocol for the massiv cluster randomized clinical trial. *JMIR Res Protoc*. 2020;9(11):e20904. doi:10.2196/20904
31. Dabira ED, Soumare HM, Conteh B, et al. Mass drug administration of ivermectin and dihydroartemisinin–piperaquine against malaria in settings with high coverage of standard control interventions: a cluster-randomised controlled trial in The Gambia. *Lancet Infect Dis*. 2021. doi:https://doi.org/10.1016/S1473-3099(21)00557-0
32. QSR International. QSR International. *NVivo*. 2012.
33. Fehr A, Nieto-Sanchez C, Muela J, et al. From informed consent to adherence: factors influencing involvement in mass drug administration with ivermectin for malaria elimination in The Gambia. *Malar J*. 2021;20(1):198. doi:10.1186/s12936-021-03732-z
34. Masunaga Y, Jaiteh F, Manneh E, et al. The Community Lab of Ideas for Health: Community-based Transdisciplinary Solutions in a Malaria Elimination Trial in The Gambia. *Front Public Heal*. 1AD;0:1042. doi:10.3389/FPUBH.2021.637714
35. Gerrets R. Charting the road to eradication: Health facility data and malaria indicator generation in rural Tanzania. In: Rottenburg R, Merry SE, Park S-J, Mugler J, eds. *The World of Indicators*. Cambridge: Cambridge University Press; :151-187. doi:10.1017/CBO9781316091265.007
36. Muela Ribera J, Hausmann-Muela S, Gryseels C, Peeters Grietens K. Re-imagining adherence to treatment from the “other side”: Local interpretations of adverse anti-malarial drug reactions in the Peruvian Amazon. *Malar J*. 2016;15(1):136. doi:10.1186/s12936-016-1193-x
37. Kaehler N, Adhikari B, Cheah PY, et al. The promise, problems and pitfalls of mass drug administration for malaria elimination: a qualitative study with scientists and policymakers. *Int Health*. 2019;11(3):166-176. doi:10.1093/inthealth/ihy079
38. Vincent R, Adhikari B, Duddy C, et al. "Working relationships" across difference - a realist review of community engagement with malaria research [version 1; peer review: 1 approved]. *Wellcome Open Res*. 2022;7(13). doi:10.12688/wellcomeopenres.17192.1
39. Krentel A, Fischer PU, Weil GJ. A Review of Factors That Influence Individual Compliance with Mass Drug Administration for Elimination of Lymphatic Filariasis. Addiss DG, ed. *PLoS Negl Trop Dis*. 2013;7(11):e2447. doi:10.1371/journal.pntd.0002447

40. Leal PA. Participation: The Ascendancy of a Buzzword in the Neo-Liberal Era. *Dev Pract*. 2007;17(4/5):539-548.
41. Adams V. Metrics: What Counts in Global Health. March 2016. doi:10.1215/9780822374480
42. Shah MP HJCLLKAKSP, Desai M. Mass drug administration for malaria. *Cochrane Database Syst Rev*. 2021;(9). doi:10.1002/14651858.CD008846.pub3

Chapter 9

Discussion

A roadscape view from our vehicle while heading to an intervention village

The overall focus of this dissertation has been to answer the research question: *How can we understand the socio-cultural and ethical aspects of participation in a mass drug administration trial for malaria elimination in The Gambia?* To do so, my team and I conducted in-depth social science research around an MDA clinical trial for malaria elimination in The Gambia (the MASSIV trial). From this research, I have composed five manuscripts that make up the previous chapters and delve deeply into this primary research question and the dissertation's sub-questions. This chapter now highlights the key findings of this study.

9.1. Summary of manuscripts

Chapter 4 provides the economic context of the trial setting and the financial repercussions malaria has on those residing in the trial villages. We found that even though malaria treatment is technically free of charge and provided by The Gambian government, 70% of the respondents in the household survey paid out-of-pocket costs and experienced prohibitive expenses the last time they or their child had malaria. These expenses included buying medication at private pharmacies due to stockouts at the health facilities and expenses related to traveling for care, such as transportation, meals, and lodging.

Chapter 5 focused on the factors that acted as facilitators or barriers to taking the MDA medication and assessed whether those factors were more or less influential at different times throughout the trial: from initial informed consent and enrolment to the final dose of the medication. The results expanded upon the previous literature that showed individual factors, such as mobility, agricultural demands, or side effects, affected medicinal intake and introduced the importance and influence of social dynamics on the decision-making process, including social cohesion. I focused on social cohesion in Chapter 6 and demonstrated how two different villages expressed this social dynamic through their involvement and engagement with the implementation of the MDA. Further, we found that this expression of social cohesion was directly correlated with the differing coverage rates of the two villages.

In Chapter 7, I described the position of the Medical Research Council Unit The Gambia (MRCG) fieldworkers in the MDA trial, including their role in the

research communities' dynamics, such as social cohesion. Based on the sociological principle of body work, we found that the fieldworkers engaged in what we labelled "reciprocity work." Reciprocity work included the day-to-day activities and labour of the fieldworkers that showed respect and established trust with the trial communities. Though these activities went beyond what would be considered in the job descriptions of the fieldworkers, we found that they were essential to the success of the MDA. Lastly, in Chapter 8, we analysed the definition of "participation" in the MDA from the communities' perspective. Unlike the binary definition based on medicinal intake used by the trial team, we found that communities considered participation to be based on one's involvement in the trial – whether they took the medication or not. Further, we found that the emic understandings of participation included both active and passive forms, and that unrelated to the activities of the trial team, the communities themselves employed internal strategies to increase participation and medicinal uptake.

The following section highlights these key findings as they are relevant to each research sub-question.

9.2. Key findings by research sub-question

9.2.1. Sub-question 1: What – and for whom – is participation in an MDA clinical trial*?*

Before addressing what factors affected participation in the MASSIV trial, it was first important to understand what participation meant and how it was defined in regard to medicinal intake. Perhaps one of the first findings of this dissertation was that *participation* was far more complicated than is otherwise assumed in the MDA literature and, for the respondents, went far beyond measurements of medicinal intake. This sub-section will first look at why it is important to measure medicinal intake, the problems with the current indicators in measuring medicinal intake or participation, and how the trial communities themselves defined and expressed participation as it related to the MDA clinical trial.

9.2.1.1. Why does medicinal intake matter?

Having a high percentage of the target population take the medication is essential for the success of an MDA. First, to be clinically and epidemiologically successful – i.e., to decrease the prevalence of malaria in

the target population – at least 80% of the target population must take the medication as prescribed[1]. Second, achieving this threshold is of ethical concern as it is necessary for the benefits of any trial medication to outweigh its potential risks. Though the risks for the medications used in the MASSIV trial are minimal, it is still not ethical to distribute them without the possibility of the MDA being successful[2]. Therefore, to achieve its desired effect and to be ethically viable, MDA requires a high percentage (i.e., at least 80%) of the targeted population to take the prescribed medication.

9.2.1.2. How is medicinal intake measured (and why is it problematic)?
Three key indicators are used in measuring malaria MDAs: coverage, compliance, and adherence. In general, they are implementation indicators used to measure the percent of people from the target population who took the MDA medication. These indicators are introduced in Chapter 2, where I also discuss some of the historical problems of these terms and their use. This includes that throughout the MDA literature, these terms are often poorly defined and used interchangeably. An initial finding from assessing the MDA literature was that this inconsistent use is problematic in that it renders comparisons of MDA impossible, therefore making it difficult to assess if the method is truly an effective form of malaria control and elimination.

This study, however, found additional reasons as to why the current use of coverage, compliance, and adherence is problematic. First, these terms are binary, focused on the individual, and time specific. They are based on an observable act as part of the directly observed therapy (DOT) method of most MDAs, including MASSIV: did this one person consume the medication at this specific time or not? In the MASSIV trial, this was used for the definition of coverage. As mentioned in Chapter 3, the MASSIV trial was comprised of three rounds of MDA per month for three months per year for two years; therefore, an individual who took the medication as prescribed in the trial protocol would have taken the medication 18 separate, unique times. As I write in Chapter 5, we found that each time an individual took the trial medication was subject to its own decision-making process, complete with its own influences. Regardless of what one consented to, medicinal intake was a process that went through multiple re-evaluations throughout the trial. A key finding of this dissertation, therefore, is that this process is not accounted for and, in fact, is masked, in the trial's definitions of coverage and compliance.

Second, we found that these indicators – coverage, compliance, and adherence – are often used as a way to measure *community participation* in the MDA. Multiple studies have reported and justified that there was "high participation" based solely upon the percent of individuals who took the medication[3–5]. Our findings show that this is not only reductionist, but also misleading. Chapters 5, 6, 7, and 8 all address the complexities of community participation in the MDA and show that the single value of the given MDA indicator does not account for the realities of what is happening on the ground. Much of this is addressed in the following sections. However, related to the definition(s) of participation, we found that the chosen indicators also do not include the perspectives of those in the target communities and how they define participation and its relationship to medicinal intake.

2.1.3. How do communities define "participation"?

A principal finding and novel contribution of this study is that those in the trial communities regarded and practiced participation in very different ways than defined by the trial implementers, and, importantly, their definition of "participation" was not based upon medicinal intake. Instead, we found that participation was a multidimensional concept, embedded within the political connotations and values related to belonging in the communities. This was most often expressed through one's position in the socio-political structure of their family and community and was more heavily focused on their involvement in or engagement with the implementation of the MDA trial.

