Effect of a community-based behavioural intervention bundle to improve antibiotic use and patient management in Burkina Faso and DR Congo: a cluster randomized controlled trial

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Summary

Background

Sub-Saharan Africa has a high burden of disease due to antimicrobial resistance that is thought to be driven by a combination of sub-optimal antibiotic use and frequent exposures to AMR in different One Health compartments. We evaluated a community-based, co-created intervention bundle to improve antibiotic use and hygiene practices, targeting all community-level healthcare providers and communities.

Methods

In a cluster-randomised, controlled trial in 44 villages, we measured the intervention effect on antibiotic use through repeated patient surveys. Simulated patient visits, mimicking common infections, were used to monitor patient management. In 22 randomised intervention villages, three rounds of intervention activities (health education campaign, educational/feedback sessions) were implemented over nine months. Provider interventions focused on infections with highest antibiotic use, introducing WHO AWaRe Book guidance. Per provider type per village, 100 patient surveys and five simulated patient visits were conducted at baseline and post-intervention. Primary outcomes were the change in Watch antibiotic use and patient management scores. CABU-EICO was registered on clinicaltrials.gov/study/NCT05378880.

Findings

During the baseline period (Oct 26, 2022 to Mar 13, 2023), 5532 patients were surveyed at 63 health centres, 60 pharmacies, and 41 informal vendors. Post-intervention (Nov 6, 2023 to Apr 3, 2024), 4898 patients were surveyed. A total of 1092 simulated patient visits were completed across both periods. Weighted prevalence of Watch-antibiotic use decreased from 26·8% (95%CI 8·8-44·8) to 17·1% (95%CI 7·7-26·5) with a prevalence ratio (PR) of 0·29 (95%CI 0·10-0·82). Use of any systemic antibiotics decreased from 56·2 (95%CI 35·9-76·5) to 37·5% (95%CI 28·3-46·7), PR 0·48 (95%CI 0·26-0·88). At intervention health centres, patient management scores increased by 1·5 points (95%CI -0·77-3·68), at informal vendors by 0·29 points (95%CI -0·21-0·78).

Interpretation

The low-cost behavioural intervention bundle more than halved Watch and overall antibiotic use and did not negatively impact patient management, highlighting the potential of antibiotic use improvements across healthcare providers.

Funding

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Research in context

Evidence before this study

Evidence on the effectiveness of interventions to improve antibiotic use in primary care in low- and middle-income countries (LMIC) is heterogenous, both in terms of intervention components and effect sizes. A systematic review of behavioural interventions in LMIC analysed eight experimental or quasi-experimental studies in health centres, two in private clinics, and three in community pharmacies. Most interventions consisted of educational sessions on treatment guidance, with or without feedback or supervision. The strongest evidence was found for combinations of education and feedback in primary care: for example, printing clinical guidance and providing educational sessions in Kenyan private clinics reduced prevalence of quinolone use from 30% to 16%. A treatment algorithm introduced in Tanzanian health centres reduced the prevalence of antibiotic use from 70% to 25% while improving checks for danger signs in children.

Evidence concerning interventions among informal healthcare providers is scarcer: provision of educational sessions for informal medicine vendors in India was not linked to a change in prevalence of antibiotic use, but did improve patient management.

A systematic review of studies in sub-Saharan Africa published up to 2020 found that self-medication with antibiotics—obtained from community pharmacies or medicine vendors—is reported by more than half of respondents. Prior studies in the Nanoro and Kimpese study sites indicated that up to 50% of antibiotics were obtained from private providers, and that as much as 75% of Watch-group antibiotic use could have been substituted by either no antibiotic or an Access-group antibiotic, when treatment would be according to WHO AWaRe Book guidance.

Added value of this study

To our knowledge, no previous intervention has simultaneously targeted both antibiotic dispensing by healthcare providers or vendors and the demand from the communities they serve. By including all community-level providers and vendors in both the intervention and its evaluation, and by adjusting community-level antibiotic-use prevalence for healthcare utilisation, we were able to estimate effects on community-wide antibiotic use.

We used simulated patient visits for five priority infections to assess changes in patient management and antibiotic dispensing. This approach enabled direct comparison of history taking, examination practices, and dispensing across provider types and intervention arms, offering clear insight into how the intervention influenced clinical management and antibiotic use. Together with detailed sub-analyses by infection and provider type, and qualitative interviews with providers and community members, the evaluation identified intervention components which appeared to be the most effective and could be prioritised in future, more targeted interventions.

Finally, this is the first experimental study to evaluate an intervention informed by the WHO AWaRe Antibiotic Book, which was published in December 2022, only two months before the study started. Our findings demonstrate that an approach focusing on a small number of common primary-care infections can reduce overall antibiotic use and improve the selection of appropriate antibiotics.

Implications of all the available evidence

Low-cost, contextualised behavioural interventions based on existing treatment guidance can substantially improve antibiotic use.

Introduction

Mortality attributable to bacterial antimicrobial resistance (AMR) is estimated to be highest in sub-Saharan Africa, though available data from the region remain limited.[1,2] Causative pathogens are predominantly community-acquired, such as *Streptococcus pneumoniae*, *Escherichia coli*, and (non-)typhoid *Salmonella*, and frequently exhibit resistance to Access and Watch group antibiotics that are essential to treat most bacterial infections.[1,3,4] High resistance levels may stem from both community- and healthcare-level drivers such as inappropriate antibiotic use leading to selective pressure favouring resistant bacteria, and poor sanitation leading to high rates of transmission between hosts and environmental reservoirs.[5–7] Core objectives of the Global Action Plan on AMR are, accordingly, to optimize the use of antimicrobials and to reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures.[8]

In 2022, the World Health Organization (WHO) introduced the AWaRe Antibiotic Book, evidence-based treatment guidelines for empiric prescribing in primary care and hospitals.[9] Its guidance for 20 common infections in primary care promotes symptomatic care without antibiotics and the use of 'Access antibiotics', which should be generally available in primary care to treat most mild infections, over 'Watch antibiotics', with broader spectrum yet higher AMR potential.[10] For most minor infections (mainly upper respiratory tract infections), no antibiotic use is recommended. Watch antibiotics are only recommended for acute severe bloody diarrhoea, enteric fever, and certain sexually transmitted infections. The UN General Assembly committed in September 2024 to expand by 2030 the use of Access antibiotics to at least 70% of overall human antibiotic use, by strengthening stewardship programmes.[11]

Unnecessary or suboptimal antibiotic use can arise from limited awareness of antimicrobial resistance, limited diagnostic capacity, and frequent self-medication in low- and middle-income countries (LMIC).[12,13] In sub-Saharan Africa, antibiotic use per capita is increasing, but overall it is not thought to be higher than in most industrialised countries.[14–16] Nevertheless, most current use of antibiotics in primary care is for conditions for which (Watch) antibiotics are not indicated: previous patient surveys in rural Burkina Faso and DR Congo indicated that respectively 69% and 75% of Watch-antibiotic use could be replaced by Access antibiotics or no antibiotic use, if treatment would have been according to guidance from the AWaRe Antibiotic Book.[15,17]

Evidence about effectiveness of interventions to improve community-level or primary care antibiotic use in LMIC is limited and heterogeneous, in terms of intervention components, healthcare providers targeted, and effect size. Intervention bundles combining enabling interventions (e.g., education, guidelines) with persuasive interventions (e.g., dispensing audits and feedback) appeared more effective than standalone interventions.[18,19]

The CABU-EICO project (clinicaltrials.gov/study/NCT05378880) developed, implemented and evaluated a community-based intervention bundle to improve human antibiotic use and prevent transmission through water, sanitation and hygiene improvements in communities in two health districts in Burkina Faso and DR Congo.[20] A nine-month behavioural intervention bundle targeted all formal or informal medicine providers (supply) as well as the communities they serve (demand) through three-monthly educational and persuasive (i.e. feedback) sessions and health education campaigns. We evaluated the intervention's effect on Watch and overall antibiotic use and on patient management. The effect on within-household ESBL-*E. coli* transmission is reported in [joint submission].

Methods

Study design

We conducted a cluster-randomised, controlled trial in 44 villages and neighbourhoods in two health districts in two countries: Kimpese in DR Congo and Nanoro in Burkina Faso (description in appendix). Study protocols were approved by Université Protestante au Congo Ethics Committee

(CEUPC0098), Burkina Faso Ethics Committee for Health Research (2022-03-050), and Antwerp University Hospital Ethics Committee (3456, 3363).

Clusters

Village or neighbourhood was the unit of randomization because the intervention was targeting all community-level healthcare providers or medicine dispensers and surrounding communities. In Kimpese, 14 rural villages and eight peri-urban neighbourhoods were selected (estimated population 54684). In Nanoro, 22 rural villages were selected (estimated population 80203). Eligible village or neighbourhood clusters had at least 500 inhabitants, and at least one community-level or primary care provider functioning as the main medicine dispenser of the population of that village/neighbourhood. For peri-urban neighbourhoods, non-neighbouring areas were selected, to avoid contamination of a potential intervention effect from intervention to control clusters. Clusters selected for the trial were different from villages where the intervention was developed. Village leaders and local community-level healthcare providers were visited to assess eligibility and willingness to participate in the study. Informed consent for intervention participation was collected orally from village leaders and documented. Participating providers provided written consent.

Randomisation

Village/neighbourhood clusters were randomised 1:1 intervention or control in two strata. In Nanoro, strata distinguished villages with a primary health centre and those without (only formal or informal medicine outlets). In Kimpese, strata distinguished peri-urban neighbourhoods and rural villages. A random number between 0 and 1 was given to each cluster using the RAND function in Excel. Per stratum, clusters with the 50% higher numbers were allocated as intervention clusters; the half with the lower numbers were therefore allocated as control clusters. Field workers conducting simulated patient visits were masked.

Intervention and participants

The study team co-created a behavioural intervention package based on extensive consultation of community members and community-level healthcare providers. Content and form of the intervention bundle were developed based on an exploratory qualitative study, interviewing and observing all healthcare providers (primary health centres, private clinics, private community pharmacies, informal medicine vendors) and community members in four villages per site.[21] Villages for intervention development shared socio-economic and geographic characteristics with trial villages. The intervention was later piloted in these villages, as a way of presenting results of the preparatory research whilst also gaining valuable feedback on the intervention. A day-to-day intervention manual detailed three rounds of educational and feedback sessions with providers and mass health education activities with community members (Table 1). Sessions with providers focused on four infections accounting for 73% (1047/1444) of any antibiotic use and 66% (210/318) of Watch antibiotics in prior patient surveys.[15,17] Priority infections were: (1) cough including bronchitis, (2) community-acquired pneumonia, (3) diarrhoea and other gastro-intestinal complaints, and (4) acute fever without other discriminating symptoms. We adapted and contextualized treatment guidance for those infections from the 2022 AWaRe Antibiotic Book, while integrating existing Integrated Management of Childhood Illness guidance in children aged <5 years (appendix).

