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The role of multidimensional poverty in antibiotic misuse: A mixed-methods study of self-medication and non-adherence in Kenya, Uganda, and Tanzania

Authors: Dominique L. Green, PhD,[1*] Katherine Keenan, PhD,[1] Sarah I. Huque, PhD,[1] Mike Kesby, PhD,[1] Martha F. Mushi, PhD,[4] Catherine Kansiime, PhD,[2] Benon Asiimwe, PhD,[2] John Kiiru, PhD,[3] Stephen E. Mshana, MD,[4] Stella Neema, PhD,[2] Joseph R. Mwanga, PhD,[4] Kathryn J. Fredricks, PhD[1] Andy G. Lynch, PhD,[1] Hannah Worthington, PhD[1], Emmanuel Olamijuwon, PhD, [1] Mary Abed Al Ahad, MSc, [1] Annette Aduda, MA,[3] Blandina T. Mmbaga, PhD,[5] Joel Bazira, PhD,[7] Alison Sandeman, PhD,[1] John Stelling, MD[8] Stephen H. Gillespie, DSc[1] Gibson Kibiki, MD,[9] Wilber Sabiiti, PhD,[1] Derek Sloan, MD,[1] Matthew T. G. Holden, PhD,[1] and HATUA Consortium[1]

[1] University of St Andrews, UK
[2] Makerere University, Uganda
[3] Kenya Medical Research Institute, Kenya
[4] Catholic University of Health and Allied Sciences, Tanzania
[5] Kilimanjaro Clinical Research Institute and Kilimanjaro Christian Medical University College, Tanzania
[6] Mbeya Medical Research Centre, Tanzania
[7] Mbarara University, Uganda
[8] Brigham and Women's Hospital, United States
[9] East African Health Commission, Burundi
* Correspondence to: Dominique L. Green, School of Geography & Sustainable Development, University of St. Andrews, St Andrews, UK KY16 9AL; dominique.green@st-andrews.ac.uk

Abstract

Background: Poverty is a proposed driver of antimicrobial resistance (AMR), influencing inappropriate antibiotic (AB) use in low and middle-income countries (LMICs). However, at sub-national levels, studies investigating poverty and AB use are sparse and the results inconsistent.

Methods: The Holistic Approach to Unravelling Antimicrobial Resistance (HATUA) Consortium collected data from 6,827 patients presenting with urinary tract infection (UTI) symptoms in Kenya, Uganda, and Tanzania. Using Bayesian hierarchical modelling, we investigated the association between multidimensional poverty and self-reported AB self-medication and treatment non-adherence (skipping a dose and not completing the course). We also analysed linked qualitative in-depth patient interviews (IDIs) (n = 82) and unlinked focus group discussions (FGDs) with community members (n = 44 groups).

Findings: AB self-medication and non-adherence to treatment courses was significantly more common in the least deprived group compared with those in severe poverty. Adjustment for AB 'knowledge', attitudes and socio-demographics diminished the association with self-medication, but not non-adherence. IDIs and FGDs suggested that self-medication and non-adherence are driven by perceived inconvenience of the healthcare system, financial barriers, and ease of unregulated AB access.

Interpretation: Structural barriers to optimal AB use exist at all levels of the socioeconomic hierarchy. Inefficiencies in public healthcare may be fuelling alternative antibiotic access points, for those who can afford it. In designing interventions to tackle AMR and reduce AB misuse, the behaviours and needs of wealthier population groups should not be neglected.

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Research in context

Evidence before this study

We searched Google Scholar, PubMed, and Web of Science with the terms “antibacterial”, “antibiotic”, “poverty,” and “socio* risk factors” for articles published between 2011 and 2021. We found several systematic reviews covering subjects relating to poverty, AMR, and factors influencing antibiotic misuse in LMICs. Among these was a systematic review (published 2018) which identified 19 research articles (seven in LMICs, none in Africa) on the impact of poverty on AMR. The reviewed studies found that various dimensions of poverty, such as lack of education and poor sanitation, have been linked to increased burden of AMR. As well as sparse evidence from LMICs, the review highlighted that poverty was measured inconsistently. We found five systematic reviews (published between 2018-2021) that focused specifically on antibiotic misuse, mainly in the form of self-medication, in LMICs. These reviews identified 103 studies from LMICs (22 from Africa) and found a high prevalence of self-medication ranging from 7% to 94%. Various socioeconomic factors were associated with self-medication, but relationships were mixed. For example, one study found a positive association between self-medication and employment, whiles others found positive associations with unemployment. Many of the reviewed studies, including those from Africa, found that low education and socioeconomic status were associated with higher self-medication. Finally, one systematic review (published 2018) which focussed on patterns of antibiotic use among patients, including 87 studies from 33 countries (13 studies covering LMICs). The review suggests lower treatment adherence among the young and those with low education/income, and that self-medication more common in younger and more highly educated patients, and those with lower knowledge. Overall, these reviews highlight mixed and contradictory evidence on the link between socioeconomic status and AB misuse. Poverty was rarely the focus of these studies and there is underrepresentation from Africa, particularly East Africa.

Added value of this study

Rather than consider individual socioeconomic indicators, we measure poverty using a standardised and internationally recognised index, which accounts for multiple dimensions of well-being: education, health and living standards. We use multi-country, harmonised data from individuals in three East African nations, with linked quantitative and qualitative evidence. Our findings show that the least deprived are the most likely to misuse antibiotics, and this is explained by a range of structural and contextual factors. This study highlights the somewhat overlooked role of higher socioeconomic status as a facilitator of inappropriate antibiotic use in contexts where public health provision is inadequate and antibiotic regulations are insufficiently enforced. Consequently, richer subgroups may contribute more to the spread of AMR in poor regions than has hitherto been appreciated.

Implications of all the available evidence

Although poverty plays an important role in the AMR crisis, we should not assume that poorer subgroups drive AB misuse. Antibiotic use is socially stratified, but patterns depend on the context. Exploring the various dimensions of poverty remains crucial in understanding the contextual and situational rationale for antibiotic misuse. Notwithstanding the role of individual decision-making, greater attention is required to the structural barriers that discourage optimal antibiotic use at all levels of the socioeconomic hierarchy in LMICs.

Introduction

Antimicrobial resistance (AMR) is a complex biosocial phenomenon that threatens global public health[1] and is accelerated by inappropriate antibiotic use.[2] Globally, human consumption of antibiotics (ABs) increased by over 60% between 2000-15, and consumption in low- and middle-income countries (LMICs) is rapidly converging with richer nations.[3] Inappropriate use of ABs, sometimes called AB 'misuse,' in LMICs includes behaviours like self-medication, accessing ABs without prescription and incomplete treatment adherence, such as skipping doses or not fully completing a course.[4] While many factors may facilitate these behavioural patterns, encouraging optimal AB use among patients has become an important policy target.[5]

Poverty is likely to play an important but complex role in the AMR nexus. Studies suggest that structural poverty - that is, poverty emergent from the way economies and societies are structured - may fuel AMR. Poor sanitation for example, may increase bacterial infection rates and transmission of drug-resistant pathogens.[5,6] Meanwhile, under-resourced healthcare and poorly-regulated dispensing systems may foster AB misuse via both inappropriate prescription and self-medication without prescription.[4,7–10] At the same time, macro-scale factors associated with socioeconomic growth, such as increasing urbanisation are associated with the development of AMR hotspots.[11]

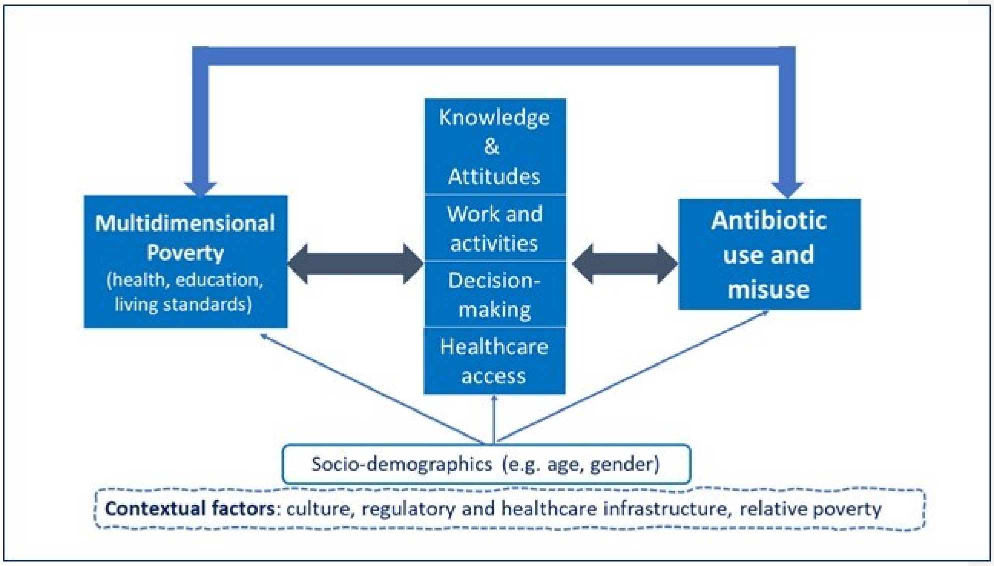
At an individual, rather than aggregate level however, evidence on the relationship between poverty and AB use behaviours is limited and often contradictory, while evidence of the relationship in Africa is sparse.[4,6,7,12–14] Some studies from LMICs suggest poorer and lower educated subgroups are more likely to self-medicate[13,15,16] and have worse AB treatment adherence,[7,14] perhaps because of an inability to purchase a whole course. Others suggest subgroups with more purchasing power may have more opportunity to self-medicate.[4] Given that AMR and AB use are strongly contextually situated,[7] generalisations across LMIC settings may obscure critical insights by ignoring inequalities within settings. Furthermore, understanding of possible relationships between poverty and AB use is limited by small scale samples, diverse study designs, and a lack of a standardised way to measure multidimensional poverty.

To address these gaps, we investigate the following research questions in this mixed-methods study:

- What is the nature of the relationship between multidimensional poverty and reported AB misuse among patient populations in East Africa (Kenya, Uganda, and Tanzania)? How do other individual and contextual factors help to account for the relationships?

Based on previous empirical evidence, we developed a conceptual framework to guide our study (Figure 1). It describes the potentially complex interplay of social, cultural, and economic factors in the poverty-AMR nexus. We conceptualise that poverty and AB misuse may be bi-directionally related, linked to economic opportunities to self-medicate,[17,18] but may also be mediated by a number of contextual, attitudinal, and structural factors. For example, poverty may be associated with poorer knowledge and understanding of ABs,[7,13,14,19–22] that may also foster misuse. Other factors, including employment and decision-making processes may be co-constitutive of poverty, influencing AB misuse directly and indirectly. Finally, the relationship between AB misuse and poverty may be influenced by socio-demographic or cultural factors and 'facilitating' contextual factors such as the disease and pathogen landscape, regulatory and healthcare infrastructures.[15]

Figure 1: Proposed conceptual framework for the relationship between multidimensional poverty and AB misuse in individuals.



Methods

Data and sample

The data were generated by the HATUA (Holistic Approach To Unravelling Antimicrobial Resistance) Consortium, an interdisciplinary, mixed-methods, three country study on the drivers of AMR, described elsewhere.[23] The HATUA study uses urinary tract infection (UTI) - a commonly occurring bacterial infection - as a clinical prism through which to investigate the drivers of AMR. Between February 2019 and September 2020, 6,827 adult outpatients (aged 18+, or those 14 -18 and pregnant) were recruited from healthcare facilities in Kenya, Uganda, and Tanzania, drawn from three sites in each country (Tanzania: Mwanza, Kilimanjaro, and Mbeya; Kenya: Nairobi, Nanyuki, and Makueni; Uganda: Mbarara, Nakapiripirit, and Nakasongola). Facilities were predominantly government-funded and included both primary and secondary levels of care (see Appendix 1). Doctors identified patients with symptomatic and probable UTI for inclusion to the study. Less than 1% declined to participate in every setting. Patients provided a urine sample and answered a questionnaire on treatment-seeking for UTI symptoms, AB use practices, attitudes, and sociodemographic characteristics. In-depth interviews (IDIs) were conducted with a purposively selected subset of patients (n = 82) who reported complex treatment pathways or were diagnosed with a multi-drug resistant UTI pathogen. IDIs were conducted using standardised topic guides in the respondent's primary language and translated by fieldworkers. Interviewees discussed their recent treatment seeking, AB use, knowledge, attitudes, and motivations for behaviours. Patient qualitative and quantitative data were linked by patient ID. Independently from the patient sample, we conducted 44 gender-stratified focus group discussions (FGDs) with community members in study sites in Tanzania (Moshi n = 8; Mbeya n = 7; Mwanza n = 8) and Uganda (Nakasongola n = 8; Mbarara n = 8; Nakapiripirit n = 5), using standardised topic guides (see Table S2.1 for characteristics). FGDs captured details of healthcare seeking among a wider group than those who recently attended healthcare facilities. Participants gave written informed consent, and ethical approval for this project was obtained from all institutions involved (see protocol).[23]

Measurement of AB misuse

All three outcomes were binary indicators. AB self-medication was derived from reported history of recent treatment for UTI-like symptoms and took the value 1 for all patients who, prior to their recruitment at health clinics, took ABs that had not been prescribed by an attending physician (i.e., from drug sellers, friends, etc.). To measure skipping a dose, patients were asked 'Have you ever skipped a dose of ABs?' and for not completing the course 'Do you usually complete the course of treatment?' to which patients answered yes or no. Interviewees discussed AB use practices during in-depth discussions of treatment-seeking pathways. FGD participants discussed self-medication without prescription, AB adherence, and taking partial courses.