Further, we found that within this variation of understanding and expressing participation, participation could also be an active or passive behaviour. For example, we found that many compound heads considered themselves active participants in the MASSIV trial, even though they did not take the medication themselves (mostly due to eligibility reasons). They considered themselves as participants, however, because through their roles as leaders, they actively encouraged others in their community and compound to take the medication. These compound heads also helped spread information on behalf of the MRCG and brought people to the distribution site. Importantly, they participated in and worked for the success of the MDA. And though we found that these compound heads were considered participants by themselves and their communities, they were not included in the trial's indicators of "participation," i.e., coverage and compliance.

We also found that there were many in the trial villages who passively participated in the MDA and took the medication because they were told to do so, because "they obey." For girls in particular, practices of participation were expressed through their positions in the socio-political structures of the communities: we found that taking the medication because their compound head told them to do so was a way for the girls to demonstrate respect and an integral part of maintaining their standing and place in their families and communities. Because this was a passive behaviour and practice of participation, we found that it may also require "surveillance" by those in positions of authority to ensure these individuals continued taking the medication throughout the trial. We found that boys, on the other hand, may passively *not* take the trial medication. Due to their responsibilities on the farm or elsewhere, and their freedom to move around as they pleased, we found that this group could easily skip the MDA. Often, their reasoning for not taking the medication was considered by respondents as an "excuse," a demonstration of a "lack of responsibility," or as "laziness." However, we found that these individuals could be "convinced" to take the medication through pressure from those in positions of authority.

Of course, there were some people who did not take the medication at all. We found that in certain instances, this was seen as acceptable by the community and did not negatively affect one's social standing. As was the case with some of the older compound heads mentioned, certain people in the villages were not eligible to participate in the MDA trial. Relatedly, we also found that there were some in the villages who "could not" take the medication. Rather than trial eligibility, they could not take the medication due to other socially acceptable or justifiable reasons, such as being "too old" or having experienced strong adverse reactions in a previous round. Lastly, we found a small minority of villagers who declined any medication or form of participation in the MDA. Their reasonings were often based on past experiences with the MRCG or intra-village politics. Others in the villages, we found, considered these individuals to be "stubborn" or otherwise disconnected from the community.

9.2.2. Sub-question 2: Based upon the socio-ecological model, what affects participation in an MDA clinical trial at different "levels"?

As has been done to increase the understanding of multiple complex health-related topics, I chose to use the socio-ecological model (SEM) as a framework for evaluating the factors that affect MDA clinical trial coverage and participation at different "levels:" the individual, the interpersonal, the community, and the societal[6,7]. The SEM was a useful "diagnostic tool" to apply to the existing literature to determine gaps in understanding. As discussed in Chapter 2, the results of the literature review demonstrated that most research regarding coverage or participation in MDAs was focused on barriers and facilitators to participation at the individual level. This included, for example, scepticism towards allopathic medicine[8], being asymptomatic at the time of drug distribution[9], or concerns regarding adverse drug reactions; it also included individual factors related to implementation, like the MDA taking place at times of high mobility or agricultural demands[10]. The results of this dissertation, particularly in Manuscript 2, have shown that these were, indeed, also factors that affected coverage in the MDA clinical trial. We found that respondents reported barriers to medicinal intake such as farming demands, preferring traditional medicines, and not wanting to do eligibility tests (Chapter 5).

However, a more important result of this dissertation is the finding that what affects coverage and participation is much more complex than previously written about and that the greatest effects are not found within one level of the SEM, but instead are a combination of multiple levels. In other words, the factors most influential in affecting medicinal intake and participation in the MDA clinical trial, both in favour of or against, were at the same time a combination of personal, interpersonal, communal, and/or societal. Therefore, for the rest of this section, I have chosen to focus on two examples of the results effecting medicinal intake and participation – one barrier and one facilitator – and demonstrate how they crossed multiple levels described in the SEM.

9.2.2.1. Pregnancy tests

An important barrier to medicinal intake for women and girls of reproductive age was the need for a pregnancy test prior to each MDA round for eligibility

purposes[9]. This was an important finding regarding barriers at the individual level that led to consequences at the interpersonal and communal levels. We found the tests proved to be problematic for several reasons. First, especially during the first year of the MDA, multiple sites lacked the private toilet facilities necessary for collecting urine samples. As we observed, even if a woman or girl went home to provide a sample, she would still have to carry the collection cup through the village on her return. Once the fieldworker had the sample, the results of the tests were often read and recorded at the same table used to register people for the MDA, allowing all those present to hear. Furthermore, in the first year of the MDA, there was only one female fieldworker, and in the second year all fieldworkers were men. Chapter 5 reports that women and girls experienced feelings of embarrassment when asked to show their urine to a man, especially if it were possible to tell by looking at the sample that they were menstruating at the time of the test. Lastly, we found many unmarried women to be bothered by the implications of being asked to take a pregnancy test when they "should not" or "could not" be pregnant; if an unmarried woman was found to be pregnant, it would likely lead to substantial social consequences for her. Therefore, we found the social ramifications of the pregnancy tests were potentially too disastrous for many women and girls to risk, demonstrating the effects on participation from the interpersonal and communal levels.

Our findings regarding the pregnancy tests in Year 1 of the MDA were used by the clinical trial team to change the trial protocol in favour of increased privacy for women and girls. In addition, our findings have been discussed in the literature surrounding the validity and possibility of conducting MDAs with ivermectin. A Correspondence in the Lancet Infectious Diseases was written as a response to the final MASSIV trial manuscript[11,12]. In it, the authors cite the results of Chapter 5 to demonstrate that pregnancy tests are too difficult to respectfully and properly administer in such communities, and that the lack of privacy, among other concerns, may deter women and girls from taking the trial medicine. They use our findings to argue that, globally, MDA with ivermectin should not be conducted until the effects of the drug during pregnancy are better established[12].[10] This Correspondence expands

[9] As specified in the trail protocol, ivermectin should not be taken by those who are pregnant or breastfeeding, and DP should not be taken during the first trimester of pregnancy[62].

[10] The MASSIV PI and trial coordinator responded to the correspondence. They agreed to the need for further tests on the safety of ivermectin during pregnancy but stated that

our findings of the pregnancy tests to larger discussions on trial protocols and the ethical implementations of such trials, representing their importance at the societal level.

We found similar findings of complexity – that one factor affected participation across levels of the SEM – when analysing the impact of the sensitization meetings on medicinal intake.

9.2.2.2. Attending sensitization meetings

It has previously been demonstrated in multiple studies that individuals who attend pre-trial sensitization meetings are more likely to take the MDA or clinical trial medication[13,14]. This is often attributed to potential participants gaining more knowledge about the trial at these meetings and that more knowledge, on the individual level, leads to overall higher MDA coverage or adherence rates[15–17]. The results of the household survey reported in Chapter 5 demonstrate this as well: those who attended the pre-trial sensitization meeting significantly knew more details of the MDA clinical trial than those who did not attend, and they were also significantly more likely to take the MDA medication and adhere to the complete drug regimen.

However, some studies have found that being able to repeat back correct information did not always lead to increased medicinal intake; this was explained as the co-existence of correct and incorrect knowledge and differences in the interpretation of information[18]. The results of this study, however, found the importance of attendance to be far more than the personal-level factor of acquisition of trial-related knowledge: attending the pre-trial sensitization meeting was also important as a community-level factor in that it was a way for someone – either as an individual or as a representative of their family (interpersonal level) – to show the village that they supported the communal decision to participate in the MDA trial. As will be discussed shortly, we found this to be an essential component of the communities' social cohesion, and one that community members were not likely to go against (Chapter 6).

---

corresponding qualitative studies (citing a different manuscript than ours) have shown these tests to be acceptable in this setting and that these groups need to be included in order to increase the potential coverage and impact of the MDA.

Additionally, we found attending the sensitization meeting to also be a demonstration to the MRCG that an individual/representative of a family supported the work the institution was doing in the village. Our results indicate this was important for two key reasons. First, attendance at the sensitization meeting was part of the interpersonal- and community-level reciprocal relationship between community members and the MRCG (discussed in more detail below). By showing their support of the institution and the MDA, that person/family would now be justified within this sense to receive any of the additional trial benefits, such as access to healthcare or transportation. Second, we found attending the sensitization meeting as a way of supporting the MRCG to be a societal-level factor affecting participation, as the continuation of this reciprocal relationship was necessitated by the trial setting's context of poverty and an insufficient healthcare infrastructure. Without this relationship with the MRCG, individuals, families, and communities felt as if they may not otherwise have access to necessary healthcare.

The "societal level" of the study setting must be taken into consideration when assessing the factors that affect participation or medicinal intake in the MDA clinical trial. The Upper River Region of The Gambia is a setting of rural poverty and endemic malaria where the majority of residents experience great difficulty in accessing basic healthcare[19,20] (Chapter 4). Previous studies have demonstrated that structural coercion[21] and an environment of poverty and vulnerability can increase the number of people who decide to take trial medications as a way of seeking access to healthcare or other monetary and material benefits[17,22–24]. We found aspects of this to be true in this MDA clinical trial as well. This study's contribution, however, is an expansion on the theory of structural coercion in that it also demonstrates how this effect at the societal level permeates through all other levels of the SEM to influence the individual and their medicinal intake. An example of this is demonstrated through the importance of the MRCG and the communities' relationship with the institution as well. Other examples will be provided in the following sections.