Table 1. Components and content of the co-created AMR control intervention bundle.

Intervention component	Topic
Face-to-face educational sessions (enabling) with healthcare providers and medicine dispensers	
- clinical case discussion (all providers), prescription audit and feedback (health centres) - training session, quizzes, and peer-to-peer discussions on the choice of antimicrobial agents using a bag of locally available antibiotics - introducing treatment guidance	1st round: Bacterial AMR and its determinants (bacteria and viruses and role of the immune system in combating infection, mechanism how inappropriate antibiotic use induces AMR); Antimicrobial agents, their spectrum of activity, the role of broad vs. narrow spectrum antibiotics, route of administration, dosing, side effects, contra-indications; Indications of antibiotic use, the distinction between Access and Watch antibiotics, and why they are used for different infections; Introduce treatment guidance for cough including bronchitis, community-acquired pneumonia, and diarrhoea or other gastro-intestinal complaints

for 4 main infections	2nd round: Introduce treatment guidance for acute fever without other discriminating symptoms, malaria, and skin or soft tissue infections. Recap previous guidance. 3rd round: Recap treatment guidance. Provider-patient communication strategies.
Health education campaign (persuasive/ enabling) in communities	
- Mass health education sessions (including video projection, quizzes, theatre plays, commitment ceremonies, distribution of soap) - Door-to-door visits - Scheduled meeting with target group - Ad hoc Q&A with residents - Role plays at schools, followed by group discussion	Across rounds: - Handwashing: the importance of using soap and important hand washing moments - Role of antibiotics to treat infections and effect on AMR - Correct use of antibiotics (e.g. role of compliance, not for any illness, …). - Role of health centre consultation versus self-medication when ill. - Safe sanitation facilities and practices, including wastewater management. - Safe drinking water sources and safe storage. 1st round: - video projection of existing songs on handwashing - theatre play depicting a dialogue between neighbours on the consequences of drinking water from dams, wells, and of taking medicines - educational group discussions using photovoice images (pictures taken by community members of day-to-day situations driving AMR) - soap distribution and setting up handwashing facilities 2nd round: - organise community clean-up days, installation of hand-washing stations - educational campaign on safe sanitation and the consequences of poor adherence to antibiotic treatment - school game on daily routines, highlighting moments of handwashing, install handwashing points in schools - video screening on all topics 3rd round: repeat all discussed drivers of AMR through all channels; Q&A; commitments on seeking (formal) healthcare consultations when ill

Three rounds of intervention activities, four days per cluster per round, were implemented by three (Nanoro) to five (Kimpese) educators. The intervention and its evaluation were rolled out in a staggered way, visiting – on average – one intervention and one control cluster per week per intervention round, hence completing all within nine months (Jan-Sep 2023 in Nanoro, Apr-Dec 2023 in Kimpese).

Intervention evaluation

At baseline and post intervention (12 months later, to account for seasonality), outcomes were recorded in three surveys. First, patient surveys recorded use of systemic antibiotics during or following patient visits to health centres, private clinics, community pharmacies or medicine stores, and informal vendors. Second, household surveys recorded healthcare visits of any household member in the previous month and previous three months, used to estimate the provider-specific rate of healthcare utilisation. Third, following provider visits by simulated patients, standardised scoring grids recorded history taking, clinical examination, counselling, medicine dispensing and duration of the visit, to assess patient management. Because 7-day phone follow-up was unreliable in prior site studies[16] and infeasible to power, we expanded the simulated-patient method of Das et al[22] to evaluate changes in patient management. Finally, a post-intervention process evaluation explored how intervention components contributed to observed effects through focus groups and in-depth interviews.

Sampling strategy and sample size

Patient surveys: At every participating community-level healthcare provider, patients or parents of paediatric patients were surveyed after completing a healthcare visit, regardless of whether they received an antibiotic. As soon as an interviewer completed a survey, the next patient finishing a visit was enrolled. Sample size calculations indicated that with 11 clusters per intervention arm per site, 100 patient surveys per provider type per village/neighbourhood cluster, a frequency of Watch antibiotic use of 24% (as observed previously in Kimpese[15]), and an assumed intraclass correlation coefficient of 0.01 there would be 80% power to detect a 40% net difference (i.e. (I_post - I_base) - (C_post - C_base)) in Watch antibiotic use. A simple difference (I_post - I_base) of >30% can be

estimated with >80% power (appendix). Patients≥18 years provided written informed consent; for patients<18 years, parents or caretakers gave written informed consent, with assent of patients 14-17 years old.

Household surveys: Per village/neighbourhood, 36 households were randomly selected from the Health Demographic Surveillance Site database (updated in 2021) in Nanoro and were randomly spatially sampled in Kimpese. GPS points were randomly distributed within a polygon with outer limits of each village, and the nearest house to each point was selected. Household heads (if not available, another adult household member present at the time of the visit) were surveyed on household structure, and healthcare provider visits (including any medicine vendors) among all household members. Adult respondents provided written informed consent.

Simulated patient visits: Field agents were trained before the visit to present at the healthcare provider and answer questions in a standardised way, each mimicking an infection according to a standardised scenario that should avoid ambiguities. Field agents were masked as to whether the visited provider received training or not. Visits were unannounced and repeated at baseline and post-intervention.. Providers consented minimum two months before baseline visits, to avoid providers altering their behaviour during visits.

Process evaluation: In five Nanoro villages, participants to focus-groups and in-depth-interviews were recruited through purposive sampling (appendix). Two external evaluators conducted 2 focus-groups, each with 5 to 8 men and women from the community, and 10 in-depth-interviews with religious leaders, community leaders, and informal medicine vendors.

Data collection, outcomes and data analysis

Patient surveys recorded in an electronic questionnaire reason for the visit (acute illness, chronic illness, no illness), clinical signs and symptoms, (if determined) clinical diagnosis, quantity of antibiotics dispensed by group of antibiotics if any, dose and duration of antibiotic treatment, mode of administration, and antimalarials used concomitantly. In Kimpese, interviewers recording patient surveys were medical doctors, who assigned an infection (or clinical presentation when no specific infection could be assigned) to each patient, based on clinical signs and symptoms and a potential diagnostic test result during the visit. In Nanoro, interviewers were generally nurses, who recorded diagnoses or clinical presentations from the patient's health booklet, when available. Based on recorded diagnoses, clinical signs and symptoms, and diagnostic test results, BI and DV independently assigned an infection to each acute illness visit, according to criteria in the Diagnosis sections in the WHO AWaRe Antibiotic Book. In case multiple infections could be assigned to the recorded clinical signs and symptoms (e.g., fever with bronchitis and a positive malaria diagnostic test), we assigned the infection that had the highest likelihood to result in antibiotic use (e.g., bronchitis). In cases of disagreement, consensus was reached through joint review. Because for certain common infections in the AWaRe Antibiotic Book, recorded clinical signs and symptoms are not specific enough to assign the specific infection, we categorised some infections in broader syndromic clinical presentations with the same treatment indications in the WHO AWaRe Antibiotic Book (e.g., bronchitis assigned as acute respiratory infection; acute diarrhoea and other acute gastro-intestinal symptoms as gastroenteritis). We excluded patient surveys at providers that were not surveyed both at baseline and endline, and at providers that had fewer than 20 surveys completed at either base- or endline.

During household surveys, interviewers completed an electronic questionnaire recording the frequency of healthcare provider visits in the previous month and previous three months of each household member, indicating the choice of provider. Using the person-months surveyed as denominator, we estimated the monthly rate of healthcare utilisation by provider type, in each study site. The overall rate is the sum of provider type-specific rates. The survey in Kimpese did not distinguish visits to public health centres from those to private clinics. Therefore, we used the distribution in healthcare utilisation by provider type from a 2020-21 Kimpese household survey (25·5 (95%CI 24·6-26·4) visits per 1000 inhabitants per month to public health centres and 31·0 (95%CI 30·0-32·0) to private clinics)

to infer the rate by type of provider.[23] We inferred the monthly number of provider visits to each of the providers in the study by multiplying the rate of provider-type-specific healthcare utilisation with the population size of the village/neighbourhood cluster.

From the patient surveys, we estimated the prevalence of (Watch) antibiotic use among patients visiting community-level healthcare providers for acute illness at baseline and post intervention, correcting for two-stage sampling and post-stratification weighting for the estimated number of provider visits. We describe the change in prevalence from baseline to post-intervention in the intervention group.

We estimated adjusted prevalence ratios (PR) of antibiotic use in intervention versus control clusters, using survey-weighted negative binomial regression, incorporating an offset for the estimated number of provider visits. The outcome was the count of patients with at least a Watch antibiotic or at least any antibiotic, with population-level healthcare utilization (village population × provider-specific utilization rate) as an offset term. Survey weights accounting for cluster size were applied using svydesign() with the provider as the primary sampling unit. The model included round (post-intervention vs. baseline), intervention/control group, and their interaction term to estimate the differential change between groups. PR and 95% confidence interval for the intervention effect were derived by exponentiating the interaction term coefficient. We used survey and MASS packages in R.

In health centres and private clinics within intervention clusters, we assessed – at baseline and post-intervention – the proportion of antibiotic use that could have been substituted (either by no antibiotic or by an antibiotic from a different AWaRe group) if prescribers had adhered to the AWaRe Antibiotic Book's recommended AWaRe group for each infection.

Combining the provider-type specific weighed prevalence of (Watch) antibiotic use and rate of provider-type-specific healthcare utilisation, we estimated the rate of antibiotic use per 1000 inhabitants per month, by study site. We estimated percentage point differences in antibiotic use rate from baseline to post-intervention. For 95% confidence intervals, we combined standard errors assuming independent samples.

In simulated patient visits, field workers mimicked five common, well-defined infections, according to a standardised scenario for which the indication for treatment, counselling or referral is clear from treatment guidance: (i) acute gastroenteritis (young child, accompanied by mother), (ii) acute severe pneumonia (caretaker seeking care for sick older adult at home), (iii) acute fever with no other symptoms, (iv) acute urinary tract infection (UTI) in an adult woman, (v) acute pharyngitis (scenarios and scoring grids in appendix). After each visit, field agents completed a scoring grid to record history taking questions, physical examinations, or actions performed during the visit (appendix). Each simulated infection had its scoring grid with specific questions, examinations and actions, based on patient management including history taking, diagnosis (including assessing the infection), treatment (or no treatment) as recommended by the WHO Antibiotic Book, WHO's Integrated Management of Childhood Illnesses (2008 and its revision of 2014). Each question or action was assigned a predefined weight—positive or negative—reflecting its relative importance in patient management, as agreed upon by DV, BM, SD and BI (three clinicians, one pharmacist, from Burkina Faso, Democratic Republic of Congo, and Belgium). Summing these weighted components produced a total patient management score that quantitatively captures the provider's adherence to established clinical standards. Patient management scores could range from −5 to 32, depending on inappropriate medicine use and completeness of recommended clinical actions.