Multidimensional poverty index (MPI)

To ensure comparability across settings, we use as a measure an internationally validated, standardised multidimensional poverty index (MPI) which captures dimensions of living standards, health and education.[24] An individual-level MPI score was calculated for each patient based on the 'counting' methodology,[25] the same used for the Acute Multidimensional Poverty Index for Developing Countries (global MPI).[24] Full details of the development of the MPI for our data (hereafter HATUA MPI), including cut-offs and weighting are in Appendix 3. Our adapted adult version contains seven binary indicators distributed under three equally weighted domains (Table S3·1). These comprised one indicator for education (no education and primary vs. secondary and tertiary), two for health (reports any chronic conditions of asthma, heart disease/stroke, cancer, and high blood pressure/hypertension; reported having a disability), and four indicators for living standards (no mains electricity, shared unimproved sanitation, unprotected public access to drinking water, and not owning more than one of these assets: TV, radio, computer, fishing boat, phone, refrigerator, or bed). Based on their weighted score, we categorised patients into four groups: not deprived if <20%, vulnerable to poverty if 20% to less than 34%, deprived if 34-49%, and living in severe poverty if more than 50%.[26]

Other socio-demographic, attitudinal and knowledge variables

After testing various model specifications, age was rarely significant, and including multiple age categories led to high model autocorrelation, so age was dichotomised to <35 years, and 35 years+ to allow for a better model fit. Alongside age and sex, other socio-economic factors that might mediate the MPI-AB use relationship included activity status (formal employment, informal employment, homemaker, not working), and difficulty in meeting healthcare costs (not difficult, some difficulties, very difficult). We measured knowledge via two variables. Familiarity with ABs included a variable measuring the number of ABs known/recognised, collected using a 'drug bag' or 'drug card' method which showed pictures and packaging of locally available ABs.[27] Patients were also asked whether they knew the term antibiotic (with answers: don't know, another name for medicine, or medicine to treat infection or germs). Healthcare attitudes were measured by responses to the question: 'What source(s) of information about medicines/drugs do you use when you are sick?' We dichotomised this to reflect those who only sought advice from doctors or formal healthcare workers vs. help from other sources such as drug sellers, traditional healers, etc. We also tested associations with other variables: awareness of the term antimicrobial resistance or AMR; believing that ABs could be used to treat colds and coughs, having health insurance, and decision-making power (needing to seek permission from others before seeking healthcare), but as these were not significant in any of the models, they were omitted.

Statistical Methods

We estimated the association between MPI and three different outcomes of AB misuse separately: the binary outcomes of skipping a dose, not completing the course, and self-medication. To do this, we used Bayesian hierarchical logistic regression models with four levels: patients nested in 25 clinics, clinics nested in nine sites, and sites nested in three countries. Approximately 9% of our sample had missing values (see Appendix 4 for how these are distributed), which we account for using a Bayesian modelling framework. Full model specifications are provided in Appendix 5. For each outcome, we fitted a series of models. We ran a series of models: Model one estimated the association between MPI and AB misuse adjusted for age, and sex. In model two, we added other socioeconomic indicators not captured in the MPI: employment and ability to meet healthcare costs. In model three, we add knowledge and attitude variables. We also repeated the analysis using frequentist multilevel modelling (full details Appendix 6) and conducted a site-level meta-analysis (full details Appendix 7).

Qualitative analysis. IDIs and FGDs were analysed using iterative thematic content analysis in NVivo,[28] with the interview/FGD guides framing initial coding and analysis. Subsequent rounds of in-depth coding were undertaken to identify challenges to patient treatment-seeking among patients in the linked sample (who had an associated MPI descriptor) and the community members in the unlinked sample (for whom we state employment as a socio-economic status indicator).

Results

Patient sample description

Across Kenya, Tanzania, and Uganda, patients were most commonly female (79·2%), aged under 35 years, worked in informal employment, and had primary-level education (Table 1). Based on the MPI categories, 42·6% of patients were not deprived, 9·5% vulnerable to poverty, 16·6% deprived, and 31·4% living in severe poverty. The most deprived participants came from Uganda and the least deprived from Kenya. We observed a similar MPI distribution in the linked qualitative sample (seen in Table 2). Across the three countries, the education indicator contributed the most to the HATUA MPI (63%). This high contribution reflects one indicator for one domain, carrying a total weight of 33% in the overall MPI score. Sanitation deprivation followed, contributing 14·3% to the HATUA MPI. Drinking water deprivation contributed the least (3%) (Appendix Table S3·4). The proportion self-medicating and skipping a dose varied significantly by country (based on bivariate analysis), whereas completing the course did not. Recent self-medication with ABs was higher in Tanzania and Kenya (7·4 and 6·9%, respectively) compared with 4·2% in Uganda. More patients from Kenya and Tanzania reported skipping a dose (both 26%) compared to Uganda (17·8%). In total, 12·7% of patients across the three countries reported not completing the course of ABs.

Table 1: Quantitative sample characteristics (complete case data)

Variable	Total N = 6,345 n (%)	Tanzania n = 2,970 n (%)	Uganda n = 1,700 n (%)	Kenya n = 1,675 n (%)
AB misuse outcomes				
Self-medicated with ABs	406 (6·4)	219 (7·4)	72 (4·2)	115 (6·9)
Skipped a dose	1,513 (23·8)	771 (26·0)	302 (17·8)	440 (26·3)
Incomplete course	803 (12·7)	359 (12·1)	224 (13·2)	220 (13·1)
Poverty status				
Not Deprived	2,701 (42·6)	918 (30·9)	392 (23·1)	1,391 (83·0)
Vulnerable	603 (9·5)	426 (14·3)	89 (5·2)	89 (5·3)
Deprived	1,052 (16·6)	679 (22·9)	252 (14·8)	121 (7·2)
Severe Poverty	1,989 (31·3)	947 (31·9)	967 (56·9)	75 (4·5)
Age				
Under 35	3,840 (60·5)	1,472 (49·6)	1,114 (65·5)	1,254 (74·9)
35 and over	2,505 (39·5)	1,498 (50·4)	586 (34·5)	421 (25·1)
Sex				
Male	1,321 (20·8)	784 (26·4)	266 (15·6)	271 (16·2)
Female	5,024 (79·2)	2,186 (73·6)	1,434 (84·4)	1,404 (83·8)
Working Status				
Formal employment	1,368 (21·6)	721 (24·3)	233 (13·7)	414 (24·7)
Informal employment	2,621 (41·3)	1,101 (37·1)	950 (55·9)	570 (34·0)
Homemaker	1,586 (25·0)	740 (24·9)	391 (23·0)	455 (27·2)
Not working	770 (12·1)	408 (13·7)	126 (7·4)	236 (14·1)
Difficulty in meeting health care costs				
Easy	2,334 (36·8)	1,443 (48·6)	261 (15·4)	630 (37·6)
Some difficulty	2,726 (43·0)	1,008 (33·9)	863 (50·8)	855 (51·0)
Very difficult	1,285 (20·3)	519 (17·5)	576 (33·9)	190 (11·3)
Source of health care advice				
Doctors only	2,219 (35)	1,146 (38·6)	692 (40·7)	381 (22·7)
Others (friends, drug sellers etc)	4,126 (65)	1,824 (61·4)	1,008 (59·3)	1,294 (77·3)
Knowledge of term 'antibiotic'				
Don't know	3,128 (49·3)	2,093 (70·5)	676 (39·8)	359 (21·4)
Another name for medicine	1,083 (17·1)	309 (10·4)	469 (27·6)	305 (18·2)
Medicine for infections/germs	2,134 (33·6)	568 (19·1)	555 (32·6)	1,012 (60·4)
Familiarity with ABs by name/packaging				
Know 0-3	3,114 (49·1)	1,637 (55·1)	580 (34·1)	897 (53·6)
Know 4 or more	3,231 (50·9)	1,333 (44·9)	1,120 (65·9)	778 (46·4)

Table 2: Qualitative sample characteristics of linked IDI patients

Variable	Total N = 82 n (%)	Tanzania n = 25 n (%)	Uganda n = 34 n (%)	Kenya n = 23 n (%)
Sex				
Male	21 (26)	8 (32)	5 (15)	8 (35)
Female	61 (74)	17 (68)	29 (85)	15 (65)
Poverty status				
Not Deprived	34 (41)	10 (40)	9 (26)	15 (65)
Vulnerable	4 (5)	1 (4)	2 (6)	1 (4)
Deprived	14 (17)	5 (20)	7 (21)	2 (9)
Severe Poverty	30 (37)	9 (36)	16 (47)	5 (22)
Age				
Under 35	42 (51)	8 (32)	22 (65)	12 (52)
35 and older	40 (49)	17 (68)	12 (35)	11 (48)
Working Status				
Formal employment	9 (11)	5 (20)	1 (3)	3 (13)
Informal employment	43 (52)	9 (36)	25 (74)	9 (39)
Homemaker	19 (23)	7 (28)	7 (21)	5 (22)
Not working	11 (13)	4 (16)	1 (3)	6 (26)

Bayesian hierarchical modelling results

Results from model three are shown in Table 3, and stepped model estimates of Models 1, 2, and 3 shown in Figure 2. In models controlling for sociodemographic characteristics, self-medication with ABs is more common those who were not severely deprived (models 1, Figure 2A). This association between MPI and self-medication diminishes when variables related to knowledge and familiarity with ABs, and attitudes are added (Model 2 & 3, Figure 2, and Table 2). Other factors associated with higher odds of self-medication are being employed (relative to being a homemaker), seeking healthcare advice from people other than doctors, and knowledge of 4 or more antibiotics.

Non-adherence to AB regimens was more common among those with lower levels of multidimensional poverty. The odds of skipping a dose increase as deprivation decreases, i.e., the better-off were most likely to skip doses. This result holds in Models 2 and 3 when further sociodemographic characteristics, knowledge and attitudes, are included (Figure 2B). Those who were not deprived (the best off) had higher odds (1.41) of not completing the course, compared with the severely deprived. Non-adherence was also more common among those who were employed (compared with other employment statuses), had a lot of difficulty meeting healthcare costs (compared with 'easy'), or sought advice from people other than doctors. These findings suggest an apparent contradiction: that those at high risk of non-adherence face difficulties meeting healthcare costs yet their poverty status is 'not deprived', which might be explained by better-off patients having higher expectations and different perceptions of healthcare compared with lower socioeconomic groups. Adjusting for knowledge and attitudes about ABs did not substantially alter the association between MPI and treatment non-adherence. We observed country, site, and clinic level variation in the outcomes, as demonstrated by the variation in the random effect estimates, but in stratified analyses (available on request) we did not detect differences in the relationship between MPI and the outcomes by country and site. The results of the fixed effects parts of the model using a frequentist multilevel approach are entirely consistent with Table 2 (Appendix 6). Site–level meta-analyses detected some differences in the associations by site but returned the same overall conclusions as regression modelling (Appendix 7).

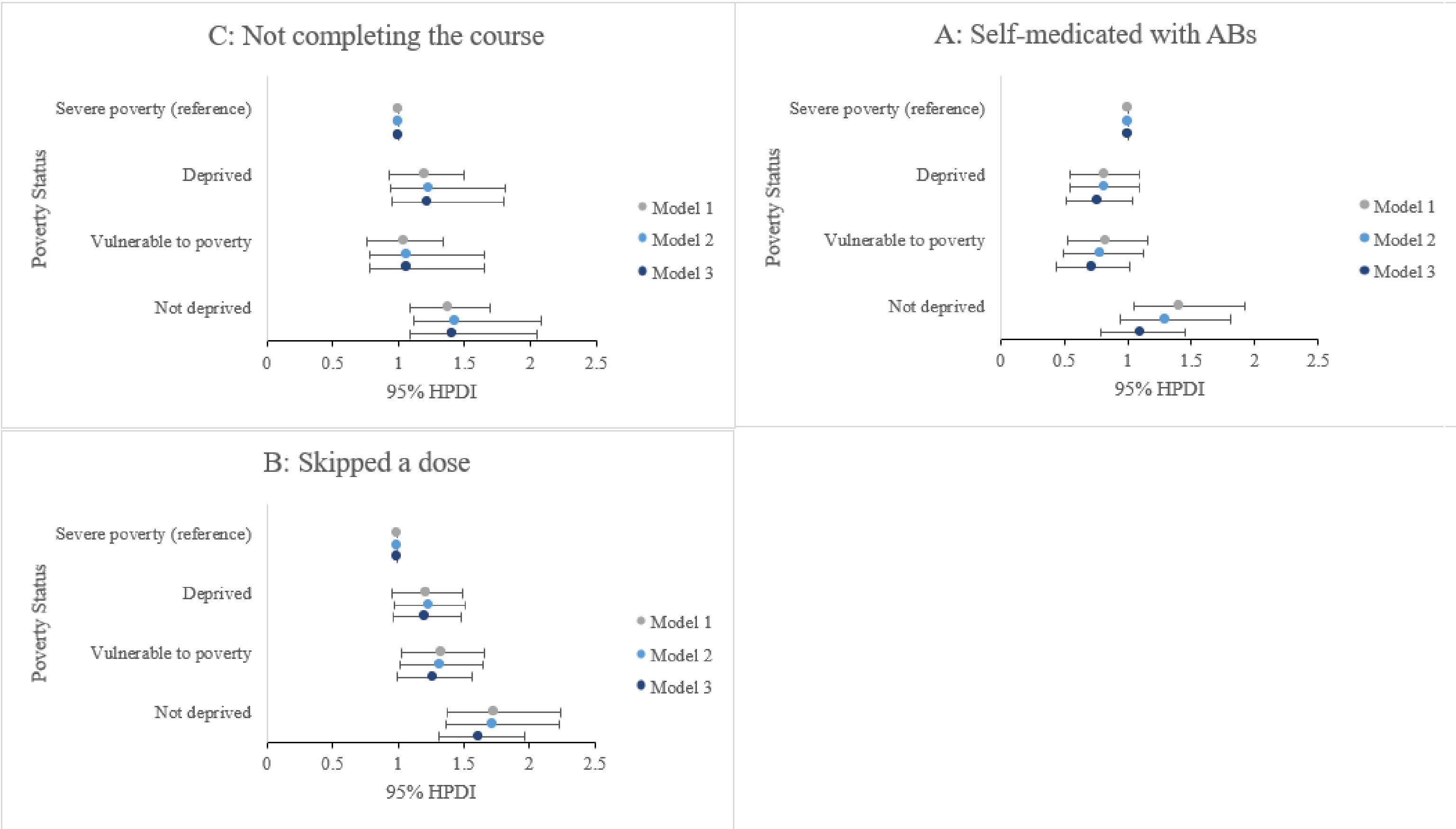
Table 3: Hierarchical regression results for associations between MPI and AB misuse (Model 3)