In summary, the usefulness of the SEM was in better understanding the complexity of the factors affecting participation and the ways in which these factors interact across its levels. This approach was recently undertaken by two systematic reviews assessing impacts on medicinal intake of MDAs for

schistosomiasis in Sub-Saharan Africa[18] and neglected tropical diseases (NTDs) in Asia-Pacific countries[25]. Many of their findings of the factors affecting medicinal intake were similar to those we found, including the effects of family endorsement, the potential influence of the implementing organization, and attendance at the sensitization meetings. However, their analyses stop there[18,25]. Torres-Vitolas, et al (2021) state that "Gathered evidence showcased the presence of multiple determinants operating simultaneously across all levels of analysis, from the individual- to the policy-level," but do not elaborate further[18]. Indeed, one of the principal results of this dissertation is that what most affects medicinal intake and participation in an MDA clinical trial – as a barrier or facilitator – is not an individual or other single-level factor. Instead, participation is extremely complex and affected by myriad identifiable factors that operate and exert influence simultaneously at the individual, interpersonal, communal, and societal/environmental "level." Moreover, our findings demonstrate *how* these factors influence both participation and medicinal intake across the levels of the SEM. The findings from this study further elaborate on their recommendations for the inclusion of social sciences in MDA implementation and show the complexities of the socio-cultural and political factors that affect MDA success.

9.2.3. Sub-question 3: What work, and from whom, is required for participation in an MDA clinical trial to occur?

A clear finding from this study is that achieving the high levels of coverage for an MDA trial to be successful takes *work*. Commonly, as found in the literature, the type of work associated with increasing coverage comes in the form of community engagement activities organized and implemented by the trial team[26–29]. Some of the activities described in other studies include sensitization meetings, as in the MASSIV trial, and other educational outreach events (e.g., radio advertisements, posters, performances, etc.), community meetings to elicit feedback, community advisory boards, and others. For malaria MDAs specifically, these activities have been shown to have various levels of success[30].

That the work required for high coverage in an MDA clinical trial is more than the traditional community engagement activities mentioned above is another important finding of this study. We found that the work to achieve the level of medicinal intake and participation necessary for a successful MDA

comes more from the day-to-day activities of the fieldworkers and from within the communities themselves.

9.2.3.1. The work from the trial communities: Social cohesion

One of the most important gaps in the MDA trial literature that this dissertation addresses is the role and type of work conducted by the trial communities that affects coverage and participation. During the first year of the MDA, we found that there was an important community dynamic taking place in the villages that was greatly affecting and leading to different rates of coverage among the villages. Based on their differing coverage rates (provided by the clinical team) and community dynamics, we theoretically chose two of these villages for more in-depth ethnographic research. Soon, it became clear the community dynamic in question was social cohesion.

The details of this finding can be found in Chapter 6. In general, we found that the two focus villages expressed social cohesion in differing ways and that this affected their involvement in engagement with the implementation of the MDA clinical trial, as well as how they viewed their individual medicinal intake. For example, we found that the village with high coverage encouraged active participation of everyone in all components of village life, MDA and otherwise. When the MDA came to this village, the expression of this ideal led to very real work being done by the individuals in the community regarding the MDA's implementation. We found that community elders and leaders, compound heads, and youth alike were involved in helping to set up the distribution centre, mobilize others to take the medication, and, importantly, tailor the implementation of the MDA trial so it better suited their needs and wants. A prime example of this was the pregnancy tests. We discovered that with the traditional birth attendant, the women in this village consulted with the assigned MRCG fieldworker on how to properly conduct the tests. They then chose a compound near the distribution centre and ran the pregnancy tests themselves. We concluded that in this way, their expression of social cohesion meant that they worked together and tailored this component of the MDA so that women and girls were more comfortable with the process and, therefore, were more likely to take the trial medication.

The effects that community dynamics such as social cohesion have on medicinal intake or participation in MDAs has not been previously established. A study on the acceptability of an MDA for malaria elimination

on the Thai-Myanmar border mentions that "more compliant villages… gave the appearance of cohesive communities"[31], and a study exploring the high coverage of another malaria MDA in Laos found that "MDA coverage was much higher in cohesive than in politically fragmented communities"[17]. Based on the observations of the study staff, the latter study attributed this to a sense of conformism in the communities and that household members or neighbours could influence individual's behaviour. The social cohesion expressed in the village described above shared similar elements, especially that individuals could be influenced by the actions of others. However, this study takes this finding further and demonstrates that it is not only a sense of conformism that effects medicinal intake, but rather that social cohesion is performed by partaking in village functions. In the case of the MDA trial, this meant that everyone was expected to participate – and to work – for the betterment of the trial in their village.

9.2.3.2. The work from the trial communities: Role of the compound heads

Early in the fieldwork, we learned that compound heads were considered to be "the most affected" by malaria. We found that this is due to their responsibility for ensuring treatment of any one in their compound who becomes ill. Relatedly, we also found the compound heads to be very concerned over lost labour or domestic chores that resulted from someone in their compound being too ill to work (made worse by the fact that malaria is most likely to occur during the peak of the agricultural season when labour is in high demand). As head of financial matters for their families, we discovered compound heads strongly felt the pressure imposed by the broader environment and the socio-economic vulnerability (established at the SEM societal level.)

The influence of the compound head on medicinal intake has been established in The Gambia[9], and we too found and described in Chapter 5 that those who had a compound head take the MDA medication were significantly more like to take it themselves. However, this study expands upon this notion by demonstrating *why* having a compound head take the medication may increase the medicinal intake of those in his compound and *how* this happens. If the compound head believed that the MDA trial did in fact prevent malaria, as we found with the "narratives of evidence" in Year 2 of the MDA (Chapter 8), the compound head would be motivated to apply hierarchal social pressure to his family members to take the medication so as

not to pay for medical care or lose valuable farm and domestic labour. Within the context of the villages' cultural values, we found that an individual in the compound, such as an adolescent girl, felt the pressure from her compound head and would obey his request to take the medicine as her way of demonstrating respect to him and his position. Further, our findings show that the MDA was an opportunity for compound heads to demonstrate leadership skills to their village and peers. By ensuring all members of his family took the trial medication, he could demonstrate the strong social cohesion in his compound and that he held the respect of his family. According to respondents, a compound head must demonstrate his ability to lead his family before he could take on a leadership role within the village.

9.2.3.3. The work of fieldworkers

Chapter 7 is part of a special issue in *Global Public Health* titled "Making global health 'work': Frontline workers' labour in research and interventions" (of which I am a co-editor) that focuses specifically on the roles of those conducting and doing global health work on the frontlines. Specifically, it concentrates on the "body work," a type of paid labour that focuses on the "assessing, diagnosing, handling, treating, manipulating, and monitoring" of bodies[32] required of fieldworkers in carrying out the roles and responsibilities of their employment. As is the case across much of global health, body work is the type of labour we found the MASSIV fieldworkers were trained and hired to do; as part of their jobs in the trial, they administered medication, measured bodies (e.g., height and weight for dosing), treated side effects, and responded to other bodily needs as necessary throughout the MDA. But body work goes beyond the corporal to also include the emotions, time, space, and "micro-political relations" that this physical labour requires[32]. As we discuss in the editorial that introduces the special issue, and as is demonstrated across the included manuscripts, fieldworkers of all types, in carrying out their physical work, must also, for example, balance cultural norms and rely on their "localness" to relate to those in the trial communities[33–35], or utilize other tacit skills that are often taken for granted by trial or institution leadership[36].

As previously discussed, we found that reciprocity was an important component of community social cohesion and relationships within the research setting – and that this included the MRCG fieldworkers as well (Chapter 6). In Chapter 7, we expanded upon this idea and related it to body

work. We found that the MASSIV fieldworkers engaged in what we labelled as *reciprocity work* throughout the entire trial process. This meant that beyond the tasks described in their job descriptions, we observed that the fieldworkers shaped and maintained complex relationships of reciprocity through showing respect and establishing trust in their day-to-day activities with the individuals in the trial villages. This work involved actions from greeting elders in the culturally appropriate way and attending village ceremonies to personally providing paracetamol to those experiencing side effects of the MDA medication. The importance of establishing trust in trial communities and treating participants well and with respect has been shown to lead to increased enrolment and participation in other studies[30], including a malaria study in Western Kenya[37], and as part of the West African Ebola epidemic[36]. As we have shown, however, this is a form of work done by the fieldworkers in ensuring a successful MDA and high medicinal intake within the communities.

A similar type of work has been found to exist among other types of frontline workers, such as social workers or police officers. In their meta-ethnographic synthesis, for example, Erasmus (2014) shows how in conducting "street-level bureaucracy," these frontline workers must operate between the demands of their employing agency and the needs of those they serve – much like how the MASSIV fieldworkers must work between the MRCG and the trial communities[38]. In doing so, street-level bureaucrats "make policy" "on the ground" in ways that may contradict their agencies' formal policies[38]. This is akin to fieldworkers "making ethics" that may contradict the protocols of the implementing institution[39]. We found this to be present in the MASSIV trial as well. To "show respect" to the local communities, we observed fieldworkers bypassing compounds during the informed consent and enrolment process if the compound head was not home. Rather than consenting and enrolling those adults who were present, the fieldworkers waited until the compound head returned and could first provide his overall consent to anyone in his compound. This was appreciated by the compound heads and viewed as a sign of respect, but based on traditional research ethics, undermines individual autonomy in that the compound head's consent was a pre-requisite of other adults' consent.

Regarding trial participation, reciprocity is most often considered in the literature as a way to alleviate power imbalances between researchers and

participants and lead to increased participant autonomy[40,41]. Studies have shown this to be done through reciprocal conversations where both parties gave and received knowledge and respect during the exchange[41,42]. However, it has also been acknowledged that in settings where reciprocity is part of the cultural norm – such as the MASSIV trial site – reciprocal relationships can influence, and perhaps undermine, the voluntariness of the informed consent process[17,30]. In other words, within settings such as ours, these relationships can affect individual autonomy.

9.2.4. Sub-question 4: What factors affect individual autonomy in the decision-making process regarding participation in an MDA clinical trial?