Using the patient management score per infection-specific simulated patient visit, we described the distribution of patient management scores during visits with the five simulated infections, comparing baseline and post intervention by simulated infection. We estimated the intervention effect on patient management scores using linear regression with an interaction term between intervention/control group and baseline/post-intervention round, adjusting for site, provider type, and type of infection. The

difference-in-differences effect and 95% confidence interval were derived from the interaction term coefficient.

Process evaluation semi-structured interviews followed an interview guide with predefined themes: perceptions of antibiotics/AMR, sales practices, social dynamics related to interventions. These themes guided initial (manual) coding of transcripts, while emergent themes were incorporated to capture unanticipated insights, to compare convergent and divergent views across participants.

Role of the funding source

The funders had no role in study design, data collection, analysis, interpretation or writing of the report.

Results

Participants

The healthcare provider intervention component enrolled 18 health centres (9 in Kimpese, 9 in Nanoro), 12 private clinics (only in Kimpese), 32 community pharmacies or medicine stores (22 in Kimpese, 2 in Nanoro), and 22 informal medicine vendors (only in Nanoro, figure 1). The health education campaign aimed to reach an estimated 30131 residents in Kimpese and 43933 in Nanoro.

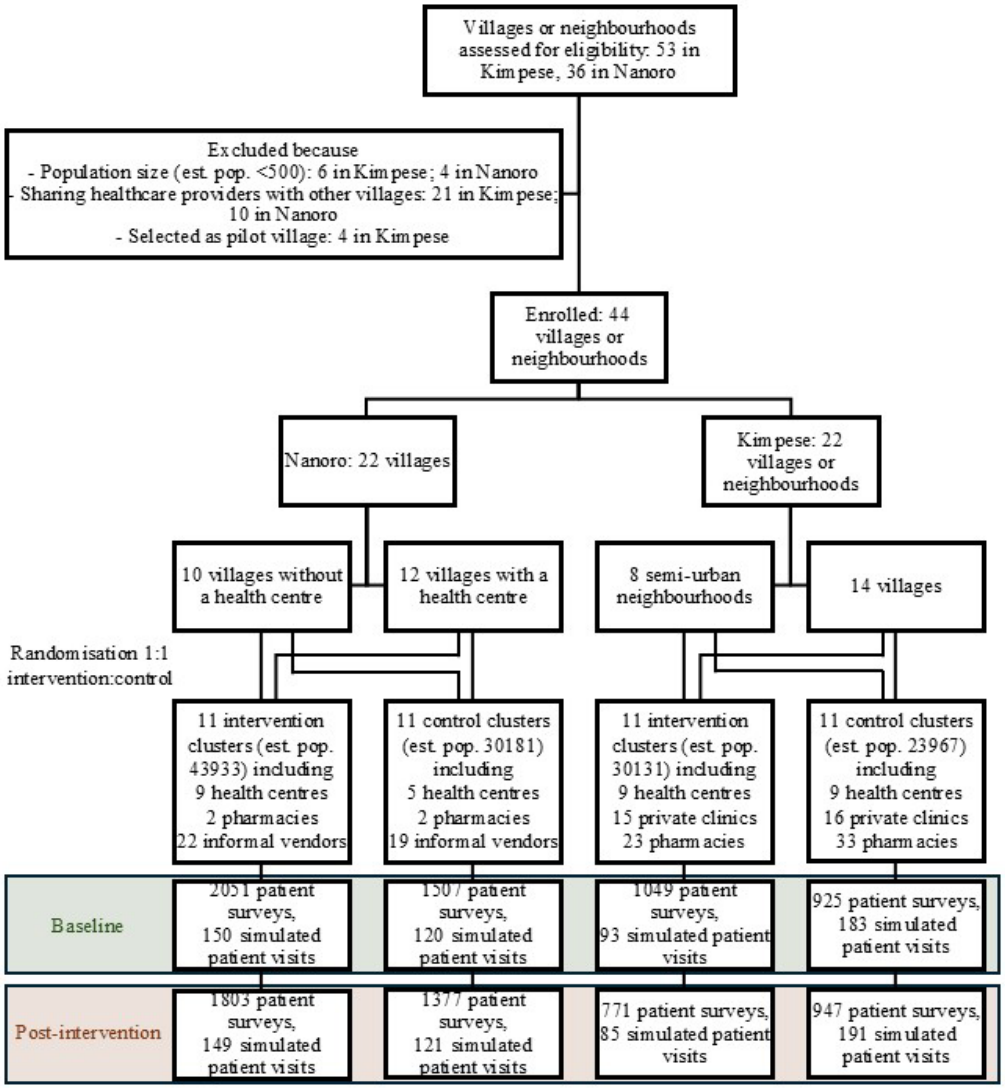

Figure 1. Trial profile

At baseline, 5532 patient surveys were completed (1974 at 105 providers in Kimpese, 3558 at 59 providers in Nanoro; Oct 26, 2022, to Mar 13, 2023) and 4898 completed patient surveys post-intervention (1718 in Kimpese, 3180 in Nanoro; Nov 6, 2023 to Apr 3, 2024). Patients were surveyed at 32 health centres (18 intervention, 14 control), 31 private clinics (15 intervention, 16 control), 60 pharmacies (25 intervention, 35 control), and 41 informal vendors (22 intervention, 19 control). Malaria, acute respiratory infections, skin or soft tissue infections, and unexplained fever were the most frequent infections recorded (Table 2).

Table 2. Characteristics of participants to patient surveys, Oct 2022-Feb 2023 and Oct 2023-Mar 2024

Patient characteristic		Kimpese								Nanoro							
		control				intervention				control				intervention			
		baseline		post		baseline		post		baseline		post		baseline		post	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Type of visit	Acute illness	876	94·7	886	93·6	993	94·7	691	89·6	1216	80·7	1246	90·5	1794	87·5	1647	91·3
	Chronic illness	24	2·6	40	4·2	20	1·9	67	8·7	123	8·2	30	2·2	101	4·9	43	2·4
	No illness (e.g. refill)	24	2·6	21	2·2	35	3·3	13	1·7	45	3	12	0·9	34	1·7	11	0·6
	Animal health	1	0·1			1	0·1			123	8·2	89	6·5	122	5·9	102	5·7
Age group*	0-4 years	179	20·4	184	20·8	229	23·1	158	22·9	112	9·2	154	12·4	216	12·0	270	16·4
	5-17 years	168	19·2	192	21·7	211	21·2	162	23·4	101	8·3	139	11·2	179	10·0	208	12·6
	18-64 years	501	57·2	496	56·0	518	52·2	354	51·2	994	81·7	927	74·4	1369	76·3	1116	67·8
	>/= 65 years	28	3·2	14	1·6	35	3·5	17	2·5	9	0·7	26	2·1	30	1·7	53	3·2
Sex*	Female	440	50·2	452	51·0	519	52·3	352	50·9	611	50·2	537	43·0	879	49·0	732	44·0
	Male	436	49·8	434	49·0	474	47·7	339	49·1	605	49·8	709	57	915	51·0	915	56·0
Assigned infection*	Malaria	217	24·8	287	32·4	293	29·5	316	45·7	164	13·5	172	13·8	346	19·3	375	22·8
	Acute respiratory infection (other than pneumonia)	117	13·4	78	8·8	92	9·3	58	8·4	418	34·4	392	31·5	592	33·0	438	26·6
	Skin/soft tissue infection	83	9·5	81	9·1	80	8·1	51	7·4	1	0·1	6	0·5	17	0·9	11	0·7
	Unexplained fever	91	10·4	63	7·1	111	11·2	43	6·2	161	13·2	198	15·9	213	11·9	217	13·2
	Unexplained gastro-intestinal complaints	56	6·4	34	3·8	64	6·4	19	2·8	47	3·9	55	4·4	67	3·7	60	3·6
	Non-bacterial infectious (viral outbreak, worms, amoebae)	47	5·4	51	5·8	62	6·2	25	3·6	2	0·2	0	0·0	1	0·1	0	0·0
	Other non-specific symptoms	24	2·7	96	10·8	49	4·9	48	7·0	289	23·8	251	20·1	341	19·0	302	18·3
	Typhoid fever or sepsis	48	5·5	58	6·6	52	5·2	34	4·9	1	0·1			6	0·3	1	0·1
	Urinary tract infection	32	3·6	27	3·0	35	3·5	15	2·2	35	2·9	62	5·0	21	1·2	79	4·8
	Gastroenteritis	30	3·4	16	1·8	30	3·0	15	2·2	29	2·4	61	4·9	79	4·4	68	4·1
	Pneumonia	3	0·3	34	3·8	6	0·6	26	3·8	1	0·1	0	0·0	1	0·1	0	0·0
	Sexually transmitted infection	8	0·9	3	0·3	16	1·6	2	0·3								
	Dental infections	7	0·8	2	0·2	1	0·1	1	0·1	7	0·6	1	0·1	6	0·3	2	0·1
	Other	104	11·9	48	5·4	87	8·8	35	5·1	61	5	48	3·9	104	5·8	94	5·7
	Not recorded	9	1·0	8	0·9	15	1·5	3	0·4								

*among patients visiting with acute illness

Healthcare visits during the past month were recorded from 5048 individuals (1326 in Kimpese, 3722 in Nanoro) from 678 households (144 in Kimpese, 534 in Nanoro). In Kimpese, 62·6 visits to health centres or private clinics (95%CI 49·1-76·1) were reported per 1000 inhabitants per month, and 26·4 to private pharmacies or medicine stores (95%CI 17·7-35·1; appendix). In Nanoro, 26·3 visits to health centres (95%CI 21·1-31·5), 2·4 visits to pharmacies (95%CI 0·8-4·0), and 5·4 visits to informal medicine vendors (95%CI 3·0-7·7) were reported per 1000 inhabitants per month.

Effect on the prevalence of (Watch) antibiotic use

The adjusted prevalence ratio (PR) for use of Watch antibiotics was 0·29 (95%CI 0·10-0·82). The weighted prevalence of use of Watch group antibiotics decreased from 26·8% (95%CI 8·8-45) of patients to 17·1% (95%CI 7·7-26). In Kimpese, use of Watch group antibiotics decreased from 41·6

(95%CI 24·7-58·4) to 28·9% (95%CI 18·5-39·4; PR 0·35, 95%CI 0·14-0·92; Figure 1). In Nanoro, the prevalence decreased from 3·3% (95%CI 1·3-5·2) to 1·7% (95%CI 0·6-2·8; PR 0·30, 95%CI 0·06-1·4).