	Self-medicated with ABs	**Skipped a Dose**	**Not completing the course**
	Posterior OR (95% HPDI[1])	Posterior OR (95% HPDI[1])	Posterior OR (95% HPDI[1])
Poverty status: (ref = severe poverty)			
Deprived	0·77 (0·52-1·04)	1·21 (0·98-1·46)	1·22 (0·95-1·53)
Vulnerable to poverty	0·72 (0·44-1·02)	**1·27 (1·10-1·56)**	1·06 (0·78-1·37)
Not deprived	1·11 (0·79-1·45)	**1·61 (1·32-1·94)**	**1·41 (1·09-1·73)**
Age (ref = less than 35 years)			
35 and over	0·86 (0·68-1·08)	0·88 (0·76-1·01)	0·90 (0·75-1·06)
Female (ref = Male)	0·89 (0·66-1·12)	1·07 (0·91-1·24)	0·94 (0·77-1·12)
Working status (ref = Formal employment)			
Informal employment	0·86 (0·63-1·09)	**0·77 (0·64-0·90)**	0·85 (0·68-1·04)
Homemakers	**0·52 (0·35-0·69)**	**0·67 (0·54-0·81)**	0·82 (0·63-1·02)
Not working	0·75 (0·50-1·03)	**0·62 (0·49-0·76)**	**0·75 (0·55-0·96)**
Able to meet healthcare costs (ref = Easy)			
Some difficulty	**1·37 (1·06-1·71)**	0·89 (0·76-1·02)	1·14 (0·94-1·35)
Very difficult	1·17 (0·80-1·57)	**1·46 (1·20-1·73)**	**1·39 (1·09-1·70)**
Source of advice: (ref = other than doctor)			
Doctor's/healthcare workers' advice only	**0·61 (0·47-0·76)**	**0·65 (0·56-0·74)**	**0·67 (0·56-0·79)**
Knowledge of term 'antibiotic' (ref = Don't know)			
Another name for medicine	1·07 (0·72-1·43)	1·02 (0·83-1·22)	1·13 (0·87-1·14)
Medicine for infections/germs	1·32 (0·95-1·71)	1·04 (0·85-1·21)	1·17 (0·93-1·41)
Familiarity with ABs (ref = Know 0-3)			
Know 4 or more	**1·62 (1·27-2·00)**	**1·30 (1·14-1·47)**	0·87 (0·73-1·02)
Random effects			
Country-level variance	2·63 (1·28-4·4)	1·28 (0·01-2·53)	1·92 (0·76-3·47)
Clinic-level variance	0·41 (0·2-0·65)	0·81 (0·51-1·15)	0·72 (0·45-1·02)
Site-level variance	0·15 (0-0·41)	0·72 (0·02-1·5)	0·63 (0·01-1·23)

[1] Highest posterior density interval. Emboldened text indicates HPDI for OR not crossing 1.

Source: HATUA data ; n = 6,827.

Figure 2: Adjusted 95% HPDI for the following outcomes A) self-medicated with ABs B) skipped a dose, and C) not completing the course.



Qualitative analysis

The qualitative data set analysed here is comparatively large. It illuminates patterns and seeming contradictions identified in the quantitative modelling, illustrating that healthcare seeking behaviours are better understood as 'situationally rational' than as 'irrational,'[29] and suggests that many barriers to 'optimal' AB use are interrelated, structural and experienced regardless of socioeconomic status.

It was common for respondents to report bypassing government healthcare centres in favour of self-medication with ABs obtained without a prescription from drug sellers or other sources closer at hand than health centres. This was driven by multiple factors, including insufficient funds to cover transport or drugs: "*Sometimes you are sick, and you don't have money to take you to the hospital and thus decide to just buy [antibiotics] thinking that you will be healed*" (Tanzania, male patient, 'severe poverty'). Financial constraints also contributed to decisions to buy and take a partial course of ABs: *"When the money becomes too much, you end up buying fewer tablets…you take less…. When you get enough money, you buy more tablets*" (Uganda, male patient, 'deprived'). As we report elsewhere,[30] the preparedness of (Tanzanian) sellers to dispense ABs without prescription and sell less than the recommended minimum course is almost universal, further rationalising decisions to bypass health professionals. Unsurprisingly, insufficient funds and ill-health can become a vicious circle: *"Something that is needed is money for treatment services and since you are sick and you cannot work you will not be having money"* (Tanzania, FGD15, female, seller). 'Insufficient funds' were cited, even amongst the better-off, as a further reason to avoid both health care facilities and drug shops: "*It is not easy [to get antibiotics] because most of the times I don't have money and that is why I go to my friend for herbal medicine*" (Kenya, male patient, not deprived). However, if these remedies are not effective, delayed medicinal treatment is then usually sought from medical centres or drug sellers if and when a person obtains the necessary resources.

Perceived inconvenience was frequently offered as a rational for accessing ABs without prescription, especially among those with other responsibilities. The better-off and those with jobs were particularly vocal about travel and waiting times associated with attending government healthcare facilities: *"Mostly when I go there, I have to sacrifice almost a whole day because of the long queues and many waiting hours"* (Kenya, male patient, 'not deprived'). The frequently reported unavailability of ABs at government healthcare centres further strengthened the rationale of going straight to private suppliers. FGD participants highlighted elements of service provision and patient care that further explained this behaviour: *"You can reach a health facility, and somebody talks to you rudely. If a person talks to you well even if he does not have treatment for you, you can feel better. Instead, a health worker [says] that 'we don't have drugs, so you can do what you want'"* (Uganda, FGD1, female, farmer).

After being questioned about their practices around AB use, patient interviewees were given some 'best practice' advice (see Figure 3) and asked: (i) whether they had heard it before and (ii) what challenges might prevent individuals following such advice. While most respondents had heard some or all of the advice, most identified difficulties stemming from a complex combination of individual and structural factors that can constrain individuals from acting on what knowledge they *do* have about AB best practices (see Table 4).

Figure 3. HATUA Interview Best Practice Advice statement given to interviewees

> Best practice is that antibiotics should be taken
>
> (a) *only* when prescribed by a doctor,
>
> (b) at a set time each day,
>
> (c) a full course should be taken (never just a couple of days - even if you start to feel better), and
>
> (d) a patient should take the full course *themselves* and not share with others.

Notes: Advice based on guidance issued by National Health Service (https://www.nhs.uk/conditions/antibiotics/) and Centre for Disease Control (https://www.cdc.gov/antibiotic-use/do-and-dont.html)

Table 4. Challenges to implementing AB use best practices reported by patient interviewees: Interrelated themes around financial constraints, work commitments and inconvenience

Financial constraint and care commitments	**Work commitments**	**Inconvenience and health facility under-resourcing**
Yes, the advice is good, but it is not voluntary that we share medicine, but our [financial] resources determine [this choice]. For instance, we can be sick and even our children are sick, and you know that the same medicine you are swallowing can also help treat the child, so you end up sharing the medicine. Financial situation[s] [might prevent people from following the doctor's advice]. (Uganda, female patient, 'deprived')	*I think when one is asked to set time each day, [it] is so unachievable especially for the people that are working during the day. For most medicine we are asked to take them three times in a day, and you find that during the day one is occupied by work, and they forget to take the medicines.* (Kenya, male patient, 'severe poverty')	*Some of them do not have enough time to go to the hospital because of the number of sick people in the hospital (long line), they want to go to the doctor direct, but they are forced to wait. And waiting - time is wasted. So, instead they decide to go to the clinic or drug shop… It is the distance and the weather.* (Uganda, female patient, 'not deprived')
Lack of knowledge and financial constraint	**Competing work and care commitments**	**Time constraints and convenience**
I think that [not following best practices] is caused by little understanding, but there are genuine reasons, for example someone taking half dose of drugs due to lack of money, it means he doesn't have money to buy [the] full course… He purchases and take[s] half [of the] course, which is way better than staying sick… Without knowing he is causing more serious effects… But the main cause is poverty. (Tanzania, male patient, 'not deprived')	*Like for us who work, you leave home in the morning at 6:00am and the child has to take the drug at 7:00am so you find you have failed to give the child the medicine in time, you end up skipping some days. The dose gets spoilt, and thus fails to cure the child.* (Uganda, female patient, 'vulnerable to poverty')	*It is a little difficult, but I can try [to buy ABs only with a prescription] … What do I do when I am not able to go to the hospital? At times I just buy due to lack of otherwise [other options].* (Kenya, female patient, 'not deprived')

Interviewees suggested that lack of knowledge about ABs and illness was a barrier to following the best practice advice. It also became clear from both qualitative and quantitative data that AB 'knowledge' is a complex phenomenon that deserves further unpacking: "*[Antibiotic] is the other word for medicine used to treat disease… I think there is no difference [between antibiotics and other drugs]"* (Kenya, male patient, 'not deprived'). This might help explain our finding from the quantitative modelling that better 'knowledge' of ABs did not predict lower AB misuse. Our 'knowledge' variables capture respondents' familiarity with pharmaceutical products included in the drug bag/card, and a very general 'knowledge' of disease, rather than any understanding that antibiotics treat bacterial diseases specifically. Our qualitative data suggest that the public wants and needs better understanding of disease types, the purpose of ABs and the importance of adherence. Overall, respondents from across the socioeconomic spectrum experienced personal and structural challenges and frustrations when seeking care from health professionals in government facilities, that in their view, rationalised the tendency to misuse antibiotics.

Discussion

This unique study uses standardised, mixed-method data from three East African countries and demonstrates that AB use patterns for a common infection (UTI) are socially stratified, but not as in previous studies which highlighted that lower socioeconomic status is associated with higher AB misuse.[4,13] Specifically, we find that AB misuse, especially treatment non-adherence, is more common among those not suffering multidimensional poverty. This finding is robust to different modelling choices and adjustment for potential mediators such as 'knowledge' and attitudes. Our qualitative analysis illuminates these associations, suggesting that, in a context of under-resourced public health provision and insufficiently regulated free market AB dispensing, financial and time considerations and the perceived relative inconvenience of accessing healthcare can drive AB misuse across the socioeconomic spectrum. Better-off subgroups have more economic opportunity to deal with these challenges through AB self-medication. Furthermore, familiarity with ABs should not be conflated with 'knowledge' of their proper use; hence, 'knowledge' of ABs is not associated with better practice in our data.

Despite the richness of the data, our study has some limitations. The linked quantitative-qualitative sample is representative of the patient population attending mainly public outpatient services with UTI-like symptoms. Findings are not necessarily generalisable to population level. Comparisons of our sample to national MPI levels shows that while the Tanzanian sample is approximately socioeconomically representative, the Ugandan sample is more-, and the Kenyan less deprived than country wide MPI levels (see Figure S2·5). However, patient populations are an important subgroup for possible interventions, and UTI is both prevalent and commonly treated with ABs in this region. Moreover, similar themes emerged from FGD where participants included non-clinic attendees. The MPI used necessarily collapses several socioeconomic indicators together; while Table S3·4 shows that the largest contributor to the HATUA MPI is education levels. Our outcomes are self-reported, and we cannot rule out reporting bias.

Poverty has been suggested as a root cause of AMR in LMICs[17] and higher deprivation seen as a driver of poor AB use.[6,7] However, previous investigations of poverty, AB misuse and AMR have tended to use designs which obscure social inequalities within contexts.[8] Consequently, policy initiatives might easily be misdirected by an assumption that links between poverty and AB misuse observable in international comparisons will hold for individual scale behaviour within national settings. This study paints a more nuanced picture and highlights the somewhat overlooked role of higher socioeconomic status as a facilitator of inappropriate AB use in contexts where public health provision is inadequate and AB regulations are insufficiently enforced. Consequently, richer subgroups may contribute more to the spread of AMR in poor regions than has hitherto been appreciated. Notwithstanding the role of individual decision-making, greater attention is required to the structural barriers that discourage optimal AB use at all levels of the socioeconomic hierarchy in such contexts. Here we show the complex interplay between poverty and AMR, and that the assumption that AB misuse is predominantly an issue for more impoverished subgroups masks the prevalence of this issue amongst those who are not deprived. The AMR crisis may be driven as much by hybrid healthcare systems, opportunity structures and marketisation of healthcare, as by knowledge, beliefs, and attitudes towards ABs. Interventions to improve AB use behaviours should therefore not focus on the latter at the expense of addressing the challenges presented by the former.

Author contributions

DLG conceptualised the paper, analysed quantitative data, and wrote the manuscript. KK co-designed the study, supervised data analysis, and wrote the manuscript. SIH analysed qualitative data and edited the manuscript. MK co-designed the study, supervised qualitative data analysis, and edited the manuscript. MFM supervised data collection and reviewed the manuscript. CK supervised data collection and reviewed the manuscript. BA co-designed the study, supervised data collection, and reviewed the manuscript. JK co-designed the study, supervised data collection, and reviewed the manuscript. SEM co-designed the study, supervised data collection, and reviewed the manuscript. SN co-designed the study, supervised data collection, and reviewed the manuscript. JRM co-designed the study, supervised data collection, and reviewed the manuscript. KJF analysed qualitative data and edited the manuscript. AGL co-designed the study, supervised quantitative data analysis, and edited the manuscript. HW provided statistical advice and edited the manuscript. EO analysed quantitative data and reviewed the manuscript. MAAA assisted with data preparation and reviewed the manuscript. AA supervised data collection and reviewed the manuscript. BTM co-designed the study, supervised data collection, and reviewed the manuscript. JB supervised data collection and reviewed the manuscript. AS coordinated the study and reviewed the manuscript. JS co-designed the study and reviewed the manuscript. SHG co-designed the study and reviewed the manuscript. GK co-designed the study and reviewed the manuscript. WS co-designed the study and reviewed the manuscript. DS co-designed the study, supervised data analysis, and reviewed the manuscript. MTGH led the design of the project, was the guarantor of the work, and reviewed the manuscript.