As discussed in Chapter 2, autonomy is the most debated of the main principals of biomedical and clinical research ethics, particularly as it relates to the informed consent process in international research[43].[11] As is the requirement for all trials, the MASSIV clinical protocol provided information on how the informed consent process would take place prior to the MDA trial. This protocol was approved by all appropriate ethics committees and was the basis for how fieldworkers were trained to carry out the activity. Consequently, we found the fieldworkers and those in the trial villages clearly understood that the MDA was voluntary and that, from the perspective of the MRCG, people were free to take the medication or not.

However, many of the long-debated topics regarding informed consent were relevant in this study. Emanuel, et al (2004) state nearly 20 years ago that "spheres of consent" – i.e., first getting permission from the village leader, then the compound head, then the head of household, etc. – may be required to conduct research in study settings such as ours[43]. In fact, obtaining consent in this manner is often considered a way to show respect and increase the ethical rigor of a study, and it is often recommended that community engagement strategies first start by obtaining "community-level consent" from the community's leader, such as the Alkalo[44–46].

In their analysis of the informed consent process through the lens of Bourdieu's theory of symbolic power[40], Brear (2018) demonstrates how this process, in contrast to increasing ethical rigor, actually perpetuates the symbolic power of community leaders and compound heads and leads to

[11] The four main principals of biomedical and clinical research include 1. Autonomy, 2. Non-maleficence, 3. Beneficence, and 4. Justice[63].

symbolic violence[47]. Because they hold the social and political capital, those in charge hold the symbolic power where individuals "under" those in power do not have the ability to autonomously decide on participating in the trial. This could perhaps be taken further still, and assessed through the idea that within the "social field"[48] of this MDA clinical trial, the MRCG also hold capital in the form of access to health and medicines. Similar arguments have been made showing how the structural environment and influence of community leaders is also a form of structural coercion[21,24], as has been demonstrated in previous sections. Furthermore, at the community and societal level, part of being in a society or citizenship is recognizing, and to an extent obeying, the cultural and social norms. Many of the settings where MDAs take place, from Southeast Asia to sub-Saharan Africa - including The Gambia - have cultures centred around communalism. Simplified, within this notion, the overall decisions and betterment of the group, such as the MDA trial village, are considered more important than the desires of the individual. As demonstrated throughout this dissertation, we found that working for the betterment of one's family or community, even at the sacrifice of oneself, was regarded as the morally right thing to do.

Therefore, the concept of individual autonomy in this case goes far beyond the informed consent process. Our findings have added to the theories of symbolic power and structural coercion by demonstrating that not only do they exist within this context and affect participation and medicinal intake in the MDA, but that they do so by triggering various other social forces that move through all levels of the SEM, from the societal level to the individual.

This does, however, raise the question: is individual autonomy the right focus in this context? The informed consent process as it is written in the numerous international guidelines for ethical research practice is based upon the Western Kantian ideals and philosophy of autonomy and free will where individuals can make decisions without the influence or coercion of outside persons or forces[49,50]. When informed consent is conducted, it is assumed that the individual being asked to participate in the research has been given all relevant information, has the capacity to make a decision on their own, and then decides without the opinions of their family members or

community, or cultural expectations[12]. The relevance of this within settings such as ours has been debated at length by African philosophers who argue in favour of a more communalistic ideal, and state that in much of sub-Saharan Africa, being an individual is based upon one's place in a community[51–53]. They argue that this is not the antithesis of individual autonomy, and other African philosophers have further opined that even with a priority on communal decision making, there is a place for self-determination through an individual-in-community approach[54]. This is an area for future research to focus. Is there a place for communal decisions in traditional research ethics? Regardless, this finding particularly highlights the need for non-Western philosophies and epistemologies to be included in debates surrounding clinical trial and MDA participation. Furthering epistemic justice within these debates and within the informed consent process is one way to aid in the decolonization of global health and clinical research.

9.3. Methodological reflections: Study approach, positionality, and validity

As mentioned in Chapter 3, validity refers to the accuracy and trustworthiness of the data collection tools, the data collected, and the research findings[55]. This study employed a variety of methods, with the addition of several measures to ensure validity throughout. Some of these included group translations of any interview guides or survey questions, pilot testing of instruments before data collection began, and regular transcription and translation quality checks.

By following a transdisciplinary approach[56–58], we necessarily spoke with and included any potential stakeholders in this study. This included those who took the trial medication and those who did not; the Alkalos and community leaders; farmers and housewives; those socially segregated from their villages; adolescent boys and girls; and the MASSIV clinical field team. This not only ensured greater validity of the study, but made for far richer data and an in-depth, layered understanding. Further, these initial findings led our team to host discussions with trial leadership on recommended changes to the MDA's implementation; these changes were then carried out between

[12] It should be noted, however, that research ethics have evolved in the past few years and that international guidelines have begun to formally recognize the importance of other factors, such as communal influence, on the informed consent and decision-making process.

Year 1 and Year 2. In essence, this meant that the opinions and feedback from the communities led to changes in the way the trial was carried out. Consequently, with the implementation issues addressed, we were able to go further in-depth in our analysis of community social dynamics and the nuances of participation in the subsequent research phases.

The emergent, iterative process of the study design was particularly useful for ensuring validity. This included regular, often daily, debriefing sessions with the team in the field. Especially in the earlier stages of the research, or whenever we were discussing a new topic, we would meet at the end of every field day and discuss the individual interviews or FGDs, our findings, what we thought these findings meant in the overall context of our study, and any issues that arose during questioning or translating. In this way, we were not only able to make changes to the IDI or FGD guides if needed, but we were also able to quickly identify any interesting or conflicting findings and discuss how we would go about future data collection to investigate further.

Certain concepts in this research were complicated and had the potential to be "lost in translation;" therefore, extra steps were taken to ensure we collected and analysed data appropriately. For example, when focusing on issues related to social cohesion, myself and JM held several, in-depth conversations with OC, EM, and DB. We reflected on and discussed our own definitions of social cohesion and what it meant to us and to the research (e.g., any potential bias we as individuals may bring into our analysis of the concept), the proper terminology to use in English, Mandinka, and Fula, and how to discuss the concept in IDIs and FGDs. We continued these conversations throughout this part of the research process. Additionally, at least two of the three Gambian members of the field team were present for IDIs and FGDs so that we could ensure translation was accurate and the relevant concepts were being properly presented and interpreted. As an additional safeguard, members of the field team transcribed the IDIs or FGDs led by their colleagues, and we all conducted regular quality checks on the translation and accuracy of the transcripts.

Another way we were able to ensure validity was through our ethnographic approach and ability to triangulate our qualitative and quantitative findings with what we were observing. Biehl and Petryna (2013) write, "Ethnographic cases untangle people from their shadow realities and representations,

capturing, for a moment and overtime, institutional designs, diseases-in-motion, and survival, implicated as these are in scarcity, politics, technology, and money." A major strength of this study in general – and for its validity – is the amount of time the team and I spent "in the field." Over the course of the trial, I spent nine months in the Upper River Region, including many nights across all the intervention villages, in times during and outside the MDA. Building rapport was essential to lower reactivity, the changes in behaviour people may make when they know they are being studied[55]. Therefore, when not conducting interviews or FGDs, we – myself, DB, EM, and OC – lived, ate, and participated in the lives of those in the villages. For the men on the team, this meant many long conversations while brewing *attaya.* There were times that I participated in the conversations over *attaya*, but I mostly spent time with the women and children. For example, I would help prepare and clean up after meals at the compound where we were staying, I was involved in braiding hair, and I regularly played dancing games with young children and soccer/football with older children; one time, I participated in the very lengthy and very social process of having my feet decorated with *fuda* (a type of skin dying, similar to henna).

Building rapport was also an essential part of the study concerning the MASSIV clinical field team. Initially hesitant of our "true" purpose, the team eventually saw us as "one of them" – fieldworkers just carrying out the tasks required of their jobs. Our study objectives – including the focus on their roles – were well known; the field team was treated as any other research participant and provided informed consent prior to participating in our research and we regularly reminded them that we were interested in their roles in the MDA trial as part of our overall study. As such, we were able to observe the clinical team's fieldworkers during DOT and hold myriad informal conversations during and between MDA rounds.

The time "in the field" and these activities certainly helped establish rapport among me, the rest of the social science team, those in the communities, and the MASSIV clinical team. However, nine months is never enough to be fully engrained in the community and it was necessary that I was always aware of my positionality. It was necessary for me to continuously reflect upon the ways in which my particular background, world view, and personal history may influence the type of data I was interested in collecting and the ways in which I interpreted it. As a white, highly educated, woman born in the United

States, my views on participation, democracy, and the meaning of individual autonomy would be naïve in this context. As part of this, I would regularly engage in reflexive exercises on my own and with my team. For example, I kept a personal journal to keep record of my own feelings and the events of my personal life. This helped to ensure that my own views were known and could be understood as much as possible during data collection and analysis. Furthermore, I regularly reflected on all aspects of the research with the social science team. This included JM and CN while they were in The Gambia, and also regularly with OC, EM, and DB. While no study is free of bias, I believe that taking these extra measures helped to at least minimize biases and increase the study's validity.

9.4. Implications and recommendations

9.4.1. For malaria control and elimination through mass drug administration

The Global Technical Strategy for Malaria 2016-2030 (GTS), as introduced in Chapter 1, prioritizes new strategies for malaria control and elimination that include the "involvement and meaningful participation of communities." As part of this focus, they argue for increased community engagement and "interventions tailored to local context"[59]. This study provides ample evidence as to the importance of involving communities in malaria control strategies from the earliest stages.