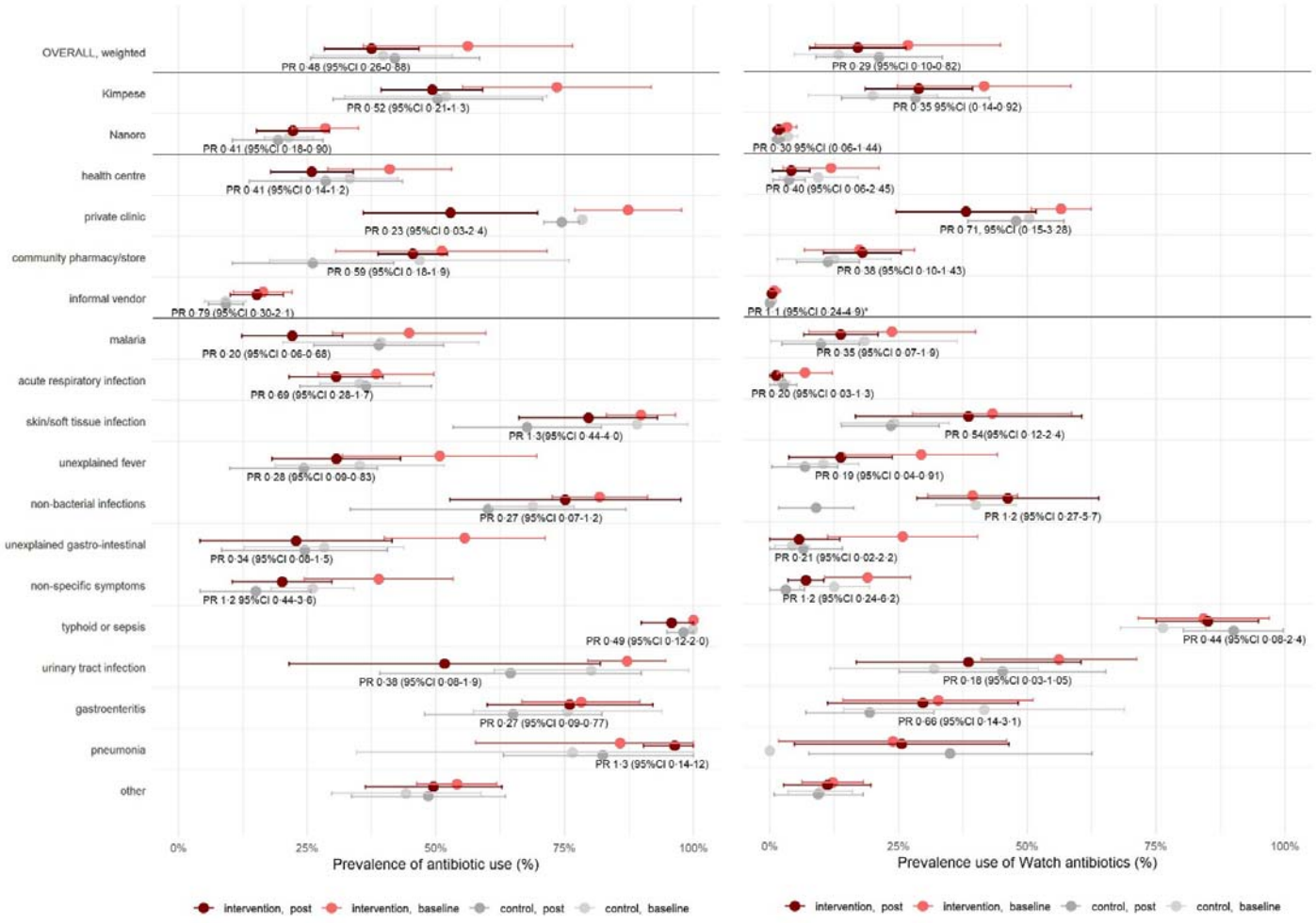

Figure 2. Prevalence of (Watch) antibiotic use during healthcare visits, overall, by site, by type of provider, or by assigned infection, corrected for cluster surveys and offset against the expected number of visits at each provider. Subgroups with <5 patients per group were excluded. PR: adjusted prevalence ratio.

The PR of any antibiotic use was 0·48 (95%CI 0·26-0·88). Weighted prevalence of use of any systemic antibiotic in intervention clusters decreased from 56·2 (95%CI 35·9-76·5) to 37·5% (95%CI 28·3-46·7). In Kimpese, prevalence decreased from 73·5 (95%CI 55·2-91·8) to 49·3% (95%CI 39·4-59·1; PR 0·52, 95%CI 0·21-1·3); in Nanoro, from 28·5 (95%CI 22·1-34·9) to 22·2% (95%CI 15·1-29·3; PR 0·41, 95%CI 0·18-0·90).

Subgroup analyses indicated stronger decreases in (Watch) antibiotic use in health centres (PR Watch antibiotic use 0·40, 95%CI 0·06-2·45, PR any antibiotic use 0·41, 95%CI 0·18-1·2) and more limited reductions at informal vendors (PR Watch 1·1, 95%CI 0·24-4·0, PR any antibiotic 0·79, 95%CI 0·30-2·1; Figure 2). The largest reduction in Watch antibiotic use was with unexplained fever, urinary tract infection, acute respiratory infection, and sexually transmitted infections (Figure 2, Table S4 in

appendix). Any antibiotic use decreased most in sexually transmitted infections, malaria, gastro-enteritis, and unexplained fever.

Appropriate treatment choice

When adhering to AWaRe Antibiotic Book treatment guidance in health centres and private clinics, 413 (65·9%) antibiotic treatment episodes could have been avoided at baseline, and 185 (54·1%) post-intervention (Figure 3). Watch antibiotics made up 240 (38·3%) antibiotic treatment episodes at baseline, of which 199 (82·9%) could have been substituted by access antibiotics or by no antibiotic treatment. Post-intervention, 116 (33·7%) treatment courses had Watch antibiotics, of which 93 (80·2%) could be substituted.

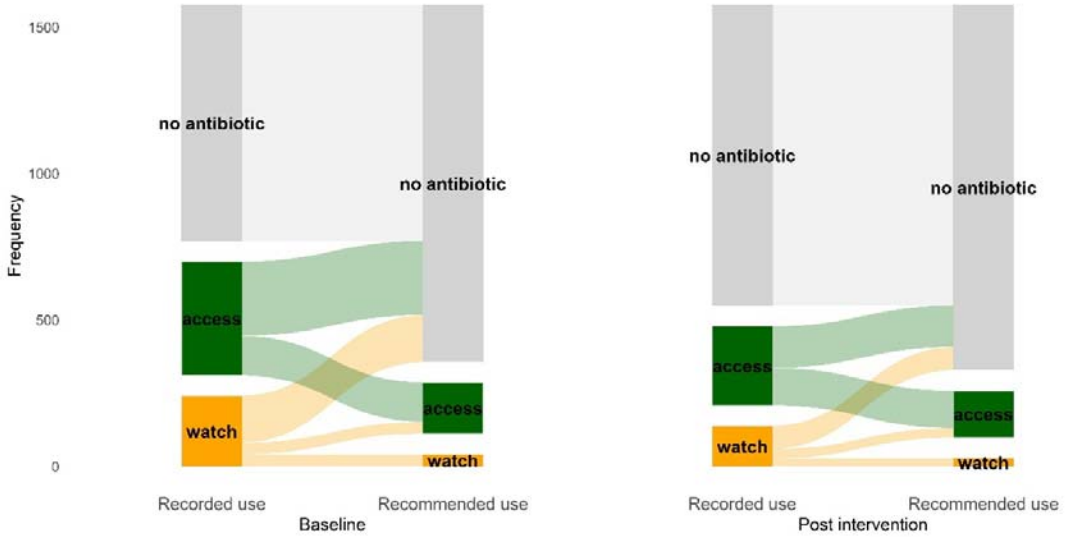

Figure 3. Distribution of recorded and of recommended use of Access/Watch Reserve antibiotics at baseline and post intervention in health centres and private clinics in intervention clusters. Recommended use was according to infection-specific AWaRe Book treatment guidance.

Effect on population-wide antibiotic use

In intervention villages in Kimpese, the rate of population-wide use of any antibiotic decreased from 61·9 treatment episodes (95%CI 61·2-62·6) to 40·6 episodes per 1000 inhabitants per month (95%CI 39·9-41·3, Figure S2 in appendix). Use of Watch antibiotics decreased from 33·3 (95%CI 24·2-47·5) to 23·1 episodes per 1000 inhabitants per month (95%CI 13·1-43·5). Most of the reduction in antibiotic use was at private clinics (decrease of 11·9 antibiotic treatment episodes, 95%CI 22·5-1·3; 6·3 Watch episodes per 1000 inhabitants per month, 95%CI-2·5-15·2) and health centres (decrease 8·0 antibiotic treatment episodes, 95%CI 0·4-16·6; 4·0 Watch episodes per 1000 inhabitants per month, 95%CI -6·2-14·1).

In Nanoro, use of any antibiotic decreased from 9·9 (95%CI 8·8-11·0) to 7·6 episodes per 1000 inhabitants per month (95%CI 6·5-8·7) and use of Watch antibiotics decreased from 1·1 (95%CI 0·0-2·3) to 0·6 per 1000 inhabitants per month (95%CI 0·0-2·6). Most of the reduction in antibiotic use was at health centres (decrease of 2·0 antibiotic treatment episodes, 95%CI 1·5-2·5; 0·5 Watch episodes per 1000 inhabitants per month, 95%CI-0·80 to 1·80, Table S5 in appendix).

Effect on patient management

We repeatedly conducted 546 simulated patient visits (Figure 1). At baseline, across providers and infections, patient management scores ranged between -4 and 24; mean 4·3 (95%CI 3·8-4·8). Scores were higher at health centres (mean 6·6, 95%CI 5·7-7·4) and community pharmacies (mean 6·3, 95%CI 5·5-7·0) than at informal medicine vendors (mean 0·1, 95%CI -0·1-0·3; Figure 4). Scores were

higher at health centres (mean 9·5, 95%CI 8·0-10·9) and pharmacies in Kimpese (mean 6·7, 95%CI 5·8-7·5) than in Nanoro (respectively 4·2, 95%CI 3·5-4·9, and 2·0, 95%CI 0·88-3·2; Fig S3 in appendix).