HATUA Consortium includes everyone listed above, plus: V. Anne Smith, Arun Gonzales Decano, Antonio Maldonando Barragan, David Aanensen, John Njeru Mwaniki, Nyanda E Ntinginya, Madeleine Clarkson, Alison Elliott.

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Conflict of Interests

None

Data Sharing

Data may be made available according to data sharing policy of the partners in the three participating countries upon request to the corresponding author.

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References

1 O'Neill J. Tackling drug-resistant infections globally: final report and recommendations. London, 2016.

2 Holmes AH, Moore LSP, Sundsfjord A, *et al.* Understanding the mechanisms and drivers of antimicrobial resistance. Lancet. 2016; **387**: 176–87.

3 Klein EY, Van Boeckel TP, Martinez EM, *et al.* Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. *Proc Natl Acad Sci U S A* 2018; **115**: E3463–70.

4 Torres NF, Chibi B, Middleton LE, Solomon VP, Mashamba-Thompson TP. Evidence of factors influencing self-medication with antibiotics in low and middle-income countries: a systematic scoping review. *Public Health* 2019; **168**: 92–101.

5 World Health Organization. Global action plan on antimicrobial resistance. 2016 https://www.who.int/publications/i/item/9789241509763.

6 Alividza V, Mariano V, Ahmad R, *et al.* Investigating the impact of poverty on colonization and infection with drug-resistant organisms in humans: A systematic review. *Infect Dis Poverty* 2018; **7**: 76.

7 Do NTT, Vu HTL, Nguyen CTK, *et al.* Community-based antibiotic access and use in six low-income and middle-income countries: a mixed-method approach. *Lancet Glob Heal* 2021; published online March 10. DOI:10.1016/S2214-109X(21)00024-3.

8 Batista AD, A. Rodrigues D, Figueiras A, Zapata-Cachafeiro M, Roque F, Herdeiro MT. Antibiotic Dispensation without a Prescription Worldwide: A Systematic Review. *Antibiotics* 2020; **9**: 786.

9 Torres NF, Chibi B, Kuupiel D, Solomon VP, Mashamba-Thompson TP, Middleton LE. The use of non-prescribed antibiotics; prevalence estimates in low-and-middle-income countries. A systematic review and meta-analysis. Arch. Public Heal. 2021; **79**: 1–15.

10 Collignon P, Beggs JJ, Walsh TR, Gandra S, Laxminarayan R. Anthropological and socioeconomic factors contributing to global antimicrobial resistance: a univariate and multivariable analysis. *Lancet Planet Heal* 2018; **2**: e398–405.

11 Nadimpalli ML, Marks SJ, Montealegre MC, *et al.* Urban informal settlements as hotspots of antimicrobial resistance and the need to curb environmental transmission. Nat. Microbiol. 2020; **5**: 787–95.

12 Ocan M, Obuku EA, Bwanga F, *et al.* Household antimicrobial self-medication: A systematic review and meta-analysis of the burden, risk factors and outcomes in developing countries. BMC Public Health. 2015; **15**: 1–11.

13 Aslam A, Gajdács M, Zin CS, *et al.* Evidence of the practice of self-medication with antibiotics among the lay public in low-and middle-income countries: A scoping review. Antibiotics. 2020; **9**: 1–17.

14 Zanichelli V, Tebano G, Gyssens IC, *et al.* Patient-related determinants of antibiotic use: a systematic review. Clin. Microbiol. Infect. 2019; **25**: 48–53.

15 Haenssgen MJ, Charoenboon N, Xayavong T, Althaus T. Precarity and clinical determinants

of healthcare-seeking behaviour and antibiotic use in rural Laos and Thailand. *BMJ Glob Heal* 2020; **5**: 3779.

16 Nepal G, Bhatta S. Self-medication with Antibiotics in WHO Southeast Asian Region: A Systematic Review. *Cureus* 2018; **10**. DOI:10.7759/CUREUS.2428.

17 Okeke IN. Poverty and root causes of resistance in developing countries. In: Antimicrobial Resistance in Developing Countries. Springer New York, 2010: 27–35.

18 Fletcher S. Understanding the contribution of environmental factors in the spread of antimicrobial resistance. Environ. Health Prev. Med. 2015; **20**: 243–52.

19 Malik B, Bhattacharyya S. Antibiotic drug-resistance as a complex system driven by socio-economic growth and antibiotic misuse. *Sci Rep* 2019; **9**: 1–12.

20 Ayukekbong JA, Ntemgwa M, Atabe AN. The threat of antimicrobial resistance in developing countries: Causes and control strategies. Antimicrob. Resist. Infect. Control. 2017; **6**: 1–8.

21 Haenssgen MJ, Charoenboon N, Zanello G, *et al.* Antibiotics and activity spaces: Protocol of an exploratory study of behaviour, marginalisation and knowledge diffusion. *BMJ Glob Heal* 2018; **3**. DOI:10.1136/bmjgh-2017-000621.

22 Mboya EA, Davies ML, Horumpende PG, Ngocho JS. Inadequate knowledge on appropriate antibiotics use among clients in the Moshi municipality Northern Tanzania. *PLoS One* 2020; **15**: e0239388.

23 Asiimwe BB, Kiiru J, Mshana SE, *et al.* Protocol for an interdisciplinary cross-sectional study investigating the social, biological and community-level drivers of antimicrobial resistance (AMR): Holistic Approach to Unravel Antibacterial Resistance in East Africa (HATUA). *BMJ Open* 2021; **11**: e041418.

24 Alkire S, Santos ME. Measuring Acute Poverty in the Developing World: Robustness and Scope of the Multidimensional Poverty Index. *World Dev* 2014; **59**: 251–74.

25 Alkire S, Foster J. Understandings and misunderstandings of multidimensional poverty measurement. *J Econ Inequal* 2011; **9**: 289–314.

26 Fransman T, Yu D. Multidimensional poverty in South Africa in 2001–16. *Dev South Afr* 2019; **36**: 50–79.

27 Dixon J, MacPherson E, Manyau S, *et al.* The 'Drug Bag' method: lessons from anthropological studies of antibiotic use in Africa and South-East Asia. *Glob Health Action* 2019; **12**: 1639388.

28 Ltd. QIP. New NVivo, release 1.0. 2020.

29 Rhodes T. Risk environments and drug harms: A social science for harm reduction approach. *Int J Drug Policy* 2009; **20**: 193–201.

30 Ndaki PM, Mushi MF, Mwanga JR, *et al.* Dispensing Antibiotics without Prescription at Community Pharmacies and Accredited Drug Dispensing Outlets in Tanzania: A Cross-Sectional Study. *Antibiot 2021, Vol 10, Page 1025* 2021; **10**: 1025.

Appendix/Supplementary material

Contents

1: HATUA patient recruitment: sites and healthcare facilities

HATUA patient recruitment took place in 9 sites (three each in Kenya, Tanzania, and Uganda). Healthcare facilities were chosen across a number of primary and secondary care levels.

Table S1.1 Patient recruitment sites in Kenya, Tanzania, and Uganda

Country/site	Number of facilities (TOTAL)	Source of funding	Levels recruited from[1]
Kenya			
Makueni	1	Public	5
Nairobi	4	Public and private	3-5, National
Nanyuki	1	Public	4
Tanzania			
Kilimanjaro/Moshi	3	Public and private	2,3, and 5
Mbeya	2	Public and private	3 and 4
Mwanza	5	Public and private	2,3, and 5
Uganda			
Mbarara	3	Public	3 and 5
Nakapiripirit	3	Public	2 and 3
Nakasongola	3	Public and private	3 and 4

[1] Levels of facilities are identified in each country following the Kenya Health Policy 2014-2013 (http://publications.universalhealth2030.org/uploads/kenya_health_policy_2014_to_2030.pdf); Tanzanian Health Sector Strategic Plan (http://www.tzdpg.or.tz/fileadmin/documents/dpg_internal/dpg_working_groups_clusters/cluster_2/health/Key_Sector_Documents/Induction_Pack/Final_HSSP_IV_Vs1.0_260815.pdf), and the Ugandan Hospital and Health Centre IV census survey (https://www.who.int/healthinfo/systems/SARA_H_UGA_Results_2014.pdf).

2: Focus group discussion characteristics

Table S2.1: Description of Focus Group Discussions conducted

	Site	Date conducted	Number of Participants	Social characteristics
Tanzania				
TZ FGD1	Moshi	Jan. 2020	11	Men (41-77 years), Farmers, Labourers
TZ FGD2	Moshi	Jan. 2020	11	Women (39-66 years), Mostly Farmers, Vendors
TZ FGD3	Moshi	Feb. 2020	6	Men (19-39 years), Mostly Farmers, Vendors, Labourers
TZ FGD4	Moshi	Feb. 2020	11	Men (35-68 years), Farmers, Bus driver
TZ FGD5	Moshi	Jan. 2020	12	Women (33-72 years), Vendors, Farmers, Housewives
TZ FGD6	Mwanza	Feb. 2020	11	Men (19-29 years), Mostly Subsistence farmers, Labourers
TZ FGD7	Mwanza	Feb. 2020	9	Women (19-32 years), Mostly Petty traders, Tailors
TZ FGD8	Mwanza	Feb. 2020	12	Men (40-78 years), Labourers, Vendors, Farmers
TZ FGD9	Mwanza	Feb. 2020	12	Men (25-40 years), Subsistence farmers
TZ FGD10	Mwanza	Feb. 2020	11	Men (42-68 years), Various occupations
TZ FGD11	Mwanza	Feb. 2020	11	Women (35-55 years), Vendors, business owners, Housewife
TZ FGD12	Mwanza	Feb. 2020	12	Women (25-45 years), Vendors, Farmers, Tailors
TZ FGD13	Mwanza	Feb. 2020	9	Women (42-59 years), Mostly Vendors, Farmers
TZ FGD14	Moshi	Feb. 2020	12	Women (20-38 years), Mostly Vendors, Shop owners
TZ FGD15	Moshi	Feb. 2020	12	Women (18-59 years), Farmers, Students, Vendors
TZ FGD16	Moshi	Jan. 2020	10	Men (41-72 years), Businessmen, Security
TZ FGD17	Mbeya	May 2020	7	Men (20-25 years), Students
TZ FGD18	Mbeya	May 2020	10	Men (44-82 years), Mostly Farmers
TZ FGD19	Mbeya	May 2020	7	Men (40-66 years), Farmers, Mechanics
TZ FGD20	Mbeya	June 2020	8	Men (18-40 years), Mostly Entrepreneurs, Students, Vendors
TZ FGD21	Mbeya	May 2020	7	Women (38-52 years), Farmers, Saloon owner
TZ FGD22	Mbeya	May 2020	6	Women (52-70 years), Farmers
TZ FGD23	Mbeya	June 2020	8	Women (25-41 years), Vendors, Housewives, Farmers
Uganda				
UG FGD1	Mbarara	July 2019	6	Women (35-65 years), Crop farmers
UG FGD2	Mbarara	June 2019	6	Women (35-67 years), Farmers
UG FGD3	Mbarara	June 2019	8	Men (22-56 years), Mostly Farmers, Casual workers
UG FGD4	Mbarara	June 2019	9	Women (20-43 years), Mostly Farmers, Housewives, Traders
UG FGD5	Mbarara	May 2019	9	Women (23-44 years), Farmers, Rural
UG FGD6	Mbarara	May 2019	7	Men, (29-51 years), Mostly Boda Boda drivers
UG FGD7	Mbarara	June 2019	7	Men (25-70 years), Farmers
UG FGD8	Mbarara	July 2019	7	Men (20-60 years), Farmers
UG FGD9	Nakasongola	Nov. 2019	7	Men, (32-55 years), Farmers
UG FGD10	Nakasongola	Nov. 2019	9	Women (32-63 years), Farmers
UG FGD11	Nakasongola	Nov. 2019	7	Men (20-30 years), Mostly Casual workers, Drivers
UG FGD12	Nakasongola	Nov. 2019	8	Men (20-61 years), Farmers, Laborers, Student, Librarian
UG FGD13	Nakasongola	Nov. 2019	9	Women (32-60 years), Farmers
UG FGD14	Nakasongola	Nov. 2019	8	Women (20-38 years), Housewives, Workers, Farmer
UG FGD15	Nakasongola	Nov. 2019	8	Men (24-59 years), Farmers, Traders, Laborers
UG FGD16	Nakasongola	Nov. 2019	8	Women (22-36), Housewives, Petty Traders
UG FGD 17	Nakapiripirit	July 2020	6	Men (27-40), No employment listed, VHT
UG FGD 18	Nakapiripirit	July 2020	5	Women (25-39), No employment listed, Housewives
UG FGD 19	Nakapiripirit	July 2020	6	Women (20-35), No employment provided
UG FGD 20	Nakapiripirit	June 2020	7	Women (21-37), Farmers, Housewives
UG FGD 21	Nakapiripirit	June 2020	7	Women (25-35), Farmers, Housewives

3: Development of the Multidimensional Poverty Index (MPI) for HATUA data

Background

We chose to use the MPI because it captures multiple dimensions of poverty, and is a relatively objective, comparable measure suitable for multi-country analysis. It is also flexible, allowing for the inclusion of any number of indicators depending on availability. The MPI identifies poverty using a two-stage 'dual' cut off approach.[1] Estimation of the MPI for HATUA data was based on the 'counting' methodology developed by Alkire and Foster,[2] which was used as a basis for the Acute Multidimensional Poverty Index for Developing Countries (global MPI).[3] The global MPI assesses people's deprivations according to ten indicators organised into three equally weighted dimensions: education, health, and living standards. The global MPI measures acute poverty based on breadth and depth of poverty within the country. The breadth of poverty communicates incidence, which corresponds to the proportion of people within a population who experience many deprivations. The depth conveys the intensity of a person's deprivation, in other words, the average proportion of deprivations they experience.[3]

The Alkire-Foster (AF) method to develop an MPI has several advantages. Firstly, it is a harmonised and relatively objective measure. It can be used to compare poverty across countries, making it ideal for multi-country analysis. Secondly, it is highly flexible which allows for the inclusion of any number of indicators. This is ideal when data limitations affect the number or type of indicators included in the measure. Lastly, the measure captures multiple dimensions of poverty, beyond income, that allows for an assessment of how various components of poverty are related to antibiotic use.