One implication of this seems obvious: implementation matters. Without proper implementation – distributing medications at the appropriate time, having enough staff to carry out all activities, informing the communities of the necessary details, etc. – it is hard to ensure that the requisite 80% of the target community receives and takes the MDA medication. In the MASSIV trial, with input from the social science team, the clinical team made improvements to the implementation of the MDA between Years 1 and 2. They increased privacy for pregnancy tests, they increased the number of field staff, and they kept field nurses in the villages for longer periods of time in order to respond to any adverse effects of the medication. This certainly helped increase the coverage rates in the second year. However, perhaps even more important, we found that these improvements also triggered social reactions within the communities that led to the target populations doing more work for the MDA. It was the work of both the field staff and the

communities that ultimately led to increases in participation and medicinal intake.

This leads to the second implication for MDAs: MDAs need to take a more emic approach to implementation. One of the most important findings of this study was that the communities did not define participation in the same way as the MDA implementers; to the communities, participation was based on engaging with the trial and not on medicinal intake. It is important to note that the MASSIV trial did not have any formal community engagement activities. It was the communities themselves, through their expressions of participation, that engaged with the trial. As such, communities with high participation were able to contextualize the MDA to their needs and wants which further increased the number of individuals who took the medication. These local preferences need to be included in the planning of future MDA trials or interventions. Increased time and space for communities to be involved – to participate – and adapt the trial to their preferences will benefit them and the intervention. It is also important that this is done per target community or village. As we found in this study, even villages within the same geographic region and demographic makeup are not at all homogenous and a "one-size-fits-all" approach would not have increased medicinal intake in the same ways.

Following this argument, this study clearly demonstrates the importance of the fieldworkers and the unique role they played in the MDA trial. Along with engaging with the community and incorporating them into trial design and implementation, the fieldworkers should also be regularly consulted by trial leadership. As they often act as the intermediaries between trial leadership/the implementing institution and the trial communities, the fieldworkers are privy to noticing community-specific nuances that affect the trial's success. In MASSIV, the fieldworkers were not blind to the impact implementation issues had on the trial communities and they had unique insights into ways that implementation could have been more community friendly and increased medicinal intake. Future trials need to create mechanisms for those "in the field" to provide potentially crucial feedback.

A more emic approach to trial implementation is also relevant for the indicators used to measure the reach and acceptability of MDAs in the target population: coverage, compliance, and adherence. This study clearly

demonstrates that there is a need to invest further research and attention to improving these critical indicators so that they more accurately report on the true success of the MDA. As the global health world continues to work towards malaria elimination, it is critical that the methods being considered or advocated for are able to be properly evaluated.

9.4.2. For research ethics and policy

First, based on our initial findings during Year 1 of the MDA, the trial team changed the protocol regarding the pregnancy tests for Year 2. Though this held specific implications for the MASSIV trial, these findings also proved to have greater implications on research ethics and policy, as demonstrated by the Commentary in The Lancet. For MDAs – and for research in general – eligibility tests need to be conducted in ways that are appropriate and sensitive to local cultures. This includes adequate privacy. Researchers and study implementers cannot expect people to participate in research when the implementation provides barriers. As already mentioned, true inclusion and engagement with communities before and throughout the trial, and allowing communities to contextualize implementation, can alleviate these barriers.

Second, throughout this dissertation, I have written on our findings regarding the non-individual factors that influence participation and medicinal intake in an MDA clinical trial. Among these factors are the familial and social pressures that one may feel regarding their own participation, including that acting for the betterment of one's family or community is a moral issue. This has severe implications for traditional research ethics. These social forces, particularly when combined with components of structural coercion, can undermine the intentions of autonomous decision making and informed consent. Future trials and interventions need to be aware of the potential impact they may have upon entering a community that makes it socially and morally difficult for an individual to make an autonomous decision. Ways to address this will include moving beyond traditional community engagement and creating meaningful and lasting bidirectional conversation. This could include, as other have argued for, treating informed consent not as a one-time event, but as a continuous process and contextualizing it the specific research setting[47,60]. Our findings support this recommendation: we found that the decision-making process for participation and medicinal intake was also not a one-time event, but instead was a process that was influenced by

external factors throughout the entirety of the MDA. An informed consent process that better reflects the nature of decision making – that it is a continuous process – and includes considerations for effects on decision making across the SEM could increase the ethical rigor of clinical trials.

9.4.3. For beyond…

Lastly, an implication of this study is that as the discipline rightfully works to decolonize, Global Health needs to immediately expand its epistemic community[52,61]. In this study, we have demonstrated the importance of emic understandings and expressions of participation through communities' social values and individual's place within socio-political structures. In addition to more thorough engagement with the trial communities and allowing them to contextualize implementation, further research needs to draw from and include emic philosophies and logics and integrate them into broader implementation practices and research policy.

9.5. Concluding remarks

This study has demonstrated that *participation* in an MDA clinical trial for malaria elimination in The Gambia was far more nuanced than the traditional binary indicators used to measure this phenomenon imply. We found that the social values and socio-political structures of the trial communities rendered the villages as accepting of the trial and created a supportive environment for it to take place. These values included community social cohesion and pyramidal social pressure, among others. Within that, participation was an expression of one's position in these structures and based upon how they engaged with the trial and its implementation – not on whether or not they took the medication. Furthermore, the type of work required for a successful MDA was far more than traditional community engagement or job description-based actions from the trial team. Communities mobilized themselves and worked to increase participation and coverage in the MDA through varying internal strategies.

This study has implications for malaria control efforts and the implementation of MDAs, as well as research ethics and policy. In addition to demonstrating the need to improve the key indicators used to measure MDAs, this dissertation shows the importance of using emic understandings and definitions of participation to understand how the MDA is truly operating

and accepted within the target community. Following, it also demonstrates the need for the Global Health discipline as a whole to expand its epistemic community and incorporate other logics and philosophies into implementation, practice, and policy.

References

1. Newby G, Hwang J, Koita K, et al. Review of Mass Drug Administration for Malaria and Its Operational Challenges. *Am J Trop Med Hyg*. 2015;93(1):125-134. doi:10.4269/ajtmh.14-0254
2. Cheah PY, White NJ. Antimalarial mass drug administration: ethical considerations. *Int Health*. 2016;8(4):235-238. doi:10.1093/inthealth/ihw027
3. Pell C, Straus L, Andrew EVW, Meñaca A, Pool R. Social and cultural factors affecting uptake of interventions for malaria in pregnancy in Africa: A systematic review of the qualitative research. *PLoS One*. 2011;6(7). doi:10.1371/journal.pone.0022452
4. Muela Ribera J, Hausmann-Muela S, Gryseels C, Peeters Grietens K. Re-imagining adherence to treatment from the "other side": local interpretations of adverse anti-malarial drug reactions in the Peruvian Amazon. *Malar J*. 2016;15(1):136. doi:10.1186/s12936-016-1193-x
5. Kaehler N, Adhikari B, Cheah PY, et al. The promise, problems and pitfalls of mass drug administration for malaria elimination: a qualitative study with scientists and policymakers. *Int Health*. 2019;11(3):166-176. doi:10.1093/inthealth/ihy079
6. Kilanowski JF. Breadth of the Socio-Ecological Model. *J Agromedicine*. 2017;22(4):295-297. doi:10.1080/1059924X.2017.1358971
7. Lee BC, Bendixsen C, Liebman AK, Gallagher SS. Using the Socio-Ecological Model to Frame Agricultural Safety and Health Interventions. *J Agromedicine*. 2017;22(4):298-303. doi:10.1080/1059924X.2017.1356780
8. Adhikari B, James N, Newby G, et al. Community engagement and population coverage in mass anti-malarial administrations: a systematic literature review. *Malar J*. 2016;15(1):523. doi:10.1186/s12936-016-1593-y
9. Jaiteh F, Masunaga Y, Okebe J, et al. Community perspectives on treating asymptomatic infections for malaria elimination in the Gambia. *Malar J*. 2019;18(1):39. doi:10.1186/s12936-019-2672-7
10. Dierickx S, Gryseels C, Mwesigwa J, et al. Factors Associated with Non-Participation and Non-Adherence in Directly Observed Mass Drug Administration for Malaria in The Gambia. Sullivan DJ, ed. *PLoS One*. 2016;11(2):e0148627. doi:10.1371/journal.pone.0148627
11. Dabira ED, Soumare HM, Conteh B, et al. Mass drug administration of

ivermectin and dihydroartemisinin–piperaquine against malaria in settings with high coverage of standard control interventions: a cluster-randomised controlled trial in The Gambia. *Lancet Infect Dis*. 2022;22(4):519-528. doi:10.1016/s1473-3099(21)00557-0