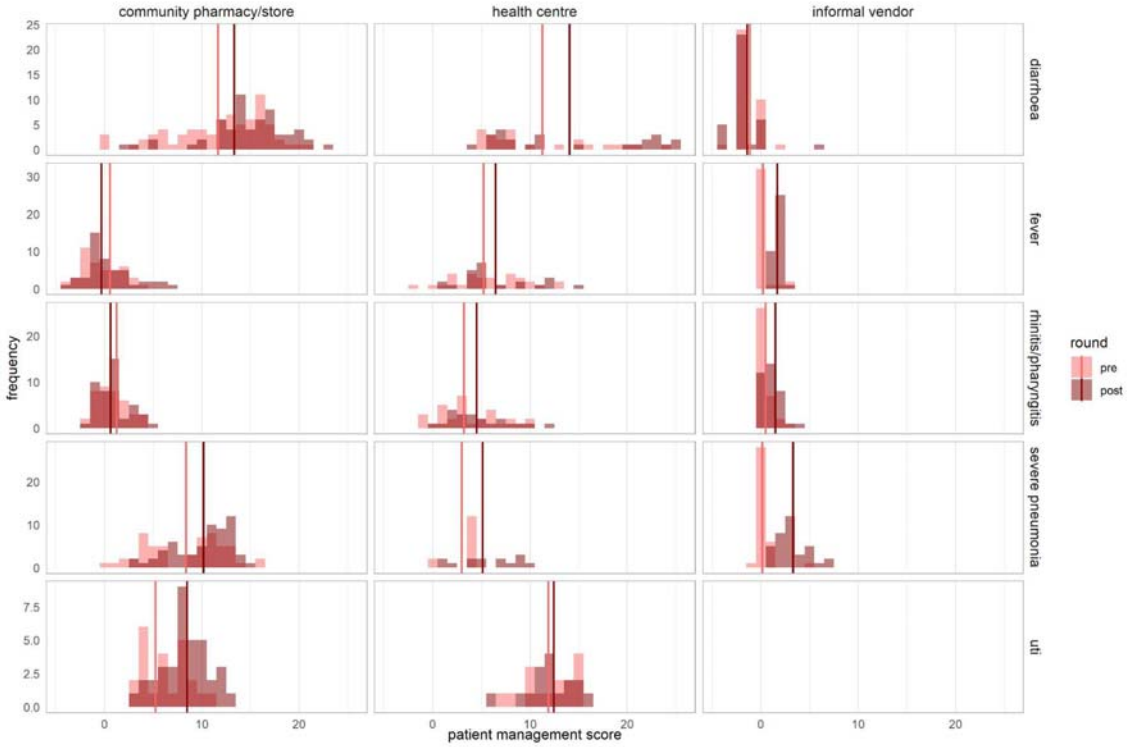

Figure 4. Distribution of patient management scores at all healthcare providers in the intervention group before vs after intervention, faceted by type of provider and by infection. Vertical lines are mean scores. Higher scores indicate better patient management.

The intervention increased patient management scores by 1·5 point (95%CI-0·77-3·68) in health centres and by 0·29 point (-0·21-0·78) during informal vendor visits. At pharmacies, there was a decrease of -1·0 point (95%CI -2·3-0·23). We did not observe major changes in use of Watch antibiotics during visits, except a possible increase during diarrhoea visits to pharmacies (0 to 13·3%, 95%CI 0-30·5%) and informal vendors (0 to 31·6%, 95% 10·7-52·5%, Fig S4 in appendix).

Process evaluation

Community members and medicine vendors consistently reported that the intervention incited partial awareness on the risks of self-medication with antibiotics, possibly resulting in a shift away from informal vendors. Some interviewees were aware that *street medicines are bad for health*, but did not understand how.

"I didn't know that street medicines at best mask the illness and end up causing problems." —female community member

"Informal street vendors are no longer common in [village] because people no longer buy their products."—village leader

Interviewees argued that greater awareness of better treatment outcomes could discourage patients from reverting to self-medication. Nevertheless, financial barriers to visiting health centers remained, even with free-of-cost healthcare for <5 year olds. Informal vendors offered more financial flexibility.

"Abandoning makeshift pharmacies in favour of health centres is possible because differences [in clinical outcome] motivated people[...]if treatment is more effective at the health centre, those who switched will continue to do so" —female community member

"There are no more medicines at the hospital. The government said to treat children for free, and the health centres go bankrupt. They prescribe and tell you to go to the [community] pharmacy. You spend 1000CFA-francs on gasoline. When you arrive, they ask for 3000CFA-francs[...]Informal vendors pharmacies gained power because of this. Even if it means buying 100CFA-francs products and dying, we'll do it, because we have no other choice." —male community member

Informal vendors highlighted they faced pressure to sell antibiotics clients asked for. Refusing to sell antibiotics or patient referrals resulted in client dissatisfaction.

"Customers usually insist on the medications they want, while others refuse to follow[...]advice. As a result, customers chose to buy elsewhere."—informal vendor

"On a daily basis, 20% of customers get angry and leave when I refer them to the health centre"— informal vendor

"Patients expect to receive medication at every visit, and this puts [vendors] in difficult situations."— informal vendor

Discussion

A co-created intervention bundle that combined repeated educational and feedback sessions targeting all community-level healthcare providers with an AMR awareness campaign in surrounding communities, was feasible and effective in reducing (Watch) antibiotic use. Patient management also showed modest improvements in health centres. Across provider types, the intervention achieved a 70% reduction in Watch-antibiotic use (PR 0·29, 95%CI 0·10-0·82), the primary study outcome. This finding is consistent with preparatory studies indicating that >75% of Watch use could be substituted by Access antibiotics or no antibiotic.[15,17] Use of any antibiotic reduced by more than half, an unexpected result given that the intervention focused on Watch antibiotics and that dispensing no antibiotic would go against patients' expectations.

Subanalyses suggested that a shift to no antibiotic treatment might have been more pronounced in health centres and private clinics than at medicine stores, and for infections that were prioritized in the provider intervention. In Nanoro, the change in per capita antibiotic use was attributable to reduced use in health centres. In Kimpese, reductions in private clinics contributed at least as much as those in health centres, consistent with prior studies indicating that half of community-wide antibiotic use stemmed from visits to private providers.[16] Quantitative and qualitative findings confirm medicine vendors' difficulties in reducing over-the-counter dispensing of (Watch) antibiotics. Educational sessions to informal vendors in India also showed no change in the prevalence of antibiotic use, but improved patient management.[22] Informal vendors highlighted difficulties in influencing antibiotic use resulting from patient expectations. Formal and informal medicine vendors are visited because of financial, (waiting) time, antibiotic availability, and proximity considerations.[13,24] Certain policies, such as free-of-charge healthcare for young children, strengthened patient-centred care, or regulation of antibiotic sales have proven successful in curbing self-medication.[24,25]

Educational and feedback sessions with communities, prescribers and dispensers were intended to enable integration in routine supervision activities by health district staff. The intervention therefore focused on infections with the largest potential antibiotic use improvements, identified in prior surveys, and integrated existing treatment guidance based on Integrated Management of Childhood Illness with the AWaRe Antibiotic Book, published months before the intervention start. Even without (costly) structural or restrictive interventions, community-wide antibiotic use can be substantially optimized at low cost.

Because unintended effects were possible, we used simulated patient visits to monitor care quality and safety. Changes in clinical outcome following primary-care or pharmacy visits are difficult to detect – often underpowered with challenging follow-up. Simulated patient visits detected no worsening of patient management, instead a modest improvement, mostly in private clinics and health centres. The extent to which clinical history was taken, examinations were performed, referrals made, and treatments provided varied widely across sites and provider types. Informal vendors rarely took an anamnesis and primarily dispensed medicines, with little or no change after the intervention.

Adjusting antibiotic-use prevalence for healthcare utilisation and village population size allowed estimation of population-wide antibiotic use, highlighting the intervention's public health implications. Our study did not measure changes in healthcare utilisation. Community feedback suggested a shift from self-medication to health-centre consultations, which—had it been incorporated into the weighting—might have yielded a more accurate estimate of post-intervention antibiotic use and may mean our current estimate is conservative. Another limitation was that we could not formally power our study for the presented sub-analyses by infection or provider type due to a limit in eligible villages and providers. Finally, some infections may have been wrongly assigned, particularly in Nanoro where surveyors had no medical background, potentially attenuating infection-specific effects.

Conclusion

A low-cost behavioural intervention targeting both supply (medicine vendors and primary care) and demand (communities served), focusing on key infections, was found to be feasible and resulted in a substantial decrease in antibiotic use, overall and of Watch group antibiotics, and a modest improvement in patient management in primary care. At formal and informal community pharmacies and medicine stores, the study found little change in antibiotic use and patient management. Despite the effect being more modest outside primary care clinics, population-wide antibiotic use was substantially reduced, highlighting the importance of addressing antibiotic use across different healthcare providers.

Contributors

BI, DV, EvK, EW, BC, DMP and MvdS conceptualised the study; BI, DV and BM developed and validated questionnaires with input from LC and SD; BI, DV and SD developed the simulated patient visit scenarios and checklists; LC, SJK, CMKM, and MM led intervention development; BI, DV and BM coordinated data collection; DV and SJK coordinated the process evaluation; BI and DV curated, validated and analysed the data, with input from VB and EvK; BI wrote the draft manuscript with input from DV; all authors revised the first and subsequent drafts of the manuscript; all authors had full access to the study data and had final responsibility for the decision to submit for publication.

Declaration of interests

We declare no competing interests.

Data sharing

Questionnaires, informed consent forms, pseudonymized datasets, data dictionaries, and data analysis scripts in R are available: https://github.com/ingelbeen/cabu_intervention.

The study protocol was published: https://doi.org/10.1186/s13063-023-07856-2

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Appendix of
Effect of a community-based behavioural intervention bundle to improve antibiotic use and patient management in Burkina Faso and DR Congo: a cluster randomized controlled trial

Study setting and population

The study was conducted in two health districts with populations followed up within Health demographic surveillance sites (HDSS) in Nanoro district, Burkina Faso, and Kimpese district, DR Congo. The HDSS in Nanoro was established in 2009. We selected 22 study villages in Nanoro health district, with a total estimated population of 80203 (2023). All villages had at least one medicine vendor (pharmacy or medicine store), and 13 had a primary health centre. The HDSS in Kimpese was established in 2018. We selected 14 villages and 8 urban neighbourhoods, with a total estimated population of 54684 (2023). District referral hospitals in each of both sites have a clinical microbiology laboratory and serve as an AMR surveillance site. Both research institutes coordinating the HDSS also had experienced social science teams prior to the study.