Methods

The MPI identifies the poor using a two-stage 'dual' cut-off approach.[1] Before the application of these cut-offs, a set of indicators are selected that are generally accepted as essential for human well-being. The first cut-off processs relates to the deprivation cut-off for each selected indicator. The cut-off point is a normative minimum level that a patient needs in order to be defined as not poor. The indicators' weights are chosen, the sum of which equals one (1). Each dimension carries an equal weight, so that if three domains are used, they each have an equal weight of 1/3. Each indicator within each domain carries an equal weight. Based on this, a deprivation score is calculated, ranging from zero to one. The second cut-off process represents the share of weighted deprivations that a patient must have to be considered multidimensionally poor. A patient is considered poor if their deprivation score is at least a third of their weighted indicators.

Following other studies,[4] this study uses an adapted version of the global MPI, where the choice of indicators and deprivation cut-offs included was guided by a) the patient population under investigation and b) indicators available in the HATUA survey data. The MPI constructed for this study contains seven indicators (Table S3·1) distributed under three domains: education, health, and living standards (distribution by country is shown in Table S3·2 and distribution by our dichotomised age variable and sex is shown in Table S3·3). We excluded child-specific indicators used in the global MPI because this study concentrates on adult outpatients. A final score was calculated for each patient based on a classification score developed elsewhere.[3] Patients are considered not deprived if they are deprived in less than 20% of the weighted score; if deprived in 20 to 33·99% of the score, patients are considered vulnerable to poverty; if deprived in 34 to 49·99% of the weighted score, patients are considered deprived; and if deprived in more than 50% of the weighted score, patients were in severe poverty.[5] Table S3·4 summarises the relative contribution of each of these indicators showing that education is the largest contributor/has the largest influence on the score across all three countries, followed by sanitation. Disability and drinking water were the lowest contributors.

Table S3.1: Dimensions of the MPI, indicators and cut-offs in HATUA data

Dimension	Indicator	Deprivation Cut-off	Weighting
Education	1) Level of education	If the patient has less than a secondary education	1/3
Health	2) Disability	If the patient is disabled	1/6
	3) Chronic illness	If the patient has one of the following illnesses: diabetes, heart disease, asthma, hypertension/high blood pressure, HIV/AIDS, heart problems, stroke, and cancer.	1/6
Standard of living	4) Sanitation	No access to private flush toilet	1/12
	5) Asset ownership	Does not own more than one of the following: TV, computer, radio, fridge, cellular phone (smart or not), fishing boat, motor	1/12
	6) Electricity	Does not have access to mains electricity	1/12
	7) Drinking water	Does not have access to private protected water sources	1/12

Table S3.2: Descriptive statistics of indicators used in the MPI

	Components of MPI measure			
	TOTAL **N = 6,345**	**Tanzania** **n = 2,970**	**Uganda** **n = 1,700**	**Kenya** **n = 1,675**
Indicators	**N(%)**	**n(%)**	**n(%)**	**n(%)**
Education Level				
None	923 (14·6)	329 (11·1)	575 (33·8)	19 (1·1)
Primary	2,488 (39·2)	1,638 (55·2)	632 (37·2)	218 (13)
Secondary	1,989 (31·4)	739 (24·9)	329 (19·4)	921 (55)
Higher/Tertiary	945 (14·9)	264 (8·9)	164 (9·7)	517 (30·9)
Deprived Health				
Chronic health	819 (12·9)	456 (15·4)	290 (17·1)	73 (4·4)
Disability	423 (6·7)	223 (7·5)	162 (9·5)	38 (2·3)
Deprived Living Standards				
Assets	907 (14·3)	365 (12·3)	418 (24·6)	124 (7·4)
Electricity	1,223 (19·3)	473 (16)	726 (42·7)	24 (1·4)
Drinking Water	847 (13·4)	365 (12·3)	370 (21·8)	112 (6·7)
Sanitation	4,386 (69·1)	1,830 (61·6)	1,676 (98·6)	880 (52·5)

Table S3.3: Descriptive associations between MPI indicator between age and sex

	Age		Sex	
	Under 35	**35 and over**	**Male**	**Female**
	n(%)	**n(%)**	**n(%)**	**n(%)**
Education Level				
None	451 (11·7)	473 (18·9)	161 (12·2)	763 (15·2)
Primary	1,230 (32)	1,262 (50·4)	537 (40·6)	1,955 (38·9)
Secondary	1,463 (38)	527 (21)	384 (29·1)	1,606 (31·9)
Higher/Tertiary	703 (18·3)	243 (9·7)	240 (18·2)	706 (14)
Deprived Health				
Chronic health	197 (5·1)	624 (24·9)	273 (20·7)	548 (10·9)
Disability	123 (3·2)	301 (12)	166 (12·6)	258 (5·1)
Deprived Living Standards				
Assets	596 (15·5)	311 (12·4)	142 (10·8)	767 (15·2)
Electricity	744 (19·4)	479 (19·1)	223 (16·9)	1,000 (19·9)
Drinking Water	439 (11·4)	408 (16·3)	188 (14·2)	659 (13·1)
Sanitation	2,799 (72·9)	1,587 (63·4)	830 (62·8)	3,556 (70·8)

Table S3.4: MPI decomposition (%) by indicator and country

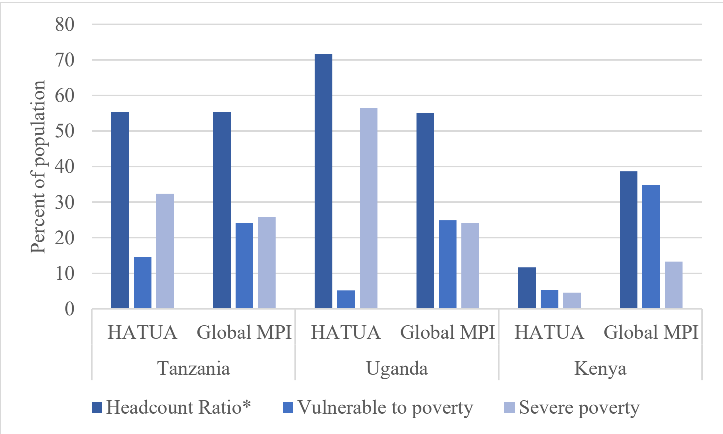
			Contribution to HATUA MPI			
Dimension	**Indicator**	**Contribution to Total Weight**	Overall	Tanzania	Uganda	Kenya
Education	1) Level of education	0·33	63·1%	65·4%	59·1%	69·1%
	2) Disability	0·17	3·6%	3·8%	3·4%	3·4%
Health	3) Chronic illness	0·17	6·7%	7·4%	6·1%	5·5%
	4) Sanitation	0·08	14·2%	13·4%	14·9%	16·5%
	5) Asset ownership	0·08	3·6%	2·9%	4·8%	2·3%
	6) Electricity	0·08	5·5%	4·2%	7·9%	0·6%
Standard of living	7) Drinking water	0·08	3·3%	3·0%	3·8%	2·6%

Table S3.5: HATUA MPI Scores and poverty classification

HATUA MPI Score	Poverty status classification
0 0·083 0·167	Not Deprived
0·250 0·333	Vulnerable to poverty
0·417	Deprived
0·500 0·583 0·667 0·75 0·833 0·917 1	Severe poverty

Our sample is composed of patients attending public clinics with suspected UTI infection, in selected study sites, hence we are not expecting national level representativity. However, to understand any direction of bias, we compared our calculated MPI scores to global (national-level) MPI scores for 2019,[6] based on data from the most recent Demographic and Health Survey data (2016 for Uganda, 2015-16 for Tanzania, and 2014 for Kenya). The proportions of patients in poverty according to various cut-offs shown are in Figure S3·5. For Tanzania, we note that global MPI headcount ratio (the percent of people in the population who experience multiple deprivations) is similar to that seen in the HATUA data. The HATUA headcount ratios for Uganda and Kenya are more and less than the global MPI, respectively. We also note that the HATUA sample contains proportionally more people in severe poverty than the global MPI in Tanzania and Uganda. For Kenya, the HATUA sample contains proportionally fewer people in severe poverty, than estimated in the DHS-based MPI. The non-comparability that we see between the DHS-based MPI and the HATUA MPI is likely to be influenced by the indicators chosen in its calculation as well as the differences between the populations.

Figure S3.5. HATUA MPI measures by country, compared to global MPI levels



*The headcount ratio refers to those within a particular population who are experiencing multiple deprivations.
Sources: HATUA data/2019 Global MPI Country Briefings for Tanzania, Uganda, and Kenya

4: Missing data

Approximately 9% of data from adult outpatients in the HATUA sample had missing data for at least one variable in this analysis. The descriptive statistics for the missing data sample compared to the analysis sample are presented in Table S4·1. Chi-square test statistics indicate those with missing data were more likely to be 35 and older, male, and to be less knowledgeable about ABs. To minimize possible bias from missing data in our analyses, we performed a Bayesian analysis of the full dataset. (see appendix 5).

Table S4.1 Distribution of variables in complete data compared to missing data.

Variable	Complete Data N = 6345 n (%)	Missing Data N =482 n (%)	Relationship (chi-square test)
Outcome Variables			
Self-medicated with ABs	406 (6·4)	15 (3·11)	p<0·001
Missing – self medicated		28 (5·81)	
Skipped a dose	1,513 (23·9)	94 (19·50)	p<0·001
Missing – skipped dose		34 (7·05)	
Incomplete course	803 (12·7)	74 (15·35)	p<0·001
Missing – incomplete course		39 (8·09)	
Poverty status			p<0·001
Not deprived	2,701 (42·6)	144 (29·88)	
Vulnerable to poverty	603 (9·5)	62 (12·86)	
Deprived	1,052 (16·6)	95 (19·71)	
Severe poverty	1,989 (31·4)	107 (22·20)	
Missing		74 (15·35)	
Age			p<0·001
Under 35	3,840 (60·5)	247 (51·24)	
35 and up	2,505 (39·5)	222 (46·06)	
Missing		13 (2·70)	
Sex			p<0·05
Male	1,321 (20·8)	122 (25·31)	
Female	5,024 (79·2)	360 (74·69)	
Working Status			p<0·001
Formal employment	1,368(21·6)	69 (14·32)	
Informal employment	2,621 (41·3)	179 (37·14)	
Homemaker	1,586 (25)	125 (25·93)	
Not working	770 (12·1)	56 (11·62)	
Missing		53 (11·00)	
Difficulty in meeting health care costs			p<0·001
Easy	2,334 (36·8)	146 (30·29)	
Little Difficult	2,726 (42·96)	146 (30·29)	
Very difficult	1,285 (20·25)	99 (20·54)	
Missing		91 (18·88)	
Source of health care advice			p<0·001
Doctors only	2,219 (34·97)	194 (40·25)	
Missing		10 (2·07)	
Knowledge of term 'antibiotic'			p<0·001
Don't know	3,128 (49·30)	344 (71·37)	
Another name for medicine	1,083 (17·07)	52 (10·79)	
Medicine for infections/germs	2,134 (33·63)	53 (11·00)	
Missing		33 (6·85)	
Knowledge of ABs by name/packaging			p<0·001
Know 0-3	3,114 (49·08)	182 (37·76)	
Know 4 or more	3,231 (50·92)	121 (25·10)	
Missing		179 (37·14)	

5: Statistical appendix: Bayesian Hierarchical Modelling

We estimated the posterior distributions of the model parameters using Markov chain Monte Carlo (MCMC) algorithms implemented in the BUGS language through the NIMBLE package in R Studio. A directed acyclic graph (DAG) of the estimated Bayesian hierarchial model is presented in Figure S5.1. No previous studies have estimated levels of AB misuse, let alone the association with poverty, in East African patient populations, so we had little information from which to draw informative priors. To avoid possible bias from missing data, we estimated the models on the sample with some incomplete values on the covariates and outcomes (see appendix 4). Five chains were initiated at different start values, with each chain run for 30,000 iterations. We assessed convergence by a visual inspection of trace- and autocorrelation-plots (see Figures S5·2-S5·7) and based on these outputs selected a burn-in period of 10,000 iterations, thus resulting in a posterior sample size of 100,000.

Commented [AL1]: Should cite: de Valpine P, Turek D, Paciorek C, Anderson-Bergman C, Temple Lang D, Bodik R (2017). "Programming with models: writing statistical algorithms for general model structures with NIMBLE." Journal of Computational and Graphical Statistics, 26, 403-413

Commented [AL2]: There isn't actually any assessment is there?

All models followed a similar four level structure, expressed as:

$$\text{Misuse}_i \sim \text{Bernoulli}(\pi_i)$$

$$log\left(\frac{\pi_i}{1-\pi_i}\right) = \boldsymbol{\beta X}_i + \beta country_{c_i} + \beta site_{s_i} + \beta clinic_{h_i}$$

where

$$\beta country_{c} \sim \boldsymbol{N}(\boldsymbol{0}, \boldsymbol{\sigma_c^2})$$

for each country, c,

$$\beta site_{s} \sim \boldsymbol{N}(\boldsymbol{0}, \boldsymbol{\sigma_s^2})$$

for each site, s, and

$$\beta clinic_{h} \sim \boldsymbol{N}(\boldsymbol{0}, \boldsymbol{\sigma_h^2})$$

for each clinic, h.