12. Erber AC, Colebunders R. Ivermectin for malaria control in mass drug administration programmes. *Lancet Infect Dis*. 2022;22(4):449-450. doi:10.1016/S1473-3099(22)00152-9
13. Dierickx S, O'Neill S, Gryseels C, et al. Community sensitization and decision-making for trial participation: A mixed-methods study from The Gambia. *Dev World Bioeth*. 2018;18(4):406-419. doi:10.1111/dewb.12160
14. Dial NJ, Ceesay SJ, Gosling RD, D'Alessandro U, Baltzell KA. A qualitative study to assess community barriers to malaria mass drug administration trials in the Gambia. *Malar J*. 2014;13(1):47. doi:10.1186/1475-2875-13-47
15. Nguyen TN, Thu PNH, Hung NT, et al. Community perceptions of targeted anti-malarial mass drug administrations in two provinces in Vietnam: A quantitative survey. *Malar J*. 2017;16(1):1-12. doi:10.1186/s12936-016-1662-2
16. Browne JL, Rees CO, Delden JJM Van, Agyepong I, Grobbee DE. The willingness to participate in biomedical research involving human beings in low- and middle-income countries : a systematic review. 2018;00(00):1-16. doi:10.1111/tmi.13195
17. Adhikari B, Phommasone K, Kommarasy P, et al. Why do people participate in mass anti-malarial administration? Findings from a qualitative study in Nong District, Savannakhet Province, Lao PDR (Laos). *Malar J*. 2018;17(1):15. doi:10.1186/s12936-017-2158-4
18. Torres-Vitolas CA, Dhanani N, Fleming FM. *Factors Affecting the Uptake of Preventive Chemotherapy Treatment for Schistosomiasis in Sub-Saharan Africa: A Systematic Review*. Vol 15.; 2021. doi:10.1371/journal.pntd.0009017
19. ICF. The Gambia Demographic and Health Survey 2019-20 . 2021. https://www.dhsprogram.com/pubs/pdf/FR369/FR369.pdf.
20. Geissler PW, Kelly A, Imoukhuede B, Pool R. "He is now like a brother, I can even give him some blood" - Relational ethics and material exchanges in a malaria vaccine "trial community" in The Gambia. *Soc Sci Med*. 2008;67(5):696-707. doi:10.1016/j.socscimed.2008.02.004
21. Fisher JA, Fisher JA. Expanding the Frame of "Voluntariness" in

Informed Consent: Structural Coercion and the Power of Social and Economic Context. 2020;23(4):355-379.
22. Mfutso-Bengo J, Ndebele P, Jumbe V, et al. Why do individuals agree to enrol in clinical trials? A qualitative study of health research participation in Blantyre, Malawi. *Malawi Med J*. 2008;20(2):37-41. doi:10.4314/mmj.v20i2.10898
23. Kingori P. The ' empty choice ': A sociological examination of choosing medical research participation in resource- limited Sub-Saharan Africa. 2015. doi:10.1177/0011392115590093
24. Nyirenda D, Sariola S, Kingori P, et al. Structural coercion in the context of community engagement in global health research conducted in a low resource setting in Africa. 2020:1-10.
25. Mitchell E, Kelly-Hanku A, Krentel A, et al. Community perceptions and acceptability of mass drug administration for the control of neglected tropical diseases in Asia-Pacific countries: A systematic scoping review of qualitative research. *PLoS Negl Trop Dis*. 2022;16(3):1-18. doi:10.1371/journal.pntd.0010215
26. Nyika A, Chilengi R, Ishengoma D, et al. Engaging diverse communities participating in clinical trials: Case examples from across Africa. *Malar J*. 2010;9(1):1-11. doi:10.1186/1475-2875-9-86
27. Peto TJ, Tripura R, Davoeung C, et al. Reflections on a Community Engagement Strategy for Mass Antimalarial Drug Administration in Cambodia. *Am J Trop Med Hyg*. 2018;98(1):100-104. doi:10.4269/ajtmh.17-0428
28. Reynolds L, Sariola S. The ethics and politics of community engagement in global health research. *Crit Public Health*. 2018;1596:1-12. doi:10.1080/09581596.2018.1449598
29. Wilkinson A, Parker M, Martineau F, Leach M. Engaging "communities": anthropological insights from the West African Ebola epidemic. *Philos Trans R Soc Lond B Biol Sci*. 2017;372(1721):20160305. doi:10.1098/rstb.2016.0305
30. Adhikari B, Pell C, Cheah PY. Community engagement and ethical global health research. *Glob Bioeth*. 2020;31(1):1-12. doi:10.1080/11287462.2019.1703504
31. Kajeechiwa L, Thwin MM, Shee PW, et al. The acceptability mass administrations of anti-malarial drug as part of targeted malaria elimination in villages along the Thai-Myanmar border. *Malar J*. 2016;15(1):1-12. doi:10.1186/s12936-016-1528-7

32. Twigg J, Wolkowitz C, Cohen RL, Nettleton S. Conceptualising body work in health and social care. *Sociol Heal Illn*. 2011;33(2):171-188. doi:10.1111/j.1467-9566.2010.01323.x
33. Kingori P, Gerrets R. The masking and making of fieldworkers and data in postcolonial Global Health research contexts. *Crit Public Health*. 2019;29(4):494-507. doi:10.1080/09581596.2019.1609650
34. Kingori P. Experiencing everyday ethics in context: Frontline data collectors perspectives and practices of bioethics. *Soc Sci Med*. 2013;98:361-370. doi:10.1016/j.socscimed.2013.10.013
35. Rilkoff H, Tukahebwa EM, Fleming FM, Leslie J, Cole DC. Exploring Gender Dimensions of Treatment Programmes for Neglected Tropical Diseases in Uganda. Gyapong M, ed. *PLoS Negl Trop Dis*. 2013;7(7):e2312. doi:10.1371/journal.pntd.0002312
36. Dada S, McKay G, Mateus A, Lees S. Lessons learned from engaging communities for Ebola vaccine trials in Sierra Leone: Reciprocity, relatability, relationships and respect (the four R's). *BMC Public Health*. 2019;19(1):1-13. doi:10.1186/s12889-019-7978-4
37. Madiega PA, Jones G, Prince RJ, Geissler PW. "She's My Sister-In-Law, My Visitor, My Friend" - Challenges of Staff Identity in Home Follow-Up in an HIV Trial in Western Kenya. *Dev World Bioeth*. 2013;13(1):21-29. doi:10.1111/dewb.12019
38. Erasmus E. The use of street-level bureaucracy theory in health policy analysis in low-and middle-income countries: A meta-ethnographic synthesis. *Health Policy Plan*. 2014;29:iii70-iii78. doi:10.1093/heapol/czu112
39. Kingori P. Experiencing everyday ethics in context: Frontline data collectors perspectives and practices of bioethics. *Soc Sci Med*. 2013;98:361-370. doi:10.1016/j.socscimed.2013.10.013
40. Bourdieu P. The forms of capital. In: Richardson JG, ed. *Handbook of Theory and Research for the Sociology of Education*. Westport, CT: Greenwood; 1986:241-258.
41. Maiter S, Simich L, Jacobson N, Wise J. Reciprocity: An ethic for community-based participatory action research. *Action Res*. 2008;6(3):305-325. doi:10.1177/1476750307083720
42. Kerasidou A. Trust me , I ' m a researcher !: The role of trust in biomedical. *Med Heal Care Philos*. 2017;20(1):43-50. doi:10.1007/s11019-016-9721-6
43. Emanuel EJ, Wendler D, Killen J, Grady C. What Makes Clinical

Research in Developing Countries Ethical? The Benchmarks of Ethical Research. *J Infect Dis*. 2004;189(5):930-937. doi:10.1086/381709
44. Gikonyo C, Bejon P, Marsh V, Molyneux S. Taking social relationships seriously: Lessons learned from the informed consent practices of a vaccine trial on the Kenyan Coast. *Soc Sci Med*. 2008;67(5):708-720. doi:10.1016/j.socscimed.2008.02.003
45. Tindana PO, Singh JA, Tracy CS, et al. Grand Challenges in Global Health: Community Engagement in Research in Developing Countries. *PLoS Med*. 2007;4(9):e273. doi:10.1371/journal.pmed.0040273
46. Tindana PO, Rozmovits L, Boulanger RF, et al. Aligning Community Engagement With Traditional Authority Structures in Global Health Research: A Case Study From Northern Ghana. *Am J Public Health*. 2011;101(10):1857-1867. doi:10.2105/AJPH.2011.300203
47. Brear M. Ethical Research Practice or Undue Influence ? Symbolic Power in Community- and Individual-Level Informed Consent Processes in Community-Based Participatory Research in Swaziland. 2018. doi:10.1177/1556264618761268
48. Bourdieu, P. Social space and symbolic power. Theory S, Spring N. 2007;7(1):14-25.
49. Princewill CW, Jegede AS, Om KN, Lanre-abass B, Elger BS. Factors affecting women's autonomous decision making in research participation amongst Yoruba women of Western Nigeria. *Dev. World Bioethics*. 2017;17(1):40-49. doi:10.1111/dewb.12112
50. Kant I. *Groundwork of the Metaphysic of Morals*. Translated. New York: Haper & RW; 1948.
51. Mbiti JS. *African Religion and Philosophy*. London: Heinemann; 1969.
52. Chimakonam JO. African philosophy and global epistemic injustice African philosophy and global epistemic injustice. 2017;9626. doi:10.1080/17449626.2017.1364660
53. Mosima P. Introduction: African Philosophy. *Philos sagacity Intercult Philos*. 2016.
54. Ujewe SJ. Ought-onomy and mental health ethics: From “respect for personal autonomy” to “preservation of person-in-community” in African ethics. *Philos Psychiatry Psychol*. 2018;25(4). doi:10.1353/ppp.2018.0032
55. Bernard HR. *Research Methods in Anthropology: Qualitative and Quantitative Approaches*. 6th ed. Rowman and Littlefield Publishers; 2017.