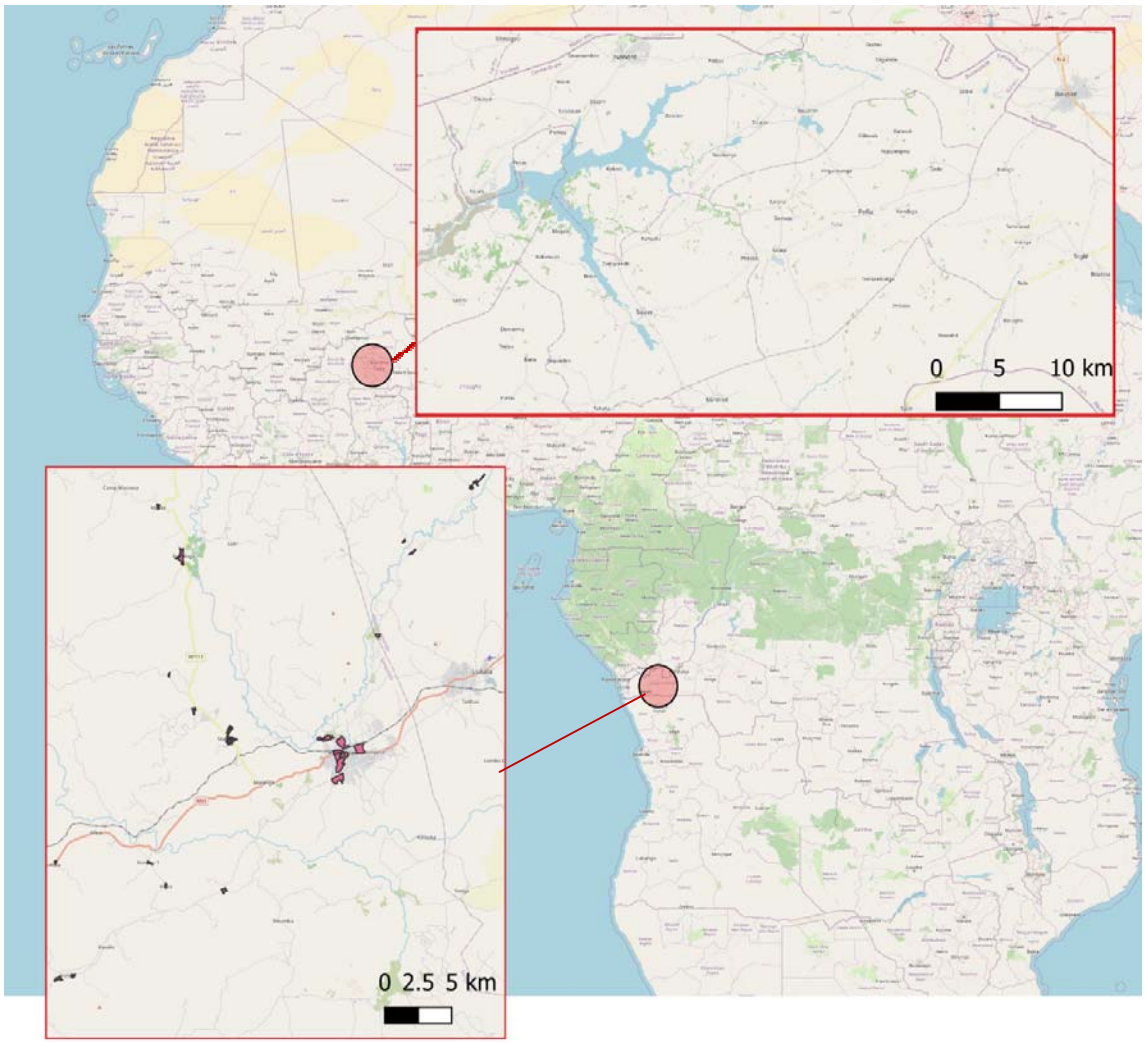

Figure S1. Study sites in DR Congo and Burkina Faso

Supplementary text 1. Treatment guidance for prioritized infections, adapted from the 2022 AWaRe Antibiotic Book, for the educational sessions with prescribers and medicine dispensers.
https://github.com/ingelbeen/cabu_intervention/blob/main/provider_intervention_guide_fr

Supplementary text 2. Simulated patient visits scenarios and checklists to assess patient management
https://github.com/ingelbeen/cabu_intervention/blob/main/simulated_patient_visit_scenarios_checklists

Supplementary text 3. Methods of the process evaluation
The process evaluation was done in five villages in Nanoro during Nov 23, 2023 – Dec 4, 2023. Participants were recruited through purposive sampling, relying on community liaisons. This recruitment method, overseen by local authorities and community leaders (village chiefs, Village Development Committees, health workers, pastors, and community informants), aimed to ensure the legitimacy and acceptability of the evaluation within the villages concerned.

A total of 12 interviews were conducted, including:

- 2 focus group discussions with men and women from the community,
- 10 in-depth individual interviews with key stakeholders, including religious leaders, community leaders, and informal medicine vendors.

Combining focus group discussions and individual interviews allowed for the integration of community perspectives with those of influential stakeholders. Data were collected in the local language, then transcribed into French and translated into English. The analysis was carried out manually, using a thematic approach aimed at highlighting the perceptions, practices and social dynamics related to the intervention.

Supplementary text 4. Estimation of statistical power to observe a reduction in Watch antibiotic use.
To ensure differences in the prevalence of Watch antibiotic use at baseline between intervention and control clusters are factored in the analysis, the planned analysis was a difference-in-differences (net difference) analysis, comparing interventions vs control while adjusting for baseline, to reduce residual variance and the required sample size. We explored the effect of different scenarios, i.e. different values of the assumed effect size (reduction in Watch antibiotics by 40%), of the baseline prevalence of Watch antibiotic use (24%), and of intra class correlation (ICC), on statistical power to observe the difference in prevalence of Watch antibiotic use. We assumed 11 intervention vs control clusters, allowing a site-specific analysis. The script with the estimation of statistical power can be found here:
https://github.com/esthervankleef/sample_size_jpiamr/blob/master/Scripts/main_trial_binary.R

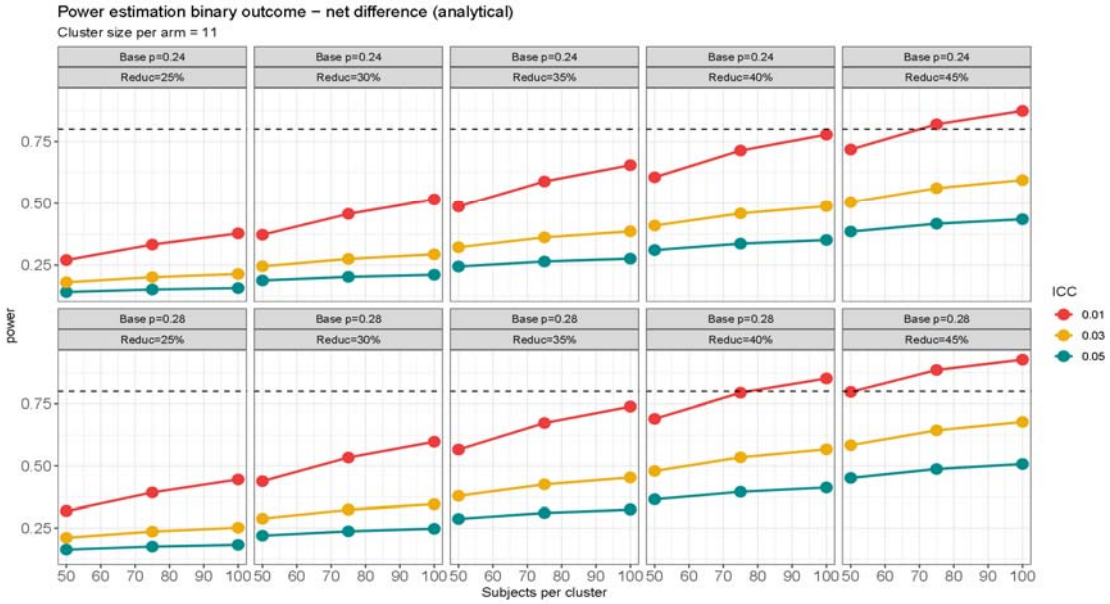

Table S1. Community-level healthcare visits per 1000 inhabitants per month estimated from household survey data. Jan 24, 2023 to Apr 6, 2023 (Kimpese) and Oct 11, 2022 to Feb 4, 2023 (Nanoro).

Type of provider	Reported visits in the last 3 months during prior survey*			Reported visits in the last 3 months			Reported visits in the last month		
	n	rate	95%CI	n	rate	95%CI	n	rate	95%CI
Kimpese (DR Congo)	N=31221 person-months						N=1326 person-months		
Health centre		25.5	24.6-26.4				83	62.6	49.1-76.1
Private clinic£		31.0	30.0-32.0						
Community pharmacy/store		17.6	16.9-18.3				35	26.4	17.7-35.1
Informal vendor		§					§	-	-
Traditional healer		13.4	12.8-14.0				1	0.8	-0.7-2.2
Hospital#		1.2	1.0-1.4						
OVERALL		88.7	81.9-95.4				119	89.7	73.6-105
Nanoro (Burkina Faso)	N=32079 person-months			N=11166 person-months			N=3722 person-months		
Health centre	1328	41.4		232	20.8	18.1-23.5	98	26.3	21.1-31.5
Community pharmacy/store	89	2.8		28	2.5	1.6-3.4	9	2.4	0.8-4.0
Informal vendor	315	9.8		54	4.8	3.5-6.1	20	5.4	3.0-7.7
Traditional healer	62	1.9		4	0.4	0.0-0.7	2	0.5	-0.2-1.3
OVERALL	1794	56.0		318	28.5	19.1-37.9	129	34.7	28.7-40.6

*The prior surveys were limited to four villages in DRC (rural Viaza, Malanga, Kavuaya, and peri-urban Nkandu) during November 2019-June 2020, and two in Burkina Faso (rural Nazoanga and peri-urban Nanoro) during October 2020-December 2021. Results were published doi.org/10.1016/j.cmi.2022.04.002 and doi.org/10.1007/978-981-16-3787-2_4

£During the 2022 household survey in Kimpese, it was not specified whether primary care clinics were public health centres or private clinics, and the specific moment of healthcare seeking during the past month could not be reliably recorded.

§In Kimpese, no informal vendors were identified and community pharmacies or stores often lack qualified staff.

#Healthcare visits to secondary care were only recorded in the prior healthcare utilisation surveys.