The variances each having a prior $\boldsymbol{\sigma_X^2} \sim \boldsymbol{exp}(\boldsymbol{1})$.

Coefficients, β, associated with covariates in the fixed effects are given a normal prior distribution with standard deviation 2·3 to give a relatively flat distribution after an inverse logit transformation. Missing data are given priors based on the empirical distributions seen in complete cases. The results of these analyses are presented as highest posterior density intervals throughout.

Figure S.51: Directed acyclic graph (DAG) of the Bayesian hierarchical model estimated

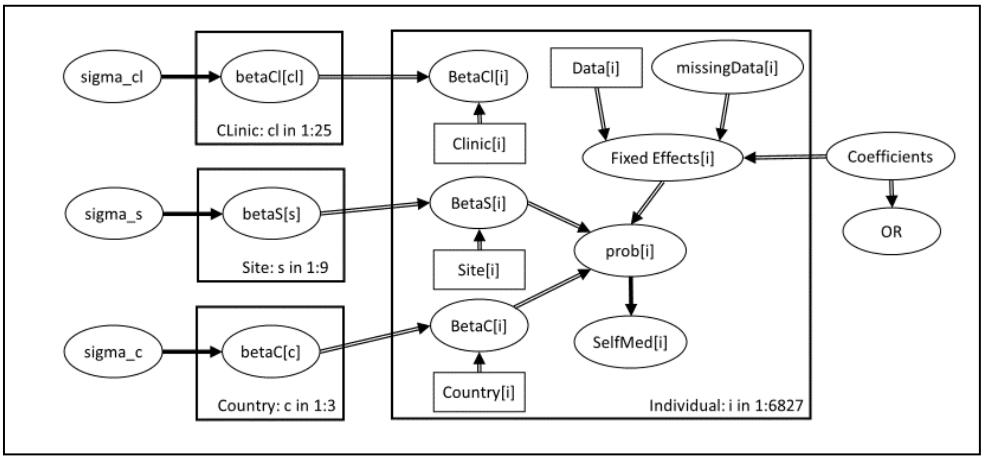


Figure S5.2A Trace plots for self-medicating with ABs- covariates with fixed effects (model 3)

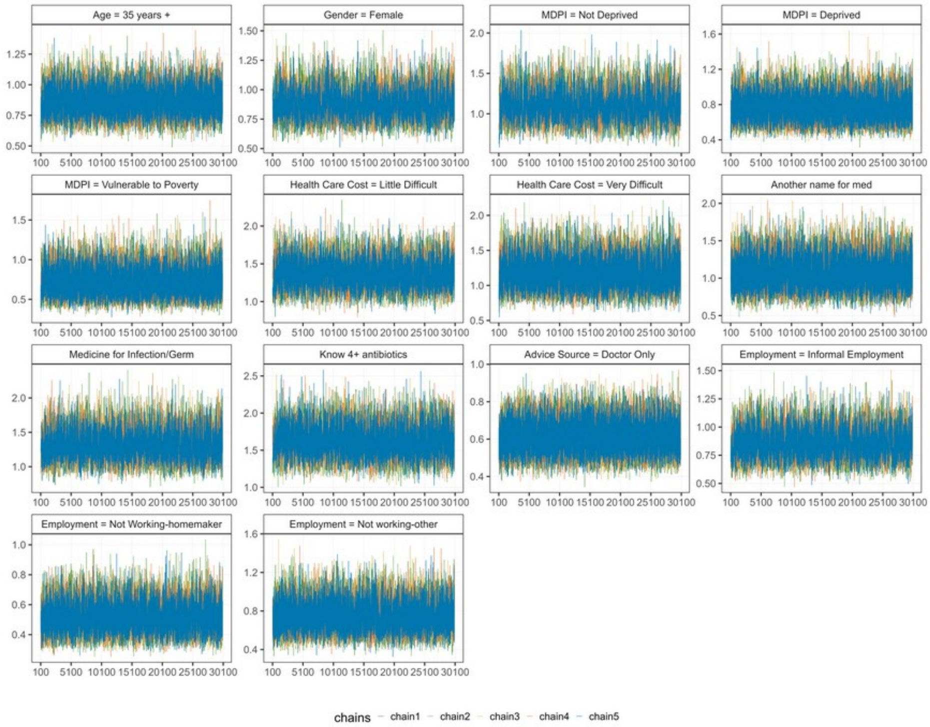


Figure S5.2B Trace plots for self-medicating with ABs (model 3)- covariates with random effects

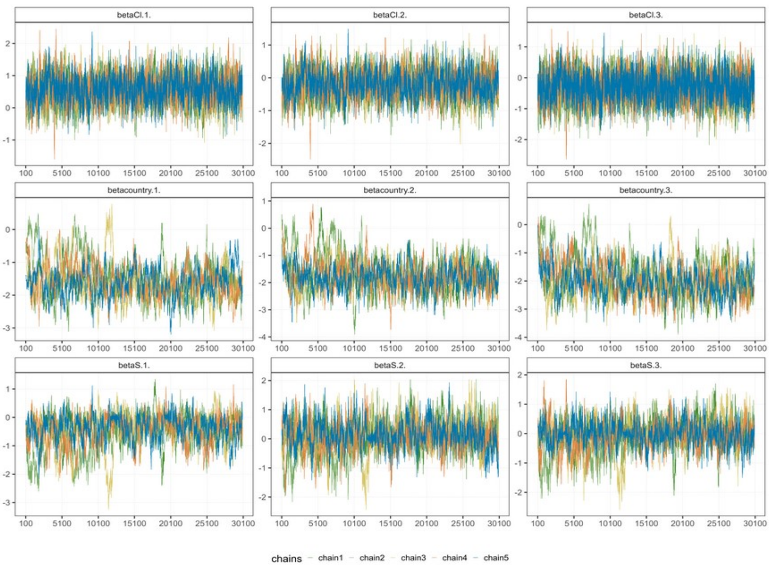


Figure S5.3 Plots of posterior distributions for outcome of self-medication, model 3

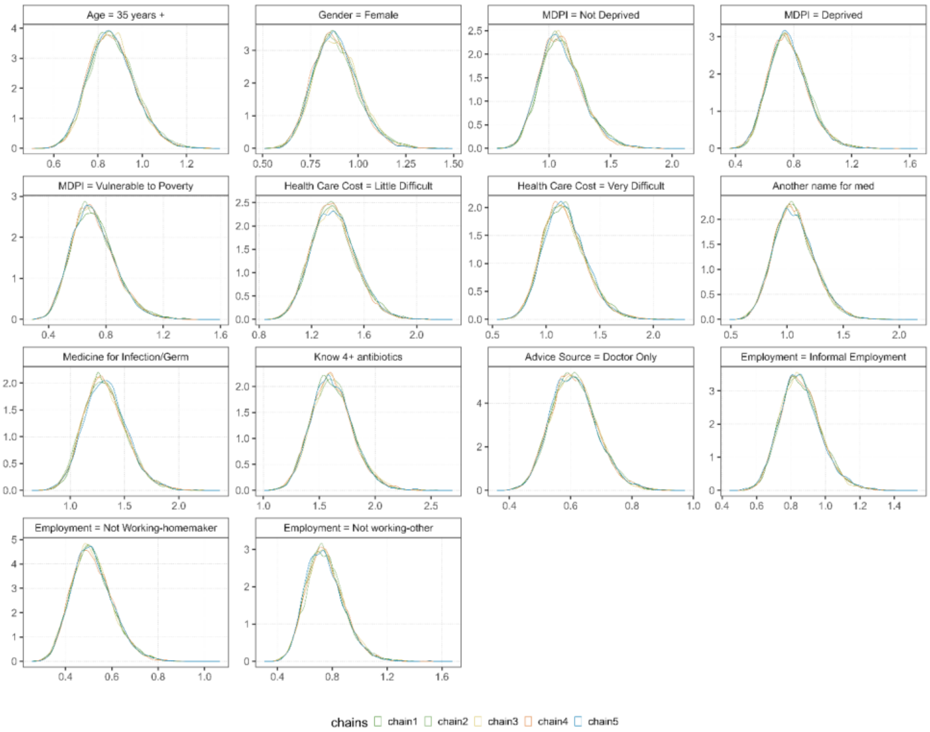


Figure S5.4A Trace plots for outcome of skipped a dose (model 3)- fixed effect covariates

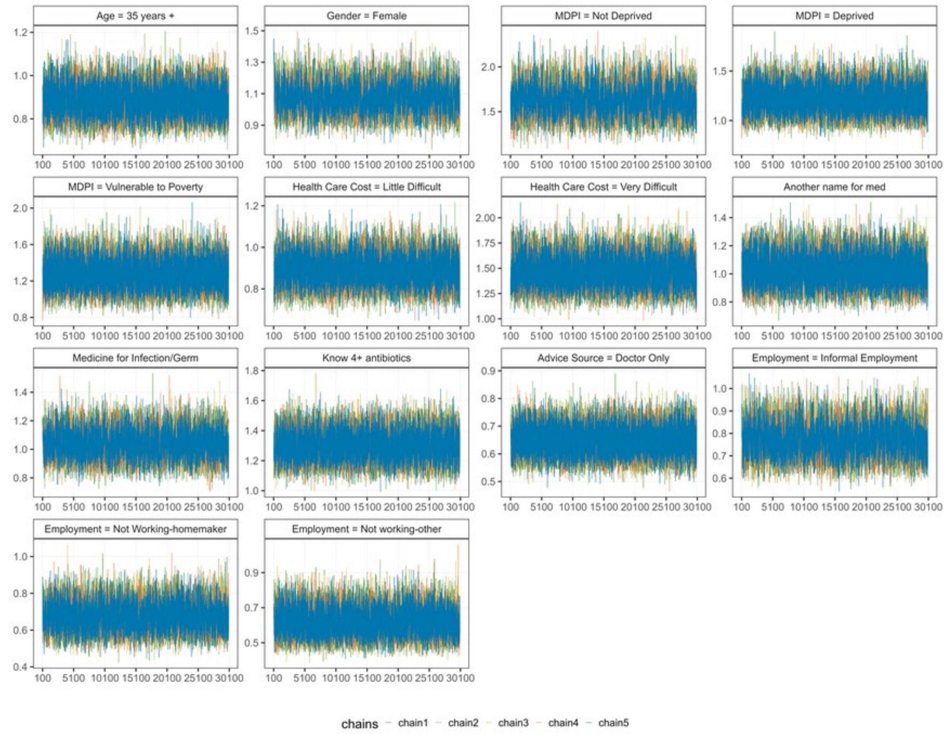


Figure S5.4B Trace plots for outcome of skipped a dose (model 3)- random effect covariates

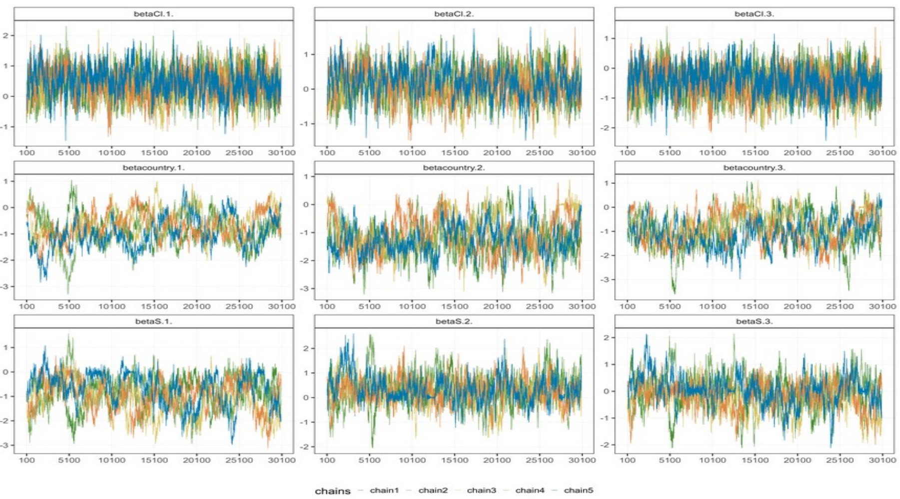


Figure S5.5 Plots of posterior distributions for outcome of skipped a dose (model 3)

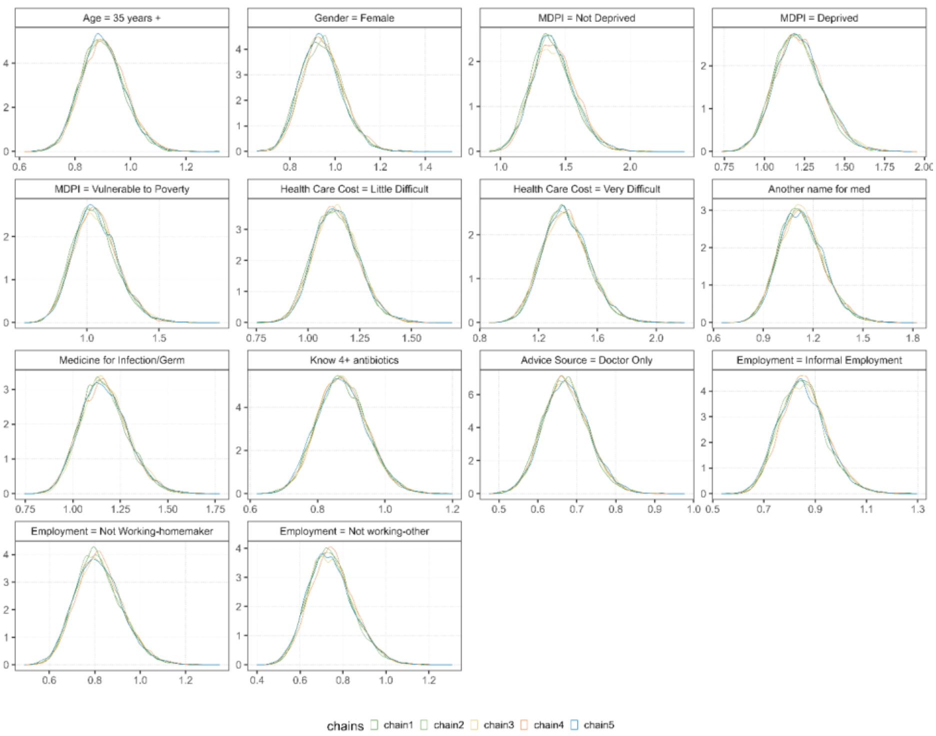


Figure S5.6A: Trace plots for not completing the course (model 3)- fixed effect covariates