56. Bunders-Aelen J, Broerse J, Keil F, Pohl C, Scholz R, Zweekhorst M. How can transdisciplinary research contribute to knowledge democracy? In: In'tveld RJ, ed. *Knowledge Democracy: Consequences for Science, Politics, and Media*. ; 2010:1-397. doi:10.1007/978-3-642-11381-9
57. Leavy P. *The Essentials of Transdisciplinary Research: Using Problem-Centered Methodologies*. New York, New York: Routledge; 2016.
58. Rosenfield PL. The potential of transdisciplinary research for sustaining and extending linkages between the health and social sciences. *Soc Sci Med*. 1992;35(11):1343-1357. doi:10.1016/0277-9536(92)90038-R
59. World Health Organization, ed. *Global Technical Strategy for Malaria 2016-2030, 2021 Update*.; 2021. https://www.who.int/publications/i/item/9789240031357.
60. Kalabuanga M, Ravinetto R, Maketa V, et al. The Challenges of Research Informed Consent in Socio-Economically Vulnerable Populations: A Viewpoint From the Democratic Republic of Congo. *Dev World Bioeth*. 2016;16(2):64-69. doi:10.1111/dewb.12090
61. Haas PM. Introduction: epistemic communities and international policy coordination. *Int Organ*. 1992;46(1):1–35. doi:10.1017/S0020818300001442
62. Dabira ED, Soumare HM, Lindsay SW, et al. Mass drug administration with high-dose ivermectin and dihydroartemisinin-piperaquine for malaria elimination in an area of low transmission with high coverage of malaria control interventions: Protocol for the massiv cluster randomized clinical trial. *JMIR Res Protoc*. 2020;9(11):e20904. doi:10.2196/20904
63. Beauchamp T, Childress J. *Principles of Biomedical Ethics*. Fifth. Oxford: Oxford University Press; 1983.

Additional sections

Summary
Acknowledgements
About the author

Two children enjoy their lunch in the courtyard of their compound

Summary

Malaria is a social disease and has been a major public health concern for centuries. Since the 1950s, countless control, elimination, and eradication campaigns have taken place across the globe. After a general trend of decline since 2000, malaria case incidence and deaths have increased since 2019. Though this is in part a consequence of the COVID-19 pandemic, progress towards malaria elimination had been stagnant since 2015. As a result, a renewed focus on new or updated interventions to combat the disease has emerged. One such intervention is mass drug administration (MDA). MDA involves administering the complete course of a given medication to an entire geographically defined target population, regardless of individual disease status. In order to be successful, at least 80% of those targeted for the MDA must take the medication as described, making the intervention highly dependent on social factors. By following a specific MDA clinical trial that took place in the Upper River Region of The Gambia, this study aims to understand all the factors involved in achieving this 80% coverage goal. The main research question of this dissertation is:

How can we understand the socio-cultural and ethical aspects of participation in a mass drug administration trial for malaria elimination in The Gambia?

This question was further divided into 4 sub-questions:

1. What – and for whom – is participation in an MDA clinical trial?
2. Based upon the socio-ecological model, what affects participation in an MDA clinical trial at different "levels" (e.g., the individual, familial, community, and societal levels)?
3. What work, and from whom, is required for participation in an MDA clinical trial to occur?
4. What factors affect individual autonomy in the decision-making process regarding participation in an MDA clinical trial?

To address these questions, this study used a mixed-methods, transdisciplinary approach while following the "Mass drug administration of ivermectin and dihydroartemisinin-piperaquine as an additional intervention for malaria elimination (MASSIV)" trial conducted by the Medical Research

Council Unit The Gambia at the London School of Hygiene and Tropical Medicine (MRCG). MASSIV was a Phase III, community-based, cluster-randomized control trial that took place in 32 villages (16 control and 16 intervention) in 2018-2019.

This thesis is comprised of 3 parts: 1. Introduction, 2. Findings, and 3. Discussion.

Part 1: Introduction

Part 1 includes Chapters 1-3. Chapter 1 provides the historical background and current status of malaria control, elimination, and eradication efforts. This provides the context for the use of MDA as an intervention and the importance of social factors in its success. The chapter also introduces the role of the MRCG and The Gambia's work in eliminating malaria. Chapter 2 provides more information and background necessary in addressing the main research question, including the terminology used to measure MDAs and medicinal intake (e.g., coverage, compliance, and adherence), a summary of the literature regarding the factors that affect MDA participation, and the informed consent process. It also introduces the socio-ecological model (SEM), the conceptual framework used throughout the study. Lastly, Chapter 3 provides a detailed description of the research phases and methods used throughout this study, including ethnography, observations, in-depth interviews (IDIs), focus group discussions (FGDs), and a quantitative household survey. Respondents for this study included all those in the trial villages, including those who took the MDA medication and those who did not. The findings are based on more than 200 IDIs, 30 FGDs, and countless observations and informal conversations; the household survey included 864 individuals in the 16 intervention villages.

Part 2: Findings

The findings of this study are found in Chapters 4-8. Chapter 4 provides the economic context of the trial villages and financial consequences that can result from malaria. Importantly, it reports our finding that though malaria treatment is technically free in The Gambia, 70% of our respondents paid out-of-pocket expenses the last time they or their child had malaria.

Chapter 5 goes on to describe the barriers and facilitators to taking the MDA medication and whether they were more or less influential at different times throughout the trial. This chapter introduced the importance of social dynamics on the decision-making process. Chapter 6 elaborates on this finding by demonstrating the unique ways two different villages expressed social cohesion through their involvement with the implementation of the MDA. Ultimately, it demonstrates that this expression of social cohesion was qualitatively correlated with the differing coverage rates of the two villages.

Chapter 7 focuses on the role of the fieldworkers in the MDA trial. It uses the principle of "body work" to demonstrate the importance of fieldworkers' "reciprocity work," including the extra day-to-day activities that were essential to the success of the MDA. Lastly, Chapter 8 describes the definitions and practices of "participation" in the MDA from the perspective of the trial communities, and the internal strategies that increased participation in the MDA – independent of the activities of the trial team.

Part 3: Discussion

This dissertation ends with a discussion of its key findings, recommendations, and concluding remarks (Chapter 9). The first key finding of this dissertation is that the trial communities found participation to be more complex than what is measured in the traditional MDA indicators (e.g., coverage, compliance, and adherence). To them, participation in the MDA was a multidimensional concept, embedded within their social values and political structures. Respondents did not consider medicinal intake relevant for participation. Instead, participation was defined and practiced in myriad ways based upon one's engagement with the MDA and involvement in its implementation.

The second key finding is that the factors that affected participation – both facilitators and barriers – were not found within one level of the SEM, but instead were a combination of personal, interpersonal, communal, and/or societal factors operating at the same time. The pregnancy tests required for eligibility purposes and attendance at the sensitization meetings were two examples of, respectively, a barrier and facilitator to participation that crossed multiple levels of the SEM.

Third, achieving the 80% coverage necessary for the MDA to be epidemiologically successful required work from the communities and from the trial fieldworkers. Trial villages were found to have internal strategies to increase participation independent of the trial team. However, the fieldworkers also practiced a type of work in navigating reciprocal relationships with the trial villages. These relationships were found to be essential in achieving MDA success, but also had implications on individual autonomy in the informed consent process and traditional research ethics.

This study has implications for malaria control and elimination through MDA and for general research ethics and policy. First, it makes clear the importance of community participation and involvement with the MDA implementation. Stemming from the ways in which communities defined and practiced participation and social cohesion, those with high coverage rates were also the ones most heavily involved in the implementation. Importantly, this meant they were able to contextualize the MDA to their needs and wants which further increased the number of people who took the medication. Second, by demonstrating the strong influence of familial and societal pressures on the decision-making process, especially when combined with components of structural coercion, this dissertation also demonstrates the importance of meaningful, bidirectional conversation between trial communities and trial implementers and treating informed consent as a continuous process contextualized to the specific setting.

Conclusion

This study has demonstrated that participation in an MDA clinical trial for malaria elimination in The Gambia was a complex phenomenon influenced by multiple individual factors, social values, socio-political structures, and the greater environment. Further, the success of the MDA was based on more than the activities of the trial team; it was heavily influenced by the work and internal strategies of the trial communities. Overall, this study demonstrates the importance of using emic definitions and understandings of participation. Furthermore, it shows the need of the Global Health discipline to expand its epistemic community and incorporate other logics and philosophies into its implementation, practice, and policy.

Acknowledgements

Life doesn't stop and the world doesn't slow down because you have decided to do a PhD. The challenges that exist when you submit your application are still there when you leave for fieldwork. I began this journey at an exceptionally difficult time in my life, and even during the course of the past 4.5 years, several big changes have happened in my family; two grandparents passed away; old relationships changed forever; new relationships blossomed. On top of that, the COVID-19 pandemic began two years in – right after I finished fieldwork – and I initially struggled to see the significance of my own research in comparison. My own country, forever occupying the global news, went through its own disasters and movements, and for the first time in my many years as an expat, I felt guilty that I was not there to do *something*. And even in this past year, I struggled with the final writing while taking on a full-time job in London and away from friends and family.

That said, I am here now, with this dissertation in hand, because of the people mentioned here. I am so thankful.

--

First and foremost, I want to thank the participants and respondents that made this study possible in the first place. Thank you for not only answering all of our questions in interviews, focus groups, or questionnaires, but in also welcoming the team and me into your communities, homes, and lives. You are what made this experience so great.

<u>In The Gambia</u>

I was so incredibly lucky to have worked with such an amazing team in The Gambia. Ebrima Manneh, Dulloh Baldeh, and Omar Ceesay – my Sunshines – you truly were the Dream Team. Thank you for your hard and excellent work and, especially, being my Gambian family over all those months. Your contributions were invaluable to the study and your kindness and fun made fieldwork such a joy and special experience. I will never forget our time together.

I would like to recognize and thank the members of the MRC The Gambia and MASSIV trial team. Thank you to the trial leadership, Umberto D'Alessandro and Jane Achan, for supporting our work. A big thank you also to Edgard Dabira and Haruna Soumare for supporting the study in the field (and for

making my 34th birthday unforgettable). Thank you Abdoulie Sillah, Kebba Naban, and others for all of your help and going above and beyond. Thank you to the MRC Drivers – Boye, Omar, Ousman, and so many others – for your kind flexibility and perpetual helpfulness. And a very special thank you to the Basse hospitality crew who always made sure I was comfortable and felt at home, including Isatou, Bintu, Tombong, and Yankuba.