Table S2. Characteristics of participants to patient surveys, by site, round, and intervention group, Oct 2022-Feb 2023 and Oct 2023-Mar 2024

Patient characteristic		Kimpese								Nanoro							
		baseline				endline				baseline				endline			
		control		intervention		control		intervention		control		intervention		control		intervention	
		n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Type of visit	Acute illness	626	96.2	741	94.4	886	93.6	691	89.6	1216	80.7	1794	87.5	1246	90.5	1647	91.3
	Chronic illness	14	2.1	15	1.9	40	4.2	67	8.7	123	8.2	101	4.9	30	2.2	43	2.4
	No illness (e.g. refill)	11	1.7	29	3.7	21	2.2	13	1.7	45	3.0	34	1.7	12	0.9	11	0.6
	Animal health									123	8.2	122	5.9	89	6.5	102	5.7
Age group*	0-4 years	138	22.0	182	24.6	184	20.8	158	22.9	112	9.2	216	12.0	154	12.4	270	16.4
	5-17 years	128	20.4	168	22.7	192	21.7	162	23.4	101	8.3	179	10.0	139	11.2	208	12.6
	18-64 years	337	53.8	365	49.3	496	56.0	354	51.2	994	81.7	1369	76.3	927	74.4	1116	67.8
	>/= 65 years	23	3.7	26	3.5	14	1.6	17	2.5	9	0.7	30	1.7	26	2.1	53	3.2
Sex*	Female	324	51.8	400	54.0	452	51.0	352	50.9	611	50.2	879	49.0	537	43.0	732	44.0
	Male	302	48.2	341	46.0	434	49.0	339	49.1	605	49.8	915	51.0	709	57.0	915	56.0
Assigned infection*	Malaria	195	31.1	256	34.5	287	32.4	316	45.7	164	13.5	346	19.3	172	13.8	375	22.8
	Acute respiratory infection (other than pneumonia)	88	14.1	71	9.6	78	8.8	58	8.4	418	34.4	592	33.0	392	31.5	438	26.6
	Skin/soft tissue infection	45	7.2	50	6.8	81	9.1	51	7.4	1	0.1	17	0.9	6	0.5	11	0.7
	Unexplained fever	53	8.5	83	11.2	63	7.1	43	6.2	161	13.2	213	11.9	198	15.9	217	13.2
	Unexplained gastro-intestinal complaints	40	6.4	50	6.8	34	3.8	19	2.8	47	3.9	67	3.7	55	4.4	60	3.6
	Non-bacterial infectious (viral outbreak, worms, amoebae)	32	5.1	34	4.6	51	5.8	25	3.6	2	0.2	1	0.1				
	Other non-specific symptoms	20	3.2	40	5.4	96	10.8	48	7.0	289	23.8	341	19.0	251	20.1	302	18.3
	Typhoid fever or sepsis	35	5.6	29	3.9	58	6.6	34	4.9	1	0.1	6	0.3			1	0.1
	Urinary tract infection	9	1.4	20	2.7	27	3.0	15	2.2	35	2.9	21	1.2	62	5.0	79	4.8
	Gastroenteritis	18	2.9	19	2.6	16	1.8	15	2.2	29	2.4	79	4.4	61	4.9	68	4.1
	Pneumonia	2	0.3	1	0.1	34	3.8	26	3.8	1	0.1	1	0.1				
	Sexually transmitted infection	4	0.6	6	0.8	3	0.3	2	0.3								
	Dental infections	6	1.0			2	0.2	1	0.1	7	0.6	6	0.3	1	0.1	2	0.1
	Other	73	11.7	71	9.6	48	5.4	35	5.1	61	5.0	104	5.8	48	3.9	94	5.7
	Not recorded	6	1.0	11	1.5	8	0.9	3	0.4								

*among patients visiting with acute illness

Table S3. Frequency and unadjusted prevalence of antibiotic use by type of provider

Type of provider		Use of any antibiotic				Use of Watch antibiotic			
		control		intervention		control		intervention	
	round	count	pct	count	pct	count	pct	count	pct
Kimpese (DR Congo)									
health centre	baseline	107/233	45.9	201/330	60.9	36/233	15.5	113/330	34.2
	post	67/152	44.1	60/200	30.0	13/152	8.6	30/200	15.0
private clinic	baseline	109/139	78.4	143/211	67.8	70/139	50.4	96/211	45.5
	post	199/273	72.9	97/178	54.5	105/273	38.5	69/178	38.8
private pharmacy	baseline	279/504	55.4	327/452	72.3	76/504	15.1	138/452	30.5
	post	158/461	34.3	152/313	48.6	52/461	11.3	66/313	21.1
Nanoro (Burkina Faso)									
health centre								3	
	baseline	139/511	27.2	283/894	31.7	26/511	5.1	1/894	3.5
	post	136/512	26.6	187/835	22.4	13/512	2.5	17/835	2.0
private pharmacy	baseline	17/88	19.3	28/113	24.8	0/88	0.0	3/113	2.7
	post	62/141	44.0	14/80	17.5	14/141	9.9	4/80	5.0
informal vendor	baseline	60/617	9.7	125/787	15.9	3/617	0.5	8/787	1.0
	post	58/593	9.8	107/732	14.6	0/593	0.0	3/732	0.4

Table S4. Frequency, crude and weighed prevalence of (Watch) antibiotic use by assigned infection

Assigned infection	control								intervention								Adjusted risk ratio	
	baseline				endline				baseline				endline					
	n	crude %	weighed %	95%CI	n	crude %	weighed %	95%CI	n	crude %	weighed %	95%CI	n	crude %	weighed %	95%CI	aRR	95%CI
ANY ANTIBIOTIC USE																		
malaria	118/381	31·0	39·3	20·2-58·3	151/459	32·9	38·9	26·2-51·5	238/639	37·2	44·8	29·9-59·7	115/691	16·6	22·1	12·3-31·9	0·20	0·06-0·68
acute respiratory infection	135/535	25·2	35·2	27·5-43·0	128/470	27·2	36·4	23·6-49·1	182/684	26·6	38·4	27·1-49·6	115/496	23·2	30·6	21·5-39·7	0·69	0·28-1·7
skin/soft tissue infection	71/84	84·5	89·1	79·3-98·9	59/87	67·8	67·7	53·3-82·1	85/97	87·6	89·8	83·1-96·5	46/62	74·2	79·6	66·1-93·0	1·33	0·44-4·0
unexplained fever	68/252	27·0	35·2	18·8-51·6	41/261	15·7	24·3	9·9-38·6	111/324	34·3	50·7	31·8-69·6	41/260	15·8	30·7	18·2-43·1	0·28	0·09-0·83
unexplained gastro-intestinal	25/103	24·3	28·3	12·8-43·8	14/89	15·7	24·5	8·4-40·5	48/131	36·6	55·6	40·0-71·2	13/79	16·5	22·8	4·1-41·5	0·34	0·07-1·5
non-bacterial infectious (viral outbreak, scabies, worms, amoebae)	33/49	67·3	68·8	60·7-76·8	26/51	51·0	60·1	33·4-86·9	51/63	81·0	81·8	72·6-91·1	19/25	76·0	75·1	52·7-97·6	0·27	0·07-1·1
non-specific symptoms or complaints	48/313	15·3	26·1	18·0-34·1	37/347	10·7	15·0	4·2-25·7	79/390	20·3	38·9	24·4-53·3	44/350	12·6	20·1	10·4-29·8	1·25	0·43-3·6
typhoid or sepsis	48/49	98·0	99·9	99·5-100	57/58	98·3	98·1	94·9-100	58/58	100·0	100·0	100-100	33/35	94·3	95·8	89·9-100	0·49	0·12-2·1
urinary tract infection	32/67	47·8	80·2	61·3-99·0	30/89	33·7	64·5	39·1-89·9	34/56	60·7	87·1	79·5-94·6	15/94	16·0	51·7	21·5-81·9	0·38	0·08-1·8
gastroenteritis	34/59	57·6	75·6	57·3-93·9	47/77	61·0	65·0	47·8-82·2	72/109	66·1	78·2	66·7-89·6	54/83	65·1	76·0	60·0-92·1	0·27	0·09-0·7
pneumonia	3/4	75·0	76·5	34·6-100	27/34	79·4	82·4	63·1-100	6/7	85·7	85·8	57·7-100	25/26	96·2	96·4	90·3-100	1·28	0·14-12
sexually transmitted infection	8/8	100·0	100·0	100-100	2/3	66·7	49·6		15/16	93·8	86·8	60·8-100	1/2	50·0	37·4		0·14	0·01-2·0
dental	5/14	35·7	77·7	46·8-100	2/3	66·7	68·8	16·9-100	1/7	14·3	40·5	0-94·1	2/3	66·7	37·5	0-94·2	2·59	0·14-47
other	74/165	44·8	44·2	29·7-58·7	54/96	56·2	48·5	33·6-63·5	114/191	59·7	54·1	46·3-61·8	92/129	71·3	49·5	36·3-62·8	1·47	0·57-3·8
NA	9/9	100·0			5/8	62·5			13/15	86·7			2/3	66·7				
WATCH ANTIBIOTIC USE																		
malaria	118/381	31·0	39·3	20·2-58·3	151/459	32·9	38·9	26·2-51·5	238/639	37·2	44·8	29·9-59·7	115/691	16·6	22·1	12·3-31·9	0·35	0·07-1·8
acute respiratory infection	135/535	25·2	35·2	27·0·5-43	128/470	27·2	36·4	23·6-49·1	182/684	26·6	38·4	27·1-49·6	115/496	23·2	30·6	21·5-39·7	0·20	0·03-1·3
skin/soft tissue infection	71/84	84·5	89·1	79·3-98·9	59/87	67·8	67·7	53·3-82·1	85/97	87·6	89·8	83·1-96·5	46/62	74·2	79·6	66·1-93·0	0·54	0·12-2·3
unexplained fever	68/252	27·0	35·2	18·8-51·6	41/261	15·7	24·3	9·9-38·6	111/324	34·3	50·7	31·8-69·6	41/260	15·8	30·7	18·2-43·1	0·19	0·04-0·9
unexplained gastro-intestinal	25/103	24·3	28·3	12·8-43·8	14/89	15·7	24·5	8·4-40·5	48/131	36·6	55·6	40-71·2	13/79	16·5	22·8	4·1-41·5	0·21	0·02-2·1
non-bacterial infectious (viral outbreak, scabies, worms, amoebae)	33/49	67·3	68·8	60·7-76·8	26/51	51·0	60·1	33·4-86·9	51/63	81·0	81·8	72·6-91·1	19/25	76·0	75·1	52·7-97·6	1·24	0·27-5·7
non-specific symptoms or complaints	48/313	15·3	26·1	18·0-34·1	37/347	10·7	15·0	4·2-25·7	79/390	20·3	38·9	24·4-53·3	44/350	12·6	20·1	10·4-29·8	1·22	0·24-6·1
typhoid or sepsis	48/49	98·0	99·9	99·5-100	57/58	98·3	98·1	94·9-100	58/58	100·0	100·0	100-100	33/35	94·3	95·8	89·9-100	0·44	0·08-2·4
urinary tract infection	32/67	47·8	80·2	61·3-99·0	30/89	33·7	64·5	39·1-89·9	34/56	60·7	87·1	79·5-94·6	15/94	16·0	51·7	21·5-81·9	0·18	0·03-1·05
gastroenteritis	34/59	57·6	75·6	57·3-93·9	47/77	61·0	65·0	47·8-82·2	72/109	66·1	78·2	66·7-89·6	54/83	65·1	76·0	60·0-92·1	0·66	0·14-3·1
pneumonia	3/4	75·0	76·5	34·6-100	27/34	79·4	82·4	63·1-100	6/7	85·7	85·8	57·7-100	25/26	96·2	96·4	90·3-100		
sexually transmitted infection	8/8	100·0	100·0	100-100	2/3	66·7	49·6	0-100	15/16	93·8	86·8	60·8-100	1/2	50·0	37·4	0-100	0·16	0·01-5·07
dental	5/14	35·7	77·7	46·8-100	2/3	66·7	68·8	16·9-100	1/7	14·3	40·5	0-94·1	2/3	66·7	37·5	0-94·2		
other	74/165	44·8	44·2	29·7-58·7	54/96	56·2	48·5	33·6-63·5	114/191	59·7	54·1	46·3-61·8	92/129	71·3	49·5	36·3-62·8	1·14	0·18-7·08
NA	9/9	100·0			5/8	62·5			13/15	86·7			2/3	66·7				

Table S5. Rate of antibiotic use episodes per 1000 inhabitants per month, by site and by type of healthcare provider, before and after intervention in intervention clusters.