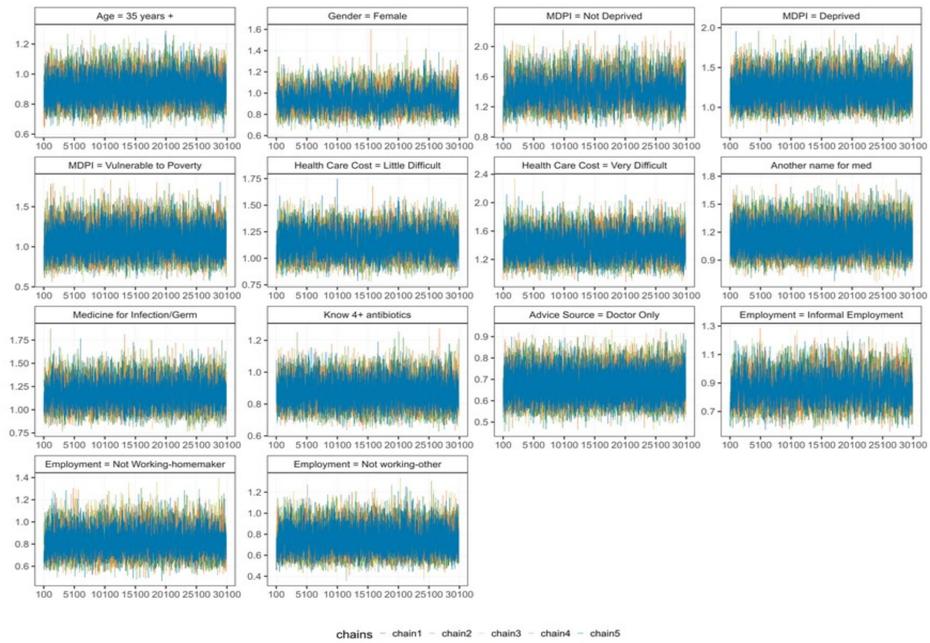


Figure S5.6B: Trace plots for not completing the course (model 3)- random effect covariates

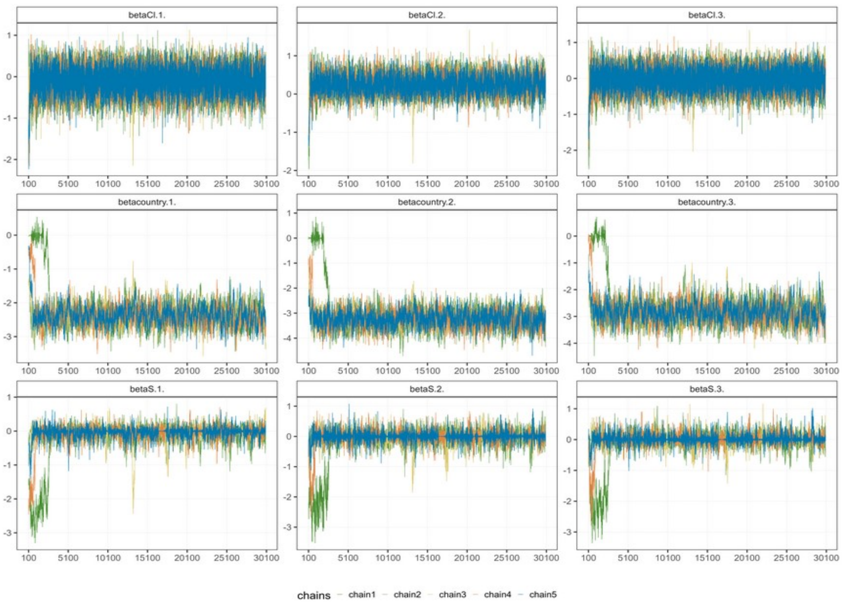
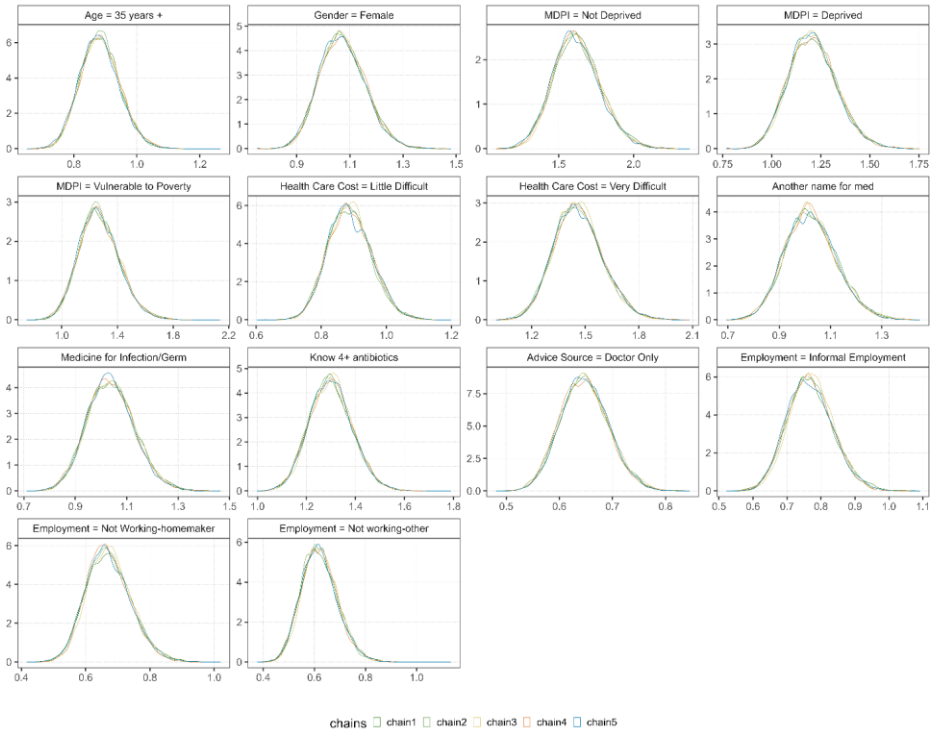


Figure S5.7 Plots of posterior distributions for outcome of not completing the course (model 3)



6: Results from frequentist multilevel modelling

Statistical approach

As far as was possible, we replicated the analysis presented in the main paper using frequentist approaches. To explore the associations between MPI and AB misuse (binary outcomes of skipping a dose, not completing the course, and self-medication separately), we used multilevel logistic regression models. However, fixed effect estimates for multilevel models may only be reliable with at least 10 level-2 units, and we have only 9 sites[7]. Subsequently, for the frequentist approach, we switched from a 4-level to use a 2-level models with patients nested in (n = 25) clinics. To account for the missing data, multiple imputation by chained equations (MICE) approach was used to account for missing data, under the missing at random assumption. MICE was estimated in STATA 15. The imputation models included all variables used in the multilevel model, with variable country deemed as an auxiliary variable as it was found to be predictive of missingness to create 10 imputed datasets for each variable.

The models followed a similar 2-level structure, expressed as:

$$\log\left[\frac{\pi_{ij}}{1-\pi_{ij}}\right] = \alpha_0 + \boldsymbol{\beta}\boldsymbol{X}_{ij} + w_j + \varepsilon_{ij}$$

where the log odds of AB misuse for the *i*th patient in the *j*th clinic, is represented as a function of fixed and random effects and $\varepsilon_{ij} \sim N(0, \sigma^2)$ independently. The fixed effects are described through a linear combination of an intercept (α_0), and a set of individual-level predictors ($\boldsymbol{X}_{ijk}$) and associated coefficients ($\boldsymbol{\beta}$), including MPI as the main independent variable, and others detailed in the methodology section.

The random effects are:

$$w_j = w + \varepsilon_j^w \qquad \text{for clinic } j,$$

where $\varepsilon_j^w \sim N(0, \sigma_w^2)$ for all clinics.

Results of multilevel modelling

The results in terms of pattern of effects (Table S6.1) are very similar to those seen using Bayesian estimation. Results were also consistent in the MICE model (Table S6.2). Skipping a dose and not completing the course was more common in the better-off sub-groups, among those who were formally employed (relative other types of employment or nor working), who had difficulties meeting healthcare costs, took medical advice from people other than doctors and healthcare workers. In fully adjusted models (model 3), self-medication was more common in the not deprived subgroup, but this was not statistically significant after inclusion of knowledge and attitude variables.

Table S6.1: Multilevel regression results for associations between MPI and AB misuse (model 3)

	Self-medicated with ABs OR (95% CI)	Skipped a Dose OR (95% CI)	Not completing the course OR (95% CI)
Poverty status: (ref = severe poverty)			
Deprived	0·78 (0·5-1·12)	1·25 (1·01-1·54)**	1·24 (0·97-1·59)*
Vulnerable to poverty	0·73 (0·48-1·12)	1·30 (1·03-1·65)**	1·09 (0·81-1·47)
Not deprived	1·11 (0·81-1·52)	1·67 (1·3-2·03)***	1·42 (1·13-1·82)**
Age (ref = less than 35 years)			
35 and over	0·85 (0·67-1·08)	0·89 (0·77-1·03)	0·89 (0·74-1·06)
Female (ref = Male)	0·89 (0·69-1·15)	1·11 (0·94-1·31)	0·95 (0·78-1·16)
Country (ref = Tanzania)			
Uganda	0·43 (0·28-0·66)***	0·68 (0·31-1·51)	0·93 (0·45–1·94)
Kenya	0·62 (0·40-0·96)**	0·78 (0·32-1·90)	0·64 (0·28–1·46)
Working status (ref = employed)			
Informal employment	0·89 (0·68-1·17)	0·77 (0·65-0·92)**	0·84 (0·67-1·04)
Homemakers	0·52 (0·37-0·73)***	0·66 (0·53-0·81)***	0·76 (0·59-0·99)**
Not working	0·79 (0·55-1·14)	0·61 (0·48-0·76)***	0·69 (0·51-0·92)**
Able to meet healthcare costs (ref = easy)			
Some difficulty	1·37 (1·07-1·74)**	0·88 (0·76-1·03)*	1·19 (0·98-1·44)*
Very difficult	1·15 (0·82-1·60)	1·47 (1·22-1·77)***	1·43 (1·13-1·80)**
Source of advice: (ref = other than doctor)			
Doctor's/healthcare workers' advice only	0·64 (0·51-0·82)***	0·66 (0·58-0·76)***	0·66 (0·55-0·79)***
Knowledge of term 'antibiotic' (ref = don't know)			
Another name for medicine	1·03 (0·73-1·44)	0·98 (0·81-1·20)	1·15 (0·91-1·46)
Medicine for infections/germs	1·26 (0·95-1·69)	1·02 (0·85-1·21)	1·18 (0·95-1·46)
Familiarity with ABs (ref = knows <4 types)			
Knows 4 or more types	1·65 (1·31-2·08)***	1·26 (1·10-1·44)**	0·87 (0·74-1·04)
Random effects			
Clinic-level variance	0·09 (0·03-0·31)	0·73(0·39-1·35)***	0·59 (0·30-1·16)***

*** p<0·01, ** p<0·05, * p<0·1
N = 6,345
Source: HATUA data

Table S6.2: Multilevel regression results with imputed values for associations between MPI and AB misuse (model 3)

	Self-medicated with ABs	Skipped a Dose	Not completing the course
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Poverty status: ref = severe poverty			
Deprived	0·77 (0·54 - 1·09)	1·23 (1·01 - 1·51)**	1·23(0·97 - 1·56)*
Vulnerable to poverty	0·72 (0·48 - 1·09)	1·29 (1·03 - 1·61)**	1·07 (0·81 - 1·42)
Not deprived	1·12 (0·82 - 1·53)	1·67 (1·38 – 2·03)***	1·44 (1·14 - 1·81)**
Age (ref: less than 35 years)			
35 and over	0·88 (0·69 - 1·11)	0·89 (0·78 - 1·03)	0·91 (0·77 - 1·08)
Female (ref = Male)	0·89 (0·69 - 1·15)	1·09 (0·93 - 1·27)	0·95 (0·79 - 1·15)
Country (ref: Tanzania)			
Uganda	0·43 (0·28 - 0·67)***	0·68 (0·31 - 1·49)	0·93 (0·45 – 1·92)
Kenya	0·62 (0·39 - 0·97)**	0·79 (0·33 - 1·90)	0·65 (0·29 – 1·47)
Working status (ref: employed)			
Informal employment	0·87 (0·67 - 1·14)	0·79 (0·66 - 0·93)**	0·87 (0·70 - 1·07)
Homemakers	0·53 (0·38 - 0·73)***	0·68 (0·56 - 0·83)***	0·82 (0·64 – 1·05)
Not working	0·76 (0·53 - 1·09)	0·62 (0·50 - 0·78)***	0·75 (0·57-0·99)**
Able to meet healthcare costs (ref: easy)			
Some difficulty	1·37 (1·08 - 1·74)**	0·89 (0·77 - 1·03)	1·14 (0·95 - 1·37)
Very difficult	1·18 (0·85 - 1·63)	1·46 (1·22 - 1·75)***	1·39 (1·12 - 1·74)**
Source of advice: (ref: other than doctor)			
Doctor's /healthcare workers' advice only	0·62 (0·49 - 0·78)***	0·66 (0·58 - 0·76)***	0·67 (0·57 - 0·80)***
Knowledge of term 'antibiotic' (ref: don't know)			
Another name for medicine	1·07 (0·76 - 1·49)	1·00 (0·83 - 1·21)	1·13 (0·90 - 1·43)
Medicine for infections/germs	1·34 (1·01 - 1·79)**	1·02 (0·86- 1·22)	1·18 (0·96 - 1·46)
Familiarity with ABs (ref: knows <4 types)			
Knows 4 or more types	1·63 (1·30 – 2·04)***	1·30 (1·14 - 1·48)***	0·87 (0·74 - 1·03)
Random effects			
Clinic-level variance	0·10 (0·03 – 0·32)	0·71(0·39 – 1·32)***	0·58 (0·30 - 1·12)***

*** p<0·01, ** p<0·05, * p<0·1
Note: Number of groups varies among imputations· Number of observations per group varies among imputations·
Source: HATUA data
N=6827

7: Results from site level meta-analysis

Another way to think about the HATUA data is a series of studies conducted in different sites. We conducted a between-site meta-analysis of associations between binary MPI and each outcome using the *ipdmetan* command in Stata version 15,[8] which pooled odds ratios from each of the sites and is designed specifically for use with individual patient data. In cross-tabulations of poverty and the outcome variables there were no patients in Makeuni identified as either in severe poverty, vulnerable to poverty, or deprived who self-medicated with antibiotics, or skipped a dose, or did not complete the course. This required a slightly modified analysis of site variation. We used random-effects models to account for within- and between-site variation; it is estimated via empirical Bayes inverse-variance model[9] and adjusted for age and sex. Our previous analysis has highlighted that the not deprived vs the other categories was an important contrast, so we regrouped the four category MPI (the 'treatment') to contrast the best-off category of not deprived vs. all the rest. Results were displayed in forest plots with I^2 statistics to indicate the proportion of heterogeneity between study sites from the total observed variation. In future analysis, we intend to further investigate explore site-level variations in antibiotic use.