In Europe

I am exceptionally grateful to the European Commission Erasmus Mundus Joint Doctorate fellowship in Transdisciplinary Global Health that provided the opportunity and funding for me to carry out this research and dissertation.

I would like to acknowledge the important role of my reading committee and to thank them immensely for their feedback on my dissertation and their participation in my defence. Thank you, Jacqueline Broerse, Rafaella Ravinetto, Shelley Lees, Dorcas Kamuya, and Sumit Kane. Your role is so greatly appreciated.

The Athena Institute

First, I would like to express my sincere gratitude to my promoters, Joske Bunders-Aelen and Teun Zuiderent-Jerak. How lucky I was to have you! Joske, you plucked me out of Rwanda and offered me the opportunity to do this research; you trusted my abilities and provided guidance; you knew when to push me and when to let me rest. Thank you now and thank you tomorrow. It has been a blessing to have you as my advisor and mentor. Teun, even if it was not originally planned, I think you were always meant to be a part of my dissertation. Thank you for your insight and intellectual contributions to the research, as well as being so wonderful to work with. I am especially grateful you were brought into this study.

I am also thankful for all of the people who make The Athena Institute so special. Jacqueline Broerse, thank you also for your involvement in TGH. Thank you, Astrid van de Wal-Kooijmans and Durwin Lynch, your help throughout these past several years has been invaluable. Durwin, you are wonderful. And thank you to the awesome Athena Secretariaat, including Justine, Evelyne, and Lotte, for all your help – especially in the final months – you keep everything running.

It feels like it was in another lifetime, but thank you to the OG greatest officemates, Nikha, Harry, and Gianni for welcoming me into Athena and for all the laughs. Thank you, Hilde and Mike, for "Writing together… apart;" our group pomodoros made all the difference in the final stretches of writing.

Lastly, thank you so much, Sarju Rai and Indu Sharma. At the beginning, I was so grateful to have your help and guidance in navigating TGH and settling into Amsterdam. Later and through now, I'm even more grateful to have had you as friends and to have gone through this whole process together. You two will always be part of my Amsterdam family.

ITM Antwerp
I would like to thank my co-promoter and the PI of the MASSIV social science study, Koen Peeters Grieten. Koen, thank you for trusting me in this work and in The Gambia, providing your anthropological insight, and for your general support, especially when I was in Antwerp. Claudia Nieto and Joan Muela, thank you from the bottom of my heart. I would love it if we could do every study together for the rest of our careers. I learned so much working with both of you in The Gambia and in Antwerp. Thank you for your support, your intelligence, your feedback, and so much more. I would also like to thank the SEHR (née MAU) group for always welcoming me in Antwerp, especially Maureen, Fatou, and Maya – especially for allowing me to stay at your place.

Barcelona
I am also grateful for my other promoter, Azucena Bardaji. Thank you, Azucena, for starting our relationship warmly and openly and for providing a wonderful, more clinical perspective that was otherwise missing. I am glad we got together on this dissertation, and I really hope to be able to meet you and thank you in person one day.

<u>Across the globe, past and present</u>
The journey to this point started well before February 2018. Indeed, I would venture to go as far as acknowledging the importance of Mrs. Gold at St. Paul's Episcopal Day School in Ventura, California... Looking back, I have been exceedingly fortunate to have had some of the best teachers and mentors in my life.

Mr. Bobbitt, thank you for mentoring me in what could be considered my first thesis. I remember we could not decide which subject my chosen topic best fit because, as you said, it was "too math for the literature people and too literature for the math people." Who knew then, but I think this was the beginning of my mixed-methods, multi-disciplinary research approach. A few years later, thank you, Lance Gravlee, for helping me learn what it might mean to be an anthropologist and also being the first to suggest, "what about an MPH?" Lastly, thank you, Neal Dickert, for not only formally introducing me into the world of research ethics, but also being my first boss to treat me as a colleague (instead of underling) and a capable academic researcher.

I am so incredibly thankful for the friends and family who have supported me in these past 4 years and beyond. Doing a PhD can feel selfish and isolating, and it would be easy to allow friendships to slide. That said, thank you, Fathores Kyle McCluskey and Krista Westmark, Anne Schuster, and Laura Whitaker for sticking by me and still being my friends. In Amsterdam, thank you, David Morel, for, if anything, being the first to say, "go focus on your thesis!" if I started to let life's other distractions get in the way. To my MHiL, Donna Holt, thank you for your love and support and always being ready with a hot toddy.

Rafael Garcia-Suarez, you came into all this mess in the thick of it and have made it better ever since. Considering I was introduced to you with "tell him about your thesis – he won't get bored," I suppose it makes sense that you may be one of the only people who has read this whole thing through. Thank you for all the love and support (and delicious meals) these last couple of years. What started as a lockdown companionship has continued to evolve into something beautiful.

Though they have passed, it's important to me to acknowledge my grandparents, Darlene and Jack Thompson (Nana and Papa) and Martha and William Fehr (Grandma and Grandpa). For the lucky ones, grandparents are a special source of love and support to their grandchildren; mine were that and more. Papa, the first scientist in the family, you always encouraged a sense of wonder and love for learning. Nana, even though you may not have always understood what I was doing "over there," you loved and supported me, nonetheless, and made sure I paid attention to the importance of things outside school and work. Grandpa, I can only imagine how proud you'd be

that I was “paid to go to school” and that this dissertation would have been next to my other awards and clippings you kept on display. And Grandma. Someone so smart and so professionally accomplished for a woman of your era and background. You always seemed to “get it,” even when that meant making sure I got on the plane to Sierra Leone, knowing full well you would not (physically) be there when I got back. I wish I could be sharing this with you now.

To my parents, Bruce Fehr and Lori Thompson. Where do I even begin? I will always be eternally grateful to you. For my whole life, you have always given me your love and support in anything I have set my mind to. From “playing school” as a toddler, to listening to and supporting my “I don’t want to be a (medical) doctor anymore” university realization/crisis, you have always believed that I would do amazing things and never allowed me to settle for less. But even with all that, what I think I am most grateful for in this moment and in this context is that you always encouraged us to “go places and do things,” even when that meant long – and sometimes very long – periods of time far away from home. This PhD – this particular life I lead – would not have been possible otherwise. Ahboo. And also to my “little sissoo” Kimberly Fehr Barnard (AKA Kimmie): you have had to put up with my special type of obnoxiousness since the day you were born but have still always loved and supported me from day 1 (unless, of course, it meant that you would be late for first period English). Grassyas.

Against all better judgement, I will also thank my dogs. Pilar and Hugo, you spoiled little mutts. Though you have no real concept of time or place or why I would ever sit at my computer instead of play with you, your never-ending cuddles and pure, uncomplicated love always brighten even my worst days. Now that this is done, I promise more walkies and time at the park.

And, lastly, to Austin Holt, the co-star of my memoirs. I do not have the ability to write in this space what you mean to the success of this dissertation let alone what you mean to me. As my best friend, partner, and husband, for more than 20 years you have loved me and supported me as I’ve chased my dreams around the globe, and I am so thankful for you. I could not have done this without you. Thank you for everything, but especially for always being able to make me laugh. I wuv ewes.

About the author

Alexandra Elizabeth Thompson Fehr

Alex on the back of a moto-taxi in Basse after the last day of fieldwork.

Alex grew up on the beaches of southern California and northwest Florida. She has always had a love for education and graduated from the International Baccalaureate Program at Pensacola High School in Pensacola, Florida in 2004. Due to her interests in science and health and a passion to help others, Alex started university with the intention of becoming a medical doctor. During that time, however, she was introduced to Anthropology and was immediately enthralled by the social science aspects of health and medicine; this would be her focus moving forward. She received her Bachelor of Arts (*magna cum laude)* from the University of Florida in Gainesville, Florida in 2008. Afterwards, Alex earned a Master of Public Health (MPH) from the Emory University Rollins School of Public Health in Atlanta, Georgia in 2011. Her MPH is in Global Health with a concentration in Community Health and Development.

After completing her MPH, Alex worked for 7 years in global health research. This included a Research Fellowship with UNICEF focused on water, sanitation, and hygiene in Timor-Leste, the Philippines, and Sierra Leone. During this time, she became increasingly interested in research ethics and took a position as a Clinical Research Coordinator at the Emory University School of Medicine. Her research focused on empirical bioethics, including issues of informed consent and the decision-making process for trial enrolment. Looking to broaden her research back into a global context, Alex next accepted the position of Research Associate for Partners in Health Rwanda where she worked for 1.5 years before beginning her doctoral studies.

In 2018, Alex began the Erasmus Mundus Joint Doctorate fellowship in Transdisciplinary Global Health at the Athena Institute, Vrije Universiteit

Amsterdam in The Netherlands, along with the Institute of Tropical Medicine, Antwerp in Belgium and the Barcelona Institute of Global Health, University of Barcelona in Spain. Using a mixed-methods, transdisciplinary approach, Alex focused her research on the socio-cultural and ethical nuances of participation in a mass drug administration clinical trial in The Gambia. Broadly speaking, her research interests focus on global health research ethics, particularly issues surrounding community engagement, the informed consent process, global health emergency settings, and decolonizing global health.

Alex is currently a Research Fellow in Social Science at the London School of Hygiene and Tropical Medicine and part of the United Kingdom Public Health Rapid Support Team. She is based in London, U.K. Outside work, she enjoys traveling, photography, sailing, scuba diving, and cooking.