			Any antibiotic use		Watch antibiotic use	
site	**provider type**	**round**	**rate**	**95% CI**	**rate**	**95% CI**
Kimpese	health centre	baseline	17·8	13·9 - 22·8	8·9	6·7 - 11·8
		post	9·8	6·2 - 15·6	4·9	1·6 - 14·6
	private clinic	baseline	30·0	23·4 - 38·5	19·4	15·2 - 24·7
		post	18·1	12·2 - 27·0	13·1	8·5 - 20·2
	private pharmacy	baseline	14·1	8·1 - 24·7	4·9	2·2 - 10·9
		post	12·7	8·9 - 18·2	5·1	3·0 - 8·7
Nanoro	health centre	baseline	8·4	6·2 - 11·5	1·0	0·5 - 2·1
		post	6·4	4·1 - 9·9	0·5	0·2 - 1·5
	informal vendor	baseline	0·9	0·5 - 1·6	0·0	0·0 - NaN
		post	0·8	0·4 - 1·4	0·0	0·0 - NaN
	private pharmacy	baseline	0·6	0·3 - 1·4	0·1	0·0 - 0·3
		post	0·4	0·2 - 0·9	0·1	0·0 - 0·5

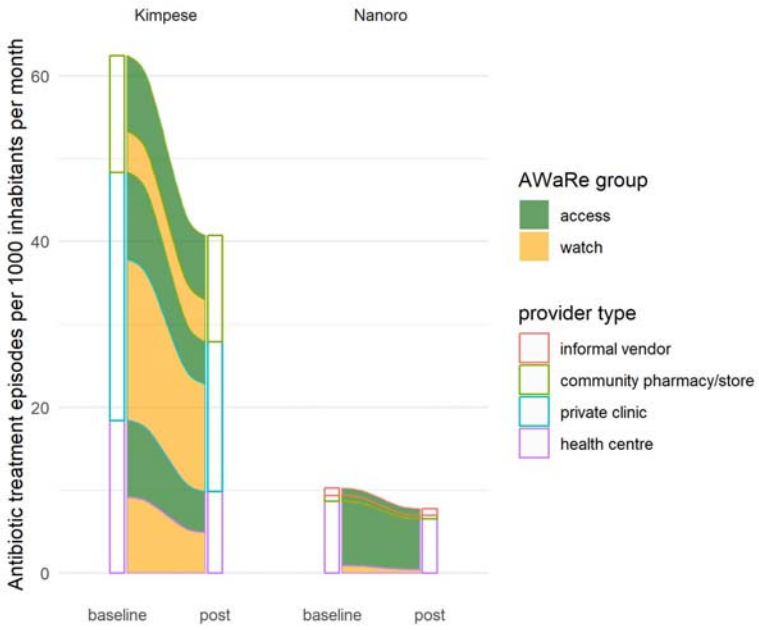

Figure S2. Rate of antibiotic use episodes per 1000 inhabitants per month, before and after the intervention bundle in intervention clusters.

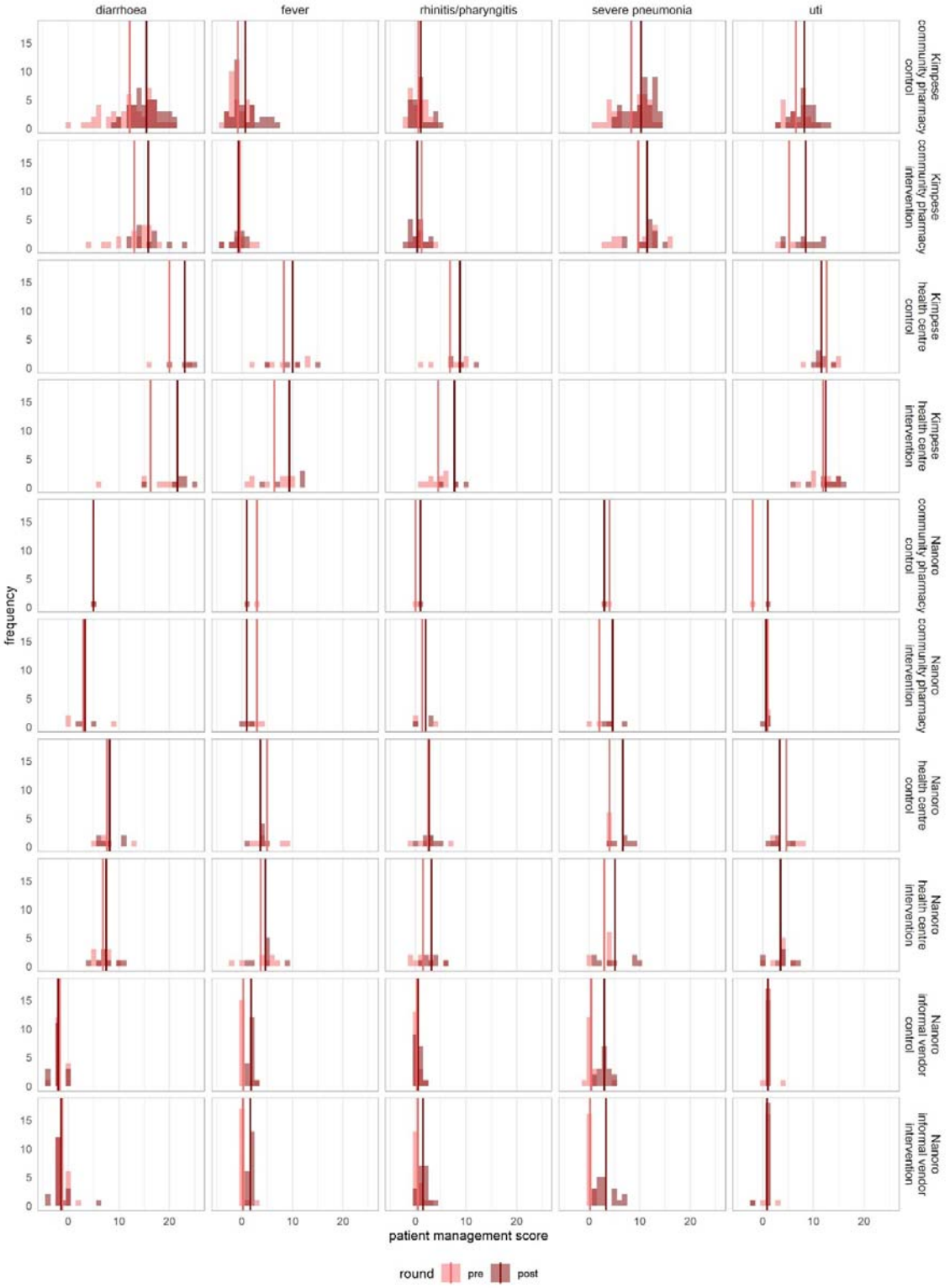

Figure S3. Patient management scores at all healthcare providers in the intervention group before vs after intervention, faceted by site, by type of provider, by intervention/control clusters, and by infection Vertical lines are mean scores.

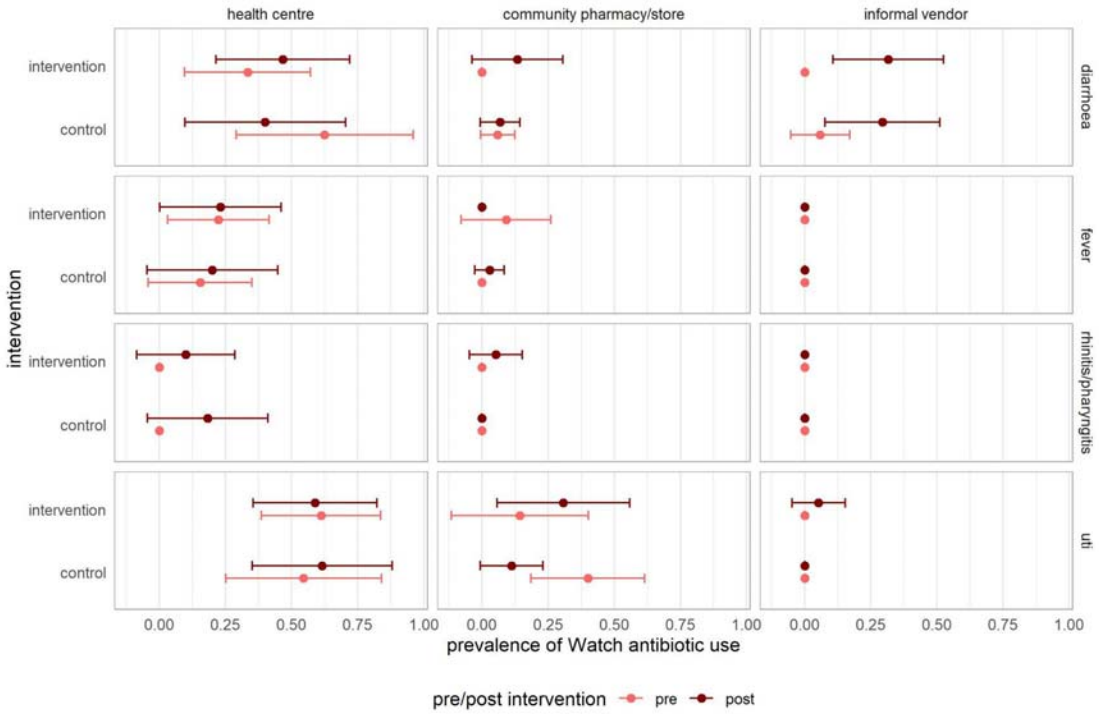

Figure S4. Prevalence of Watch antibiotic use during simulated patient visits before and after the intervention, at providers in the intervention and control group