Figure S7.1: Random effects meta-analysis of the effects of 'not deprived' poverty on self-medication with ABs

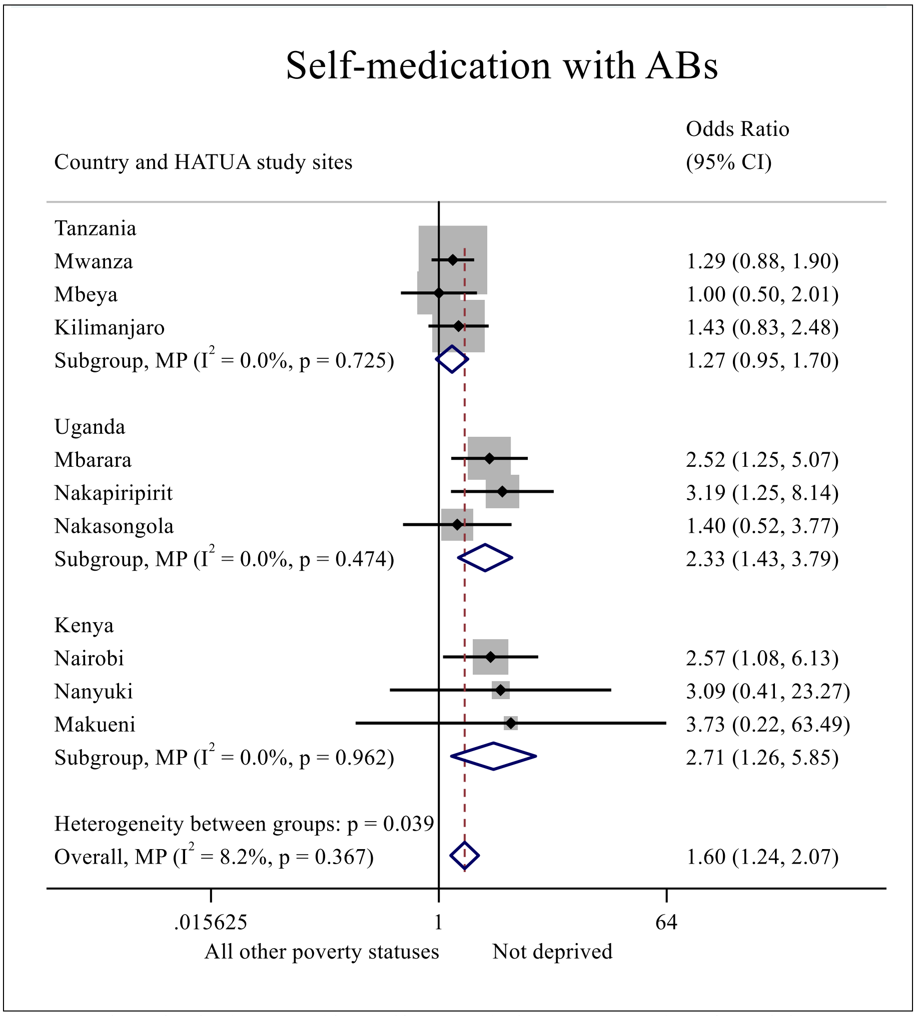


Figure S7·1 shows that despite some evidence of heterogeneity between groups (sites), the pooled OR estimates (the overall rhombus at the bottom of the Figure) indicated a pooled OR of 1.60 (95% CI 1.24-2.07), corroborating our findings from Bayesian estimation and frequentist multilevel modelling (Model 1), that the 'not deprived' group are more likely to self-medicate.

Figure S7.2: Random effects meta-analysis of the effects of 'not deprived' poverty on skipping a dose

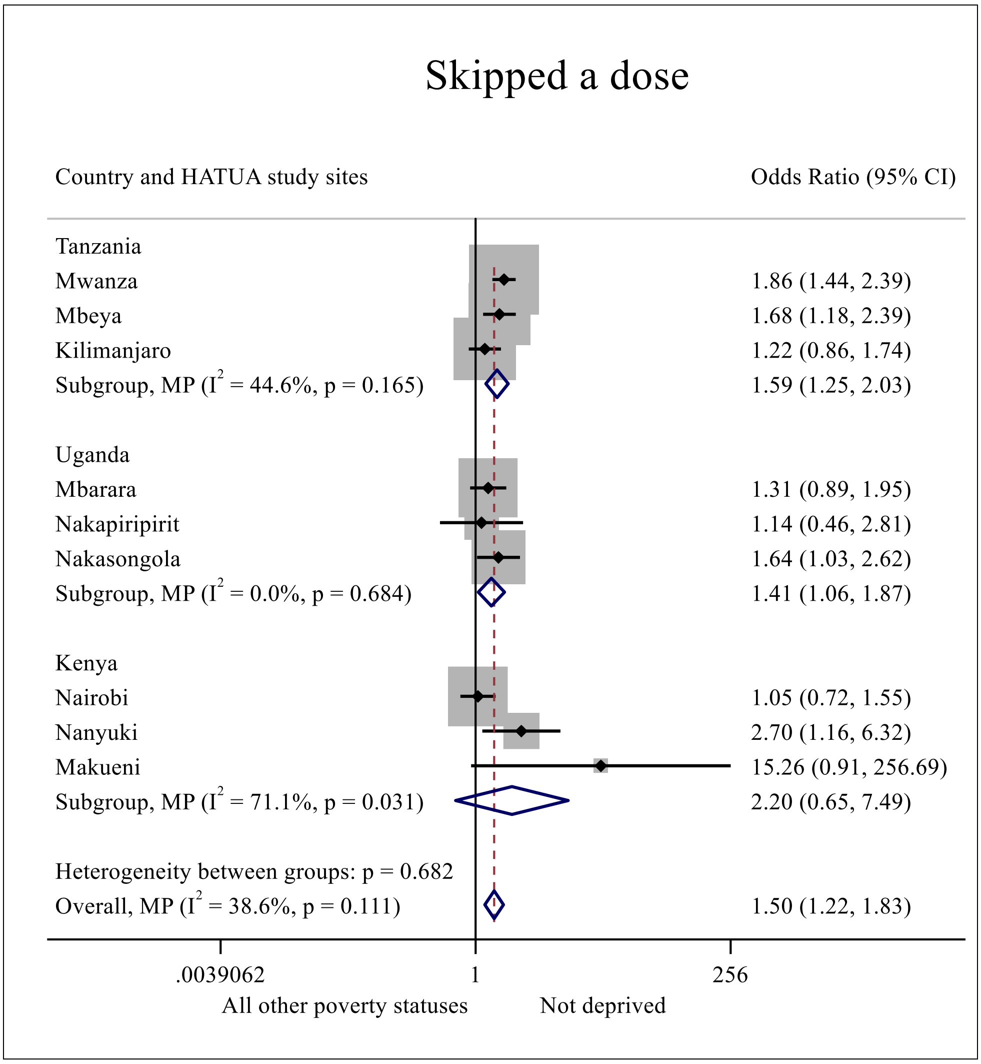
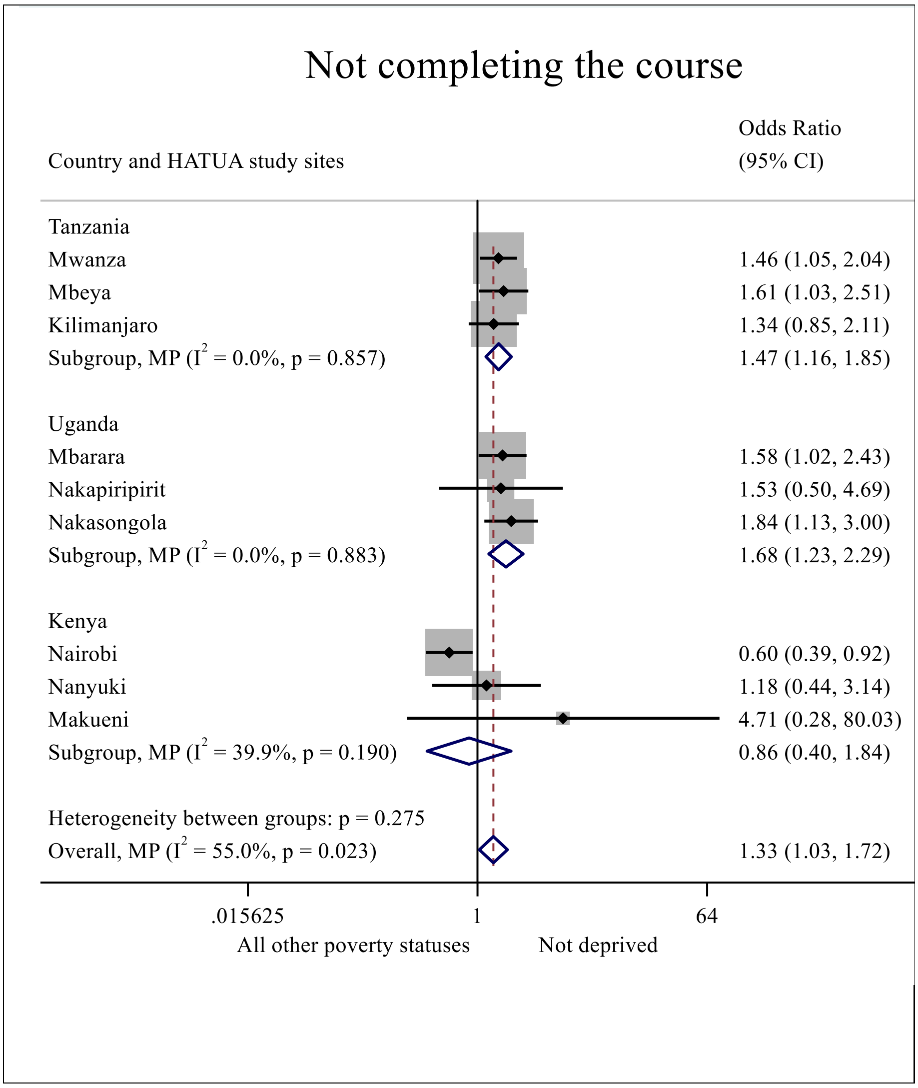


Figure S7·2 confirms the results seen in other analyses, that the not deprived group are more likely to skip a dose (pooled OR 1.50 (1.22-1.83). There was some evidence of between site heterogeneity in Tanzania and Kenya.

Figure S7.3: Random effects meta-analysis of the effects of 'not deprived' poverty on not completing the course



Finally, Figure S7·3 shows that despite some site level heterogeneity in Kenya, those who are 'not deprived' generally show higher odds (pooled OR: 1·33; CI: 1·03-1·72) of not completing the course.

References

1 Alkire S, Foster J. Understandings and misunderstandings of multidimensional poverty measurement. *J Econ Inequal* 2011; **9**: 289–314.

2 Alkire S, Foster J. Counting and multidimensional poverty measurement. *J Public Econ* 2011; **95**: 476–87.

3 Alkire S, Santos ME. Measuring Acute Poverty in the Developing World: Robustness and Scope of the Multidimensional Poverty Index. *World Dev* 2014; **59**: 251–74.

4 Mushongera D, Zikhali P, Ngwenya P. A Multidimensional Poverty Index for Gauteng Province, South Africa: Evidence from Quality of Life Survey Data. *Soc Indic Res* 2017; **130**: 277–303.

5 Fransman T, Yu D. Multidimensional poverty in South Africa in 2001–16. *Dev South Afr* 2019; **36**: 50–79.

6 United Nations Development Program UNDP, Oxford Poverty and Human Development Initiative OP and HDI. Multidimensional Poverty Index: Developing countries (2019). Washington, D. C., 2019 http://hdr.undp.org/sites/default/files/mpi_2019_publication.pdf.

7 Bell BA, Morgan GB, Schoeneberger JA, Kromrey JD, Ferron JM. How low can you go?: An investigation of the influence of sample size and model complexity on point and interval estimates in two-level linear models. *Methodology* 2014; **10**: 1–11.

8 Fisher DJ. Two-stage Individual Participant Data Meta-analysis and Generalized Forest Plots: *https://doi.org/101177/1536867X1501500203* 2015; **15**: 369–96.

9 Sidik K, Jonkman JN. A comparison of heterogeneity variance estimators in combining results of studies. *Stat Med* 2007; **26**: 1964–81.